付録 2.7.4.2
Related Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Study 304
Safety Analysis Set

	All				Japanese			
	Lenvatinib (N=476)		Sorafenib (N=475)		Lenvatinib (N=81)		Sorafenib (N=87)	
System organ Class Preferred Term	Any Grade n (%)	Grade >= 3 n (%)	Any Grade n (%)	Grade >= 3 n (%)	Any Grade n (%)	Grade >= 3 n (%)	Any Grade n (%)	Grade >= 3 n (%)
脳血管発作	1 (0.2)	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
平衡障害	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
灼熱感	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
肝性昏睡	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ジスキネジア	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
顔面麻痺	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
蟻走感	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
頭蓋内出血	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)
味覚減退	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
末梢性ニューロパチー	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
末梢性運動ニューロパチー	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)
末梢性感覚運動ニューロパチー	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
可逆性後白質脳症症候群	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
痙攣発作	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
緊張性頭痛	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
中毒性ニューロパチー	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
振戦	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
三叉神経痛	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)
知覚過敏	0 (0.0)	0 (0.0)	3 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
失声症	0 (0.0)	0 (0.0)	2 (0.4)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
大脳基底核出血	0 (0.0)	0 (0.0)	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
認知障害	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
注意力障害	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

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Study 304
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System organ Class Preferred Term	Any Grade n (%)	Grade >= 3 n (%)	Any Grade n (%)	Grade >= 3 n (%)	Any Grade n (%)	Grade >= 3 n (%)	Any Grade n (%)	Grade >= 3 n (%)
虚血性脳卒中	0 (0.0)	0 (0.0)	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
意識消失	0 (0.0)	0 (0.0)	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
代謝性脳症	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
神経毒性	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
失神寸前の状態	0 (0.0)	0 (0.0)	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血栓性脳梗塞	0 (0.0)	0 (0.0)	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
精神障害	15 (3.2)	2 (0.4)	4 (0.8)	1 (0.2)	2 (2.5)	0 (0.0)	0 (0.0)	0 (0.0)
不眠症	11 (2.3)	0 (0.0)	1 (0.2)	0 (0.0)	2 (2.5)	0 (0.0)	0 (0.0)	0 (0.0)
錯乱状態	2 (0.4)	1 (0.2)	2 (0.4)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
うつ病	2 (0.4)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
無感情	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
抑うつ気分	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
易刺激性	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
腎および尿路障害	123 (25.8)	30 (6.3)	51 (10.7)	6 (1.3)	38 (46.9)	8 (9.9)	20 (23.0)	1 (1.1)
蛋白尿	114 (23.9)	27 (5.7)	44 (9.3)	6 (1.3)	37 (45.7)	7 (8.6)	19 (21.8)	1 (1.1)
血尿	15 (3.2)	0 (0.0)	5 (1.1)	0 (0.0)	3 (3.7)	0 (0.0)	3 (3.4)	0 (0.0)
腎機能障害	2 (0.4)	0 (0.0)	3 (0.6)	0 (0.0)	2 (2.5)	0 (0.0)	3 (3.4)	0 (0.0)
ビリルビン尿	2 (0.4)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
急性腎障害	2 (0.4)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
着色尿	2 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
夜間頻尿	2 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
白血球尿	1 (0.2)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
無尿	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

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System organ Class Preferred Term	Any Grade n (%)	Grade >= 3 n (%)	Any Grade n (%)	Grade >= 3 n (%)	Any Grade n (%)	Grade >= 3 n (%)	Any Grade n (%)	Grade >= 3 n (%)
慢性腎臓病	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)
排尿困難	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
糖尿	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
腎仙痛	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
腎不全	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	1 (1.2)	1 (1.2)	0 (0.0)	0 (0.0)
腎梗塞	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)
腎尿細管壊死	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
頻尿	0 (0.0)	0 (0.0)	3 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
多尿	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
生殖系および乳房障害	14 (2.9)	1 (0.2)	9 (1.9)	0 (0.0)	3 (3.7)	0 (0.0)	1 (1.1)	0 (0.0)
女性化乳房	2 (0.4)	0 (0.0)	1 (0.2)	0 (0.0)	1 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)
骨盤痛	2 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
陰嚢潰瘍	1 (0.2)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
後天性陰嚢水瘤	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)
性器発疹	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
不規則月経	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
骨盤液貯留	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
前立腺閉塞	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
陰部そう痒症	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
陰嚢血瘤	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)
陰嚢浮腫	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
精巣痛	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
無月経	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

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乳房痛	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
性器紅斑	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
乳頭の炎症	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)
乳頭痛	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
陰嚢障害	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
陰嚢紅斑	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
外陰部障害	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
呼吸器、胸郭および縦隔障害	134 (28.2)	7 (1.5)	84 (17.7)	4 (0.8)	38 (46.9)	1 (1.2)	26 (29.9)	0 (0.0)
発声障害	104 (21.8)	0 (0.0)	52 (10.9)	0 (0.0)	35 (43.2)	0 (0.0)	21 (24.1)	0 (0.0)
鼻出血	12 (2.5)	0 (0.0)	7 (1.5)	0 (0.0)	2 (2.5)	0 (0.0)	2 (2.3)	0 (0.0)
呼吸困難	12 (2.5)	2 (0.4)	5 (1.1)	0 (0.0)	2 (2.5)	0 (0.0)	0 (0.0)	0 (0.0)
口腔咽頭痛	9 (1.9)	0 (0.0)	7 (1.5)	0 (0.0)	1 (1.2)	0 (0.0)	1 (1.1)	0 (0.0)
喀血	6 (1.3)	1 (0.2)	2 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)
咳嗽	5 (1.1)	0 (0.0)	13 (2.7)	0 (0.0)	2 (2.5)	0 (0.0)	2 (2.3)	0 (0.0)
胸水	5 (1.1)	0 (0.0)	1 (0.2)	0 (0.0)	3 (3.7)	0 (0.0)	1 (1.1)	0 (0.0)
肺塞栓症	3 (0.6)	3 (0.6)	2 (0.4)	2 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
呼吸不全	2 (0.4)	2 (0.4)	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
しゃっくり	1 (0.2)	0 (0.0)	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
喉頭の炎症	1 (0.2)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)
鼻痛	1 (0.2)	0 (0.0)	1 (0.2)	0 (0.0)	1 (1.2)	0 (0.0)	1 (1.1)	0 (0.0)
慢性気管支炎	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
特発性肺線維症	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
壊死性細気管支炎	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

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非心原性肺水腫	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	1 (1.2)	1 (1.2)	0 (0.0)	0 (0.0)
口腔咽頭不快感	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
肺臓炎	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
肺梗塞	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
肺腫瘤	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
上気道の炎症	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)
鼻の炎症	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
湿性咳嗽	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
皮膚および皮下組織障害	211 (44.3)	16 (3.4)	339 (71.4)	64 (13.5)	51 (63.0)	6 (7.4)	76 (87.4)	17 (19.5)
手掌・足底発赤知覚不全症候群	126 (26.5)	14 (2.9)	249 (52.4)	54 (11.4)	42 (51.9)	6 (7.4)	64 (73.6)	15 (17.2)
発疹	38 (8.0)	0 (0.0)	64 (13.5)	2 (0.4)	7 (8.6)	0 (0.0)	11 (12.6)	0 (0.0)
そう痒症	23 (4.8)	0 (0.0)	25 (5.3)	1 (0.2)	4 (4.9)	0 (0.0)	3 (3.4)	0 (0.0)
皮膚乾燥	13 (2.7)	0 (0.0)	18 (3.8)	0 (0.0)	1 (1.2)	0 (0.0)	1 (1.1)	0 (0.0)
脱毛症	12 (2.5)	0 (0.0)	115 (24.2)	0 (0.0)	5 (6.2)	0 (0.0)	32 (36.8)	0 (0.0)
紅斑	7 (1.5)	0 (0.0)	10 (2.1)	0 (0.0)	1 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)
斑状丘疹状皮疹	6 (1.3)	0 (0.0)	16 (3.4)	4 (0.8)	1 (1.2)	0 (0.0)	5 (5.7)	2 (2.3)
ざ瘡様皮膚炎	4 (0.8)	0 (0.0)	8 (1.7)	0 (0.0)	3 (3.7)	0 (0.0)	4 (4.6)	0 (0.0)
過角化	4 (0.8)	0 (0.0)	7 (1.5)	0 (0.0)	1 (1.2)	0 (0.0)	2 (2.3)	0 (0.0)
皮膚剥脱	4 (0.8)	0 (0.0)	3 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
皮膚反応	4 (0.8)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
爪変色	4 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)
水疱	3 (0.6)	0 (0.0)	4 (0.8)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
丘疹性皮疹	2 (0.4)	0 (0.0)	5 (1.1)	2 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

Related TEAEs include TEAEs that were considered by the Investigator to be possibly or probably related to study drug or TEAEs with a missing causality.
Percentages are based on the total number of subjects in the Safety Analysis Set within the relevant treatment group.
Subject with two or more TEAEs reported in the same SOC or PT term will be only counted once.
Adverse Events terms were coded using Medical Dictionary for Regulatory Activities (MedDRA) version 19.1.
TEAE = Treatment-emergent adverse event.

付録 2.7.4.2
Related Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Study 304
Safety Analysis Set

	All				Japanese			
	Lenvatinib (N=476)		Sorafenib (N=475)		Lenvatinib (N=81)		Sorafenib (N=87)	
System organ Class Preferred Term	Any Grade n (%)	Grade >= 3 n (%)	Any Grade n (%)	Grade >= 3 n (%)	Any Grade n (%)	Grade >= 3 n (%)	Any Grade n (%)	Grade >= 3 n (%)
多形紅斑	2 (0.4)	0 (0.0)	3 (0.6)	1 (0.2)	0 (0.0)	0 (0.0)	1 (1.1)	1 (1.1)
ざ瘡	2 (0.4)	0 (0.0)	2 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
湿疹	2 (0.4)	0 (0.0)	2 (0.4)	0 (0.0)	2 (2.5)	0 (0.0)	1 (1.1)	0 (0.0)
そう痒性皮疹	2 (0.4)	0 (0.0)	2 (0.4)	0 (0.0)	1 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)
皮膚炎	2 (0.4)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)
皮膚疼痛	1 (0.2)	0 (0.0)	4 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
蕁麻疹	1 (0.2)	0 (0.0)	4 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
顔面腫脹	1 (0.2)	0 (0.0)	2 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
爪線状隆起	1 (0.2)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
手掌紅斑	1 (0.2)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
紫斑	1 (0.2)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
脂漏性皮膚炎	1 (0.2)	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)
皮膚障害	1 (0.2)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)
皮膚色素減少	1 (0.2)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)
皮膚刺激	1 (0.2)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
乾皮症	1 (0.2)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
皮膚血管炎	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
皮膚嚢腫	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
接触皮膚炎	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)
異汗性湿疹	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
間擦疹	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
寝汗	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
爪破損	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

Related TEAEs include TEAEs that were considered by the Investigator to be possibly or probably related to study drug or TEAEs with a missing causality.
Percentages are based on the total number of subjects in the Safety Analysis Set within the relevant treatment group.
Subject with two or more TEAEs reported in the same SOC or PT term will be only counted once.
Adverse Events terms were coded using Medical Dictionary for Regulatory Activities (MedDRA) version 19.1.
TEAE = Treatment-emergent adverse event.

Program: T2_7_4_2.sas 18MAY2017 11:01

付録 2.7.4.2
Related Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Study 304
Safety Analysis Set

	All				Japanese			
	Lenvatinib (N=476)		Sorafenib (N=475)		Lenvatinib (N=81)		Sorafenib (N=87)	
System organ Class Preferred Term	Any Grade n (%)	Grade >= 3 n (%)	Any Grade n (%)	Grade >= 3 n (%)	Any Grade n (%)	Grade >= 3 n (%)	Any Grade n (%)	Grade >= 3 n (%)
点状出血	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
紅斑性皮疹	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
皮膚びらん	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)
薬疹	0 (0.0)	0 (0.0)	4 (0.8)	1 (0.2)	0 (0.0)	0 (0.0)	4 (4.6)	1 (1.1)
水疱性皮膚炎	0 (0.0)	0 (0.0)	3 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
多汗症	0 (0.0)	0 (0.0)	2 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
乾癬	0 (0.0)	0 (0.0)	2 (0.4)	1 (0.2)	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)
皮膚病変	0 (0.0)	0 (0.0)	2 (0.4)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
皮膚潰瘍	0 (0.0)	0 (0.0)	2 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	2 (2.3)	0 (0.0)
アレルギー性皮膚炎	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
斑状出血	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
剥脱性発疹	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
全身紅斑	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)
陰茎潰瘍形成	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)
斑状皮疹	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
痂皮	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
皮膚癒着	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
皮膚変色	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)
皮膚不快感	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
皮膚亀裂	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
皮膚硬結	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
皮膚感作	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
毛細血管拡張症	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

Related TEAEs include TEAEs that were considered by the Investigator to be possibly or probably related to study drug or TEAEs with a missing causality.
Percentages are based on the total number of subjects in the Safety Analysis Set within the relevant treatment group.
Subject with two or more TEAEs reported in the same SOC or PT term will be only counted once.
Adverse Events terms were coded using Medical Dictionary for Regulatory Activities (MedDRA) version 19.1.
TEAE = Treatment-emergent adverse event.

Eisai

Protocol: Lenvatinib (E7080) Integrated Summary of Safety

付録 2.7.4.2
Related Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Study 304
Safety Analysis Set

	All				Japanese			
	Lenvatinib (N=476)		Sorafenib (N=475)		Lenvatinib (N=81)		Sorafenib (N=87)	
System organ Class Preferred Term	Any Grade n (%)	Grade >= 3 n (%)	Any Grade n (%)	Grade >= 3 n (%)	Any Grade n (%)	Grade >= 3 n (%)	Any Grade n (%)	Grade >= 3 n (%)
血管障害	197 (41.4)	108 (22.7)	135 (28.4)	63 (13.3)	40 (49.4)	26 (32.1)	42 (48.3)	23 (26.4)
高血圧	191 (40.1)	105 (22.1)	131 (27.6)	62 (13.1)	40 (49.4)	26 (32.1)	42 (48.3)	23 (26.4)
潮紅	2 (0.4)	0 (0.0)	2 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
循環虚脱	2 (0.4)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
大動脈解離	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
動脈解離	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)
深部静脈血栓症	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
静脈塞栓症	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)
起立性低血圧	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血栓性静脈炎	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
充血	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血液量減少性ショック	0 (0.0)	0 (0.0)	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
末梢冷感	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

Related TEAEs include TEAEs that were considered by the Investigator to be possibly or probably related to study drug or TEAEs with a missing causality.
Percentages are based on the total number of subjects in the Safety Analysis Set within the relevant treatment group.
Subject with two or more TEAEs reported in the same SOC or PT term will be only counted once.
Adverse Events terms were coded using Medical Dictionary for Regulatory Activities (MedDRA) version 19.1.
TEAE = Treatment-emergent adverse event.

Program: T2_7_4_2.sas

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付録 2.7.4.3
Fatal Serious Treatment-Emergent Adverse Events by Preferred Term
Study 304
Safety Analysis Set

	All		Japanese	
Preferred Term	Lenvatinib (N=476) n (%)	Sorafenib (N=475) n (%)	Lenvatinib (N=81) n (%)	Sorafenib (N=87) n (%)
Subjects with Any Fatal TEAEs	61 (12.8)	36 (7.6)	5 (6.2)	2 (2.3)
悪性新生物進行	10 (2.1)	14 (2.9)	0 (0.0)	0 (0.0)
肝不全	10 (2.1)	2 (0.4)	1 (1.2)	1 (1.1)
敗血症	5 (1.1)	1 (0.2)	1 (1.2)	0 (0.0)
呼吸不全	3 (0.6)	3 (0.6)	0 (0.0)	0 (0.0)
脳出血	3 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)
上部消化管出血	2 (0.4)	2 (0.4)	0 (0.0)	0 (0.0)
全身健康状態低下	2 (0.4)	1 (0.2)	0 (0.0)	0 (0.0)
多臓器機能不全症候群	2 (0.4)	1 (0.2)	0 (0.0)	0 (0.0)
脳血管発作	2 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)
肝性昏睡	2 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)
肝性脳症	2 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)
誤嚥性肺炎	2 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)
門脈血栓症	2 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)
腎機能障害	1 (0.2)	2 (0.4)	1 (1.2)	1 (1.1)
突然死	1 (0.2)	2 (0.4)	0 (0.0)	0 (0.0)
急性呼吸不全	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)
肝癌破裂	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)

Percentages are based on the total number of subjects in the Safety Analysis Set within the relevant treatment group.
Subjects with two or more adverse events in the same preferred term will be counted only once.
Adverse Events terms were coded using Medical Dictionary for Regulatory Activities (MedDRA) version 19.1.
TEAE = Treatment-emergent adverse event.

付録 2.7.4.3
Fatal Serious Treatment-Emergent Adverse Events by Preferred Term
Study 304
Safety Analysis Set

	All		Japanese	
Preferred Term	Lenvatinib (N=476) n (%)	Sorafenib (N=475) n (%)	Lenvatinib (N=81) n (%)	Sorafenib (N=87) n (%)
腫瘍出血	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)
急性肝不全	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
胆管閉塞	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
悪液質	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
心肺不全	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
胆管炎	1 (0.2)	0 (0.0)	1 (1.2)	0 (0.0)
慢性肝不全	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
循環虚脱	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
死亡	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
播種性血管内凝固	1 (0.2)	0 (0.0)	1 (1.2)	0 (0.0)
呼吸困難	1 (0.2)	0 (0.0)	1 (1.2)	0 (0.0)
大腸菌性敗血症	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
肝硬変	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
腸出血	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
中枢神経系転移	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
心筋梗塞	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
臓器不全	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
急性膵炎	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)

Percentages are based on the total number of subjects in the Safety Analysis Set within the relevant treatment group.
Subjects with two or more adverse events in the same preferred term will be counted only once.
Adverse Events terms were coded using Medical Dictionary for Regulatory Activities (MedDRA) version 19.1.
TEAE = Treatment-emergent adverse event.

付録 2.7.4.3
Fatal Serious Treatment-Emergent Adverse Events by Preferred Term
Study 304
Safety Analysis Set

	All		Japanese	
Preferred Term	Lenvatinib (N=476) n (%)	Sorafenib (N=475) n (%)	Lenvatinib (N=81) n (%)	Sorafenib (N=87) n (%)
細菌性腹膜炎	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
肺塞栓症	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
肺梗塞	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
腹水	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)
肝機能異常	0 (0.0)	1 (0.2)	0 (0.0)	1 (1.1)
虚血性脳卒中	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)
食道静脈瘤出血	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)
敗血症性ショック	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)
くも膜下出血	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)
外傷性血腫	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)

Percentages are based on the total number of subjects in the Safety Analysis Set within the relevant treatment group.
Subjects with two or more adverse events in the same preferred term will be counted only once.
Adverse Events terms were coded using Medical Dictionary for Regulatory Activities (MedDRA) version 19.1.
TEAE = Treatment-emergent adverse event.

Eisai
Protocol: Lenvatinib (E7080) Integrated Summary of Safety

付録 2.7.4.4
Fatal Serious Related Treatment-Emergent Adverse Events by Preferred Term
Study 304
Safety Analysis Set

	All		Japanese	
	Lenvatinib (N=476)	Sorafenib (N=475)	Lenvatinib (N=81)	Sorafenib (N=87)
Preferred Term	n (%)	n (%)	n (%)	n (%)
Subjects with Any Fatal Related TEAEs	11 (2.3)	4 (0.8)	0 (0.0)	0 (0.0)
脳出血	3 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)
肝不全	3 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)
呼吸不全	2 (0.4)	1 (0.2)	0 (0.0)	0 (0.0)
脳血管発作	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
循環虚脱	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
心筋梗塞	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
敗血症	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
上部消化管出血	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
虚血性脳卒中	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)
突然死	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)
腫瘍出血	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)

Related TEAEs include TEAEs that were considered by the Investigator to be possibly or probably related to study drug or TEAEs with a missing causality.
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付録 2.7.4.5
Serious Treatment-Emergent Adverse Events by Preferred Term
Study 304
Safety Analysis Set

	All		Japanese	
Preferred Term	Lenvatinib (N=476) n (%)	Sorafenib (N=475) n (%)	Lenvatinib (N=81) n (%)	Sorafenib (N=87) n (%)
Subjects with Any Serious TEAEs	205 (43.1)	144 (30.3)	31 (38.3)	25 (28.7)
肝性脳症	21 (4.4)	3 (0.6)	5 (6.2)	1 (1.1)
肝不全	14 (2.9)	8 (1.7)	3 (3.7)	1 (1.1)
腹水	12 (2.5)	11 (2.3)	3 (3.7)	4 (4.6)
食欲減退	11 (2.3)	2 (0.4)	2 (2.5)	0 (0.0)
悪性新生物進行	10 (2.1)	14 (2.9)	0 (0.0)	0 (0.0)
下痢	8 (1.7)	2 (0.4)	0 (0.0)	0 (0.0)
食道静脈瘤出血	7 (1.5)	5 (1.1)	0 (0.0)	1 (1.1)
胆汁うっ滞性黄疸	7 (1.5)	3 (0.6)	2 (2.5)	2 (2.3)
敗血症	7 (1.5)	3 (0.6)	1 (1.2)	0 (0.0)
無力症	7 (1.5)	1 (0.2)	0 (0.0)	0 (0.0)
血中ビリルビン増加	7 (1.5)	1 (0.2)	1 (1.2)	0 (0.0)
腹痛	6 (1.3)	10 (2.1)	0 (0.0)	1 (1.1)
発熱	6 (1.3)	5 (1.1)	2 (2.5)	2 (2.3)
嘔吐	6 (1.3)	0 (0.0)	0 (0.0)	0 (0.0)
肺炎	5 (1.1)	4 (0.8)	2 (2.5)	1 (1.1)
全身健康状態低下	5 (1.1)	3 (0.6)	0 (0.0)	0 (0.0)
呼吸困難	5 (1.1)	2 (0.4)	1 (1.2)	0 (0.0)

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付録 2.7.4.5
Serious Treatment-Emergent Adverse Events by Preferred Term
Study 304
Safety Analysis Set

	All		Japanese	
Preferred Term	Lenvatinib (N=476) n (%)	Sorafenib (N=475) n (%)	Lenvatinib (N=81) n (%)	Sorafenib (N=87) n (%)
上部消化管出血	5 (1.1)	2 (0.4)	2 (2.5)	0 (0.0)
肺塞栓症	4 (0.8)	2 (0.4)	0 (0.0)	0 (0.0)
心筋梗塞	4 (0.8)	1 (0.2)	0 (0.0)	0 (0.0)
癌疼痛	4 (0.8)	0 (0.0)	3 (3.7)	0 (0.0)
門脈血栓症	4 (0.8)	0 (0.0)	2 (2.5)	0 (0.0)
呼吸不全	3 (0.6)	3 (0.6)	0 (0.0)	0 (0.0)
腫瘍出血	3 (0.6)	3 (0.6)	1 (1.2)	1 (1.1)
急性腎障害	3 (0.6)	2 (0.4)	0 (0.0)	0 (0.0)
胆管炎	3 (0.6)	2 (0.4)	3 (3.7)	1 (1.1)
肝性昏睡	3 (0.6)	1 (0.2)	0 (0.0)	0 (0.0)
出血性十二指腸潰瘍	3 (0.6)	1 (0.2)	1 (1.2)	0 (0.0)
低ナトリウム血症	3 (0.6)	1 (0.2)	1 (1.2)	0 (0.0)
末梢性浮腫	3 (0.6)	1 (0.2)	0 (0.0)	0 (0.0)
脳出血	3 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)
肝硬変	3 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)
悪心	3 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)
誤嚥性肺炎	3 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)
蛋白尿	3 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)

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付録 2.7.4.5
Serious Treatment-Emergent Adverse Events by Preferred Term
Study 304
Safety Analysis Set

	All		Japanese	
Preferred Term	Lenvatinib (N=476) n (%)	Sorafenib (N=475) n (%)	Lenvatinib (N=81) n (%)	Sorafenib (N=87) n (%)
背部痛	2 (0.4)	5 (1.1)	0 (0.0)	0 (0.0)
病的骨折	2 (0.4)	5 (1.1)	0 (0.0)	0 (0.0)
疲労	2 (0.4)	2 (0.4)	0 (0.0)	1 (1.1)
腎機能障害	2 (0.4)	2 (0.4)	2 (2.5)	1 (1.1)
アスパラギン酸アミノトランスフェラーゼ増加	2 (0.4)	1 (0.2)	0 (0.0)	0 (0.0)
脳血管発作	2 (0.4)	1 (0.2)	0 (0.0)	0 (0.0)
胃腸炎	2 (0.4)	1 (0.2)	0 (0.0)	0 (0.0)
肝膿瘍	2 (0.4)	1 (0.2)	1 (1.2)	1 (1.1)
肝癌破裂	2 (0.4)	1 (0.2)	0 (0.0)	0 (0.0)
肺感染	2 (0.4)	1 (0.2)	0 (0.0)	0 (0.0)
脊椎転移	2 (0.4)	1 (0.2)	0 (0.0)	0 (0.0)
多臓器機能不全症候群	2 (0.4)	1 (0.2)	0 (0.0)	0 (0.0)
筋力低下	2 (0.4)	1 (0.2)	1 (1.2)	0 (0.0)
痙攣発作	2 (0.4)	1 (0.2)	0 (0.0)	0 (0.0)
上腹部痛	2 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)
偶発的過量投与	2 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)
胆管閉塞	2 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)
胆管結石	2 (0.4)	0 (0.0)	2 (2.5)	0 (0.0)

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Serious Treatment-Emergent Adverse Events by Preferred Term
Study 304
Safety Analysis Set

	All		Japanese	
Preferred Term	Lenvatinib (N=476) n (%)	Sorafenib (N=475) n (%)	Lenvatinib (N=81) n (%)	Sorafenib (N=87) n (%)
蜂巣炎	2 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)
脳梗塞	2 (0.4)	0 (0.0)	1 (1.2)	0 (0.0)
胆嚢炎	2 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)
脱水	2 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)
十二指腸潰瘍	2 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)
胃潰瘍	2 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)
頭痛	2 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)
肝肺症候群	2 (0.4)	0 (0.0)	1 (1.2)	0 (0.0)
高カリウム血症	2 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)
中枢神経系転移	2 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)
骨盤痛	2 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)
細菌性腹膜炎	2 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)
腎不全	2 (0.4)	0 (0.0)	1 (1.2)	0 (0.0)
脊髄圧迫	2 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)
臍ヘルニア	2 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)
尿路感染	2 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)
貧血	1 (0.2)	4 (0.8)	1 (1.2)	1 (1.1)
肝機能異常	1 (0.2)	4 (0.8)	1 (1.2)	3 (3.4)

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Serious Treatment-Emergent Adverse Events by Preferred Term
Study 304
Safety Analysis Set

	All		Japanese	
Preferred Term	Lenvatinib (N=476) n (%)	Sorafenib (N=475) n (%)	Lenvatinib (N=81) n (%)	Sorafenib (N=87) n (%)
黄疸	1 (0.2)	4 (0.8)	0 (0.0)	0 (0.0)
胃出血	1 (0.2)	3 (0.6)	1 (1.2)	1 (1.1)
腹部膨満	1 (0.2)	2 (0.4)	0 (0.0)	0 (0.0)
急性胆嚢炎	1 (0.2)	2 (0.4)	0 (0.0)	0 (0.0)
錯乱状態	1 (0.2)	2 (0.4)	0 (0.0)	0 (0.0)
骨転移	1 (0.2)	2 (0.4)	0 (0.0)	0 (0.0)
突然死	1 (0.2)	2 (0.4)	0 (0.0)	0 (0.0)
腫瘍疼痛	1 (0.2)	2 (0.4)	0 (0.0)	1 (1.1)
急性呼吸不全	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)
心房細動	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)
胆道感染	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)
両麻痺	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)
低血糖	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)
感染	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)
感染性胸水	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)
肺膿瘍	1 (0.2)	1 (0.2)	1 (1.2)	0 (0.0)
頚部痛	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)
末梢腫脹	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)

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Preferred Term	Lenvatinib (N=476) n (%)	Sorafenib (N=475) n (%)	Lenvatinib (N=81) n (%)	Sorafenib (N=87) n (%)
敗血症性ショック	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)
下腹部痛	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
急性肝不全	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
アラニンアミノトランスフェラーゼ増加	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
大動脈解離	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
虫垂膿瘍	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
菌血症	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
胆管拡張	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
血圧低下	1 (0.2)	0 (0.0)	1 (1.2)	0 (0.0)
骨髄機能不全	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
骨痛	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
悪液質	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
心肺不全	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
慢性肝不全	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
循環虚脱	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
クロストリジウム検査陽性	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
死亡	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
深部静脈血栓症	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)

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Preferred Term	Lenvatinib (N=476) n (%)	Sorafenib (N=475) n (%)	Lenvatinib (N=81) n (%)	Sorafenib (N=87) n (%)
デング熱	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
糖尿病	1 (0.2)	0 (0.0)	1 (1.2)	0 (0.0)
播種性血管内凝固	1 (0.2)	0 (0.0)	1 (1.2)	0 (0.0)
注意力障害	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
憩室炎	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
浮動性めまい	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
消化不良	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
大腸菌性敗血症	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
顔面麻痺	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
転倒	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
側腹部痛	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
ウイルス性消化管感染	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
全身性浮腫	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
鼠径部膿瘍	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
血尿	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
血性胆汁	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
肝酵素上昇	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
肝臓痛	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)

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Preferred Term	Lenvatinib (N=476) n (%)	Sorafenib (N=475) n (%)	Lenvatinib (N=81) n (%)	Sorafenib (N=87) n (%)
肝腎症候群	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
しゃっくり	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
水腫性胆嚢炎	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
高ビリルビン血症	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
高カルシウム血症	1 (0.2)	0 (0.0)	1 (1.2)	0 (0.0)
低アルブミン血症	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
低カルシウム血症	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
低マグネシウム血症	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
ＩｇＡ腎症	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
感染性新生物	1 (0.2)	0 (0.0)	1 (1.2)	0 (0.0)
企図的過量投与	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
間擦疹	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
椎間板突出	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
腸出血	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
頭蓋内腫瘍出血	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
肝損傷	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
腰部脊柱管狭窄症	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
大うつ病	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)

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Preferred Term	Lenvatinib (N=476) n (%)	Sorafenib (N=475) n (%)	Lenvatinib (N=81) n (%)	Sorafenib (N=87) n (%)
髄膜腫	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
壊死性細気管支炎	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
好中球数減少	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
非心原性肺水腫	1 (0.2)	0 (0.0)	1 (1.2)	0 (0.0)
臓器不全	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
口腔咽頭痛	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
変形性関節症	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
四肢痛	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
急性膵炎	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
反回神経麻痺	1 (0.2)	0 (0.0)	1 (1.2)	0 (0.0)
肝周囲膿瘍	1 (0.2)	0 (0.0)	1 (1.2)	0 (0.0)
歯周炎	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
胸膜感染	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
気胸	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
可逆性後白質脳症症候群	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
術後膿瘍	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
肺梗塞	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
肺結核	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)

Percentages are based on the total number of subjects in the Safety Analysis Set within the relevant treatment group.
Subjects with two or more adverse events in the same preferred term will be counted only once.
Adverse Events terms were coded using Medical Dictionary for Regulatory Activities (MedDRA) version 19.1.
TEAE = Treatment-emergent adverse event.

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付録 2.7.4.5
Serious Treatment-Emergent Adverse Events by Preferred Term
Study 304
Safety Analysis Set

	All		Japanese	
Preferred Term	Lenvatinib (N=476) n (%)	Sorafenib (N=475) n (%)	Lenvatinib (N=81) n (%)	Sorafenib (N=87) n (%)
腎細胞癌	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
腎尿細管壊死	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
横紋筋融解症	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
サルモネラ症	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
陰嚢感染	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
脂漏性皮膚炎	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
脊柱管狭窄症	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
脊椎圧迫骨折	1 (0.2)	0 (0.0)	1 (1.2)	0 (0.0)
自殺企図	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
失神	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
胸椎骨折	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
血栓性静脈炎	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
一過性脳虚血発作	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
結核	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
腫瘍壊死	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
腫瘍破裂	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
腸球菌性尿路感染	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
尿路性敗血症	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)

Percentages are based on the total number of subjects in the Safety Analysis Set within the relevant treatment group.
Subjects with two or more adverse events in the same preferred term will be counted only once.
Adverse Events terms were coded using Medical Dictionary for Regulatory Activities (MedDRA) version 19.1.
TEAE = Treatment-emergent adverse event.

Program: T2_7_4_5.sas 18MAY2017 11:07

付録 2.7.4.5
Serious Treatment-Emergent Adverse Events by Preferred Term
Study 304
Safety Analysis Set

	All		Japanese	
Preferred Term	Lenvatinib (N=476) n (%)	Sorafenib (N=475) n (%)	Lenvatinib (N=81) n (%)	Sorafenib (N=87) n (%)
食道静脈瘤	1 (0.2)	0 (0.0)	1 (1.2)	0 (0.0)
体重減少	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
手掌・足底発赤知覚不全症候群	0 (0.0)	3 (0.6)	0 (0.0)	1 (1.1)
薬疹	0 (0.0)	2 (0.4)	0 (0.0)	2 (2.3)
発熱性好中球減少症	0 (0.0)	2 (0.4)	0 (0.0)	0 (0.0)
胃腸出血	0 (0.0)	2 (0.4)	0 (0.0)	0 (0.0)
下部消化管出血	0 (0.0)	2 (0.4)	0 (0.0)	2 (2.3)
血小板数減少	0 (0.0)	2 (0.4)	0 (0.0)	1 (1.1)
胸水	0 (0.0)	2 (0.4)	0 (0.0)	1 (1.1)
脊椎骨折	0 (0.0)	2 (0.4)	0 (0.0)	0 (0.0)
急性心筋梗塞	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)
急性副鼻腔炎	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)
ビタミンＢ１２欠乏性貧血	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)
アスペルギルス感染	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)
心房粗動	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)
大脳基底核出血	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)
気管支炎	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)
心不全	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)

Percentages are based on the total number of subjects in the Safety Analysis Set within the relevant treatment group.
Subjects with two or more adverse events in the same preferred term will be counted only once.
Adverse Events terms were coded using Medical Dictionary for Regulatory Activities (MedDRA) version 19.1.
TEAE = Treatment-emergent adverse event.

付録 2.7.4.5
Serious Treatment-Emergent Adverse Events by Preferred Term
Study 304
Safety Analysis Set

	All		Japanese	
Preferred Term	Lenvatinib (N=476) n (%)	Sorafenib (N=475) n (%)	Lenvatinib (N=81) n (%)	Sorafenib (N=87) n (%)
白内障	0 (0.0)	1 (0.2)	0 (0.0)	1 (1.1)
大腸炎	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)
医療機器関連感染	0 (0.0)	1 (0.2)	0 (0.0)	1 (1.1)
糖尿病性足感染	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)
脳症	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)
腸炎	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)
多形紅斑	0 (0.0)	1 (0.2)	0 (0.0)	1 (1.1)
食中毒	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)
体内異物	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)
胃穿孔	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)
出血性胃潰瘍	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)
血便排泄	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)
ヘモグロビン減少	0 (0.0)	1 (0.2)	0 (0.0)	1 (1.1)
痔核	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)
心臓弁狭窄	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)
聴力低下	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)
低蛋白血症	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)
低血圧	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)

Percentages are based on the total number of subjects in the Safety Analysis Set within the relevant treatment group.
Subjects with two or more adverse events in the same preferred term will be counted only once.
Adverse Events terms were coded using Medical Dictionary for Regulatory Activities (MedDRA) version 19.1.
TEAE = Treatment-emergent adverse event.

付録 2.7.4.5
Serious Treatment-Emergent Adverse Events by Preferred Term
Study 304
Safety Analysis Set

	All		Japanese	
Preferred Term	Lenvatinib (N=476) n (%)	Sorafenib (N=475) n (%)	Lenvatinib (N=81) n (%)	Sorafenib (N=87) n (%)
虚血性脳卒中	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)
意識消失	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)
下気道感染	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)
肺の悪性新生物	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)
悪性腹水	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)
悪性胸水	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)
眼部単純ヘルペス	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)
会陰膿瘍	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)
腹膜出血	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)
形質細胞性骨髄腫	0 (0.0)	1 (0.2)	0 (0.0)	1 (1.1)
大腸菌性肺炎	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)
肺臓炎	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)
外傷性気胸	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)
乾癬	0 (0.0)	1 (0.2)	0 (0.0)	1 (1.1)
ショック	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)
変形性脊椎症	0 (0.0)	1 (0.2)	0 (0.0)	1 (1.1)
くも膜下出血	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)
表在性血栓性静脈炎	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)

Percentages are based on the total number of subjects in the Safety Analysis Set within the relevant treatment group.
Subjects with two or more adverse events in the same preferred term will be counted only once.
Adverse Events terms were coded using Medical Dictionary for Regulatory Activities (MedDRA) version 19.1.
TEAE = Treatment-emergent adverse event.

付録 2.7.4.5
Serious Treatment-Emergent Adverse Events by Preferred Term
Study 304
Safety Analysis Set

	All		Japanese	
	Lenvatinib (N=476)	Sorafenib (N=475)	Lenvatinib (N=81)	Sorafenib (N=87)
Preferred Term	n (%)	n (%)	n (%)	n (%)
血栓性脳梗塞	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)
外傷性血腫	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)
上気道感染	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)
回転性めまい	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)

Percentages are based on the total number of subjects in the Safety Analysis Set within the relevant treatment group.
Subjects with two or more adverse events in the same preferred term will be counted only once.
Adverse Events terms were coded using Medical Dictionary for Regulatory Activities (MedDRA) version 19.1.
TEAE = Treatment-emergent adverse event.

付録 2.7.4.6
Serious Related Treatment-Emergent Adverse Events by Preferred Term
Study 304
Safety Analysis Set

	All		Japanese	
Preferred Term	Lenvatinib (N=476) n (%)	Sorafenib (N=475) n (%)	Lenvatinib (N=81) n (%)	Sorafenib (N=87) n (%)
Subjects with Any Serious Related TEAEs	84 (17.6)	48 (10.1)	15 (18.5)	13 (14.9)
肝性脳症	9 (1.9)	1 (0.2)	2 (2.5)	0 (0.0)
食欲減退	8 (1.7)	1 (0.2)	1 (1.2)	0 (0.0)
下痢	7 (1.5)	2 (0.4)	0 (0.0)	0 (0.0)
腹水	6 (1.3)	3 (0.6)	3 (3.7)	2 (2.3)
肝不全	5 (1.1)	3 (0.6)	1 (1.2)	0 (0.0)
無力症	4 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)
発熱	3 (0.6)	4 (0.8)	2 (2.5)	1 (1.1)
血中ビリルビン増加	3 (0.6)	1 (0.2)	0 (0.0)	0 (0.0)
肺塞栓症	3 (0.6)	1 (0.2)	0 (0.0)	0 (0.0)
上部消化管出血	3 (0.6)	1 (0.2)	2 (2.5)	0 (0.0)
脳出血	3 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)
心筋梗塞	3 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)
食道静脈瘤出血	3 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)
蛋白尿	3 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)
呼吸不全	2 (0.4)	1 (0.2)	0 (0.0)	0 (0.0)
脳梗塞	2 (0.4)	0 (0.0)	1 (1.2)	0 (0.0)
胆嚢炎	2 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)

Percentages are based on the total number of subjects in the Safety Analysis Set within the relevant treatment group.
Related TEAEs include TEAEs that were considered by the Investigator to be possibly or probably related to study drug or TEAEs with a missing causality.
Subjects with two or more adverse events in the same preferred term will be counted only once.
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TEAE = Treatment-emergent adverse event.

付録 2.7.4.6
Serious Related Treatment-Emergent Adverse Events by Preferred Term
Study 304
Safety Analysis Set

	All		Japanese	
Preferred Term	Lenvatinib (N=476) n (%)	Sorafenib (N=475) n (%)	Lenvatinib (N=81) n (%)	Sorafenib (N=87) n (%)
胆汁うっ滞性黄疸	2 (0.4)	0 (0.0)	1 (1.2)	0 (0.0)
嘔吐	2 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)
肝機能異常	1 (0.2)	3 (0.6)	1 (1.2)	2 (2.3)
胃出血	1 (0.2)	2 (0.4)	1 (1.2)	0 (0.0)
腫瘍出血	1 (0.2)	2 (0.4)	1 (1.2)	1 (1.1)
脳血管発作	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)
出血性十二指腸潰瘍	1 (0.2)	1 (0.2)	1 (1.2)	0 (0.0)
疲労	1 (0.2)	1 (0.2)	0 (0.0)	1 (1.1)
肺炎	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)
急性腎障害	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
大動脈解離	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
胆管結石	1 (0.2)	0 (0.0)	1 (1.2)	0 (0.0)
骨髄機能不全	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
胆管炎	1 (0.2)	0 (0.0)	1 (1.2)	0 (0.0)
循環虚脱	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
肝性昏睡	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
深部静脈血栓症	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
脱水	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)

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Related TEAEs include TEAEs that were considered by the Investigator to be possibly or probably related to study drug or TEAEs with a missing causality.
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TEAE = Treatment-emergent adverse event.

付録 2.7.4.6
Serious Related Treatment-Emergent Adverse Events by Preferred Term
Study 304
Safety Analysis Set

	All		Japanese	
Preferred Term	Lenvatinib (N=476) n (%)	Sorafenib (N=475) n (%)	Lenvatinib (N=81) n (%)	Sorafenib (N=87) n (%)
十二指腸潰瘍	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
呼吸困難	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
顔面麻痺	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
胃潰瘍	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
全身健康状態低下	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
全身性浮腫	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
血尿	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
血性胆汁	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
肝硬変	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
肝酵素上昇	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
肝臓痛	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
肝腎症候群	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
しゃっくり	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
高カリウム血症	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
低カルシウム血症	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
低血糖	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
低マグネシウム血症	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
低ナトリウム血症	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)

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付録 2.7.4.6

Serious Related Treatment-Emergent Adverse Events by Preferred Term

Study 304

Safety Analysis Set

	All		Japanese	
Preferred Term	Lenvatinib (N=476) n (%)	Sorafenib (N=475) n (%)	Lenvatinib (N=81) n (%)	Sorafenib (N=87) n (%)
間擦疹	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
肺感染	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
筋力低下	1 (0.2)	0 (0.0)	1 (1.2)	0 (0.0)
悪心	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
壊死性細気管支炎	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
好中球数減少	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
非心原性肺水腫	1 (0.2)	0 (0.0)	1 (1.2)	0 (0.0)
末梢性浮腫	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
骨盤痛	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
門脈血栓症	1 (0.2)	0 (0.0)	1 (1.2)	0 (0.0)
可逆性後白質脳症症候群	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
術後膿瘍	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
腎不全	1 (0.2)	0 (0.0)	1 (1.2)	0 (0.0)
腎機能障害	1 (0.2)	0 (0.0)	1 (1.2)	0 (0.0)
腎尿細管壊死	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
陰嚢感染	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
脂漏性皮膚炎	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
敗血症	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)

Percentages are based on the total number of subjects in the Safety Analysis Set within the relevant treatment group.
Related TEAEs include TEAEs that were considered by the Investigator to be possibly or probably related to study drug or TEAEs with a missing causality.
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付録 2.7.4.6
Serious Related Treatment-Emergent Adverse Events by Preferred Term
Study 304
Safety Analysis Set

	All		Japanese	
Preferred Term	Lenvatinib (N=476) n (%)	Sorafenib (N=475) n (%)	Lenvatinib (N=81) n (%)	Sorafenib (N=87) n (%)
血栓性静脈炎	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
食道静脈瘤	1 (0.2)	0 (0.0)	1 (1.2)	0 (0.0)
手掌・足底発赤知覚不全症候群	0 (0.0)	3 (0.6)	0 (0.0)	1 (1.1)
貧血	0 (0.0)	2 (0.4)	0 (0.0)	1 (1.1)
錯乱状態	0 (0.0)	2 (0.4)	0 (0.0)	0 (0.0)
薬疹	0 (0.0)	2 (0.4)	0 (0.0)	2 (2.3)
血小板数減少	0 (0.0)	2 (0.4)	0 (0.0)	1 (1.1)
腹痛	0 (0.0)	1 (0.2)	0 (0.0)	1 (1.1)
ビタミンＢ１２欠乏性貧血	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)
心房細動	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)
大脳基底核出血	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)
心不全	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)
大腸炎	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)
医療機器関連感染	0 (0.0)	1 (0.2)	0 (0.0)	1 (1.1)
多形紅斑	0 (0.0)	1 (0.2)	0 (0.0)	1 (1.1)
胃穿孔	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)
胃腸出血	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)
血便排泄	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)

Percentages are based on the total number of subjects in the Safety Analysis Set within the relevant treatment group.
Related TEAEs include TEAEs that were considered by the Investigator to be possibly or probably related to study drug or TEAEs with a missing causality.
Subjects with two or more adverse events in the same preferred term will be counted only once.
Adverse Events terms were coded using Medical Dictionary for Regulatory Activities (MedDRA) version 19.1.
TEAE = Treatment-emergent adverse event.

付録 2.7.4.6
Serious Related Treatment-Emergent Adverse Events by Preferred Term
Study 304
Safety Analysis Set

	All		Japanese	
Preferred Term	Lenvatinib (N=476) n (%)	Sorafenib (N=475) n (%)	Lenvatinib (N=81) n (%)	Sorafenib (N=87) n (%)
ヘモグロビン減少	0 (0.0)	1 (0.2)	0 (0.0)	1 (1.1)
痔核	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)
心臓弁狭窄	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)
聴力低下	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)
感染	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)
虚血性脳卒中	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)
黄疸	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)
意識消失	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)
下部消化管出血	0 (0.0)	1 (0.2)	0 (0.0)	1 (1.1)
腹膜出血	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)
乾癬	0 (0.0)	1 (0.2)	0 (0.0)	1 (1.1)
突然死	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)
血栓性脳梗塞	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)

Percentages are based on the total number of subjects in the Safety Analysis Set within the relevant treatment group.
Related TEAEs include TEAEs that were considered by the Investigator to be possibly or probably related to study drug or TEAEs with a missing causality.
Subjects with two or more adverse events in the same preferred term will be counted only once.
Adverse Events terms were coded using Medical Dictionary for Regulatory Activities (MedDRA) version 19.1.
TEAE = Treatment-emergent adverse event.

付録 2.7.4.7
Treatment-Emergent Adverse Events Leading to Treatment Discontinuation by Preferred Term
Study 304
Safety Analysis Set

	All		Japanese	
Preferred Term	Lenvatinib (N=476) n (%)	Sorafenib (N=475) n (%)	Lenvatinib (N=81) n (%)	Sorafenib (N=87) n (%)
Subjects with Any TEAEs Leading to Treatment Discontinuation	94 (19.7)	69 (14.5)	15 (18.5)	18 (20.7)
疲労	7 (1.5)	5 (1.1)	1 (1.2)	2 (2.3)
肝性脳症	7 (1.5)	0 (0.0)	2 (2.5)	0 (0.0)
血中ビリルビン増加	6 (1.3)	1 (0.2)	1 (1.2)	0 (0.0)
肝不全	5 (1.1)	3 (0.6)	2 (2.5)	1 (1.1)
胆汁うっ滞性黄疸	3 (0.6)	1 (0.2)	1 (1.2)	0 (0.0)
蛋白尿	3 (0.6)	1 (0.2)	1 (1.2)	0 (0.0)
脳出血	3 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)
心筋梗塞	3 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)
敗血症	3 (0.6)	0 (0.0)	1 (1.2)	0 (0.0)
腹痛	2 (0.4)	5 (1.1)	0 (0.0)	1 (1.1)
全身健康状態低下	2 (0.4)	4 (0.8)	0 (0.0)	1 (1.1)
ＥＣＯＧパフォーマンスステータス悪化	2 (0.4)	1 (0.2)	0 (0.0)	0 (0.0)
悪性新生物進行	2 (0.4)	1 (0.2)	0 (0.0)	0 (0.0)
多臓器機能不全症候群	2 (0.4)	1 (0.2)	0 (0.0)	0 (0.0)
上部消化管出血	2 (0.4)	1 (0.2)	1 (1.2)	0 (0.0)
上腹部痛	2 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)
胆管閉塞	2 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)

Percentages are based on the total number of subjects in the Safety Analysis Set within the relevant treatment group.
Subjects with two or more adverse events in the same preferred term will be counted only once.
Adverse Events terms were coded using Medical Dictionary for Regulatory Activities (MedDRA) version 19.1.
TEAE = Treatment-emergent adverse event.

付録 2.7.4.7
Treatment-Emergent Adverse Events Leading to Treatment Discontinuation by Preferred Term
Study 304
Safety Analysis Set

	All		Japanese	
Preferred Term	Lenvatinib (N=476) n (%)	Sorafenib (N=475) n (%)	Lenvatinib (N=81) n (%)	Sorafenib (N=87) n (%)
脳血管発作	2 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)
門脈血栓症	2 (0.4)	0 (0.0)	1 (1.2)	0 (0.0)
腹水	1 (0.2)	4 (0.8)	1 (1.2)	0 (0.0)
腎機能障害	1 (0.2)	2 (0.4)	1 (1.2)	2 (2.3)
呼吸不全	1 (0.2)	2 (0.4)	0 (0.0)	0 (0.0)
突然死	1 (0.2)	2 (0.4)	0 (0.0)	0 (0.0)
無力症	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)
脳症	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)
肝機能異常	1 (0.2)	1 (0.2)	1 (1.2)	1 (1.1)
食道静脈瘤出血	1 (0.2)	1 (0.2)	0 (0.0)	1 (1.1)
四肢痛	1 (0.2)	1 (0.2)	0 (0.0)	1 (1.1)
肺炎	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)
肺塞栓症	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)
腹部膨満	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
副腎腺腫	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
血中アルカリホスファターゼ増加	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
骨髄機能不全	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
気管支肺アスペルギルス症	1 (0.2)	0 (0.0)	1 (1.2)	0 (0.0)

Percentages are based on the total number of subjects in the Safety Analysis Set within the relevant treatment group.
Subjects with two or more adverse events in the same preferred term will be counted only once.
Adverse Events terms were coded using Medical Dictionary for Regulatory Activities (MedDRA) version 19.1.
TEAE = Treatment-emergent adverse event.

付録 2.7.4.7
Treatment-Emergent Adverse Events Leading to Treatment Discontinuation by Preferred Term
Study 304
Safety Analysis Set

	All		Japanese	
Preferred Term	Lenvatinib (N=476) n (%)	Sorafenib (N=475) n (%)	Lenvatinib (N=81) n (%)	Sorafenib (N=87) n (%)
癌疼痛	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
脳梗塞	1 (0.2)	0 (0.0)	1 (1.2)	0 (0.0)
後天性胆管拡張症	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
胆管炎	1 (0.2)	0 (0.0)	1 (1.2)	0 (0.0)
慢性肝不全	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
循環虚脱	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
肝性昏睡	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
死亡	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
食欲減退	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
両麻痺	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
播種性血管内凝固	1 (0.2)	0 (0.0)	1 (1.2)	0 (0.0)
薬物不耐性	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
呼吸困難	1 (0.2)	0 (0.0)	1 (1.2)	0 (0.0)
大腸菌性敗血症	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
γ－グルタミルトランスフェラーゼ増加	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
頭痛	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
高血圧	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
治癒不良	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)

Percentages are based on the total number of subjects in the Safety Analysis Set within the relevant treatment group.
Subjects with two or more adverse events in the same preferred term will be counted only once.
Adverse Events terms were coded using Medical Dictionary for Regulatory Activities (MedDRA) version 19.1.
TEAE = Treatment-emergent adverse event.

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付録 2.7.4.7
Treatment-Emergent Adverse Events Leading to Treatment Discontinuation by Preferred Term
Study 304
Safety Analysis Set

	All		Japanese	
Preferred Term	Lenvatinib (N=476) n (%)	Sorafenib (N=475) n (%)	Lenvatinib (N=81) n (%)	Sorafenib (N=87) n (%)
肝膿瘍	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
肝癌破裂	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
肝損傷	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
中枢神経系転移	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
口腔内潰瘍形成	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
好中球数減少	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
末梢性浮腫	1 (0.2)	0 (0.0)	1 (1.2)	0 (0.0)
臓器不全	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
急性膵炎	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
肺梗塞	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
発熱	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
腎細胞癌	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
腎不全	1 (0.2)	0 (0.0)	1 (1.2)	0 (0.0)
脊髄圧迫	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
腫瘍出血	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
腫瘍壊死	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
腫瘍破裂	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
臍ヘルニア	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)

Percentages are based on the total number of subjects in the Safety Analysis Set within the relevant treatment group.
Subjects with two or more adverse events in the same preferred term will be counted only once.
Adverse Events terms were coded using Medical Dictionary for Regulatory Activities (MedDRA) version 19.1.
TEAE = Treatment-emergent adverse event.

付録 2.7.4.7
Treatment-Emergent Adverse Events Leading to Treatment Discontinuation by Preferred Term
Study 304
Safety Analysis Set

	All		Japanese	
Preferred Term	Lenvatinib (N=476) n (%)	Sorafenib (N=475) n (%)	Lenvatinib (N=81) n (%)	Sorafenib (N=87) n (%)
黄疸	0 (0.0)	3 (0.6)	0 (0.0)	0 (0.0)
手掌・足底発赤知覚不全症候群	0 (0.0)	3 (0.6)	0 (0.0)	0 (0.0)
下痢	0 (0.0)	2 (0.4)	0 (0.0)	0 (0.0)
薬疹	0 (0.0)	2 (0.4)	0 (0.0)	2 (2.3)
胃腸出血	0 (0.0)	2 (0.4)	0 (0.0)	0 (0.0)
斑状丘疹状皮疹	0 (0.0)	2 (0.4)	0 (0.0)	2 (2.3)
腫瘍疼痛	0 (0.0)	2 (0.4)	0 (0.0)	1 (1.1)
急性腎障害	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)
急性心筋梗塞	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)
アラニンアミノトランスフェラーゼ増加	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)
アスパラギン酸アミノトランスフェラーゼ増加	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)
心房細動	0 (0.0)	1 (0.2)	0 (0.0)	1 (1.1)
心不全	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)
皮膚炎	0 (0.0)	1 (0.2)	0 (0.0)	1 (1.1)
医療機器関連感染	0 (0.0)	1 (0.2)	0 (0.0)	1 (1.1)
心電図T波逆転	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)
多形紅斑	0 (0.0)	1 (0.2)	0 (0.0)	1 (1.1)
眼痛	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)

Percentages are based on the total number of subjects in the Safety Analysis Set within the relevant treatment group.
Subjects with two or more adverse events in the same preferred term will be counted only once.
Adverse Events terms were coded using Medical Dictionary for Regulatory Activities (MedDRA) version 19.1.
TEAE = Treatment-emergent adverse event.

付録 2.7.4.7
Treatment-Emergent Adverse Events Leading to Treatment Discontinuation by Preferred Term
Study 304
Safety Analysis Set

	All		Japanese	
Preferred Term	Lenvatinib (N=476) n (%)	Sorafenib (N=475) n (%)	Lenvatinib (N=81) n (%)	Sorafenib (N=87) n (%)
顔面痛	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)
胃穿孔	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)
虚血性脳卒中	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)
肺の悪性新生物	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)
錯感覚	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)
病的骨折	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)
腹膜出血	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)
血小板数減少	0 (0.0)	1 (0.2)	0 (0.0)	1 (1.1)
頻尿	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)
乾癬	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)
丘疹性皮疹	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)
痙攣発作	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)
敗血症性ショック	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)
ショック	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)
血栓性脳梗塞	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)
外傷性血腫	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)

Percentages are based on the total number of subjects in the Safety Analysis Set within the relevant treatment group.
Subjects with two or more adverse events in the same preferred term will be counted only once.
Adverse Events terms were coded using Medical Dictionary for Regulatory Activities (MedDRA) version 19.1.
TEAE = Treatment-emergent adverse event.

付録 2.7.4.8
Treatment-Emergent Adverse Events Leading to Treatment Modification (Interruption or Reduction) by Preferred Term
Study 304
Safety Analysis Set

	All		Japanese	
Preferred Term	Lenvatinib (N=476) n (%)	Sorafenib (N=475) n (%)	Lenvatinib (N=81) n (%)	Sorafenib (N=87) n (%)
Subjects with Any TEAEs Leading to Treatment Modification	294 (61.8)	264 (55.6)	65 (80.2)	65 (74.7)
下痢	36 (7.6)	35 (7.4)	7 (8.6)	6 (6.9)
食欲減退	36 (7.6)	15 (3.2)	16 (19.8)	4 (4.6)
蛋白尿	33 (6.9)	7 (1.5)	7 (8.6)	3 (3.4)
高血圧	29 (6.1)	18 (3.8)	1 (1.2)	4 (4.6)
疲労	27 (5.7)	17 (3.6)	6 (7.4)	2 (2.3)
手掌・足底発赤知覚不全症候群	25 (5.3)	88 (18.5)	8 (9.9)	26 (29.9)
血小板数減少	22 (4.6)	12 (2.5)	5 (6.2)	6 (6.9)
血中ビリルビン増加	20 (4.2)	14 (2.9)	4 (4.9)	1 (1.1)
体重減少	20 (4.2)	4 (0.8)	6 (7.4)	0 (0.0)
肝性脳症	20 (4.2)	3 (0.6)	6 (7.4)	1 (1.1)
無力症	16 (3.4)	9 (1.9)	0 (0.0)	0 (0.0)
悪心	16 (3.4)	9 (1.9)	2 (2.5)	1 (1.1)
嘔吐	12 (2.5)	6 (1.3)	0 (0.0)	1 (1.1)
発熱	12 (2.5)	5 (1.1)	2 (2.5)	1 (1.1)
好中球数減少	11 (2.3)	5 (1.1)	4 (4.9)	1 (1.1)
腹水	10 (2.1)	5 (1.1)	4 (4.9)	2 (2.3)
アスパラギン酸アミノトランスフェラーゼ増加	9 (1.9)	18 (3.8)	0 (0.0)	4 (4.6)

Percentages are based on the total number of subjects in the Safety Analysis Set within the relevant treatment group.
Subjects with two or more adverse events in the same preferred term will be counted only once.
Adverse Events terms were coded using Medical Dictionary for Regulatory Activities (MedDRA) version 19.1.
TEAE = Treatment-emergent adverse event.

付録 2.7.4.8
Treatment-Emergent Adverse Events Leading to Treatment Modification (Interruption or Reduction) by Preferred Term
Study 304
Safety Analysis Set

	All		Japanese	
Preferred Term	Lenvatinib (N=476) n (%)	Sorafenib (N=475) n (%)	Lenvatinib (N=81) n (%)	Sorafenib (N=87) n (%)
呼吸困難	8 (1.7)	4 (0.8)	2 (2.5)	0 (0.0)
γ－グルタミルトランスフェラーゼ増加	7 (1.5)	4 (0.8)	0 (0.0)	2 (2.3)
アラニンアミノトランスフェラーゼ増加	6 (1.3)	9 (1.9)	0 (0.0)	2 (2.3)
腹痛	6 (1.3)	8 (1.7)	0 (0.0)	1 (1.1)
血小板減少症	6 (1.3)	4 (0.8)	2 (2.5)	1 (1.1)
白血球数減少	6 (1.3)	4 (0.8)	2 (2.5)	2 (2.3)
末梢性浮腫	6 (1.3)	3 (0.6)	2 (2.5)	2 (2.3)
口内炎	6 (1.3)	2 (0.4)	1 (1.2)	0 (0.0)
脱水	6 (1.3)	0 (0.0)	2 (2.5)	0 (0.0)
好中球減少症	6 (1.3)	0 (0.0)	1 (1.2)	0 (0.0)
上腹部痛	5 (1.1)	2 (0.4)	1 (1.2)	0 (0.0)
食道静脈瘤出血	5 (1.1)	1 (0.2)	0 (0.0)	0 (0.0)
低ナトリウム血症	5 (1.1)	0 (0.0)	1 (1.2)	0 (0.0)
倦怠感	5 (1.1)	0 (0.0)	5 (6.2)	0 (0.0)
筋肉痛	5 (1.1)	0 (0.0)	2 (2.5)	0 (0.0)
血中アルカリホスファターゼ増加	4 (0.8)	2 (0.4)	0 (0.0)	0 (0.0)
高ビリルビン血症	4 (0.8)	2 (0.4)	1 (1.2)	0 (0.0)
四肢痛	4 (0.8)	2 (0.4)	0 (0.0)	0 (0.0)

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TEAE = Treatment-emergent adverse event.

付録 2.7.4.8

Treatment-Emergent Adverse Events Leading to Treatment Modification (Interruption or Reduction) by Preferred Term

Study 304

Safety Analysis Set

	All		Japanese	
	Lenvatinib (N=476)	Sorafenib (N=475)	Lenvatinib (N=81)	Sorafenib (N=87)
Preferred Term	n (%)	n (%)	n (%)	n (%)
急性腎障害	4 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)
高アンモニア血症	4 (0.8)	0 (0.0)	4 (4.9)	0 (0.0)
貧血	3 (0.6)	8 (1.7)	1 (1.2)	2 (2.3)
肝不全	3 (0.6)	2 (0.4)	0 (0.0)	1 (1.1)
胆管炎	3 (0.6)	1 (0.2)	2 (2.5)	1 (1.1)
出血性十二指腸潰瘍	3 (0.6)	1 (0.2)	1 (1.2)	0 (0.0)
喀血	3 (0.6)	1 (0.2)	0 (0.0)	0 (0.0)
低アルブミン血症	3 (0.6)	1 (0.2)	2 (2.5)	1 (1.1)
黄疸	3 (0.6)	1 (0.2)	0 (0.0)	0 (0.0)
嗜眠	3 (0.6)	1 (0.2)	0 (0.0)	0 (0.0)
筋力低下	3 (0.6)	1 (0.2)	1 (1.2)	0 (0.0)
便秘	3 (0.6)	0 (0.0)	1 (1.2)	0 (0.0)
尿路感染	3 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)
発疹	2 (0.4)	10 (2.1)	1 (1.2)	1 (1.1)
肝機能異常	2 (0.4)	9 (1.9)	0 (0.0)	9 (10.3)
鼻咽頭炎	2 (0.4)	3 (0.6)	0 (0.0)	1 (1.1)
胆管閉塞	2 (0.4)	1 (0.2)	0 (0.0)	0 (0.0)
脳血管発作	2 (0.4)	1 (0.2)	0 (0.0)	0 (0.0)

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付録 2.7.4.8

Treatment-Emergent Adverse Events Leading to Treatment Modification (Interruption or Reduction) by Preferred Term

Study 304

Safety Analysis Set

	All		Japanese	
	Lenvatinib (N=476)	Sorafenib (N=475)	Lenvatinib (N=81)	Sorafenib (N=87)
Preferred Term	n (%)	n (%)	n (%)	n (%)
錯乱状態	2 (0.4)	1 (0.2)	0 (0.0)	0 (0.0)
血尿	2 (0.4)	1 (0.2)	0 (0.0)	0 (0.0)
高カリウム血症	2 (0.4)	1 (0.2)	0 (0.0)	0 (0.0)
上部消化管出血	2 (0.4)	1 (0.2)	2 (2.5)	0 (0.0)
胆管結石	2 (0.4)	0 (0.0)	2 (2.5)	0 (0.0)
骨髄機能不全	2 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)
脳梗塞	2 (0.4)	0 (0.0)	1 (1.2)	0 (0.0)
胆嚢炎	2 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)
十二指腸潰瘍	2 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)
消化不良	2 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)
胃潰瘍	2 (0.4)	0 (0.0)	1 (1.2)	0 (0.0)
肝硬変	2 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)
リパーゼ増加	2 (0.4)	0 (0.0)	1 (1.2)	0 (0.0)
頚部痛	2 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)
歯周炎	2 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)
誤嚥性肺炎	2 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)
肺塞栓症	2 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)
上気道感染	1 (0.2)	4 (0.8)	1 (1.2)	0 (0.0)

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付録 2.7.4.8
Treatment-Emergent Adverse Events Leading to Treatment Modification (Interruption or Reduction) by Preferred Term
Study 304
Safety Analysis Set

	All		Japanese	
	Lenvatinib (N=476)	Sorafenib (N=475)	Lenvatinib (N=81)	Sorafenib (N=87)
Preferred Term	n (%)	n (%)	n (%)	n (%)
心房細動	1 (0.2)	3 (0.6)	0 (0.0)	1 (1.1)
背部痛	1 (0.2)	2 (0.4)	0 (0.0)	0 (0.0)
低血圧	1 (0.2)	2 (0.4)	0 (0.0)	0 (0.0)
胆汁うっ滞性黄疸	1 (0.2)	2 (0.4)	0 (0.0)	2 (2.3)
肛門膿瘍	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)
関節痛	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)
癌疼痛	1 (0.2)	1 (0.2)	1 (1.2)	0 (0.0)
急性胆嚢炎	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)
浮動性めまい	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)
口内乾燥	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)
心電図ＱＴ延長	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)
低リン酸血症	1 (0.2)	1 (0.2)	0 (0.0)	1 (1.1)
甲状腺機能低下症	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)
感染	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)
感染性胸水	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)
白血球減少症	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)
肝膿瘍	1 (0.2)	1 (0.2)	1 (1.2)	1 (1.1)
リンパ球数減少	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)

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付録 2.7.4.8
Treatment-Emergent Adverse Events Leading to Treatment Modification (Interruption or Reduction) by Preferred Term
Study 304
Safety Analysis Set

	All		Japanese	
Preferred Term	Lenvatinib (N=476) n (%)	Sorafenib (N=475) n (%)	Lenvatinib (N=81) n (%)	Sorafenib (N=87) n (%)
悪性新生物進行	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)
肺炎	1 (0.2)	1 (0.2)	0 (0.0)	1 (1.1)
門脈血栓症	1 (0.2)	1 (0.2)	1 (1.2)	0 (0.0)
腎機能障害	1 (0.2)	1 (0.2)	1 (1.2)	1 (1.1)
敗血症	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)
腫瘍出血	1 (0.2)	1 (0.2)	1 (1.2)	1 (1.1)
腹部膨満	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
下腹部痛	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
偶発的過量投与	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
急性呼吸不全	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
大動脈解離	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
虫垂膿瘍	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
菌血症	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
胆管拡張	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
左脚ブロック	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
慢性腎臓病	1 (0.2)	0 (0.0)	1 (1.2)	0 (0.0)
循環虚脱	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
クロストリジウム検査陽性	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)

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付録 2.7.4.8
Treatment-Emergent Adverse Events Leading to Treatment Modification (Interruption or Reduction) by Preferred Term
Study 304
Safety Analysis Set

	All		Japanese	
Preferred Term	Lenvatinib (N=476) n (%)	Sorafenib (N=475) n (%)	Lenvatinib (N=81) n (%)	Sorafenib (N=87) n (%)
肝性昏睡	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
細菌性結膜炎	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
皮膚血管炎	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
深部静脈血栓症	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
デング熱	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
注意力障害	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
湿疹	1 (0.2)	0 (0.0)	1 (1.2)	0 (0.0)
ウイルス性消化管感染	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
全身性浮腫	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
鼠径部膿瘍	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
吐血	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
頭痛	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
肝肺症候群	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
肝腎症候群	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
水腫性胆嚢炎	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
高カルシウム血症	1 (0.2)	0 (0.0)	1 (1.2)	0 (0.0)
低カルシウム血症	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
低カリウム血症	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)

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付録 2.7.4.8

Treatment-Emergent Adverse Events Leading to Treatment Modification (Interruption or Reduction) by Preferred Term

Study 304

Safety Analysis Set

	All		Japanese	
	Lenvatinib (N=476)	Sorafenib (N=475)	Lenvatinib (N=81)	Sorafenib (N=87)
Preferred Term	n (%)	n (%)	n (%)	n (%)
特発性肺線維症	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
インフルエンザ	1 (0.2)	0 (0.0)	1 (1.2)	0 (0.0)
鼠径ヘルニア	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
企図的過量投与	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
椎間板突出	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
腎感染	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
肺感染	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
リンパ球減少症	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
大うつ病	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
精神状態変化	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
口腔内潰瘍形成	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
心筋梗塞	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
壊死性細気管支炎	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
非心臓性胸痛	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
肝疾患による浮腫	1 (0.2)	0 (0.0)	1 (1.2)	0 (0.0)
口腔咽頭痛	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
変形性関節症	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
手掌紅斑	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)

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Treatment-Emergent Adverse Events Leading to Treatment Modification (Interruption or Reduction) by Preferred Term
Study 304
Safety Analysis Set

	All		Japanese	
	Lenvatinib (N=476)	Sorafenib (N=475)	Lenvatinib (N=81)	Sorafenib (N=87)
Preferred Term	n (%)	n (%)	n (%)	n (%)
急性膵炎	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
反回神経麻痺	1 (0.2)	0 (0.0)	1 (1.2)	0 (0.0)
末梢腫脹	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
細菌性腹膜炎	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
胸膜感染	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
可逆性後白質脳症症候群	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
術後膿瘍	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
尿中蛋白陽性	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
プロトロンビン量増加	1 (0.2)	0 (0.0)	1 (1.2)	0 (0.0)
腎尿細管壊死	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
横紋筋融解症	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
サルモネラ症	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
陰嚢感染	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
痙攣発作	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
傾眠	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
自殺企図	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
全身性炎症反応症候群	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
胸椎骨折	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)

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Treatment-Emergent Adverse Events Leading to Treatment Modification (Interruption or Reduction) by Preferred Term
Study 304
Safety Analysis Set

	All		Japanese	
Preferred Term	Lenvatinib (N=476) n (%)	Sorafenib (N=475) n (%)	Lenvatinib (N=81) n (%)	Sorafenib (N=87) n (%)
歯痛	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
トランスアミナーゼ上昇	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
一過性脳虚血発作	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
結核	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
尿中ビリルビン増加	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
尿中蛋白／クレアチニン比増加	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
食道静脈瘤	1 (0.2)	0 (0.0)	1 (1.2)	0 (0.0)
外陰腟真菌感染	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
体重増加	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
斑状丘疹状皮疹	0 (0.0)	5 (1.1)	0 (0.0)	1 (1.1)
胃出血	0 (0.0)	3 (0.6)	0 (0.0)	1 (1.1)
そう痒症	0 (0.0)	3 (0.6)	0 (0.0)	0 (0.0)
水疱	0 (0.0)	2 (0.4)	0 (0.0)	0 (0.0)
咳嗽	0 (0.0)	2 (0.4)	0 (0.0)	0 (0.0)
水疱性皮膚炎	0 (0.0)	2 (0.4)	0 (0.0)	0 (0.0)
薬疹	0 (0.0)	2 (0.4)	0 (0.0)	2 (2.3)
薬物過敏症	0 (0.0)	2 (0.4)	0 (0.0)	0 (0.0)
腸炎	0 (0.0)	2 (0.4)	0 (0.0)	0 (0.0)

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付録 2.7.4.8
Treatment-Emergent Adverse Events Leading to Treatment Modification (Interruption or Reduction) by Preferred Term
Study 304
Safety Analysis Set

	All		Japanese	
Preferred Term	Lenvatinib (N=476) n (%)	Sorafenib (N=475) n (%)	Lenvatinib (N=81) n (%)	Sorafenib (N=87) n (%)
下部消化管出血	0 (0.0)	2 (0.4)	0 (0.0)	2 (2.3)
口腔カンジダ症	0 (0.0)	2 (0.4)	0 (0.0)	1 (1.1)
胸水	0 (0.0)	2 (0.4)	0 (0.0)	1 (1.1)
急性副鼻腔炎	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)
脱毛症	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)
狭心症	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)
失声症	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)
アスペルギルス感染	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)
心房粗動	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)
細菌感染	0 (0.0)	1 (0.2)	0 (0.0)	1 (1.1)
大脳基底核出血	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)
胆管狭窄	0 (0.0)	1 (0.2)	0 (0.0)	1 (1.1)
気管支炎	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)
クロストリジウム・ディフィシレ感染	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)
大腸炎	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)
齲歯	0 (0.0)	1 (0.2)	0 (0.0)	1 (1.1)
糖尿病性足感染	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)
皮膚乾燥	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)

Percentages are based on the total number of subjects in the Safety Analysis Set within the relevant treatment group.
Subjects with two or more adverse events in the same preferred term will be counted only once.
Adverse Events terms were coded using Medical Dictionary for Regulatory Activities (MedDRA) version 19.1.
TEAE = Treatment-emergent adverse event.

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付録 2.7.4.8

Treatment-Emergent Adverse Events Leading to Treatment Modification (Interruption or Reduction) by Preferred Term

Study 304

Safety Analysis Set

	All		Japanese	
	Lenvatinib (N=476)	Sorafenib (N=475)	Lenvatinib (N=81)	Sorafenib (N=87)
Preferred Term	n (%)	n (%)	n (%)	n (%)
嚥下障害	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)
心窩部不快感	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)
変色便	0 (0.0)	1 (0.2)	0 (0.0)	1 (1.1)
発熱性好中球減少症	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)
食中毒	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)
排便回数増加	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)
胃炎	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)
胃腸炎	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)
ノロウイルス性胃腸炎	0 (0.0)	1 (0.2)	0 (0.0)	1 (1.1)
全身紅斑	0 (0.0)	1 (0.2)	0 (0.0)	1 (1.1)
舌炎	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)
舌痛	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)
血便排泄	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)
心臓弁狭窄	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)
肝酵素上昇	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)
肝毒性	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)
帯状疱疹	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)
しゃっくり	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)

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TEAE = Treatment-emergent adverse event.

付録 2.7.4.8

Treatment-Emergent Adverse Events Leading to Treatment Modification (Interruption or Reduction) by Preferred Term

Study 304

Safety Analysis Set

	All		Japanese	
	Lenvatinib (N=476)	Sorafenib (N=475)	Lenvatinib (N=81)	Sorafenib (N=87)
Preferred Term	n (%)	n (%)	n (%)	n (%)
高尿酸血症	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)
聴力低下	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)
低血糖	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)
虚血性脳卒中	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)
意識消失	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)
悪性胸水	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)
代謝性脳症	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)
骨転移	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)
筋痙縮	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)
神経痛	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)
食道カンジダ症	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)
口腔扁平苔癬	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)
口腔粘膜水疱形成	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)
口腔内痛	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)
膵炎	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)
病的骨折	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)
活動状態低下	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)
会陰膿瘍	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)

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Subjects with two or more adverse events in the same preferred term will be counted only once.
Adverse Events terms were coded using Medical Dictionary for Regulatory Activities (MedDRA) version 19.1.
TEAE = Treatment-emergent adverse event.

付録 2.7.4.8
Treatment-Emergent Adverse Events Leading to Treatment Modification (Interruption or Reduction) by Preferred Term
Study 304
Safety Analysis Set

	All		Japanese	
	Lenvatinib (N=476)	Sorafenib (N=475)	Lenvatinib (N=81)	Sorafenib (N=87)
Preferred Term	n (%)	n (%)	n (%)	n (%)
末梢性感覚ニューロパチー	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)
大腸菌性肺炎	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)
肺臓炎	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)
外傷性気胸	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)
失神寸前の状態	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)
前立腺炎	0 (0.0)	1 (0.2)	0 (0.0)	1 (1.1)
乾癬	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)
丘疹性皮疹	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)
ウイルス性気道感染	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)
陰嚢紅斑	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)
敗血症性ショック	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)
皮膚剥脱	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)
皮膚病変	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)
脊椎骨折	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)
ストーマ部出血	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)
滑膜炎	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)
扁桃炎	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)
外傷性血腫	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)

Percentages are based on the total number of subjects in the Safety Analysis Set within the relevant treatment group.
Subjects with two or more adverse events in the same preferred term will be counted only once.
Adverse Events terms were coded using Medical Dictionary for Regulatory Activities (MedDRA) version 19.1.
TEAE = Treatment-emergent adverse event.

付録 2.7.4.8
Treatment-Emergent Adverse Events Leading to Treatment Modification (Interruption or Reduction) by Preferred Term
Study 304
Safety Analysis Set

	All		Japanese	
Preferred Term	Lenvatinib (N=476) n (%)	Sorafenib (N=475) n (%)	Lenvatinib (N=81) n (%)	Sorafenib (N=87) n (%)
腫瘍壊死	0 (0.0)	1 (0.2)	0 (0.0)	1 (1.1)
腫瘍疼痛	0 (0.0)	1 (0.2)	0 (0.0)	1 (1.1)
上気道の炎症	0 (0.0)	1 (0.2)	0 (0.0)	1 (1.1)
蕁麻疹	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)
創傷感染	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)

Percentages are based on the total number of subjects in the Safety Analysis Set within the relevant treatment group.
Subjects with two or more adverse events in the same preferred term will be counted only once.
Adverse Events terms were coded using Medical Dictionary for Regulatory Activities (MedDRA) version 19.1.
TEAE = Treatment-emergent adverse event.

付録 2.7.4.9
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
HCC Lenvatinib Safety Set
ISS Safety Set

System organ Class Preferred Term	Lenvatinib (N=496) Any Grade n (%)	Lenvatinib (N=496) Grade >= 3 n (%)
Subjects with Any TEAEs	490 (98.8)	376 (75.8)
血液およびリンパ系障害	94 (19.0)	42 (8.5)
血小板減少症	39 (7.9)	14 (2.8)
貧血	34 (6.9)	16 (3.2)
好中球減少症	24 (4.8)	6 (1.2)
白血球減少症	16 (3.2)	1 (0.2)
赤血球増加症	3 (0.6)	0 (0.0)
骨髄機能不全	2 (0.4)	2 (0.4)
白血球増加症	2 (0.4)	2 (0.4)
凝血異常	1 (0.2)	0 (0.0)
播種性血管内凝固	1 (0.2)	1 (0.2)
発熱性好中球減少症	1 (0.2)	1 (0.2)
低プロトロンビン血症	1 (0.2)	0 (0.0)
リンパ節症	1 (0.2)	0 (0.0)
リンパ球減少症	1 (0.2)	1 (0.2)
汎血球減少症	1 (0.2)	0 (0.0)
心臓障害	38 (7.7)	7 (1.4)
洞性徐脈	6 (1.2)	0 (0.0)
洞性頻脈	5 (1.0)	0 (0.0)
心房細動	4 (0.8)	1 (0.2)
心筋梗塞	4 (0.8)	4 (0.8)
心筋虚血	3 (0.6)	0 (0.0)
上室性期外収縮	3 (0.6)	0 (0.0)
頻脈	3 (0.6)	0 (0.0)
徐脈	2 (0.4)	0 (0.0)
左室肥大	2 (0.4)	0 (0.0)

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Subject with two or more TEAEs reported in the same SOC or PT term will be only counted once.
Adverse Events terms were coded using Medical Dictionary for Regulatory Activities (MedDRA) version 19.1.
TEAE = Treatment-emergent adverse event.

付録 2.7.4.9
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
HCC Lenvatinib Safety Set
ISS Safety Set

System organ Class Preferred Term	Lenvatinib (N=496) Any Grade n (%)	 Grade >= 3 n (%)
動悸	2 (0.4)	0 (0.0)
不整脈	1 (0.2)	0 (0.0)
第一度房室ブロック	1 (0.2)	0 (0.0)
左脚ブロック	1 (0.2)	0 (0.0)
うっ血性心不全	1 (0.2)	0 (0.0)
心原性ショック	1 (0.2)	1 (0.2)
心肺不全	1 (0.2)	1 (0.2)
冠動脈疾患	1 (0.2)	0 (0.0)
期外収縮	1 (0.2)	0 (0.0)
結節性不整脈	1 (0.2)	0 (0.0)
プリンツメタル狭心症	1 (0.2)	0 (0.0)
洞性不整脈	1 (0.2)	0 (0.0)
心室性不整脈	1 (0.2)	0 (0.0)
心室性期外収縮	1 (0.2)	0 (0.0)
耳および迷路障害	16 (3.2)	0 (0.0)
耳鳴	6 (1.2)	0 (0.0)
回転性めまい	4 (0.8)	0 (0.0)
難聴	2 (0.4)	0 (0.0)
耳不快感	2 (0.4)	0 (0.0)
耳痛	2 (0.4)	0 (0.0)
耳の障害	1 (0.2)	0 (0.0)
耳出血	1 (0.2)	0 (0.0)
内分泌障害	86 (17.3)	0 (0.0)
甲状腺機能低下症	79 (15.9)	0 (0.0)
甲状腺機能亢進症	4 (0.8)	0 (0.0)
甲状腺炎	2 (0.4)	0 (0.0)

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Subject with two or more TEAEs reported in the same SOC or PT term will be only counted once.
Adverse Events terms were coded using Medical Dictionary for Regulatory Activities (MedDRA) version 19.1.
TEAE = Treatment-emergent adverse event.

付録 2.7.4.9
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
HCC Lenvatinib Safety Set
ISS Safety Set

System organ Class Preferred Term	Lenvatinib (N=496) Any Grade n (%)	Lenvatinib (N=496) Grade >= 3 n (%)
甲状腺腫	1 (0.2)	0 (0.0)
抗利尿ホルモン不適合分泌	1 (0.2)	0 (0.0)
眼障害	18 (3.6)	0 (0.0)
白内障	2 (0.4)	0 (0.0)
瞳孔動揺	2 (0.4)	0 (0.0)
眼充血	2 (0.4)	0 (0.0)
霧視	2 (0.4)	0 (0.0)
動脈硬化性網膜症	1 (0.2)	0 (0.0)
眼瞼炎	1 (0.2)	0 (0.0)
結膜出血	1 (0.2)	0 (0.0)
眼の炎症	1 (0.2)	0 (0.0)
眼刺激	1 (0.2)	0 (0.0)
眼痛	1 (0.2)	0 (0.0)
眼瞼浮腫	1 (0.2)	0 (0.0)
眼瞼そう痒症	1 (0.2)	0 (0.0)
角膜炎	1 (0.2)	0 (0.0)
黄斑変性	1 (0.2)	0 (0.0)
近視	1 (0.2)	0 (0.0)
網膜静脈閉塞	1 (0.2)	0 (0.0)
視力障害	1 (0.2)	0 (0.0)
胃腸障害	390 (78.6)	76 (15.3)
下痢	189 (38.1)	21 (4.2)
悪心	103 (20.8)	4 (0.8)
腹痛	85 (17.1)	8 (1.6)
便秘	84 (16.9)	3 (0.6)
嘔吐	82 (16.5)	6 (1.2)

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Subject with two or more TEAEs reported in the same SOC or PT term will be only counted once.
Adverse Events terms were coded using Medical Dictionary for Regulatory Activities (MedDRA) version 19.1.
TEAE = Treatment-emergent adverse event.

付録 2.7.4.9
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
HCC Lenvatinib Safety Set
ISS Safety Set

System organ Class Preferred Term	Lenvatinib (N=496) Any Grade n (%)	 Grade >= 3 n (%)
腹水	71 (14.3)	18 (3.6)
上腹部痛	59 (11.9)	6 (1.2)
口内炎	50 (10.1)	1 (0.2)
腹部膨満	39 (7.9)	1 (0.2)
消化不良	35 (7.1)	1 (0.2)
口内乾燥	32 (6.5)	0 (0.0)
歯肉出血	20 (4.0)	1 (0.2)
腹部不快感	11 (2.2)	0 (0.0)
痔核	11 (2.2)	0 (0.0)
歯肉腫脹	10 (2.0)	0 (0.0)
歯痛	10 (2.0)	0 (0.0)
歯肉痛	9 (1.8)	0 (0.0)
齲歯	8 (1.6)	0 (0.0)
鼓腸	8 (1.6)	0 (0.0)
胃潰瘍	8 (1.6)	1 (0.2)
食道静脈瘤出血	8 (1.6)	8 (1.6)
胃食道逆流性疾患	7 (1.4)	0 (0.0)
胃炎	6 (1.2)	0 (0.0)
痔出血	6 (1.2)	0 (0.0)
歯周病	6 (1.2)	0 (0.0)
おくび	5 (1.0)	0 (0.0)
口腔内出血	5 (1.0)	0 (0.0)
口腔内潰瘍形成	5 (1.0)	1 (0.2)
直腸出血	5 (1.0)	0 (0.0)
上部消化管出血	5 (1.0)	4 (0.8)
十二指腸潰瘍	4 (0.8)	0 (0.0)

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Subject with two or more TEAEs reported in the same SOC or PT term will be only counted once.
Adverse Events terms were coded using Medical Dictionary for Regulatory Activities (MedDRA) version 19.1.
TEAE = Treatment-emergent adverse event.

付録 2.7.4.9
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
HCC Lenvatinib Safety Set
ISS Safety Set

System organ Class Preferred Term	Lenvatinib (N=496) Any Grade n (%)	 Grade >= 3 n (%)
直腸炎	4 (0.8)	0 (0.0)
食道静脈瘤	4 (0.8)	1 (0.2)
慢性胃炎	3 (0.6)	0 (0.0)
出血性十二指腸潰瘍	3 (0.6)	2 (0.4)
腸炎	3 (0.6)	0 (0.0)
心窩部不快感	3 (0.6)	0 (0.0)
消化器痛	3 (0.6)	0 (0.0)
舌痛	3 (0.6)	0 (0.0)
嚥下痛	3 (0.6)	0 (0.0)
口腔内痛	3 (0.6)	0 (0.0)
下腹部痛	2 (0.4)	1 (0.2)
腹部圧痛	2 (0.4)	0 (0.0)
肛門の炎症	2 (0.4)	0 (0.0)
嚥下障害	2 (0.4)	0 (0.0)
軟便	2 (0.4)	0 (0.0)
排便回数増加	2 (0.4)	0 (0.0)
舌炎	2 (0.4)	0 (0.0)
吐血	2 (0.4)	0 (0.0)
血便排泄	2 (0.4)	0 (0.0)
臍ヘルニア	2 (0.4)	1 (0.2)
腹部硬直	1 (0.2)	0 (0.0)
異常便	1 (0.2)	0 (0.0)
急性腹症	1 (0.2)	0 (0.0)
裂肛	1 (0.2)	0 (0.0)
痔瘻	1 (0.2)	0 (0.0)
肛門失禁	1 (0.2)	1 (0.2)

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Subject with two or more TEAEs reported in the same SOC or PT term will be only counted once.
Adverse Events terms were coded using Medical Dictionary for Regulatory Activities (MedDRA) version 19.1.
TEAE = Treatment-emergent adverse event.

付録 2.7.4.9
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
HCC Lenvatinib Safety Set
ISS Safety Set

System organ Class Preferred Term	Lenvatinib (N=496) Any Grade n (%)	 Grade >= 3 n (%)
口唇のひび割れ	1 (0.2)	0 (0.0)
排便障害	1 (0.2)	0 (0.0)
糞塊	1 (0.2)	0 (0.0)
変色便	1 (0.2)	0 (0.0)
硬便	1 (0.2)	0 (0.0)
白色便	1 (0.2)	0 (0.0)
胃出血	1 (0.2)	0 (0.0)
胃静脈瘤	1 (0.2)	0 (0.0)
びらん性胃炎	1 (0.2)	0 (0.0)
胃腸出血	1 (0.2)	1 (0.2)
消化管運動障害	1 (0.2)	0 (0.0)
歯肉潰瘍	1 (0.2)	0 (0.0)
イレウス	1 (0.2)	0 (0.0)
単径ヘルニア	1 (0.2)	0 (0.0)
腸出血	1 (0.2)	1 (0.2)
過敏性腸症候群	1 (0.2)	0 (0.0)
口唇出血	1 (0.2)	0 (0.0)
口唇痛	1 (0.2)	0 (0.0)
下部消化管出血	1 (0.2)	0 (0.0)
口腔腫脹	1 (0.2)	0 (0.0)
食道炎	1 (0.2)	0 (0.0)
急性膵炎	1 (0.2)	1 (0.2)
門脈圧亢進性胃障害	1 (0.2)	0 (0.0)
肛門周囲痛	1 (0.2)	0 (0.0)
直腸ポリープ	1 (0.2)	0 (0.0)
直腸潰瘍	1 (0.2)	0 (0.0)

Percentages are based on the total number of subjects in the Safety Analysis Set within the relevant treatment group.
Subject with two or more TEAEs reported in the same SOC or PT term will be only counted once.
Adverse Events terms were coded using Medical Dictionary for Regulatory Activities (MedDRA) version 19.1.
TEAE = Treatment-emergent adverse event.

付録 2.7.4.9
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
HCC Lenvatinib Safety Set
ISS Safety Set

System organ Class Preferred Term	Lenvatinib (N=496) Any Grade n (%)	Lenvatinib (N=496) Grade >= 3 n (%)
逆流性胃炎	1 (0.2)	0 (0.0)
舌嚢胞	1 (0.2)	0 (0.0)
舌不快感	1 (0.2)	0 (0.0)
一般・全身障害および投与部位の状態	300 (60.5)	48 (9.7)
疲労	152 (30.6)	18 (3.6)
末梢性浮腫	72 (14.5)	4 (0.8)
発熱	71 (14.3)	0 (0.0)
無力症	54 (10.9)	14 (2.8)
倦怠感	21 (4.2)	0 (0.0)
悪寒	11 (2.2)	0 (0.0)
非心臓性胸痛	11 (2.2)	0 (0.0)
インフルエンザ様疾患	7 (1.4)	0 (0.0)
全身健康状態低下	6 (1.2)	6 (1.2)
疼痛	6 (1.2)	0 (0.0)
胸部不快感	5 (1.0)	0 (0.0)
全身性浮腫	4 (0.8)	0 (0.0)
肝疾患による浮腫	3 (0.6)	0 (0.0)
末梢腫脹	3 (0.6)	1 (0.2)
口渇	3 (0.6)	0 (0.0)
カテーテル留置部位疼痛	2 (0.4)	0 (0.0)
早期満腹	2 (0.4)	0 (0.0)
顔面浮腫	2 (0.4)	0 (0.0)
冷感	2 (0.4)	0 (0.0)
限局性浮腫	2 (0.4)	0 (0.0)
多臓器機能不全症候群	2 (0.4)	2 (0.4)
乾燥症	2 (0.4)	0 (0.0)

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Adverse Events terms were coded using Medical Dictionary for Regulatory Activities (MedDRA) version 19.1.
TEAE = Treatment-emergent adverse event.

付録 2.7.4.9
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
HCC Lenvatinib Safety Set
ISS Safety Set

System organ Class Preferred Term	Lenvatinib (N=496) Any Grade n (%)	 Grade >= 3 n (%)
突出痛	1 (0.2)	0 (0.0)
胸痛	1 (0.2)	0 (0.0)
死亡	1 (0.2)	1 (0.2)
薬物不耐性	1 (0.2)	1 (0.2)
顔面痛	1 (0.2)	0 (0.0)
肉芽腫	1 (0.2)	0 (0.0)
高熱	1 (0.2)	0 (0.0)
治癒不良	1 (0.2)	1 (0.2)
注入部位血管外漏出	1 (0.2)	0 (0.0)
注射部位内出血	1 (0.2)	0 (0.0)
粘膜の炎症	1 (0.2)	0 (0.0)
小結節	1 (0.2)	0 (0.0)
臓器不全	1 (0.2)	1 (0.2)
異物感	1 (0.2)	0 (0.0)
突然死	1 (0.2)	1 (0.2)
全身性炎症反応症候群	1 (0.2)	0 (0.0)
温度変化不耐症	1 (0.2)	0 (0.0)
肝胆道系障害	85 (17.1)	54 (10.9)
肝不全	15 (3.0)	15 (3.0)
肝機能異常	12 (2.4)	8 (1.6)
高ビリルビン血症	11 (2.2)	6 (1.2)
胆汁うっ滞性黄疸	9 (1.8)	8 (1.6)
門脈血栓症	9 (1.8)	4 (0.8)
肝臓痛	8 (1.6)	1 (0.2)
胆管炎	6 (1.2)	3 (0.6)
黄疸	6 (1.2)	1 (0.2)

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付録 2.7.4.9
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
HCC Lenvatinib Safety Set
ISS Safety Set

System organ Class Preferred Term	Lenvatinib (N=496) Any Grade n (%)	 Grade >= 3 n (%)
肝硬変	4 (0.8)	3 (0.6)
胆管閉塞	3 (0.6)	3 (0.6)
胆管結石	2 (0.4)	2 (0.4)
胆嚢炎	2 (0.4)	1 (0.2)
急性肝不全	1 (0.2)	1 (0.2)
胆管狭窄	1 (0.2)	0 (0.0)
胆管拡張	1 (0.2)	1 (0.2)
後天性胆管拡張症	1 (0.2)	1 (0.2)
急性胆嚢炎	1 (0.2)	1 (0.2)
胆石症	1 (0.2)	0 (0.0)
胆汁うっ滞	1 (0.2)	0 (0.0)
慢性肝不全	1 (0.2)	1 (0.2)
血性胆汁	1 (0.2)	1 (0.2)
肝出血	1 (0.2)	1 (0.2)
肝腫大	1 (0.2)	0 (0.0)
肝腎症候群	1 (0.2)	1 (0.2)
水腫性胆嚢炎	1 (0.2)	1 (0.2)
肝障害	1 (0.2)	0 (0.0)
肝損傷	1 (0.2)	1 (0.2)
黄疸眼	1 (0.2)	0 (0.0)
門脈圧亢進症	1 (0.2)	1 (0.2)
免疫系障害	3 (0.6)	0 (0.0)
季節性アレルギー	2 (0.4)	0 (0.0)
造影剤アレルギー	1 (0.2)	0 (0.0)
感染症および寄生虫症	155 (31.3)	40 (8.1)
鼻咽頭炎	34 (6.9)	0 (0.0)

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付録 2.7.4.9
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
HCC Lenvatinib Safety Set
ISS Safety Set

System organ Class Preferred Term	Lenvatinib (N=496) Any Grade n (%)	Lenvatinib (N=496) Grade >= 3 n (%)
上気道感染	21 (4.2)	1 (0.2)
肺炎	12 (2.4)	4 (0.8)
尿路感染	12 (2.4)	1 (0.2)
胃腸炎	9 (1.8)	3 (0.6)
インフルエンザ	9 (1.8)	0 (0.0)
咽頭炎	8 (1.6)	0 (0.0)
敗血症	7 (1.4)	7 (1.4)
細菌性腹膜炎	6 (1.2)	4 (0.8)
口角口唇炎	4 (0.8)	0 (0.0)
気管支炎	4 (0.8)	0 (0.0)
膀胱炎	4 (0.8)	0 (0.0)
歯肉炎	4 (0.8)	0 (0.0)
毛包炎	3 (0.6)	0 (0.0)
単純ヘルペス	3 (0.6)	0 (0.0)
感染	3 (0.6)	1 (0.2)
口腔カンジダ症	3 (0.6)	0 (0.0)
歯周炎	3 (0.6)	0 (0.0)
膿疱性皮疹	3 (0.6)	0 (0.0)
副鼻腔炎	3 (0.6)	1 (0.2)
皮膚感染	3 (0.6)	0 (0.0)
蜂巣炎	2 (0.4)	2 (0.4)
細菌性胃腸炎	2 (0.4)	0 (0.0)
ウイルス性胃腸炎	2 (0.4)	0 (0.0)
帯状疱疹	2 (0.4)	0 (0.0)
喉頭炎	2 (0.4)	0 (0.0)
肝膿瘍	2 (0.4)	2 (0.4)

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付録 2.7.4.9
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
HCC Lenvatinib Safety Set
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System organ Class Preferred Term	Lenvatinib (N=496) Any Grade n (%)	 Grade >= 3 n (%)
肺感染	2 (0.4)	2 (0.4)
鼻炎	2 (0.4)	0 (0.0)
足部白癬	2 (0.4)	0 (0.0)
歯感染	2 (0.4)	0 (0.0)
外陰腟真菌感染	2 (0.4)	0 (0.0)
腹壁感染	1 (0.2)	1 (0.2)
肛門膿瘍	1 (0.2)	0 (0.0)
虫垂膿瘍	1 (0.2)	1 (0.2)
虫垂炎	1 (0.2)	1 (0.2)
菌血症	1 (0.2)	1 (0.2)
細菌性腟症	1 (0.2)	0 (0.0)
胆道感染	1 (0.2)	1 (0.2)
体部白癬	1 (0.2)	0 (0.0)
気管支肺アスペルギルス症	1 (0.2)	0 (0.0)
男性外性器蜂巣炎	1 (0.2)	0 (0.0)
慢性B型肝炎	1 (0.2)	1 (0.2)
シトロバクター感染	1 (0.2)	0 (0.0)
結膜炎	1 (0.2)	0 (0.0)
細菌性結膜炎	1 (0.2)	0 (0.0)
デング熱	1 (0.2)	1 (0.2)
憩室炎	1 (0.2)	1 (0.2)
耳感染	1 (0.2)	1 (0.2)
大腸菌性敗血症	1 (0.2)	1 (0.2)
真菌感染	1 (0.2)	0 (0.0)
せつ	1 (0.2)	0 (0.0)
ウイルス性消化管感染	1 (0.2)	0 (0.0)

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付録 2.7.4.9
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
HCC Lenvatinib Safety Set
ISS Safety Set

System organ Class Preferred Term	Lenvatinib (N=496) Any Grade n (%)	 Grade >= 3 n (%)
単径部膿瘍	1 (0.2)	1 (0.2)
単径部感染	1 (0.2)	0 (0.0)
B型肝炎	1 (0.2)	0 (0.0)
麦粒腫	1 (0.2)	0 (0.0)
感染性皮膚嚢腫	1 (0.2)	0 (0.0)
感染性胸水	1 (0.2)	1 (0.2)
腎感染	1 (0.2)	1 (0.2)
限局性感染	1 (0.2)	1 (0.2)
肺膿瘍	1 (0.2)	1 (0.2)
医療機器使用部位膿瘍	1 (0.2)	0 (0.0)
爪感染	1 (0.2)	0 (0.0)
口腔真菌感染	1 (0.2)	0 (0.0)
口腔ヘルペス	1 (0.2)	0 (0.0)
中咽頭カンジダ症	1 (0.2)	0 (0.0)
爪囲炎	1 (0.2)	0 (0.0)
肝周囲膿瘍	1 (0.2)	1 (0.2)
胸膜感染	1 (0.2)	0 (0.0)
術後膿瘍	1 (0.2)	1 (0.2)
肺結核	1 (0.2)	0 (0.0)
腎盂腎炎	1 (0.2)	0 (0.0)
ウイルス性気道感染	1 (0.2)	0 (0.0)
サルモネラ症	1 (0.2)	1 (0.2)
陰嚢感染	1 (0.2)	1 (0.2)
敗血症性ショック	1 (0.2)	1 (0.2)
扁桃炎	1 (0.2)	0 (0.0)
歯膿瘍	1 (0.2)	0 (0.0)

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付録 2.7.4.9
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
HCC Lenvatinib Safety Set
ISS Safety Set

System organ Class Preferred Term	Lenvatinib (N=496) Any Grade n (%)	 Grade >= 3 n (%)
気管炎	1 (0.2)	0 (0.0)
結核	1 (0.2)	0 (0.0)
腸球菌性尿路感染	1 (0.2)	1 (0.2)
尿路性敗血症	1 (0.2)	1 (0.2)
傷害、中毒および処置合併症	31 (6.3)	7 (1.4)
転倒	8 (1.6)	1 (0.2)
挫傷	3 (0.6)	0 (0.0)
皮膚擦過傷	3 (0.6)	0 (0.0)
偶発的過量投与	2 (0.4)	2 (0.4)
処置による疼痛	2 (0.4)	0 (0.0)
創傷	2 (0.4)	0 (0.0)
節足動物刺傷	1 (0.2)	0 (0.0)
大腿骨骨折	1 (0.2)	0 (0.0)
頭部損傷	1 (0.2)	0 (0.0)
熱射病	1 (0.2)	0 (0.0)
切開部位痛	1 (0.2)	0 (0.0)
注入に伴う反応	1 (0.2)	0 (0.0)
企図的過量投与	1 (0.2)	1 (0.2)
裂傷	1 (0.2)	0 (0.0)
四肢損傷	1 (0.2)	0 (0.0)
処置後血尿	1 (0.2)	0 (0.0)
外傷後疼痛	1 (0.2)	0 (0.0)
処置による悪心	1 (0.2)	0 (0.0)
放射線性食道炎	1 (0.2)	0 (0.0)
放射線性肺臓炎	1 (0.2)	1 (0.2)
肋骨骨折	1 (0.2)	0 (0.0)

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付録 2.7.4.9
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
HCC Lenvatinib Safety Set
ISS Safety Set

System organ Class Preferred Term	Lenvatinib (N=496) Any Grade n (%)	 Grade >= 3 n (%)
交通事故	1 (0.2)	0 (0.0)
皮膚損傷	1 (0.2)	0 (0.0)
脊椎圧迫骨折	1 (0.2)	1 (0.2)
サンバーン	1 (0.2)	0 (0.0)
腱断裂	1 (0.2)	0 (0.0)
胸椎骨折	1 (0.2)	1 (0.2)
歯牙破折	1 (0.2)	0 (0.0)
各種物質毒性	1 (0.2)	1 (0.2)
外傷性血腫	1 (0.2)	0 (0.0)
創傷血腫	1 (0.2)	0 (0.0)
手首関節骨折	1 (0.2)	0 (0.0)
臨床検査	320 (64.5)	155 (31.3)
体重減少	151 (30.4)	37 (7.5)
血小板数減少	90 (18.1)	29 (5.8)
血中ビリルビン増加	71 (14.3)	31 (6.3)
アスパラギン酸アミノトランスフェラーゼ増加	68 (13.7)	24 (4.8)
アラニンアミノトランスフェラーゼ増加	55 (11.1)	16 (3.2)
白血球数減少	48 (9.7)	12 (2.4)
好中球数減少	43 (8.7)	16 (3.2)
γ－グルタミルトランスフェラーゼ増加	38 (7.7)	26 (5.2)
心電図ＱＴ延長	33 (6.7)	5 (1.0)
血中アルカリホスファターゼ増加	32 (6.5)	10 (2.0)
血中甲状腺刺激ホルモン増加	31 (6.3)	0 (0.0)
国際標準比増加	19 (3.8)	1 (0.2)
リパーゼ増加	18 (3.6)	13 (2.6)
血中アルブミン減少	14 (2.8)	1 (0.2)

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付録 2.7.4.9
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
HCC Lenvatinib Safety Set
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System organ Class Preferred Term	Lenvatinib (N=496) Any Grade n (%)	 Grade >= 3 n (%)
Ｃ－反応性蛋白増加	14 (2.8)	0 (0.0)
リンパ球数減少	12 (2.4)	8 (1.6)
血中クレアチニン増加	11 (2.2)	1 (0.2)
血中乳酸脱水素酵素増加	11 (2.2)	1 (0.2)
血圧上昇	11 (2.2)	1 (0.2)
尿中蛋白陽性	11 (2.2)	1 (0.2)
血中コレステロール増加	7 (1.4)	0 (0.0)
血中尿素増加	6 (1.2)	0 (0.0)
体重増加	6 (1.2)	0 (0.0)
アミラーゼ増加	5 (1.0)	2 (0.4)
血中カリウム減少	5 (1.0)	2 (0.4)
血中ナトリウム減少	5 (1.0)	4 (0.8)
プロトロンビン時間延長	5 (1.0)	0 (0.0)
尿中ビリルビン増加	5 (1.0)	1 (0.2)
尿中血陽性	4 (0.8)	0 (0.0)
ＥＣＯＧパフォーマンスステータス悪化	4 (0.8)	3 (0.6)
抱合ビリルビン増加	2 (0.4)	0 (0.0)
血中カルシウム減少	2 (0.4)	0 (0.0)
血中クロール減少	2 (0.4)	1 (0.2)
血中甲状腺刺激ホルモン減少	2 (0.4)	0 (0.0)
ヘモグロビン減少	2 (0.4)	0 (0.0)
ヘモグロビン増加	2 (0.4)	0 (0.0)
赤血球数減少	2 (0.4)	0 (0.0)
白血球数増加	2 (0.4)	0 (0.0)
尿中白血球陽性	2 (0.4)	0 (0.0)
活性化部分トロンボプラスチン時間短縮	1 (0.2)	0 (0.0)

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付録 2.7.4.9
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
HCC Lenvatinib Safety Set
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System organ Class Preferred Term	Lenvatinib (N=496) Any Grade n (%)	 Grade >= 3 n (%)
アンモニア増加	1 (0.2)	0 (0.0)
血中カルシウム増加	1 (0.2)	0 (0.0)
血中コリンエステラーゼ減少	1 (0.2)	0 (0.0)
血中クレアチニン減少	1 (0.2)	0 (0.0)
血中電解質減少	1 (0.2)	0 (0.0)
血中フィブリノゲン増加	1 (0.2)	0 (0.0)
血中ブドウ糖増加	1 (0.2)	1 (0.2)
血中カリウム増加	1 (0.2)	1 (0.2)
血圧低下	1 (0.2)	0 (0.0)
拡張期血圧上昇	1 (0.2)	0 (0.0)
体温上昇	1 (0.2)	0 (0.0)
心雑音	1 (0.2)	0 (0.0)
クロストリジウム検査陽性	1 (0.2)	1 (0.2)
薬物スクリーニング陽性	1 (0.2)	0 (0.0)
心電図ＳＴ部分下降	1 (0.2)	0 (0.0)
心電図ＳＴ－Ｔ変化	1 (0.2)	0 (0.0)
心電図異常Ｔ波	1 (0.2)	0 (0.0)
尿中ブドウ糖	1 (0.2)	0 (0.0)
尿中ブドウ糖陽性	1 (0.2)	0 (0.0)
ヘリコバクター検査陽性	1 (0.2)	0 (0.0)
肝酵素上昇	1 (0.2)	1 (0.2)
国際標準比減少	1 (0.2)	0 (0.0)
リパーゼ減少	1 (0.2)	0 (0.0)
リンパ球数増加	1 (0.2)	0 (0.0)
好中球数増加	1 (0.2)	0 (0.0)
尿中亜硝酸塩陽性	1 (0.2)	0 (0.0)

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付録 2.7.4.9
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
HCC Lenvatinib Safety Set
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System organ Class Preferred Term	Lenvatinib (N=496) Any Grade n (%)	 Grade >= 3 n (%)
プロテインC増加	1 (0.2)	0 (0.0)
総蛋白減少	1 (0.2)	0 (0.0)
プロトロンビン量減少	1 (0.2)	0 (0.0)
プロトロンビン量増加	1 (0.2)	0 (0.0)
トランスアミナーゼ上昇	1 (0.2)	1 (0.2)
トリヨードチロニン増加	1 (0.2)	0 (0.0)
トロポニンT増加	1 (0.2)	0 (0.0)
尿量減少	1 (0.2)	0 (0.0)
尿中蛋白／クレアチニン比増加	1 (0.2)	1 (0.2)
尿中ウロビリノーゲン増加	1 (0.2)	0 (0.0)
代謝および栄養障害	235 (47.4)	68 (13.7)
食欲減退	173 (34.9)	22 (4.4)
低アルブミン血症	47 (9.5)	4 (0.8)
低ナトリウム血症	24 (4.8)	21 (4.2)
脱水	19 (3.8)	4 (0.8)
低血糖	13 (2.6)	4 (0.8)
高カリウム血症	12 (2.4)	6 (1.2)
高アンモニア血症	10 (2.0)	0 (0.0)
低カリウム血症	8 (1.6)	5 (1.0)
低カルシウム血症	5 (1.0)	2 (0.4)
低マグネシウム血症	5 (1.0)	1 (0.2)
高血糖	4 (0.8)	1 (0.2)
高尿酸血症	4 (0.8)	0 (0.0)
低蛋白血症	4 (0.8)	1 (0.2)
糖尿病	3 (0.6)	1 (0.2)
高脂血症	3 (0.6)	0 (0.0)

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付録 2.7.4.9
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
HCC Lenvatinib Safety Set
ISS Safety Set

System organ Class Preferred Term	Lenvatinib (N=496) Any Grade n (%)	 Grade >= 3 n (%)
悪液質	2 (0.4)	2 (0.4)
痛風	2 (0.4)	0 (0.0)
高カルシウム血症	2 (0.4)	0 (0.0)
過小食	2 (0.4)	0 (0.0)
低リン酸血症	2 (0.4)	2 (0.4)
アシドーシス	1 (0.2)	0 (0.0)
糖尿病性代謝代償不全	1 (0.2)	1 (0.2)
高コレステロール血症	1 (0.2)	1 (0.2)
高ナトリウム血症	1 (0.2)	0 (0.0)
高トリグリセリド血症	1 (0.2)	1 (0.2)
低クロール血症	1 (0.2)	0 (0.0)
代謝性アシドーシス	1 (0.2)	0 (0.0)
筋骨格系および結合組織障害	190 (38.3)	18 (3.6)
背部痛	53 (10.7)	1 (0.2)
筋骨格痛	48 (9.7)	0 (0.0)
関節痛	47 (9.5)	0 (0.0)
四肢痛	38 (7.7)	3 (0.6)
筋肉痛	24 (4.8)	1 (0.2)
筋痙縮	13 (2.6)	0 (0.0)
筋力低下	13 (2.6)	2 (0.4)
筋骨格系胸痛	11 (2.2)	0 (0.0)
頚部痛	11 (2.2)	2 (0.4)
側腹部痛	8 (1.6)	0 (0.0)
骨痛	6 (1.2)	2 (0.4)
変形性関節症	4 (0.8)	1 (0.2)
関節炎	3 (0.6)	0 (0.0)

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付録 2.7.4.9
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
HCC Lenvatinib Safety Set
ISS Safety Set

System organ Class Preferred Term	Lenvatinib (N=496) Any Grade n (%)	 Grade >= 3 n (%)
筋骨格不快感	3 (0.6)	0 (0.0)
骨粗鬆症	3 (0.6)	0 (0.0)
病的骨折	3 (0.6)	2 (0.4)
尾骨痛	2 (0.4)	0 (0.0)
椎間板突出	2 (0.4)	2 (0.4)
関節腫脹	2 (0.4)	0 (0.0)
腰部脊柱管狭窄症	2 (0.4)	1 (0.2)
筋攣縮	2 (0.4)	0 (0.0)
脊柱管狭窄症	2 (0.4)	0 (0.0)
脊椎痛	2 (0.4)	0 (0.0)
脊椎すべり症	2 (0.4)	1 (0.2)
滑液包炎	1 (0.2)	0 (0.0)
痛風性関節炎	1 (0.2)	0 (0.0)
関節可動域低下	1 (0.2)	0 (0.0)
運動性低下	1 (0.2)	0 (0.0)
筋萎縮	1 (0.2)	0 (0.0)
筋緊張	1 (0.2)	0 (0.0)
筋骨格硬直	1 (0.2)	0 (0.0)
関節周囲炎	1 (0.2)	0 (0.0)
横紋筋融解症	1 (0.2)	1 (0.2)
肩回旋筋腱板症候群	1 (0.2)	0 (0.0)
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	54 (10.9)	30 (6.0)
癌疼痛	19 (3.8)	5 (1.0)
悪性新生物進行	10 (2.0)	10 (2.0)
腫瘍疼痛	4 (0.8)	1 (0.2)
悪性腹水	3 (0.6)	1 (0.2)

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付録 2.7.4.9
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
HCC Lenvatinib Safety Set
ISS Safety Set

System organ Class Preferred Term	Lenvatinib (N=496) Any Grade n (%)	Lenvatinib (N=496) Grade >= 3 n (%)
腫瘍熱	3 (0.6)	0 (0.0)
腫瘍出血	3 (0.6)	3 (0.6)
肝癌破裂	2 (0.4)	2 (0.4)
悪性胸水	2 (0.4)	0 (0.0)
中枢神経系転移	2 (0.4)	2 (0.4)
脊椎転移	2 (0.4)	2 (0.4)
腫瘍破裂	2 (0.4)	2 (0.4)
副腎腺腫	1 (0.2)	0 (0.0)
基底細胞癌	1 (0.2)	0 (0.0)
感染性新生物	1 (0.2)	1 (0.2)
頭蓋内腫瘍出血	1 (0.2)	0 (0.0)
リンパ腫	1 (0.2)	1 (0.2)
髄膜腫	1 (0.2)	1 (0.2)
骨転移	1 (0.2)	0 (0.0)
腫瘍随伴症候群	1 (0.2)	1 (0.2)
腎細胞癌	1 (0.2)	1 (0.2)
腫瘍壊死	1 (0.2)	1 (0.2)
神経系障害	172 (34.7)	50 (10.1)
頭痛	51 (10.3)	3 (0.6)
肝性脳症	41 (8.3)	26 (5.2)
浮動性めまい	30 (6.0)	1 (0.2)
味覚異常	24 (4.8)	0 (0.0)
錯感覚	9 (1.8)	2 (0.4)
傾眠	8 (1.6)	1 (0.2)
感覚鈍麻	6 (1.2)	0 (0.0)
嗜眠	6 (1.2)	0 (0.0)

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付録 2.7.4.9
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
HCC Lenvatinib Safety Set
ISS Safety Set

System organ Class Preferred Term	Lenvatinib (N=496) Any Grade n (%)	 Grade >= 3 n (%)
末梢性感覚ニューロパチー	5 (1.0)	0 (0.0)
脳出血	3 (0.6)	3 (0.6)
脳梗塞	3 (0.6)	2 (0.4)
肝性昏睡	3 (0.6)	3 (0.6)
注意力障害	3 (0.6)	0 (0.0)
多発ニューロパチー	3 (0.6)	0 (0.0)
痙攣発作	3 (0.6)	1 (0.2)
失神	3 (0.6)	3 (0.6)
失語症	2 (0.4)	0 (0.0)
固定姿勢保持困難	2 (0.4)	0 (0.0)
脳血管発作	2 (0.4)	2 (0.4)
意識レベルの低下	2 (0.4)	0 (0.0)
過眠症	2 (0.4)	0 (0.0)
睡眠の質低下	2 (0.4)	0 (0.0)
脊髄圧迫	2 (0.4)	2 (0.4)
緊張性頭痛	2 (0.4)	0 (0.0)
振戦	2 (0.4)	0 (0.0)
意識変容状態	1 (0.2)	0 (0.0)
健忘	1 (0.2)	0 (0.0)
運動失調	1 (0.2)	0 (0.0)
平衡障害	1 (0.2)	0 (0.0)
灼熱感	1 (0.2)	0 (0.0)
認知障害	1 (0.2)	0 (0.0)
昏睡	1 (0.2)	1 (0.2)
両麻痺	1 (0.2)	1 (0.2)
ジスキネジア	1 (0.2)	0 (0.0)

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Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
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System organ Class Preferred Term	Lenvatinib (N=496) Any Grade n (%)	 Grade >= 3 n (%)
測定障害	1 (0.2)	0 (0.0)
脳症	1 (0.2)	1 (0.2)
顔面麻痺	1 (0.2)	1 (0.2)
蟻走感	1 (0.2)	0 (0.0)
頭蓋内出血	1 (0.2)	0 (0.0)
味覚減退	1 (0.2)	0 (0.0)
第３脳神経麻痺	1 (0.2)	1 (0.2)
記憶障害	1 (0.2)	0 (0.0)
末梢性ニューロパチー	1 (0.2)	0 (0.0)
反回神経麻痺	1 (0.2)	1 (0.2)
末梢性運動ニューロパチー	1 (0.2)	0 (0.0)
末梢性感覚運動ニューロパチー	1 (0.2)	0 (0.0)
可逆性後白質脳症症候群	1 (0.2)	0 (0.0)
坐骨神経痛	1 (0.2)	0 (0.0)
中毒性ニューロパチー	1 (0.2)	0 (0.0)
一過性脳虚血発作	1 (0.2)	0 (0.0)
三叉神経痛	1 (0.2)	0 (0.0)
白質病変	1 (0.2)	0 (0.0)
精神障害	60 (12.1)	6 (1.2)
不眠症	37 (7.5)	1 (0.2)
不安	9 (1.8)	0 (0.0)
うつ病	7 (1.4)	1 (0.2)
錯乱状態	6 (1.2)	2 (0.4)
譫妄	4 (0.8)	0 (0.0)
精神状態変化	3 (0.6)	1 (0.2)
失見当識	2 (0.4)	0 (0.0)

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