Supplementary Information S4 (Table)| **Clinical trials with farnesyltransferase inhibitors**

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	Acute leukaemia	I	34	63	2	8			FT↓ and HDJ2↓	29.4 %	No *NRAS* mutations in patient tumours	1
	Advanced bladder cancer	II	34	64		2	13		n/d	5.9	Response rate does not warrant further investigation	2
	Advanced breast cancer	II	76	54		9	9		n/d	11.8 %	All responders had wt *RAS* genes	3
	Advanced colon cancer	II	55	69		1	11	31	n/d	1.8 %	Tipifarnib is ineffective	4
	Advanced NSCLC	II	44	71			7		HDJ2↓ and PrelaminA↓. FT↓ in 83% of pts.	0 %	No objective response. Future studies should be done with combinations	5
	Advanced solid tumours	I	25	58	0	0	8	17	Data not shown	0 %	No objective response	6
	Advanced solid tumours	I	9	53			1	8	n/d	0 %	No objective response	7
	Advanced solid tumours	I	28	56		2	3		n/d	7.1 %	5/15 pts have *KRAS* mutation	8
	Advanced solid tumours	I	21				6		n/d	0 %	No objective response. Phase II trial recommended	9
	AML	II	~~252~~	~~62~~	11	8			n/d	7.5 %	MS for pts with CR: 369 d	10
	AML	II			22	3	50	58	HDJ2↓	17. 2 %	Median duration of CR: 7.3 mos	11
	AML	III			18	20	105	36	n/d	16.7 %	MS: 107 d. 8 % of pts have a CR with an MS of 666 d	12
					0	3	130	46		1.3 %	MS: 109 d	
	Brain tumours	II				2			n/d	2.5 %	Very little activity	13
	CML, myelofibrosis, MM	~~?~~	~~40~~	~~57~~	7				n/d	17.5 %	Clinical activity in CML and meylofibrosis	14
	Metastatic pancreatic cancer	II	20	61			1		FT↓ by 50% HDJ2↓ by 33%	0 %	No objective response. MS: 19.7 wks	15

should read "II"

	MM	II	36	62	0	0	23	13	FT↓ and HDJ2↓	0 %	No objective response. No correlation between FT↓ and disease stabilisation	16
	MDS	I	20	66	1	5		1	FT↓ and HDJ2↓	30 %	No correlation between FT↓ and response. No correlation between *Ras* mutation status and response	17
	MDS	II	27	66	2	1			n/d	11.1 %	Modest anti-tumour activity	18
	MDS	II	82	67		26	37		n/d	31.7 %	Median duration of CR: 11.5 mos	19
	MDS	I	61	68	3	13			FT↓ by 75 %	26.2 %	Only 1 responder with a *KRAS* mutation. No correlation between FT↓ and dose	20
	Neurofibromatosis, neurofibromas	I	40	≤15					FT↓ by 43% HDJ2↓	0 %	No objective response	21
	Pancreatic cancer	II	53	6					n/d	0 %	No objective response. MS: 2.6 mos.	22
	Small-cell lung cancer	II	20	6					n/d	0 %	No objective response. MS: 6.8 mos, progression-free MS: 1.4 mos.	23
	Advanced colon cancer	III	235	6				55	n/d	0.4 %	MS: 174 24%	
			133 2	62	0	0	17	107		0 %	MS: 185 13 %	
Lonafarnib	Advanced solid tumours	I	24	57	0	0	2		n/d	0 %	No objec	
	Advanced solid tumours	I	12	61	0	0			PrelaminA↓	0 %	No objec	
	Advanced solid tumours	I	22	54	1	1			FT↓	12.5 % 3	Sponsor study ea negative interim efficacy. FT↓ not correlated to response	27
	Advanced solid tumours	II	15	57	0	0	7		n/d	0 %	No objective response	28
	CML	Pilot	13	62	0	2			n/d	15.5 %		29

The "2" should be in superscript

The "3" should be in superscript

	CNS tumours	I	48	12	0	1	9		n/d	2.1 %		30
	Metastatic colon cancer	II	21	64	0	0	3		n/d	0 %	No objective response	31
	MDS or sAML	II	16	70		1			n/d	6.7 %		32
	NSCLC	II	29	58		3	11	15	n/d	10.3 %	MS: 39 mos. Well-tolerated. Further clinical trials recommended.	33
	Refractory urothelial cancer (transitional cell carcinoma)	II	10	65	0	0	2	8	Small HDJ2↓	0 %	No objective response	34
	Solid tumours	I	20	59		1	8		PrelaminA↓	5.0 %		35
BMS-214662	Acute leukaemia	I	30	53	4	1			Short-lived FT↓	16.7 %		36
	Advanced solid tumours	I	44	54	0	0	1		transient FT↓ by 89.5%	0 %	No objective response. 1 pt w/ pancreatic cancer survives for >3.5 yrs	37
	Advanced solid tumours	I	68	60	0	0	5		Short-lived FT↓	0 %	No objective response	38
	Advanced solid tumours	I	19	55			1	18	n/d	0 %	No objective response	39
	Solid tumours	I	25	57		1	16	8	Short-lived FT↓	4.0 %	Response was minor	40

This table is only about FTIs because so far, to our knowledge, only one GGTI, GGTI-2418, is in clinical trials. Studies that did not evaluate tumour response 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 best supportive care. [2] In this study all patients received best supportive care, with 235 receiving tipifarnib, and 133 receiving a placebo. [3] Number differs from the authors’ calculation who included SD, resulting in a response rate of 37.5 %.

AML, acute myeloid leukaemia; BSC, best supportive care; CML, chronic myeloid leukaemia; CNS, central nervous system, CR, complete response; FNTB, farnesyltransferase β-subunit; FT, farnesyltransferase activity; HI, haematological improvement; MD, metastatic disease; MDS, myelodysplastic syndrome; MM; multiple myeloma; MS, median survival; n/d, not determined; NSCLC, non-small cell lung cancer; OS, overall survival; PD, progressive disease; PR, partial response; Pt, pts, patient(s); sAML, secondary acute myeloid leukaemia; SD, stable disease; TTP, median time to progression.

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