Supplementary Information S5 (Table) | **Clinical trials with combinations including FTIs**

Drug(s)	Disease	Phase	Patients	Median Age	Clinical response				FT or Prenylation	Response rate	Other Comments or Quotes	Refs.
					CR	PR HI	SD	PD MD				
Tipifarnib + Capecitabine	Advanced solid tumours	I	41	57		5	11		FT↓ and HDJ2↓	12.2 %	No correlation between FT↓ and response	1
Tipifarnib + Doxorubicin, Cyclophosphamide	Advanced breast cancer	I, II	32	51	7				FT↓ by 55-100%	21.9 %		2
	Stage IIB-IIIC breast cancer	II	44	51	11				Median FT↓ by 91%	25 %		3
Tipifarnib + Etoposide	AML	I	84	77	20				p-S6↓	23.4 %		4
Tipifarnib + Gemcitabine	Advanced solid tumours	I	19	59		2			HDJ2↓	10.5 %		5
Tipifarnib + Gemcitabine	Advanced pancreatic cancer	III	341	61	6		53	28	n/d	1.8 %	MS: 193 d, 6mo survival: 53%, 1yr survival: 27 %	6
			347 [1]	62	8		52	30		2.3 %	MS: 182 d, 6 mo survival: 49%, 1yr survival: 24 %	
Tipifarnib + Gemcitabine, Cisplatin	Advanced solid tumours	I	27	58	1	8			PrelaminA↓	33.3 %		7
	Advanced solid tumours	I	31	58		8	12		n/d	25.8 %	Phase II trial recommended	8
Tipifarnib + Idarubicin + Cytarabine	AML, MDS	I-II	95	50	61 [3]	9 [3]			n/d	74 %	MS: 17 mos	9
			108 [2]	52	65 [3]	11 [3]				70 %	MS: 13 mos	
Tipifarnib + Imatinib	CML	I	25	62		17			n/d	68 %	11 pts withdrew (lack of response)	10
Tipifarnib + Irinotecan	Solid tumours	I	35	52		3	14	13	n/d	8.6 %		11
Tipifarnib + letrozole	Advanced breast cancer	II	74	60	3	19	29	23	n/d	29.7 %	No improvement by Tipifarnib	12
			39 [1]	61	1	14	15	9		38.5 %		
Tipifarnib + Sorafenib	Advanced solid tumours	I	43	56		3	15	20	25% of pts with > 50% FT↓	7.0 %		13
Tipifarnib + Tamoxifen	Metastatic breast cancer	I	12	50		2	1		FT↓ 42-54%	16.7 %		14

Lonafarnib + Carboplatin + Paclitaxel	Advanced NSCLC	III	308	?					n/a	n/a	OS: 144 d, TTP: 137 d	15
			308 [1]	?						n/a	OS: 168 d, TTP: 152 d	
Lonafarnib + Docetaxel	Advanced solid tumours	I	29		1		6			3.4 %	Response (CR+SD) correlates with low FNTB mRNA levels	16
Lonafarnib + Gemcitabine	Advanced bladder cancer	II	31	64	1	9			n/d	32.3 %	MS: 11.5 mos, TTP: 7 mos	17
Lonafarnib + Imatinib	CML	I	23	55	6	2			n/d	34.7 %		18
Lonafarnib + Paclitaxel	Solid tumours	I	21	60		6			n/d	28.6 %	6 pts previously treated	19
BMS-214662 + Cisplatin	Advanced solid tumours	I	23	57			15		Short-lived FT↓	0 %	No objective response	20
BMS-214662 + Paclitaxel	Advanced solid tumours	I	26	60		2 ?			Short-lived FT↓	≤ 7.7 %		21
BMS-214662 + Paclitaxel, Carboplatin	Advanced solid tumours	I	30	58		3	8		Short-lived FT↓ and HDJ2↓	10.0 %	No correlation between dose and HDJ2↓	22
L-778,123 + radiotherapy	Advanced solid tumours	I	7	59	5	1		6	n/d	85.7 %	No *RAS* mutations	23
	Advanced pancreatic cancer	I	10	59		1	5	4	HDJ2↓	10.0 %	~~3/4 pts~~ have *KRAS* mutation	24

This table is only about FTIs because so far, to our knowledge, only one GGTI, GGTI-2418, is in clinical trials. Studies where tumour response was not evaluated are not included. Median ages are rounded to the closest integer. In the "patients" column the number of evaluable patients are stated whenever possible. The response rate was calculated by dividing the sum of complete and partial responses by the number of evaluable patients.

Downward arrows indicate reduction of enzyme activity (in the case of FT) or reduction in farnesylation (in the case of HDJ2 or prelamin A).

[1] This patient cohort received a placebo instead of the FTI. [2] This patient cohort received idarubicin + cytarabine (referred to by the authors as 'historical control'). [3] Since the reference only provides % response rates, the patient numbers were calculated

should read 3 out of 4 pts examined have KRAS mutations

AML, acute myeloid leukaemia; CML, chronic myeloid leukaemia; CR, complete response; FNTB, farnesyltransferase β-subunit; FT, farnesyltransferase activity; HI, haematological improvement; MD, metastatic disease; MDS, myelodysplastic syndrome; MS, median survival; n/d, not determined; NSCLC, non-small cell lung cancer; OS, overall survival; p-, phopsphorylated form of a protein; PD, progressive disease; PR, partial response; Pt, pts, patient(s); SD, stable disease; TTP, median time to progression.

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