

Electronic Supplementary Material (ESI) for RSC advances.

Computational analysis of binding between benzamide-based derivatives and Abl wt and T315I mutant kinases

Shengfu Zhou,^a Shepei Tan,^a Danqing Fang,^b Rong Zhang,^a WeicongLin,^a Wenjuan Wu^{*a} and Kangcheng Zheng^c

^a: Department of Physical Chemistry, College of Pharmacy, Guangdong Pharmaceutical University, Guangzhou 510006, China. E-mail: wuwenjuan83@126.com; Tel: +86 20 39352119

^b: Department of Cardiothoracic Surgery, Affiliated Second Hospital of Guangzhou Medical University, Guangzhou 510260, China

^c: School of Chemistry and Chemical Engineering, Sun Yat-Sen University, Guangzhou 510275, China

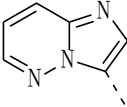
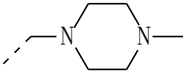
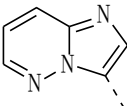
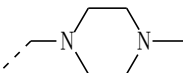
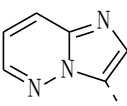
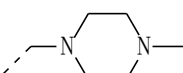
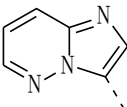
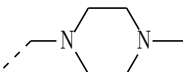
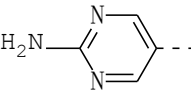
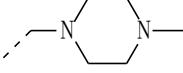
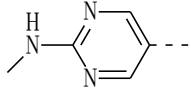
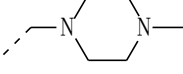
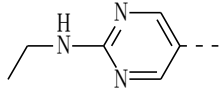
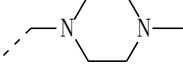
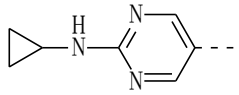
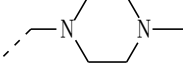
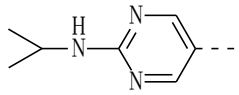
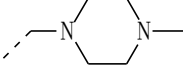
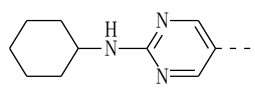
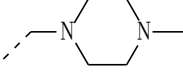
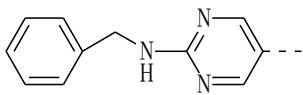
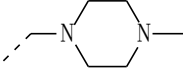
Electronic Supplementary Information

Table of Contents

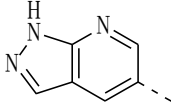
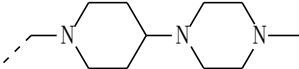
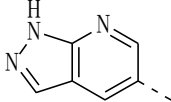
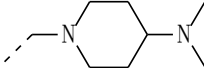
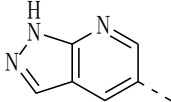
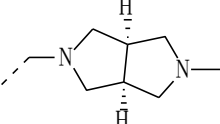
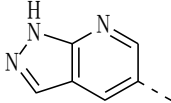
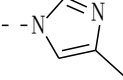
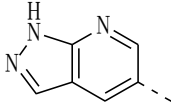
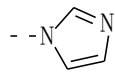
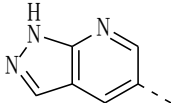
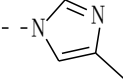
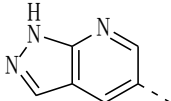
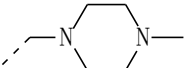
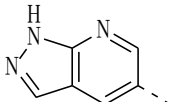
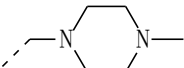
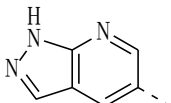
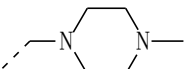
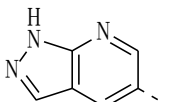
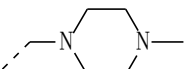
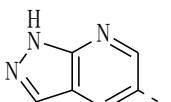
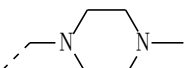
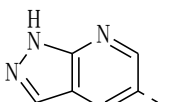
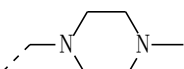

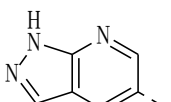
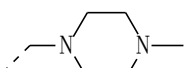

Supplementary tables (Table S1-S2)

S2-S6

Table S1 Molecular structure of compounds with their experimental activities.

No.	Het	R ₁	R ₂	R ₃	IC ₅₀ (nM)	
					Abl_wt	Abl_T315I
1			H	Me	2.67	92.2
2*			H	Me	3.44	95.7
3*			H	Me	2.25	122
4			H	Me	0.52	14.4
5			H	Me	0.78	10.6
6*			H	Me	0.54	25.2
7			H	Me	1.18	29.6
8			H	Me	1.01	89.4
9*			H	Me	5.96	341
10			H	Me	12.8	342
11			H	Me	19.1	486

12			H	Me	1629	2130
13			H	Me	22.6	206
14			H	Me	0.69	1.22
15			H	Me	302	334
16			H	Me	17.8	250
17*			H	Me	0.60	1.12
18			H	Me	0.52	2.18
19			H	Me	0.72	31.5
20			H	Me	0.52	5.09
21*			H	Me	0.45	14.2
22			H	Me	2.56	272
23			H	Me	1.42	32.8
24			H	Me	0.45	0.94

25			H	Me	0.52	18.0
26			H	Me	0.33	11.4
27			H	Me	0.41	18.7
28*		H		Me	1.66	12.7
29*		H		Me	1.03	10.6
30*		H		Me	1.94	7.93
31			H	H	1.01	38.9
32*			H	F	0.42	9.83
33			H	Cl	0.36	0.98
34			H	Br	0.70	1.94
35			H	Et	0.98	38.0
36			H		15.0	659
37			H		66.0	130

Compounds with "*" are included in the test set.

Table S2 The actual p/C_{50} , predicted p/C_{50} and their residuals of the studied compounds for CoMSIA analyses.

No.	CoMSIA (Abl_wt)			CoMSIA (Abl_T315I)		
	Expt. p/C_{50}	Pred. p/C_{50}	Res. *	Expt. p/C_{50}	Pred. p/C_{50}	Res.
Training set						
1	8.57	8.45	0.12	7.04	7.06	-0.02
4	9.28	8.95	0.34	7.84	7.87	-0.03
5	9.11	8.98	0.13	7.97	7.96	0.01
7	8.93	8.99	-0.07	7.53	7.50	0.03
8	9.00	9.22	-0.23	7.05	7.15	-0.10
10	7.89	8.32	-0.43	6.47	6.37	0.10
11	7.72	7.72	0.00	6.31	6.30	0.01
12	5.79	6.05	-0.26	5.67	5.66	0.01
13	7.65	7.89	-0.25	6.69	6.63	0.06
14	9.16	9.03	0.13	8.91	8.86	0.05
15	6.52	6.91	-0.39	6.48	6.52	-0.04
16	7.75	8.03	-0.28	6.60	6.59	0.01
18	9.28	9.24	0.04	8.66	8.76	-0.10
19	9.14	8.95	0.20	7.50	7.62	-0.12
20	9.28	9.42	-0.13	8.29	8.22	0.07
22	8.59	8.47	0.12	6.57	6.59	-0.02
23	8.85	8.87	-0.02	7.48	7.52	-0.04
24	9.35	8.81	0.53	9.03	8.86	0.17
25	9.28	9.32	-0.04	7.74	7.75	-0.01
26	9.48	9.38	0.10	7.94	7.82	0.12
27	9.39	9.04	0.35	7.73	7.87	-0.14
31	9.00	8.88	0.11	7.41	7.50	-0.09
33	9.44	9.15	0.30	9.01	8.99	0.02
34	9.15	8.96	0.20	8.71	8.67	0.04
35	9.01	8.76	0.24	7.42	7.50	-0.08
36	7.82	7.89	-0.07	6.18	6.06	0.12
37	7.18	7.40	-0.22	6.89	6.89	0.00
Test set						
2	8.46	7.90	0.56	7.55	7.02	0.53
3	8.65	8.99	-0.34	7.45	6.91	0.54
6	9.27	9.35	-0.08	7.52	7.60	-0.08
9	8.22	8.20	0.02	7.05	6.47	0.58
17	9.22	9.41	-0.19	8.40	8.95	-0.55
21	9.35	9.18	0.17	7.77	7.85	-0.08
28	8.78	8.83	-0.05	8.05	7.90	0.15
29	8.99	9.31	-0.32	8.21	7.97	0.24
30	8.71	8.94	-0.23	7.99	8.10	-0.11
32	9.38	9.14	0.24	7.65	8.01	-0.36

$$* \text{Res} = \text{Expt. } p/C_{50} - \text{Pred. } p/C_{50}$$