

Table 1. Summary of dabrafenib and trametinib clinical trial results

Drug	Dabrafenib	Dabrafenib	Dabrafenib	Dabrafenib	Trametinib	Trametinib	Trametinib	Dabrafenib + trametinib (150/2)	
Phase	1	2	2 active ^a brain mets	3	1	2 ^b	3	2	
No. of melanoma patients	156	92	172	187 ^c	97	57	214 ^c	54	
V600E	130	76	139	187	19	46	NR	47	
V600K	18	16	33	0	6	8	NR	7	
Other <i>BRAF</i> mutations	2 K601E 1 V600_K601E	0	0	0	1 L597V	1 V600R 1 K601E	0	0	
Efficacy			Untreated	Previously treated and progressed					
Response rate (%)	78 V600E 22 V600K	59 V600E 13 V600K	39 V600E ^d 7 V600K ^d	31 V600E ^d 22 V600K ^d	59	40	25	22	76
PFS (mo)	5.5 V600E 5.6 V600K	6.3 V600E 4.5 V600K	3.7 V600E 1.8 V600K	3.8 V600E 3.7 V600K	6.9	5.7	4.0	4.8	9.4
OS (mo)	NR	13.1 V600E 12.9 V600K	7.6 V600E 3.7 V600K	7.2 V600E 5.0 V600K	18.2	NR	14.2	15.6	23.8
Toxicity% (all grades; G3)									
cuSCC/KA	11	10	6		10	0	0	0	7
Pyrexia	20 (4)	24 (3)	26 (6)		16 (3)	NR	NR	NR	71 (5)
Arthralgia	20 (0)	33 (1)	(1)		19 (1)	NR	NR	NR	27 (0)
Fatigue	33 (2)	22 (1)	(<1)		18 (1)	31 (4)	26 (2)	26 (4)	53 (4)
Rash ^e	30 (0)	27 (1)	(3)		30 (0)	88 (8)	75 (9)	57 (8)	27 (0)
Diarrhoea	21 (0)	11 (1)	(1)		NR	45 (0)	52 (4)	43 (0)	36 (2)
Serous retinopathy ^f	NR	NR	NR		NR	10 (0)	2 (0)	9 (<1)	2 (2)
Cardiac	NR	NR	NR		NR	7 (0)	(3)	7 (1)	0
Peripheral oedema	NR	NR	NR		NR	35 (0)	29 (3)	26 (1)	29 (0)
Dose reduction	7	22	32		28	12	15	27	58
Permanent discontinuation	0	NR	2		3	NR	NR	NR	9%

NOTE: For phase I trials, toxicity data are from all doing cohorts.

Abbreviations: G3, grade 3 or greater; KA, cutaneous keratoacanthoma; mets, metastases; NR, not reported.

^aActive indicates untreated, or previously treated but progressed brain metastases.

^bData from the BRAF inhibitor-naïve cohort.

^cNumber receiving drug.

^dInvestigator-assessed intracranial response rate.

^eNonspecific term for any skin rash, and includes hyperkeratosis (dabrafenib) and acneiform dermatitis (trametinib).

^fNo cases of retinal vein occlusion were reported in any patients with melanoma on the phase I to III trials of trametinib.