

Supplementary

Table S1 General characteristics of cell lines

Cell lines	Organism	Cell type	EGFR mutations
Ba/F3 (EGFR L858R/T790M/C797S)	Mouse	Primary B cell	L858R/T790M/C797S
Ba/F3 (EGFR Del19/T790M/C797S)	Mouse	Primary B cell	Del19/T790M/C797S
NCI-H1975 (EGFR L858R/T790M/C797S)	Human	Non-small cell lung cancer cell	L858R/T790M/C797S
H1975 (EGFR Del19/T790M/C797S)	Human	Non-small cell lung cancer cell	Del19/T790M/C797S
PC9 (EGFR Del19/T790M/C797S)	Human	Lung cancer cell	Del19/T790M/C797S

Table S2 Summary of the tumor growth and therapeutic efficacy on the 21st day after treatment in the different groups using the H1975 EGFR (Del19/T790M/C797S) model

Group	Tumor volume (mm ³) ^a	T/C (%)	TGI (%)	P ^b	P ^c	P ^d	P ^e	P ^f	P ^g	P ^h
Vehicle	1683±201	-	-	-	-	-	-	-	-	-
WX-0593 (25 mg/kg)	1639±256	97.37	2.9	0.999	-	-	-	-	-	-
WX-0593 (75 mg/kg)	798±124	47.34	59.1	0.001	0.010	-	-	-	-	-
QL1203 (0.1 mg/mouse)	1,955±282	115.36	-18.1	0.999	0.999	0.010	-	-	-	-
Vectibix (0.1 mg/mouse)	2,202±305	130.78	-34.6	0.999	0.999	0.012	0.999	-	-	-
WX-0593 (25 mg/kg) + QL1203 (0.1 mg/mouse)	1,272±232	75.46	27.5	0.229	0.697	0.410	0.477	0.415	-	-
WX-0593 (75 mg/kg) + QL1203 (0.1 mg/mouse)	262±103	15.57	94.8	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	-
WX-0593 (25 mg/kg) + Vectibix (0.1 mg/mouse)	1,419±339	83.86	17.7	0.3302	0.771	0.737	0.555	0.481	0.999	0.001
WX-0593 (75 mg/kg) + Vectibix (0.1 mg/mouse)	196±46	11.65	99.2	<0.001	0.01	<0.001	<0.001	<0.001	<0.001	0.982

^a, tumor volume (on the 21st day after treatment) presented as the median value ± SEM; ^b, P value compared to the vehicle group; ^c, P value compared to the WX-0593 (25 mg/kg) group; ^d, P value compared to the WX-0593 (75 mg/kg) group; ^e, P value compared to the QL1203 group; ^f, P value compared to the Vectibix group; ^g, P value compared to the WX-0593 (25 mg/kg) + QL1203 group; ^h, P value compared to the WX-0593 (75 mg/kg) + QL1203 group.

Table S3 Body weight of each individual mouse during treatment in the H1975 (EGFR-Del19/T790M/C797S) model

BW	Animal No.	0 ^a	4	7	11	14	18	21
Group 1, Vehicle, PO, QD, n=6	326	21.8	21.8	21.1	21.9	21.4	22.6	22.7
	359	24.1	23.5	23.0	23.6	24.4	24.7	25.3
	332	22.1	21.9	21.8	22.5	21.8	22.7	23.0
	309	21.8	21.5	21.0	21.8	21.6	22.3	22.1
	342	20.6	20.5	20.0	20.3	20.7	20.5	20.7
	329	22.9	23.2	22.7	23.3	23.5	24.8	24.0
	Mean	22.2	22.1	21.6	22.2	22.2	22.9	23.0
	SEM	0.5	0.5	0.5	0.5	0.6	0.7	0.6

Table S3 (continued)

Table S3 (continued)

BW	Animal No.	0 ^a	4	7	11	14	18	21
Group 2, WX-0593 25 mg/kg PO, QD, n=6	358	22.0	21.9	21.9	23.0	23.1	23.3	23.5
	334	22.2	22.9	22.8	24.7	24.7	24.9	25.7
	348	23.2	23.0	22.2	24.0	23.8	23.7	24.5
	351	22.5	22.1	22.1	23.2	23.3	22.7	22.9
	371	20.8	21.9	22.2	22.8	23.2	23.1	24.0
	352	23.5	22.9	22.9	23.6	23.1	23.4	23.8
	Mean	22.4	22.5	22.4	23.5	23.5	23.5	24.1
	SEM	0.4	0.2	0.2	0.3	0.3	0.3	0.4
Group 3, WX-0593 75 mg/kg PO, QD, n=6	301	22.3	21.9	22.5	22.8	23.4	22.3	22.1
	350	19.9	19.1	18.6	19.9	19.8	20.0	20.2
	340	22.2	22.5	23.3	24.8	24.8	24.1	24.0
	307	21.8	21.3	21.2	23.3	21.2	20.9	22.0
	304	23.1	22.6	22.7	23.5	22.7	22.7	23.3
	372	23.8	23.8	23.3	23.7	22.7	23.1	24.8
	Mean	22.2	21.9	21.9	23.0	22.4	22.2	22.7
	SEM	0.5	0.7	0.7	0.7	0.7	0.6	0.7
Group 4, QL1203 0.1 mg/mouse IV, BIW, n=6	382	22.7	22.9	22.9	23.5	24.7	24.4	24.3
	357	22.1	21.9	21.9	22.8	23.3	22.9	23.3
	321	20.9	21.5	21.5	22.6	22.4	23.4	23.6
	362	24.8	23.5	23.1	24.4	24.8	25.2	24.0
	335	22.6	22.2	22.6	23.2	23.4	24.5	22.7
	325	20.3	20.4	19.9	20.6	21.3	22.0	23.2
	Mean	22.2	22.1	22.0	22.8	23.3	23.7	23.5
	SEM	0.6	0.4	0.5	0.5	0.6	0.5	0.2
Group 5, Vectibix 0.1 mg/mouse IV, BIW, n=6	387	19.8	19.8	19.9	20.9	21.5	21.4	21.9
	377	22.6	21.8	22.0	22.9	23.8	25.0	26.6
	315	23.1	22.2	22.2	23.1	23.3	24.6	27.2
	327	21.5	21.1	22.0	23.5	22.9	22.5	22.9
	363	22.8	22.9	23.4	23.9	23.3	24.9	26.2
	373	23.1	22.9	22.9	23.4	23.0	23.3	24.0
	Mean	22.1	21.8	22.1	22.9	23.0	23.6	24.8
	SEM	0.5	0.5	0.5	0.4	0.3	0.6	0.9

Table S3 (continued)

Table S3 (continued)

BW	Animal No.	0 ^a	4	7	11	14	18	21
Group 6, WX-0593, 25 mg/kg PO, QD + QL1203, 0.1 mg/mouse IV, BIW, n=6	302	21.5	21.5	22.0	22.4	22.8	23.4	24.5
	313	19.5	19.3	19.4	19.3	19.8	20.4	20.7
	316	21.5	21.1	21.5	21.8	21.9	22.3	22.7
	337	24.0	23.4	23.4	24.9	24.8	24.9	25.5
	374	21.4	21.3	21.0	21.4	21.7	21.8	21.9
	383	24.2	24.5	24.0	25.1	25.3	25.4	26.1
	Mean	22.0	21.8	21.9	22.5	22.7	23.0	23.6
	SEM	0.7	0.7	0.7	0.9	0.8	0.8	0.9
Group 7, WX-0593, 75 mg/kg PO, QD + QL1203, 0.1 mg/mouse IV, BIW, n=6	380	22.8	22.5	21.5	21.1	21.2	21.4	21.5
	338	24.8	24.7	23.7	25.0	24.9	23.5	21.7
	360	20.2	20.3	19.7	19.6	18.5	18.5	19.5
	356	20.1	20.3	19.1	19.1	18.1	17.1	16.6
	393	21.4	22.3	21.6	21.9	21.4	20.0	22.2
	368	23.1	23.6	22.9	23.7	22.9	23.6	24.6
	Mean	22.1	22.3	21.4	21.7	21.2	20.7	21.0
	SEM	0.7	0.7	0.7	0.9	1.1	1.1	1.1
Group 8, WX-0593, 25 mg/kg PO, QD + Vectibix, 0.1 mg/mouse IV, BIW, n=6	346	23.5	23.4	22.7	24.1	25.1	23.8	24.8
	323	20.5	20.7	20.4	21.2	20.9	21.8	22.1
	306	21.2	21.1	20.8	20.8	21.4	22.4	23.5
	381	20.3	20.7	21.2	22.0	22.4	22.0	23.7
	365	24.7	23.9	23.3	24.2	24.7	23.7	24.6
	308	22.4	22.1	21.5	22.2	22.3	22.6	24.2
	Mean	22.1	22.0	21.7	22.4	22.8	22.7	23.8
	SEM	0.7	0.6	0.5	0.6	0.7	0.4	0.4
Group 9, WX-0593, 75 mg/kg PO, QD + Vectibix, 0.1 mg/mouse IV, BIW n=6	328	23.6	21.6	21.8	22.4	21.4	20.9	20.6
	349	22.2	21.9	21.3	21.3	22.2	20.9	21.4
	394	23.7	23.7	22.8	24.4	24.8	21.9	21.5
	345	20.3	19.7	19.2	18.9	18.3	18.6	18.8
	386	21.6	21.5	20.4	20.2	20.8	21.6	21.5
	336	22.9	22.6	21.6	22.0	21.4	21.5	22.3
	Mean	22.4	21.8	21.2	21.5	21.5	20.9	21.0
	SEM	0.5	0.5	0.5	0.8	0.8	0.5	0.5

^a, days after the initiation of treatment. BW, body weight; BIW, twice a week; SEM, standard error of mean.

Table S4 Summary of the tumor growth and therapeutic efficacy on the 10th day after treatment in the different groups using the Baf3 EGFR (L858R/T790M/C797S) model

Group	Tumor volume (mm ³) ^a	T/C (%)	TGI (%)	P ^b	P ^c	P ^d	P ^e
Vehicle	449±30	–	–	–	–	–	–
WX-0593 (75 mg/kg)	289±27	64.26	46.55	<0.001	–	–	–
QL1203 (0.1 mg/mouse)	123±14	27.27	95.01	<0.001	<0.001	–	–
Vectibix (0.1 mg/mouse)	98±19	21.84	102.12	<0.001	<0.001	0.946	–
WX-0593 (75 mg/kg) + QL1203 (0.1 mg/mouse)	58±3	12.86	113.86	<0.001	<0.001	0.193	0.685
WX-0593 (75 mg/kg) + Vectibix (0.1 mg/mouse)	56±5	12.54	114.24	<0.001	<0.001	0.174	0.652

^a, tumor volume (on the 10th day after treatment) presented as the median value ± SEM; ^b, P value compared to the vehicle group; ^c, P value compared to the WX-0593 (75 mg/kg) group; ^d, P value compared to the QL1203 group; ^e, P value compared to the Vectibix group. SEM, standard error of mean; EGFR, epidermal growth factor receptor.

Table S5 Summary of the tumor growth and therapeutic efficacy on the 14th day after treatment in the different groups using the Baf3 EGFR (L858R/T790M/C797S) model

Group	Tumor volume (mm ³) ^a	P ^b	P ^c	P ^d	Partial regression ^e	Complete regression ^f
WX-0593 (75 mg/kg)	483±34	–	–	–	0	0
QL1203 (0.1 mg/mouse)	225±28	<0.001	–	–	0	0
Vectibix (0.1 mg/mouse)	171±40	<0.001	0.747	–	25%	0
WX-0593 (75 mg/kg) + QL1203 (0.1 mg/mouse)	51±14	<0.001	0.004	0.082	75%	12.5%
WX-0593 (75 mg/kg) + Vectibix (0.1 mg/mouse)	58±18	<0.001	0.006	0.115	62.5%	25%

^a, tumor volume (on the 14th day after treatment) presented as the median value ± SEM; ^b, P value compared to the WX-0593 (75 mg/kg) group; ^c, P value compared to QL1203 group; ^d, P value compared to the Vectibix group; ^e, tumor is partially regressed with a tumor volume at the endpoint (on the 14th day after treatment) greater than 0 but less than the tumor volume when the treatment was first initiated; ^f, tumor is completely regressed with a tumor volume at the endpoint (on the 14th day after treatment) being 0; EGFR, epidermal growth factor receptor.

Table S6 Body weight of each individual mouse during treatment in the Ba/F3 (EGFR-L858R/T790M/C797S) model

TV	Animal No.	0 ^a	3	5	7	10	12	14
Group 1 Vehicle PO, QDX2W, n=8	404	122	184	259	363	596	833	1172
	413	86	146	221	314	427	529	–
	416	102	165	252	359	519	657	931
	417	119	164	241	373	498	630	–
	426	94	124	178	222	329	430	603
	431	85	133	204	280	375	– ^b	–
	441	130	175	241	351	425	550	677
	472	104	152	202	296	420	–	–
	Mean	105	155	225	320	449	605	846
	SEM	6	7	10	18	30	56	130
Group 2, WX-0593 75 mg/kg PO, QDX2W, n=8	407	113	127	166	204	239	276	370
	434	132	157	229	272	369	491	717
	436	98	113	159	201	269	365	493
	450	85	94	129	147	196	286	381
	456	89	139	185	228	321	409	567
	461	121	181	259	315	421	518	656
	469	94	129	163	186	216	289	383
	473	111	125	187	212	281	377	503
	Mean	105	133	185	221	289	376	509
	SEM	6	9	15	18	27	33	46
Group 3, QL1203 0.1 mg/mouse IV, QWX2W, n=8	403	104	111	138	150	132	164	250
	410	112	131	147	178	202	236	350
	427	82	91	103	108	98	104	166
	437	100	98	107	116	89	112	181
	439	97	80	87	96	118	147	228
	443	133	111	120	129	124	154	230
	452	125	98	109	136	146	210	295
	462	92	72	82	85	71	73	99
	Mean	105	99	112	125	123	150	225
	SEM	6	7	8	11	14	19	28

Table S6 (continued)

Table S6 (continued)

TV	Animal No.	0 ^a	3	5	7	10	12	14
Group 4, Vectibix 0.1 mg/mouse IV, QWX2W, n=8	409	93	83	103	111	126	153	229
	414	137	164	215	241	219	291	412
	428	117	100	97	97	71	65	66
	440	103	93	98	107	76	88	120
	447	88	85	97	98	86	85	88
	448	104	86	74	75	59	88	154
	449	88	69	58	61	47	48	82
	463	112	104	111	124	99	147	213
	Mean	105	98	107	114	98	121	171
	SEM	6	10	17	19	19	28	40
Group 5, WX-0593 + QL1203 75 mg/kg + 0.1 mg/mouse PO + IV, QD + QWX2W, n=8	411	126	103	91	68	55	35	0
	420	126	115	96	91	58	49	59
	432	87	80	68	56	46	26	9
	433	108	86	84	82	71	84	129
	442	82	72	66	62	51	49	57
	445	101	120	107	79	68	60	57
	467	95	74	69	56	48	35	34
	476	118	93	87	76	65	56	64
	Mean	105	93	84	71	58	49	51
	SEM	6	6	5	5	3	6	14
Group 6, WX-0593 + Vectibix 75 mg/kg + 0.1 mg/mouse PO + IV, QD + QWX2W, n=8	402	86	66	55	44	37	27	0
	419	95	74	60	51	37	27	17
	435	119	96	76	60	53	43	55
	454	132	112	92	82	75	92	99
	465	85	78	69	59	50	40	0
	470	98	74	61	57	55	83	137
	474	107	84	73	63	67	51	53
	485	119	94	90	80	77	72	105
	Mean	105	85	72	62	56	54	58
	SEM	6	5	5	5	5	9	18

^a, days after the initiation of treatment; ^b, animal death. TV, tumor volume.