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Table 1. Dose-escalation protocol

<b>Dose Level</b>	<b>Sorafenib dose</b>	<b>Dosing schedule</b>		<b>Radiation therapy schedule</b>
1	200mg	Once daily	Days 1-28	Days 8-12, 15-19
2	200mg	Twice daily	Days 1-28	Days 8-12, 15-19
3	400mg	Twice daily	Days 1-28	Days 8-12, 15-19
4	400mg	Twice daily	Days 1-77	Days 8-12, 15-19

Table 2. Radiotherapy dose constraints

<b>Organ</b>	<b>Endpoint</b>	<b>Constraint</b>
Spinal cord	Maximum dose	<30Gy
Lung minus GTV	Volume receiving at least 20Gy (V20)	≤33%
Liver	Mean dose	<22Gy
Liver (if parallel-opposed pair)	Total liver volume receiving <1Gy	≥35%
Each kidney	Volume receiving at least 20Gy (V20)	<33%
Small bowel	Volume receiving at least 30Gy (V30)	<1/3 of total volume

Table 3. Baseline characteristics

Characteristic		Number	%
Median age (range)		64 years (40,83)	
Gender	Female: Male	14:20	41%: 59%
ECOG Performance status	0:1	11:23	32%: 68%
Concurrent therapeutic anti-coagulation	Coumarin	0	0%
	Heparin	1	3%
Primary malignancy	Lung	8	24%
	Hepatobiliary	6	18%
	Colorectal	5	15%
	Head and neck	4	12%
	Renal	3	9%
	Upper gastro-intestinal	2	6%
	Other	6	18%
Site of palliative radiotherapy	Thorax	14	41%
	Metastatic lesion(s)	8	24%
	Primary lesion alone	2	6%
	Primary and metastatic lesions in field	4	12%
	Abdomen	16	47%
	Metastatic lesion(s)	11	32%
	Primary and metastatic lesions in field	5	15%
	Pelvis	4	12%
	Metastatic lesion(s)	3	9%
	Primary and metastatic lesions in field	1	3%

ECOG: Eastern Cooperative Oncology Group

Table 4. Treatment outcomes

Patient no.	Dose Level	Radiotherapy completed	Sorafenib completed	Sorafenib dose completed (% of planned)	Reason for early discontinuation or dose modification of drug	Best evaluable in-field response	DLT
<i>Thorax</i>							
1	1	Yes	Yes	100	NA	PD	
2	1	Yes	Stopped early	50	Grade 2 rash	IE	
3	1	Yes	Yes	100	NA	PR	
4***	2	Yes	Stopped early	47	Grade 3 rash	IE	
5***	2	Yes	Stopped early	38	Grade 1 dizziness and infection	IE	
6	2	Yes	Yes	100	NA	PD	
7	2	Yes	Yes	100	NA	SD	
8***	2	Yes	Stopped early	39	Grade 2 rash (out of field)	IE	
9	2	Yes	Yes, minor dose modification	91	Grade 2 anxiety and dyspnoea	SD	Grade 3 oesophagitis
10	2	Yes	Yes	100	NA	SD	
11	2	Yes	Yes	100	NA	SD	
12	2	Yes	Yes	100	NA	SD	
13	3	Yes	Stopped early	43	Grade 2 HFS	IE	
14	3	Yes	Stopped early	36	Grade 3 hypertension	IE	
<i>Abdomen</i>							
1	1	Yes	Yes	100	NA	PR	
2	1	Yes	Yes	100	NA	IE	
3***	1	No: 0/10 fractions	Stopped early	3.5	Removed from trial as liver volume too large	IE	
4	1	Yes	Yes	100	NA	SD	
5	2	Yes	Yes, minor dose modification	95	Missed 3 doses due to PE	SD	
6	2	Yes	Yes	100	NA	SD	

7	2	Yes	Yes, minor dose modification	98	Grade 1-2 nausea	PD	
8	2	Yes	Stopped early	20	Grade 3 abdominal pain	IE	
9	3	Yes	Yes	100	NA	PR	
10	3	Yes	Yes	100	NA	SD	
11	3	Yes	Yes, minor dose modification	100	Completed over 30 days instead of 28, patient error	PR	Grade 3 elevated transaminases
12	3	Yes	Yes, substantial dose modification	50	Grade 3 thrombocytopaenia	SD	
13***	3	Yes	Yes, substantial dose modification	57	Grade 2 HFS	PD	
14***	3	Yes	Yes, substantial dose modification	64	Grade 3 rash	PD	
15	3	Yes	Yes	100	NA	PD	
16	3	Yes	Stopped early	50	Grade 3 HFS	IE	
<i>Pelvis</i>							
1	1	No: 9/10 fractions**	Stopped early	61	Grade 2 HFS	PR	
2	1	Yes	Yes	100	NA	PR	
3	1	Yes	Yes	100	NA	SD	
4	2	Yes	Stopped early	66	Grade 3 diarrhoea	IE	Grade 5 bowel perforation

\*\* : final fraction omitted as patient could not attend due to sorafenib systemic toxicity, \*\*\* : patient replaced in Dose Level, HFS: hand-foot syndrome, IE: inevaluable, NA: not applicable PD: progressive disease, PR: partial response, SD: stable disease.

Table 5. Dose-limiting toxicities

Toxicity	Cohort	Dose Level	No. patients affected		
			Grade 3	Grade 4	Grade 5
Oesophagitis	Thorax	2	1	-	-
Transaminase elevation	Abdomen	3	1	-	-
Bowel perforation	Pelvis	2	-	-	1