Supplementary Information S3 (Table) | **Effects of PTIs *in vivo***

Compound	Animal model	Molecular targets and effects	Phenotype	Refs.
FTIs				
L-739,749	Xenografts with *Nras*-transformed Rat-1 cells	n/d	Tumour growth↓	1
FTI-276	Xenografts with CaLu-1 cells [2]	HRAS-F↓	Tumour growth↓	2
	Xenografts with *Kras*-transformed NIH 3T3 cells	n/d	Tumour growth↓	3
L-744,832	*MMTV-Hras* transgenic mice	n/d	Tumour regression	4
	MMTV-Nras transgenic mice	HRAS-F↓	Tumour growth↓	5
	MMTV-Hras transgenic mice	n/d	Apoptosis↑, tumour regression	6
	MMTV-Hras; *Trp53*$^{-/-}$ transgenic mice	n/d	Apoptosis↑, G1 arrest, tumour regression	
	MMTV-Hras; *Myc* transgenic mice	n/d	Number of cells in S-phase↓, tumour regression	
	MMTV-Erbb2 transgenic mice	n/d	No response	
	MMTV-Kras transgenic mice	No effect on KRAS	Tumour growth↓	7
	Xenografts with HT-29 [1] or RT-4 cells [1]	HRAS-F not affected	No effect on oxygenation	8
	Xenografts with T24 [3] or 141-1 cells [3]	HRAS-F↓	Oxygenation of tumours↑	
FTI-2148	Xenografts with A549 cells		Tumour growth↓	9
	MMTV-Hras transgenic mice	HRAS-F↓, HDJ2-F↓	Tumour regression	10
BMS-214662	Xenografts with HT-29 [1], HCT-116 [2], MiaPaCa-2 [2], CaLu-1 [2], EJ-1 cells [3]	HRAS-F↓	Tumour regression	11
	Murine tumours (Lewis lung carcinoma and M5076 sarcoma)	n/d	No or very little effect	
Tipifarnib	Xenografts with human cancer cells	n/d	Tumour growth↓ independent of RAS mutation	12
	Xenografts with U87 cells	HRAS-F↓, HIF-1α↓	Vessel density↓	13
L-778,123	Dogs, i.v. infusion with canine PBMCs	HDJ2-F↓, RAP1A-GG↓,	n/d	14
	PBMCs from human patients	No effect on KRAS		
GGTIs				

GGTI-297	Xenografts with *Hras*-transformed NIH 3T3 cells and A549 [2] and CaLu-1 [2] cells	n/d	Tumour growth↓	3
GGTI-2154	Xenografts	n/d	Tumour growth↓	9
	MMTV-Hras transgenic mice	RHOA-GG↓, RAP1-GG↓	Tumour regression, apoptosis	10
GGTI-2418	Xenografts with MDA-MB-231 cells	n/d	Tumour growth↓	15
	MMTV-ErbB2 transgenic mice	p27Kip1↑, p-AKT↓	Tumour regression	
P61-A6	Xenografts with PANC-1 cells	RAP1-GG↓, RHOA-GG↓	Tumour growth↓	16
Combination strategies				
FTI-276 + GGTI-297	Xenografts with *Kras*-transformed NIH 3T3 cells	n/d	Tumour growth↓ more pronounced than with either drug alone	3
Lonafarnib + cyclophosphamide, 5-FU, vincristine	Xenografts with human cancer cells		Tumour growth↓. Synergy	17
	Hras transgenic mice		Tumour regression	
Lonafarnib + taxanes	Xenografts with NCI-H460 cells		Tumour growth↓. Synergy	18
FTI-2148 + cisplatin, gemcita-bine & taxane	Xenografts with A549 cells [2]		Tumour growth↓. Synergy	9
Tipifarnib + taxane	SCID-hu bone mice reconstituted with RPMI8226/S cells	n/d	Tumour growth↓. Synergy	19
Tipifarnib + budesonide	Vinyl carbamate-induced lung tumours	n/d	Lung tumour prevention. Synergy	20
Tipifarnib + tamoxifen	Xenografts with MCF-7 cells	n/d	Tumour growth↓. Synergy	21
Tipifarnib + TCN	*MMTV-Erbb2* transgenic mice	n/d	Tumour regression, Synergy	22
GGTI-2154 + cisplatin, gemcita-bine & taxane	Xenografts with A549 cells [2]	n/d	Tumour growth↓. Synergy	9

sould read "S2"

In studies that did not determine the effect of a drug on its molecular target(s) in the animal model, this was done in intact cells. See ~~TABLE 2 and~~ Supplementary Information S3 (Table).

Downward arrows indicate inhibition of the indicated process, upward arrows indicate increase.

[1] Cell line expressing wild-type HRAS and KRAS,

[2] Cell line expressing oncogenic KRAS,

[3] Cell line expressing oncogenic HRAS (COSMIC database).

Cell lines: 141-1, prostate tumour; A549, human lung adenocarcinoma; CaLu-1, NCI-H460, human non-small cell lung cancer; EJ-1, human bladder cancer; HT-29, HT-116, human colon cancer; MCF-7, MDA-MB-231, human breast cancer; MiaPaCa2, PANC-1, human pancreatic cancer; RPMI8226/S, human multiple myeloma; RT-4, human bladder carcinoma; U87, human glioblastoma

5-FU, 5-fluorouracil; MMTV, mouse mammary tumour virus; n/d, not determined; p-, phosphorylated form of a protein; PBMCs, peripheral blood mononuclear cells

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