表 2.7.4-104 データの更新に基づく主な有害事象（国際共同 304 試験：安全性解析対象集団）

器官別大分類 基本語	全体集団				日本人集団			
	本薬群 (N=476)		ソラフェニブ群 (N=475)		本薬群 (N=81)		ソラフェニブ群 (N=87)	
	全 Grade	Grade 3 以上	全 Grade	Grade 3 以上	全 Grade	Grade 3 以上	全 Grade	Grade 3 以上
全ての有害事象	470 (98.7)	359 (75.4)	472 (99.4)	318 (66.9)	81 (100.0)	63 (77.8)	87 (100.0)	66 (75.9)
血液およびリンパ系障害								
貧血	35 (7.4)	17 (3.6)	44 (9.3)	17 (3.6)	9 (11.1)	5 (6.2)	8 (9.2)	4 (4.6)
内分泌障害								
甲状腺機能低下症	80 (16.8)	0 (0.0)	8 (1.7)	0 (0.0)	33 (40.7)	0 (0.0)	4 (4.6)	0 (0.0)
胃腸障害								
下痢	184 (38.7)	20 (4.2)	223 (46.9)	20 (4.2)	37 (45.7)	3 (3.7)	34 (39.1)	2 (2.3)
悪心	92 (19.3)	4 (0.8)	70 (14.7)	4 (0.8)	14 (17.3)	0 (0.0)	9 (10.3)	0 (0.0)
腹痛	82 (17.2)	8 (1.7)	87 (18.3)	13 (2.7)	5 (6.2)	0 (0.0)	8 (9.2)	1 (1.1)
嘔吐	79 (16.6)	6 (1.3)	36 (7.6)	5 (1.1)	15 (18.5)	0 (0.0)	5 (5.7)	0 (0.0)
便秘	76 (16.0)	3 (0.6)	52 (10.9)	0 (0.0)	20 (24.7)	0 (0.0)	10 (11.5)	0 (0.0)
腹水	69 (14.5)	18 (3.8)	45 (9.5)	14 (2.9)	17 (21.0)	4 (4.9)	5 (5.7)	2 (2.3)
上腹部痛	58 (12.2)	6 (1.3)	40 (8.4)	6 (1.3)	5 (6.2)	0 (0.0)	3 (3.4)	0 (0.0)
口内炎	45 (9.5)	1 (0.2)	56 (11.8)	2 (0.4)	15 (18.5)	0 (0.0)	12 (13.8)	0 (0.0)
一般・全身障害および投与部位の状態								
疲労	142 (29.8)	18 (3.8)	119 (25.1)	17 (3.6)	15 (18.5)	1 (1.2)	8 (9.2)	4 (4.6)
発熱	69 (14.5)	0 (0.0)	63 (13.3)	1 (0.2)	13 (16.0)	0 (0.0)	15 (17.2)	0 (0.0)
末梢性浮腫	66 (13.9)	4 (0.8)	33 (6.9)	1 (0.2)	23 (28.4)	2 (2.5)	7 (8.0)	0 (0.0)
無力症	54 (11.3)	14 (2.9)	48 (10.1)	11 (2.3)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
倦怠感	21 (4.4)	0 (0.0)	9 (1.9)	0 (0.0)	15 (18.5)	0 (0.0)	7 (8.0)	0 (0.0)
肝胆道系障害								
肝機能異常	12 (2.5)	8 (1.7)	13 (2.7)	9 (1.9)	10 (12.3)	6 (7.4)	12 (13.8)	8 (9.2)
感染症および寄生虫症								
鼻咽頭炎	25 (5.3)	0 (0.0)	19 (4.0)	0 (0.0)	15 (18.5)	0 (0.0)	12 (13.8)	0 (0.0)
臨床検査								
体重減少	149 (31.3)	36 (7.6)	107 (22.5)	14 (2.9)	25 (30.9)	9 (11.1)	17 (19.5)	0 (0.0)
血小板数減少	87 (18.3)	26 (5.5)	59 (12.4)	16 (3.4)	24 (29.6)	6 (7.4)	16 (18.4)	9 (10.3)
血中ビリルビン増加	72 (15.1)	31 (6.5)	63 (13.3)	23 (4.8)	11 (13.6)	3 (3.7)	5 (5.7)	2 (2.3)
アスパラギン酸アミノトランスフェラーゼ増加	65 (13.7)	24 (5.0)	80 (16.8)	39 (8.2)	5 (6.2)	2 (2.5)	8 (9.2)	6 (6.9)
アラニンアミノトランスフェラーゼ増加	53 (11.1)	16 (3.4)	51 (10.7)	16 (3.4)	2 (2.5)	1 (1.2)	6 (6.9)	2 (2.3)
好中球数減少	41 (8.6)	15 (3.2)	11 (2.3)	8 (1.7)	11 (13.6)	6 (7.4)	2 (2.3)	1 (1.1)
代謝および栄養障害								
食欲減退	163 (34.2)	22 (4.6)	127 (26.7)	6 (1.3)	40 (49.4)	8 (9.9)	20 (23.0)	0 (0.0)
低アルブミン血症	44 (9.2)	4 (0.8)	38 (8.0)	2 (0.4)	14 (17.3)	3 (3.7)	8 (9.2)	0 (0.0)
脱水	17 (3.6)	4 (0.8)	5 (1.1)	0 (0.0)	9 (11.1)	2 (2.5)	3 (3.4)	0 (0.0)

表 2.7.4-104 データの更新に基づく主な有害事象（国際共同 304 試験：安全性解析対象集団）（続き）

器官別大分類 基本語	全体集団				日本人集団			
	本薬群 (N=476)		ソラフェニブ群 (N=475)		本薬群 (N=81)		ソラフェニブ群 (N=87)	
	全 Grade	Grade 3 以上	全 Grade	Grade 3 以上	全 Grade	Grade 3 以上	全 Grade	Grade 3 以上
筋骨格系および結合組織障害								
背部痛	50 (10.5)	1 (0.2)	31 (6.5)	5 (1.1)	5 (6.2)	0 (0.0)	3 (3.4)	0 (0.0)
神経系障害								
肝性脳症	38 (8.0)	23 (4.8)	9 (1.9)	7 (1.5)	9 (11.1)	5 (6.2)	2 (2.3)	2 (2.3)
味覚異常	22 (4.6)	0 (0.0)	13 (2.7)	0 (0.0)	10 (12.3)	0 (0.0)	7 (8.0)	0 (0.0)
腎および尿路障害								
蛋白尿	117 (24.6)	27 (5.7)	54 (11.4)	8 (1.7)	38 (46.9)	7 (8.6)	19 (21.8)	1 (1.1)
呼吸器，胸郭および縦隔障害								
発声障害	113 (23.7)	1 (0.2)	57 (12.0)	0 (0.0)	35 (43.2)	0 (0.0)	22 (25.3)	0 (0.0)
皮膚および皮下組織障害								
手掌・足底発赤知覚不全症候群	128 (26.9)	14 (2.9)	249 (52.4)	54 (11.4)	42 (51.9)	6 (7.4)	64 (73.6)	15 (17.2)
発疹	46 (9.7)	0 (0.0)	76 (16.0)	2 (0.4)	10 (12.3)	0 (0.0)	14 (16.1)	0 (0.0)
脱毛症	14 (2.9)	0 (0.0)	120 (25.3)	0 (0.0)	5 (6.2)	0 (0.0)	32 (36.8)	0 (0.0)
血管障害								
高血圧	199 (41.8)	111 (23.3)	145 (30.5)	68 (14.3)	42 (51.9)	28 (34.6)	42 (48.3)	23 (26.4)

MedDRA Version 19.1
数字は例数，(　)内は発現率(%)
全体集団又は日本人集団のいずれかの群で全 Grade の発現率が 10%以上の有害事象を記載
（添付資料 5.3.5.3.4 の Table 5.1.2.2 を引用）

2.7.4.7.2 副作用

国際共同 304 試験の主な副作用（全体集団又は日本人集団のいずれかの群で発現率が 10%以上）を表 2.7.4-105 に示した。

(1)全体集団

全体集団において，副作用発現率は両群で同程度であった（本薬群 93.9%，ソラフェニブ群 95.2%）。Grade 3 以上の副作用の発現率は本薬群で 56.9%，ソラフェニブ群で 48.6%であった。

全体集団において，本薬群で発現率が 30%以上の副作用（本薬群，ソラフェニブ群の順で記載）は，高血圧（39.7%，27.8%），下痢（30.0%，41.9%）であった。また，ソラフェニブ群で発現率が 30%以上の副作用は手掌・足底発赤知覚不全症候群（26.5%，52.4%），下痢であった。

ソラフェニブ群と比べ本薬群で発現率が 10%以上高い副作用は，高血圧（39.7%，27.8%），蛋白尿（23.9%，9.3%），発声障害（21.8%，10.9%），甲状腺機能低下症（15.1%，1.7%）であった。本薬群と比べソラフェニブ群で発現率が 10%以上高い副作用は，手掌・足底発赤知覚不全症候群（26.5%，52.4%），下痢（30.0%，41.9%），脱毛症（2.5%，24.2%）であった。

本薬群で発現率が 10%以上の Grade 3 以上の副作用は，高血圧（22.1%，13.1%）であった。ソラフェニブ群で発現率が 10%以上の Grade 3 以上の副作用は，高血圧，手掌・足底発赤知覚不

全症候群（2.9%，11.4%）であった。また，ソラフェニブ群と比べ本薬群で発現率が 5%以上高い Grade 3 以上の副作用は，高血圧であった。本薬群と比べソラフェニブ群で発現率が 5%以上高い Grade 3 以上の副作用は，手掌・足底発赤知覚不全症候群であった。

(2)日本人集団

日本人集団では，本薬群，ソラフェニブ群の全例に副作用が発現した。Grade 3 以上の副作用の発現率は本薬群で 63.0%，ソラフェニブ群で 69.0%であった。

本薬群で発現率が 30%以上の副作用（本薬群，ソラフェニブ群の順で記載）は，手掌・足底発赤知覚不全症候群（51.9%，73.6%），高血圧（49.4%，48.3%），食欲減退（48.1%，17.2%），蛋白尿（45.7%，21.8%），発声障害（43.2%，24.1%），甲状腺機能低下症（40.7%，4.6%），下痢（37.0%，36.8%）であった。本薬群で発現率が 10%以上の Grade 3 以上の副作用は，高血圧（32.1%，26.4%）であった。

全体集団と比べ日本人集団で本薬群の発現率が 10%以上高い副作用（全体集団，日本人集団の順に記載）は，手掌・足底発赤知覚不全症候群（26.5%，51.9%），食欲減退（25.6%，48.1%），蛋白尿（23.9%，45.7%），発声障害（21.8%，43.2%），甲状腺機能低下症（15.1%，40.7%），血小板数減少（13.9%，28.4%），末梢性浮腫（6.5%，22.2%），低アルブミン血症（4.4%，16.0%），倦怠感（4.4%，18.5%）であった。日本人集団と比べ全体集団で本薬の発現率が 10%以上高い副作用は認められなかった。

全体集団と比べ日本人集団で本薬群の発現率が 5%以上高い Grade 3 以上の副作用は，高血圧（22.1%，32.1%）であった。日本人集団と比べ全体集団で本薬群の発現率が 5%以上高い Grade 3 以上の副作用は認められなかった。

表 2.7.4-105 データの更新に基づく主な副作用（国際共同 304 試験：全体集団，安全性解析対象集団）

	全体集団				日本人集団			
	本薬群 (N=476)		ソラフェニブ群 (N=475)		本薬群 (N=81)		ソラフェニブ群 (N=87)	
器官別大分類 基本語	全 Grade	Grade 3 以上	全 Grade	Grade 3 以上	全 Grade	Grade 3 以上	全 Grade	Grade 3 以上
全ての副作用	447 (93.9)	271 (56.9)	452 (95.2)	231 (48.6)	81 (100.0)	51 (63.0)	87 (100.0)	60 (69.0)
内分泌障害								
甲状腺機能低下症	72 (15.1)	0 (0.0)	8 (1.7)	0 (0.0)	33 (40.7)	0 (0.0)	4 (4.6)	0 (0.0)
胃腸障害								
下痢	143 (30.0)	20 (4.2)	199 (41.9)	17 (3.6)	30 (37.0)	3 (3.7)	32 (36.8)	2 (2.3)
悪心	64 (13.4)	2 (0.4)	55 (11.6)	3 (0.6)	12 (14.8)	0 (0.0)	8 (9.2)	0 (0.0)
口内炎	43 (9.0)	1 (0.2)	54 (11.4)	2 (0.4)	14 (17.3)	0 (0.0)	11 (12.6)	0 (0.0)
腹水	31 (6.5)	7 (1.5)	8 (1.7)	2 (0.4)	12 (14.8)	2 (2.5)	2 (2.3)	0 (0.0)
一般・全身障害および投与部位の状態								
疲労	111 (23.3)	10 (2.1)	99 (20.8)	12 (2.5)	12 (14.8)	0 (0.0)	6 (6.9)	2 (2.3)
末梢性浮腫	31 (6.5)	1 (0.2)	9 (1.9)	0 (0.0)	18 (22.2)	1 (1.2)	5 (5.7)	0 (0.0)
発熱	28 (5.9)	0 (0.0)	23 (4.8)	1 (0.2)	8 (9.9)	0 (0.0)	9 (10.3)	0 (0.0)
倦怠感	21 (4.4)	0 (0.0)	6 (1.3)	0 (0.0)	15 (18.5)	0 (0.0)	6 (6.9)	0 (0.0)
肝胆道系障害								
肝機能異常	8 (1.7)	6 (1.3)	11 (2.3)	8 (1.7)	6 (7.4)	4 (4.9)	10 (11.5)	7 (8.0)
臨床検査								
体重減少	86 (18.1)	19 (4.0)	67 (14.1)	6 (1.3)	16 (19.8)	4 (4.9)	13 (14.9)	0 (0.0)
血小板数減少	66 (13.9)	21 (4.4)	47 (9.9)	12 (2.5)	23 (28.4)	6 (7.4)	16 (18.4)	9 (10.3)
アスパラギン酸アミノトランスフェラーゼ増加	40 (8.4)	10 (2.1)	53 (11.2)	22 (4.6)	5 (6.2)	2 (2.5)	7 (8.0)	5 (5.7)
好中球数減少	38 (8.0)	13 (2.7)	9 (1.9)	6 (1.3)	10 (12.3)	5 (6.2)	2 (2.3)	1 (1.1)
代謝および栄養障害								
食欲減退	122 (25.6)	16 (3.4)	100 (21.1)	4 (0.8)	39 (48.1)	6 (7.4)	15 (17.2)	0 (0.0)
低アルブミン血症	21 (4.4)	2 (0.4)	13 (2.7)	0 (0.0)	13 (16.0)	2 (2.5)	5 (5.7)	0 (0.0)
神経系障害								
味覚異常	19 (4.0)	0 (0.0)	13 (2.7)	0 (0.0)	10 (12.3)	0 (0.0)	7 (8.0)	0 (0.0)
腎および尿路障害								
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)
呼吸器，胸郭および縦隔障害								
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)
皮膚および皮下組織障害								
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)
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)
血管障害								
高血圧	189 (39.7)	105 (22.1)	132 (27.8)	62 (13.1)	40 (49.4)	26 (32.1)	42 (48.3)	23 (26.4)

MedDRA Version 19.1
数字は例数，( )内は発現率(%)
全体集団又は日本人集団のいずれかの群で全 Grade の発現率が 10%以上の副作用を記載
（添付資料 5.3.5.3.4 の Table 5.1.3.2 を引用）

2.7.4.7.3 結論

以上，国際共同 304 試験の安全性データに関して，データの更新を反映した内容と申請時データで大きく異なることはなかった。

2.7.4.8 付録

付録 2.7.4.1　Treatment-Emergent Adverse Events by System Organ Class and Preferred Term – Study 304
付録 2.7.4.2　Related Treatment-Emergent Adverse Events by System Organ Class and Preferred Term – Study 304
付録 2.7.4.3　Fatal Serious Treatment-Emergent Adverse Events by Preferred Term – Study 304
付録 2.7.4.4　Fatal Serious Related Treatment-Emergent Adverse Events by Preferred Term – Study 304
付録 2.7.4.5　Serious Treatment-Emergent Adverse Events by Preferred Term – Study 304
付録 2.7.4.6　Serious Related Treatment-Emergent Adverse Events by Preferred Term – Study 304
付録 2.7.4.7　Treatment-Emergent Adverse Events Leading to Treatment Discontinuation by Preferred Term – Study 304
付録 2.7.4.8　Treatment-Emergent Adverse Events Leading to Treatment Modification (Interruption or Reduction) by Preferred Term – Study 304
付録 2.7.4.9　Treatment-Emergent Adverse Events by System Organ Class and Preferred Term – All HCC
付録 2.7.4.10　Related Treatment-Emergent Adverse Events by System Organ Class and Preferred Term – All HCC
付録 2.7.4.11　Fatal Serious Treatment-Emergent Adverse Events by Preferred Term　All HCC
付録 2.7.4.12　Fatal Serious Related Treatment-Emergent Adverse Events by Preferred Term – All HCC
付録 2.7.4.13　Serious Treatment-Emergent Adverse Events by Preferred Term – All HCC
付録 2.7.4.14　Serious Related Treatment-Emergent Adverse Events by Preferred Term – All HCC
付録 2.7.4.15　Treatment-Emergent Adverse Events Leading to Treatment Discontinuation by Preferred Term – All HCC
付録 2.7.4.16　Treatment-Emergent Adverse Events Leading to Treatment Modification (Interruption or Reduction) by Preferred Term – All HCC
付録 2.7.4.17　特に関心のある有害事象の定義

付録 2.7.4.1
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 (%)
Subjects with Any TEAEs	470 (98.7)	357 (75.0)	472 (99.4)	316 (66.5)	81 (100.0)	63 (77.8)	87 (100.0)	66 (75.9)
血液およびリンパ系障害	84 (17.6)	37 (7.8)	78 (16.4)	26 (5.5)	15 (18.5)	9 (11.1)	13 (14.9)	5 (5.7)
貧血	34 (7.1)	16 (3.4)	43 (9.1)	17 (3.6)	9 (11.1)	5 (6.2)	8 (9.2)	4 (4.6)
血小板減少症	33 (6.9)	9 (1.9)	28 (5.9)	6 (1.3)	3 (3.7)	2 (2.5)	3 (3.4)	1 (1.1)
好中球減少症	18 (3.8)	6 (1.3)	7 (1.5)	0 (0.0)	1 (1.2)	1 (1.2)	1 (1.1)	0 (0.0)
白血球減少症	14 (2.9)	1 (0.2)	12 (2.5)	1 (0.2)	2 (2.5)	0 (0.0)	2 (2.3)	0 (0.0)
赤血球増加症	3 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)
白血球増加症	2 (0.4)	2 (0.4)	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
骨髄機能不全	2 (0.4)	2 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
発熱性好中球減少症	1 (0.2)	1 (0.2)	2 (0.4)	2 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
リンパ節症	1 (0.2)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
リンパ球減少症	1 (0.2)	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
汎血球減少症	1 (0.2)	0 (0.0)	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
凝血異常	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
播種性血管内凝固	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	1 (1.2)	1 (1.2)	0 (0.0)	0 (0.0)
低プロトロンビン血症	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)
ビタミンＢ１２欠乏性貧血	0 (0.0)	0 (0.0)	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
出血性貧血	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
脾機能亢進	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
リンパ節痛	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
心臓障害	38 (8.0)	7 (1.5)	30 (6.3)	7 (1.5)	8 (9.9)	0 (0.0)	5 (5.7)	0 (0.0)
洞性徐脈	6 (1.3)	0 (0.0)	3 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
洞性頻脈	5 (1.1)	0 (0.0)	0 (0.0)	0 (0.0)	2 (2.5)	0 (0.0)	0 (0.0)	0 (0.0)
心房細動	4 (0.8)	1 (0.2)	7 (1.5)	1 (0.2)	3 (3.7)	0 (0.0)	3 (3.4)	0 (0.0)
心筋梗塞	4 (0.8)	4 (0.8)	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	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 2.7.4.1
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 (%)
頻脈	3 (0.6)	0 (0.0)	2 (0.4)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
心筋虚血	3 (0.6)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
上室性期外収縮	3 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
左室肥大	2 (0.4)	0 (0.0)	2 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
動悸	2 (0.4)	0 (0.0)	2 (0.4)	0 (0.0)	1 (1.2)	0 (0.0)	1 (1.1)	0 (0.0)
徐脈	2 (0.4)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
結節性不整脈	1 (0.2)	0 (0.0)	2 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
心室性不整脈	1 (0.2)	0 (0.0)	1 (0.2)	1 (0.2)	1 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)
心室性期外収縮	1 (0.2)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)
不整脈	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
第一度房室ブロック	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	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)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
うっ血性心不全	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
心原性ショック	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
心肺不全	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
冠動脈疾患	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
期外収縮	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
プリンツメタル狭心症	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)
洞性不整脈	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
心房粗動	0 (0.0)	0 (0.0)	2 (0.4)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
急性心筋梗塞	0 (0.0)	0 (0.0)	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
狭心症	0 (0.0)	0 (0.0)	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
徐脈性不整脈	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
右脚ブロック	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
心不全	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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付録 2.7.4.1
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 (%)
心臓弁狭窄	0 (0.0)	0 (0.0)	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
頻脈性不整脈	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
先天性、家族性および遺伝性障害	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
大理石骨病	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
耳および迷路障害	15 (3.2)	0 (0.0)	10 (2.1)	2 (0.4)	3 (3.7)	0 (0.0)	1 (1.1)	0 (0.0)
耳鳴	6 (1.3)	0 (0.0)	2 (0.4)	0 (0.0)	1 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)
回転性めまい	4 (0.8)	0 (0.0)	4 (0.8)	1 (0.2)	2 (2.5)	0 (0.0)	0 (0.0)	0 (0.0)
耳痛	2 (0.4)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
難聴	2 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
耳不快感	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
耳の障害	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
耳出血	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
耳管開放	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)
聴覚過敏	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
聴力低下	0 (0.0)	0 (0.0)	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
内分泌障害	84 (17.6)	0 (0.0)	12 (2.5)	1 (0.2)	35 (43.2)	0 (0.0)	5 (5.7)	0 (0.0)
甲状腺機能低下症	78 (16.4)	0 (0.0)	8 (1.7)	0 (0.0)	33 (40.7)	0 (0.0)	4 (4.6)	0 (0.0)
甲状腺機能亢進症	4 (0.8)	0 (0.0)	2 (0.4)	0 (0.0)	3 (3.7)	0 (0.0)	0 (0.0)	0 (0.0)
甲状腺腫	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
抗利尿ホルモン不適合分泌	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
甲状腺炎	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
自己免疫性甲状腺炎	0 (0.0)	0 (0.0)	2 (0.4)	1 (0.2)	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)
副甲状腺機能亢進症	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
男性性腺機能低下	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
眼障害	17 (3.6)	0 (0.0)	13 (2.7)	1 (0.2)	3 (3.7)	0 (0.0)	3 (3.4)	1 (1.1)

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付録 2.7.4.1
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 (%)
霧視	2 (0.4)	0 (0.0)	3 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
白内障	2 (0.4)	0 (0.0)	2 (0.4)	1 (0.2)	1 (1.2)	0 (0.0)	2 (2.3)	1 (1.1)
瞳孔動揺	2 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
眼充血	2 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
眼瞼炎	1 (0.2)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
眼痛	1 (0.2)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
動脈硬化性網膜症	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
眼の炎症	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
眼刺激	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
眼瞼浮腫	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)
眼瞼そう痒症	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)
角膜炎	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
黄斑変性	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
近視	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
網膜静脈閉塞	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
視力障害	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
黒内障	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
眼乾燥	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)
眼瞼嚢胞	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
緑内障	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
眼窩周囲浮腫	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ぶどう膜炎	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
胃腸障害	371 (77.9)	75 (15.8)	357 (75.2)	78 (16.4)	66 (81.5)	8 (9.9)	64 (73.6)	7 (8.0)
下痢	184 (38.7)	20 (4.2)	220 (46.3)	20 (4.2)	37 (45.7)	3 (3.7)	34 (39.1)	2 (2.3)
悪心	93 (19.5)	4 (0.8)	68 (14.3)	4 (0.8)	14 (17.3)	0 (0.0)	9 (10.3)	0 (0.0)

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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 (%)
腹痛	81 (17.0)	8 (1.7)	87 (18.3)	13 (2.7)	5 (6.2)	0 (0.0)	8 (9.2)	1 (1.1)
嘔吐	77 (16.2)	6 (1.3)	36 (7.6)	5 (1.1)	15 (18.5)	0 (0.0)	5 (5.7)	0 (0.0)
便秘	76 (16.0)	3 (0.6)	52 (10.9)	0 (0.0)	20 (24.7)	0 (0.0)	10 (11.5)	0 (0.0)
腹水	68 (14.3)	18 (3.8)	44 (9.3)	14 (2.9)	17 (21.0)	4 (4.9)	5 (5.7)	2 (2.3)
上腹部痛	58 (12.2)	6 (1.3)	40 (8.4)	6 (1.3)	5 (6.2)	0 (0.0)	3 (3.4)	0 (0.0)
口内炎	45 (9.5)	1 (0.2)	56 (11.8)	2 (0.4)	15 (18.5)	0 (0.0)	12 (13.8)	0 (0.0)
腹部膨満	38 (8.0)	1 (0.2)	26 (5.5)	2 (0.4)	4 (4.9)	0 (0.0)	4 (4.6)	0 (0.0)
口内乾燥	32 (6.7)	0 (0.0)	8 (1.7)	0 (0.0)	5 (6.2)	0 (0.0)	0 (0.0)	0 (0.0)
消化不良	31 (6.5)	1 (0.2)	18 (3.8)	0 (0.0)	1 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)
歯肉出血	18 (3.8)	1 (0.2)	9 (1.9)	0 (0.0)	1 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)
腹部不快感	11 (2.3)	0 (0.0)	9 (1.9)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
痔核	10 (2.1)	0 (0.0)	9 (1.9)	1 (0.2)	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)
歯痛	10 (2.1)	0 (0.0)	5 (1.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
歯肉腫脹	10 (2.1)	0 (0.0)	2 (0.4)	0 (0.0)	1 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)
歯肉痛	9 (1.9)	0 (0.0)	3 (0.6)	0 (0.0)	1 (1.2)	0 (0.0)	1 (1.1)	0 (0.0)
鼓腸	8 (1.7)	0 (0.0)	8 (1.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
食道静脈瘤出血	8 (1.7)	8 (1.7)	5 (1.1)	4 (0.8)	0 (0.0)	0 (0.0)	1 (1.1)	1 (1.1)
胃食道逆流性疾患	7 (1.5)	0 (0.0)	6 (1.3)	0 (0.0)	1 (1.2)	0 (0.0)	1 (1.1)	0 (0.0)
胃潰瘍	7 (1.5)	1 (0.2)	2 (0.4)	1 (0.2)	1 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)
齲歯	6 (1.3)	0 (0.0)	4 (0.8)	1 (0.2)	4 (4.9)	0 (0.0)	2 (2.3)	0 (0.0)
胃炎	5 (1.1)	0 (0.0)	5 (1.1)	1 (0.2)	4 (4.9)	0 (0.0)	0 (0.0)	0 (0.0)
口腔内潰瘍形成	5 (1.1)	1 (0.2)	4 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
上部消化管出血	5 (1.1)	4 (0.8)	4 (0.8)	3 (0.6)	2 (2.5)	1 (1.2)	1 (1.1)	0 (0.0)
歯周病	5 (1.1)	0 (0.0)	3 (0.6)	0 (0.0)	2 (2.5)	0 (0.0)	1 (1.1)	0 (0.0)
痔出血	5 (1.1)	0 (0.0)	2 (0.4)	1 (0.2)	3 (3.7)	0 (0.0)	0 (0.0)	0 (0.0)

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付録 2.7.4.1
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 (%)
おくび	5 (1.1)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
口腔内出血	5 (1.1)	0 (0.0)	1 (0.2)	0 (0.0)	2 (2.5)	0 (0.0)	0 (0.0)	0 (0.0)
直腸出血	5 (1.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
十二指腸潰瘍	4 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
慢性胃炎	3 (0.6)	0 (0.0)	4 (0.8)	0 (0.0)	1 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)
心窩部不快感	3 (0.6)	0 (0.0)	3 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
口腔内痛	3 (0.6)	0 (0.0)	3 (0.6)	0 (0.0)	1 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)
舌痛	3 (0.6)	0 (0.0)	2 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
直腸炎	3 (0.6)	0 (0.0)	2 (0.4)	0 (0.0)	2 (2.5)	0 (0.0)	0 (0.0)	0 (0.0)
出血性十二指腸潰瘍	3 (0.6)	2 (0.4)	1 (0.2)	1 (0.2)	1 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)
消化器痛	3 (0.6)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
嚥下痛	3 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
食道静脈瘤	2 (0.4)	1 (0.2)	6 (1.3)	2 (0.4)	1 (1.2)	1 (1.2)	2 (2.3)	0 (0.0)
嚥下障害	2 (0.4)	0 (0.0)	3 (0.6)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
排便回数増加	2 (0.4)	0 (0.0)	3 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
舌炎	2 (0.4)	0 (0.0)	3 (0.6)	0 (0.0)	1 (1.2)	0 (0.0)	2 (2.3)	0 (0.0)
下腹部痛	2 (0.4)	1 (0.2)	2 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
肛門の炎症	2 (0.4)	0 (0.0)	2 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血便排泄	2 (0.4)	0 (0.0)	2 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)
軟便	2 (0.4)	0 (0.0)	1 (0.2)	0 (0.0)	1 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)
腹部圧痛	2 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
吐血	2 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
臍ヘルニア	2 (0.4)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
門脈圧亢進性胃障害	1 (0.2)	0 (0.0)	4 (0.8)	2 (0.4)	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)
胃出血	1 (0.2)	0 (0.0)	3 (0.6)	3 (0.6)	1 (1.2)	0 (0.0)	1 (1.1)	1 (1.1)

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付録 2.7.4.1
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 (%)
下部消化管出血	1 (0.2)	0 (0.0)	3 (0.6)	3 (0.6)	0 (0.0)	0 (0.0)	3 (3.4)	3 (3.4)
腸炎	1 (0.2)	0 (0.0)	2 (0.4)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
びらん性胃炎	1 (0.2)	0 (0.0)	2 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
胃腸出血	1 (0.2)	1 (0.2)	2 (0.4)	1 (0.2)	1 (1.2)	1 (1.2)	0 (0.0)	0 (0.0)
単径ヘルニア	1 (0.2)	0 (0.0)	2 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
肛門周囲痛	1 (0.2)	0 (0.0)	2 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
肛門失禁	1 (0.2)	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
変色便	1 (0.2)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)
消化管運動障害	1 (0.2)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
口腔腫脹	1 (0.2)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
食道炎	1 (0.2)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
逆流性胃炎	1 (0.2)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
腹部硬直	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
異常便	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
急性腹症	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
裂肛	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)
痔瘻	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)
口唇のひび割れ	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
排便障害	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
糞塊	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
硬便	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
白色便	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
胃静脈瘤	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
歯肉潰瘍	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
イレウス	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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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 (%)
腸出血	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
過敏性腸症候群	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
口唇出血	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
口唇痛	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
急性膵炎	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
直腸ポリープ	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
直腸潰瘍	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
舌嚢胞	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)
舌不快感	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
食中毒	0 (0.0)	0 (0.0)	3 (0.6)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
メレナ	0 (0.0)	0 (0.0)	3 (0.6)	1 (0.2)	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)
大腸炎	0 (0.0)	0 (0.0)	2 (0.4)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
小腸炎	0 (0.0)	0 (0.0)	2 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
口唇潰瘍	0 (0.0)	0 (0.0)	2 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
膵炎	0 (0.0)	0 (0.0)	2 (0.4)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
肛門そう痒症	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
肛門皮膚垂	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
肛門潰瘍	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
アフタ性潰瘍	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
小腸瘻	0 (0.0)	0 (0.0)	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
胃穿孔	0 (0.0)	0 (0.0)	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
胃ポリープ	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
出血性胃潰瘍	0 (0.0)	0 (0.0)	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
胃十二指腸炎	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
異所性胃食道	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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付録 2.7.4.1
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 (%)
歯肉びらん	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
歯肉紅斑	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
歯肉退縮	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
胃酸過多	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
腹腔内血腫	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
弛緩歯	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
口腔知覚不全	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
口腔扁平苔癬	0 (0.0)	0 (0.0)	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
口腔粘膜水疱形成	0 (0.0)	0 (0.0)	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
口の錯感覚	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
腹膜出血	0 (0.0)	0 (0.0)	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ひだ舌	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
直腸裂	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
レッチング	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
舌浮腫	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
変色歯	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
一般・全身障害および投与部位の状態	284 (59.7)	48 (10.1)	243 (51.2)	37 (7.8)	50 (61.7)	3 (3.7)	33 (37.9)	5 (5.7)
疲労	141 (29.6)	18 (3.8)	119 (25.1)	17 (3.6)	15 (18.5)	1 (1.2)	8 (9.2)	4 (4.6)
発熱	69 (14.5)	0 (0.0)	63 (13.3)	1 (0.2)	13 (16.0)	0 (0.0)	15 (17.2)	0 (0.0)
末梢性浮腫	66 (13.9)	4 (0.8)	33 (6.9)	1 (0.2)	23 (28.4)	2 (2.5)	7 (8.0)	0 (0.0)
無力症	54 (11.3)	14 (2.9)	48 (10.1)	11 (2.3)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
倦怠感	21 (4.4)	0 (0.0)	9 (1.9)	0 (0.0)	15 (18.5)	0 (0.0)	7 (8.0)	0 (0.0)
悪寒	11 (2.3)	0 (0.0)	5 (1.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
非心臓性胸痛	11 (2.3)	0 (0.0)	4 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
全身健康状態低下	6 (1.3)	6 (1.3)	5 (1.1)	5 (1.1)	0 (0.0)	0 (0.0)	1 (1.1)	1 (1.1)

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付録 2.7.4.1
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 (%)
インフルエンザ様疾患	6 (1.3)	0 (0.0)	5 (1.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
胸部不快感	5 (1.1)	0 (0.0)	4 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
疼痛	4 (0.8)	0 (0.0)	4 (0.8)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
全身性浮腫	4 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	2 (2.5)	0 (0.0)	0 (0.0)	0 (0.0)
末梢腫脹	3 (0.6)	1 (0.2)	6 (1.3)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
口渇	3 (0.6)	0 (0.0)	5 (1.1)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)
肝疾患による浮腫	3 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	3 (3.7)	0 (0.0)	0 (0.0)	0 (0.0)
多臓器機能不全症候群	2 (0.4)	2 (0.4)	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
カテーテル留置部位疼痛	2 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)
早期満腹	2 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
冷感	2 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
乾燥症	2 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
胸痛	1 (0.2)	0 (0.0)	2 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
顔面痛	1 (0.2)	0 (0.0)	2 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
突然死	1 (0.2)	1 (0.2)	2 (0.4)	2 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
顔面浮腫	1 (0.2)	0 (0.0)	1 (0.2)	0 (0.0)	1 (1.2)	0 (0.0)	1 (1.1)	0 (0.0)
治癒不良	1 (0.2)	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)
限局性浮腫	1 (0.2)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	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)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
突出痛	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
死亡	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
薬物不耐性	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
肉芽腫	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)
高熱	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
注入部位血管外漏出	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)

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付録 2.7.4.1
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 (%)
注射部位内出血	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
小結節	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
臓器不全	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
異物感	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
温度変化不耐症	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
歩行障害	0 (0.0)	0 (0.0)	2 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
注射部位漏出	0 (0.0)	0 (0.0)	2 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)
腋窩痛	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
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)
注入部位腫脹	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)
注射部位反応	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
粘膜の炎症	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
浮腫	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
活動状態低下	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
肝胆道系障害	85 (17.9)	54 (11.3)	54 (11.4)	37 (7.8)	19 (23.5)	13 (16.0)	14 (16.1)	10 (11.5)
肝不全	15 (3.2)	15 (3.2)	12 (2.5)	12 (2.5)	3 (3.7)	3 (3.7)	1 (1.1)	1 (1.1)
肝機能異常	12 (2.5)	8 (1.7)	13 (2.7)	9 (1.9)	10 (12.3)	6 (7.4)	12 (13.8)	8 (9.2)
高ビリルビン血症	11 (2.3)	6 (1.3)	6 (1.3)	1 (0.2)	1 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)
胆汁うっ滞性黄疸	9 (1.9)	8 (1.7)	3 (0.6)	3 (0.6)	4 (4.9)	3 (3.7)	2 (2.3)	2 (2.3)
門脈血栓症	9 (1.9)	4 (0.8)	3 (0.6)	1 (0.2)	3 (3.7)	2 (2.5)	0 (0.0)	0 (0.0)
肝臓痛	8 (1.7)	1 (0.2)	3 (0.6)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
黄疸	6 (1.3)	1 (0.2)	7 (1.5)	5 (1.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
胆管炎	6 (1.3)	3 (0.6)	3 (0.6)	3 (0.6)	3 (3.7)	3 (3.7)	1 (1.1)	1 (1.1)
肝硬変	4 (0.8)	3 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
胆管閉塞	3 (0.6)	3 (0.6)	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

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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 (%)
胆嚢炎	2 (0.4)	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
胆管結石	2 (0.4)	2 (0.4)	0 (0.0)	0 (0.0)	2 (2.5)	2 (2.5)	0 (0.0)	0 (0.0)
急性胆嚢炎	1 (0.2)	1 (0.2)	2 (0.4)	2 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
胆管狭窄	1 (0.2)	0 (0.0)	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	1 (1.1)	1 (1.1)
血性胆汁	1 (0.2)	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)
肝腫大	1 (0.2)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
肝腎症候群	1 (0.2)	1 (0.2)	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
肝損傷	1 (0.2)	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
黄疸眼	1 (0.2)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
急性肝不全	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
胆管拡張	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
後天性胆管拡張症	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
胆石症	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
胆汁うっ滞	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
慢性肝不全	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
肝出血	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
水腫性胆嚢炎	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
肝障害	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)
門脈圧亢進症	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
慢性胆嚢炎	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
肝毒性	0 (0.0)	0 (0.0)	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
免疫系障害	3 (0.6)	0 (0.0)	5 (1.1)	0 (0.0)	1 (1.2)	0 (0.0)	1 (1.1)	0 (0.0)
季節性アレルギー	2 (0.4)	0 (0.0)	2 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)
造影剤アレルギー	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)
薬物過敏症	0 (0.0)	0 (0.0)	2 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

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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 (%)
過敏症	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
感染症および寄生虫症	144 (30.3)	40 (8.4)	134 (28.2)	27 (5.7)	38 (46.9)	6 (7.4)	32 (36.8)	4 (4.6)
鼻咽頭炎	25 (5.3)	0 (0.0)	19 (4.0)	0 (0.0)	15 (18.5)	0 (0.0)	12 (13.8)	0 (0.0)
上気道感染	21 (4.4)	1 (0.2)	24 (5.1)	2 (0.4)	6 (7.4)	0 (0.0)	5 (5.7)	0 (0.0)
肺炎	12 (2.5)	4 (0.8)	9 (1.9)	4 (0.8)	4 (4.9)	2 (2.5)	3 (3.4)	1 (1.1)
尿路感染	12 (2.5)	1 (0.2)	8 (1.7)	0 (0.0)	1 (1.2)	0 (0.0)	1 (1.1)	0 (0.0)
胃腸炎	9 (1.9)	3 (0.6)	3 (0.6)	1 (0.2)	4 (4.9)	0 (0.0)	0 (0.0)	0 (0.0)
インフルエンザ	8 (1.7)	0 (0.0)	2 (0.4)	0 (0.0)	2 (2.5)	0 (0.0)	0 (0.0)	0 (0.0)
咽頭炎	7 (1.5)	0 (0.0)	6 (1.3)	0 (0.0)	3 (3.7)	0 (0.0)	1 (1.1)	0 (0.0)
敗血症	7 (1.5)	7 (1.5)	4 (0.8)	4 (0.8)	1 (1.2)	1 (1.2)	0 (0.0)	0 (0.0)
細菌性腹膜炎	6 (1.3)	4 (0.8)	1 (0.2)	1 (0.2)	1 (1.2)	1 (1.2)	1 (1.1)	1 (1.1)
膀胱炎	4 (0.8)	0 (0.0)	3 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)
気管支炎	3 (0.6)	0 (0.0)	6 (1.3)	1 (0.2)	1 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)
口腔カンジダ症	3 (0.6)	0 (0.0)	6 (1.3)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)
毛包炎	3 (0.6)	0 (0.0)	4 (0.8)	0 (0.0)	1 (1.2)	0 (0.0)	2 (2.3)	0 (0.0)
歯肉炎	3 (0.6)	0 (0.0)	3 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)
膿疱性皮疹	3 (0.6)	0 (0.0)	3 (0.6)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
皮膚感染	3 (0.6)	0 (0.0)	2 (0.4)	0 (0.0)	1 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)
口角口唇炎	3 (0.6)	0 (0.0)	1 (0.2)	0 (0.0)	2 (2.5)	0 (0.0)	1 (1.1)	0 (0.0)
感染	3 (0.6)	1 (0.2)	1 (0.2)	1 (0.2)	1 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)
単純ヘルペス	3 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
肺感染	2 (0.4)	2 (0.4)	5 (1.1)	2 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
蜂巣炎	2 (0.4)	2 (0.4)	4 (0.8)	1 (0.2)	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)
足部白癬	2 (0.4)	0 (0.0)	3 (0.6)	0 (0.0)	2 (2.5)	0 (0.0)	2 (2.3)	0 (0.0)
帯状疱疹	2 (0.4)	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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	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 (%)
肝膿瘍	2 (0.4)	2 (0.4)	1 (0.2)	1 (0.2)	1 (1.2)	1 (1.2)	1 (1.1)	1 (1.1)
歯周炎	2 (0.4)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
副鼻腔炎	2 (0.4)	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
細菌性胃腸炎	2 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
喉頭炎	2 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)
歯感染	2 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
外陰膣真菌感染	2 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
結膜炎	1 (0.2)	0 (0.0)	4 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
真菌感染	1 (0.2)	0 (0.0)	4 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
鼻炎	1 (0.2)	0 (0.0)	2 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
扁桃炎	1 (0.2)	0 (0.0)	2 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
肛門膿瘍	1 (0.2)	0 (0.0)	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
胆道感染	1 (0.2)	1 (0.2)	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
体部白癬	1 (0.2)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
せつ	1 (0.2)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ウイルス性胃腸炎	1 (0.2)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	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)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
感染性胸水	1 (0.2)	1 (0.2)	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
限局性感染	1 (0.2)	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
肺膿瘍	1 (0.2)	1 (0.2)	1 (0.2)	1 (0.2)	1 (1.2)	1 (1.2)	0 (0.0)	0 (0.0)
爪囲炎	1 (0.2)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ウイルス性気道感染	1 (0.2)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
敗血症性ショック	1 (0.2)	1 (0.2)	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
腹壁感染	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
虫垂膿瘍	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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Adverse Events terms were coded using Medical Dictionary for Regulatory Activities (MedDRA) version 19.1.
TEAE = Treatment-emergent adverse event.

付録 2.7.4.1
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 (%)
虫垂炎	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
菌血症	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
細菌性膣症	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
気管支肺アスペルギルス症	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)
男性外性器蜂巣炎	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
慢性B型肝炎	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
シトロバクター感染	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	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)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
デング熱	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
憩室炎	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
耳感染	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
大腸菌性敗血症	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
肛径部膿瘍	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
肛径部感染	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
B型肝炎	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
感染性皮膚嚢腫	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)
腎感染	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
医療機器使用部位膿瘍	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
爪感染	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)
口腔真菌感染	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
口腔ヘルペス	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
中咽頭カンジダ症	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
肝周囲膿瘍	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	1 (1.2)	1 (1.2)	0 (0.0)	0 (0.0)
胸膜感染	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
術後膿瘍	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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付録 2.7.4.1
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 (%)
肺結核	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
腎盂腎炎	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
サルモネラ症	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
陰嚢感染	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
歯膿瘍	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
気管炎	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
結核	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
腸球菌性尿路感染	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
尿路性敗血症	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
急性副鼻腔炎	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
アスペルギルス感染	0 (0.0)	0 (0.0)	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
細菌感染	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)
バクテロイデス感染	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	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)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
医療機器関連感染	0 (0.0)	0 (0.0)	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	1 (1.1)	1 (1.1)
糖尿病性足感染	0 (0.0)	0 (0.0)	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
眼瞼毛包炎	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
皮膚真菌感染	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ノロウイルス性胃腸炎	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)
C型肝炎	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ヘルペスウイルス感染	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
麦粒腫	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
感染性大腸炎	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)
下気道感染	0 (0.0)	0 (0.0)	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
髄膜炎	0 (0.0)	0 (0.0)	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

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付録 2.7.4.1
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 (%)
食道カンジダ症	0 (0.0)	0 (0.0)	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
眼部単純ヘルペス	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
中耳炎	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
慢性中耳炎	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
会陰膿瘍	0 (0.0)	0 (0.0)	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
大腸菌性肺炎	0 (0.0)	0 (0.0)	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
術後創感染	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
癜風	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)
細菌性尿路感染	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ウイルス感染	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
創傷感染	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
傷害、中毒および処置合併症	30 (6.3)	7 (1.5)	25 (5.3)	4 (0.8)	6 (7.4)	1 (1.2)	9 (10.3)	0 (0.0)
転倒	8 (1.7)	1 (0.2)	4 (0.8)	0 (0.0)	1 (1.2)	0 (0.0)	1 (1.1)	0 (0.0)
挫傷	3 (0.6)	0 (0.0)	3 (0.6)	0 (0.0)	2 (2.5)	0 (0.0)	1 (1.1)	0 (0.0)
皮膚擦過傷	3 (0.6)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)
偶発的過量投与	2 (0.4)	2 (0.4)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
創傷	2 (0.4)	0 (0.0)	1 (0.2)	0 (0.0)	1 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)
処置による疼痛	2 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
外傷後疼痛	1 (0.2)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
肋骨骨折	1 (0.2)	0 (0.0)	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
脊椎圧迫骨折	1 (0.2)	1 (0.2)	1 (0.2)	0 (0.0)	1 (1.2)	1 (1.2)	1 (1.1)	0 (0.0)
外傷性血腫	1 (0.2)	0 (0.0)	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
大腿骨骨折	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
頭部損傷	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
熱射病	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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付録 2.7.4.1
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 (%)
切開部位痛	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
注入に伴う反応	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
企図的過量投与	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
裂傷	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
四肢損傷	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
処置後血尿	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)
処置による悪心	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
放射線性食道炎	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
放射線性肺臓炎	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
交通事故	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
皮膚損傷	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
サンバーン	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
腱断裂	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
胸椎骨折	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
歯牙破折	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)
各種物質毒性	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
創傷血腫	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
手首関節骨折	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
創合併症	0 (0.0)	0 (0.0)	3 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)
脊椎骨折	0 (0.0)	0 (0.0)	2 (0.4)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
動物咬傷	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
節足動物咬傷	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)
焼痂	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
眼挫傷	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)
体内異物	0 (0.0)	0 (0.0)	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	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 2.7.4.1
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 (%)
上腕骨骨折	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
腰椎骨折	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
外傷性気胸	0 (0.0)	0 (0.0)	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
放射線宿酔症候群	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)
皮膚創傷	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)
ストーマ部出血	0 (0.0)	0 (0.0)	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
くも膜下出血	0 (0.0)	0 (0.0)	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
熱傷	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)
外傷性骨折	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)
臨床検査	304 (63.9)	150 (31.5)	255 (53.7)	121 (25.5)	54 (66.7)	28 (34.6)	44 (50.6)	24 (27.6)
体重減少	147 (30.9)	36 (7.6)	106 (22.3)	14 (2.9)	25 (30.9)	9 (11.1)	17 (19.5)	0 (0.0)
血小板数減少	87 (18.3)	26 (5.5)	58 (12.2)	16 (3.4)	24 (29.6)	6 (7.4)	16 (18.4)	9 (10.3)
血中ビリルビン増加	71 (14.9)	31 (6.5)	63 (13.3)	23 (4.8)	11 (13.6)	3 (3.7)	5 (5.7)	2 (2.3)
アスパラギン酸アミノトランスフェラーゼ増加	65 (13.7)	24 (5.0)	80 (16.8)	38 (8.0)	5 (6.2)	2 (2.5)	8 (9.2)	6 (6.9)
アラニンアミノトランスフェラーゼ増加	53 (11.1)	16 (3.4)	52 (10.9)	16 (3.4)	2 (2.5)	1 (1.2)	6 (6.9)	2 (2.3)
白血球数減少	46 (9.7)	12 (2.5)	23 (4.8)	8 (1.7)	8 (9.9)	3 (3.7)	4 (4.6)	3 (3.4)
好中球数減少	40 (8.4)	15 (3.2)	11 (2.3)	8 (1.7)	11 (13.6)	6 (7.4)	2 (2.3)	1 (1.1)
γ－グルタミルトランスフェラーゼ増加	37 (7.8)	26 (5.5)	26 (5.5)	19 (4.0)	5 (6.2)	4 (4.9)	3 (3.4)	3 (3.4)
心電図ＱＴ延長	33 (6.9)	5 (1.1)	24 (5.1)	5 (1.1)	4 (4.9)	0 (0.0)	1 (1.1)	0 (0.0)
血中アルカリホスファターゼ増加	32 (6.7)	10 (2.1)	29 (6.1)	7 (1.5)	1 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)
血中甲状腺刺激ホルモン増加	23 (4.8)	0 (0.0)	4 (0.8)	0 (0.0)	7 (8.6)	0 (0.0)	0 (0.0)	0 (0.0)
国際標準比増加	19 (4.0)	1 (0.2)	14 (2.9)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

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付録 2.7.4.1
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 (%)
リパーゼ増加	18 (3.8)	13 (2.7)	18 (3.8)	9 (1.9)	5 (6.2)	5 (6.2)	5 (5.7)	4 (4.6)
Ｃ－反応性蛋白増加	14 (2.9)	0 (0.0)	12 (2.5)	1 (0.2)	1 (1.2)	0 (0.0)	4 (4.6)	0 (0.0)
血中アルブミン減少	14 (2.9)	1 (0.2)	9 (1.9)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)
リンパ球数減少	12 (2.5)	8 (1.7)	10 (2.1)	6 (1.3)	3 (3.7)	2 (2.5)	4 (4.6)	2 (2.3)
血中乳酸脱水素酵素増加	11 (2.3)	1 (0.2)	12 (2.5)	2 (0.4)	1 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)
尿中蛋白陽性	11 (2.3)	1 (0.2)	4 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血圧上昇	11 (2.3)	1 (0.2)	3 (0.6)	1 (0.2)	1 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)
血中クレアチニン増加	10 (2.1)	0 (0.0)	4 (0.8)	0 (0.0)	4 (4.9)	0 (0.0)	1 (1.1)	0 (0.0)
血中コレステロール増加	7 (1.5)	0 (0.0)	1 (0.2)	0 (0.0)	2 (2.5)	0 (0.0)	0 (0.0)	0 (0.0)
体重増加	6 (1.3)	0 (0.0)	1 (0.2)	0 (0.0)	1 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)
プロトロンビン時間延長	5 (1.1)	0 (0.0)	7 (1.5)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
アミラーゼ増加	5 (1.1)	2 (0.4)	4 (0.8)	2 (0.4)	2 (2.5)	0 (0.0)	1 (1.1)	1 (1.1)
血中カリウム減少	5 (1.1)	2 (0.4)	3 (0.6)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血中尿素増加	5 (1.1)	0 (0.0)	2 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
尿中ビリルビン増加	5 (1.1)	1 (0.2)	2 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血中ナトリウム減少	5 (1.1)	4 (0.8)	1 (0.2)	1 (0.2)	1 (1.2)	1 (1.2)	0 (0.0)	0 (0.0)
ＥＣＯＧパフォーマンスステータス悪化	4 (0.8)	3 (0.6)	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血中クロール減少	2 (0.4)	1 (0.2)	3 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ヘモグロビン減少	2 (0.4)	0 (0.0)	3 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)
血中甲状腺刺激ホルモン減少	2 (0.4)	0 (0.0)	2 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
赤血球数減少	2 (0.4)	0 (0.0)	2 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
尿中血陽性	2 (0.4)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ヘモグロビン増加	2 (0.4)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
抱合ビリルビン増加	2 (0.4)	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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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 (%)
白血球数増加	2 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
尿中白血球陽性	2 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血中カルシウム減少	1 (0.2)	0 (0.0)	4 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
体温上昇	1 (0.2)	0 (0.0)	2 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
好中球数増加	1 (0.2)	0 (0.0)	2 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
尿中ウロビリノーゲン増加	1 (0.2)	0 (0.0)	2 (0.4)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血中コリンエステラーゼ減少	1 (0.2)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血中クレアチニン減少	1 (0.2)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血中ブドウ糖増加	1 (0.2)	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血中カリウム増加	1 (0.2)	1 (0.2)	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
尿中ブドウ糖陽性	1 (0.2)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
肝酵素上昇	1 (0.2)	1 (0.2)	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
尿中亜硝酸塩陽性	1 (0.2)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
トランスアミナーゼ上昇	1 (0.2)	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
尿量減少	1 (0.2)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	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)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
アンモニア増加	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)
血中カルシウム増加	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血中電解質減少	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血中フィブリノゲン増加	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血圧低下	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)
拡張期血圧上昇	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
心雑音	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
クロストリジウム検査陽性	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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Study 304
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	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 (%)
薬物スクリーニング陽性	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
心電図ＳＴ部分下降	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
心電図ＳＴ－Ｔ変化	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
心電図異常Ｔ波	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
尿中ブドウ糖	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ヘリコバクター検査陽性	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
国際標準比減少	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
リパーゼ減少	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
リンパ球数増加	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
プロテインＣ増加	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
総蛋白減少	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
プロトロンビン量減少	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	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)	0 (0.0)	0 (0.0)	1 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)
トリヨードチロニン増加	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
トロポニンＴ増加	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	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)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
膵酵素増加	0 (0.0)	0 (0.0)	2 (0.4)	2 (0.4)	0 (0.0)	0 (0.0)	2 (2.3)	2 (2.3)
活性化部分トロンボプラスチン時間延長	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
α１フェトプロテイン増加	0 (0.0)	0 (0.0)	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血中クレアチンホスホキナーゼ増加	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)
血中リン減少	0 (0.0)	0 (0.0)	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	1 (1.1)	1 (1.1)
チャイルド・ピュー・ターコットスコア増加	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
凝固因子増加	0 (0.0)	0 (0.0)	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	1 (1.1)	1 (1.1)

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Adverse Events terms were coded using Medical Dictionary for Regulatory Activities (MedDRA) version 19.1.
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付録 2.7.4.1
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 (%)
凝固時間延長	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
心電図T波逆転	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
肝機能検査値上昇	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)
血小板数増加	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
総蛋白増加	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
遊離トリヨードチロニン減少	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
遊離トリヨードチロニン増加	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
尿中ケトン体陽性	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
代謝および栄養障害	220 (46.2)	65 (13.7)	196 (41.3)	38 (8.0)	53 (65.4)	17 (21.0)	33 (37.9)	6 (6.9)
食欲減退	162 (34.0)	22 (4.6)	127 (26.7)	6 (1.3)	40 (49.4)	8 (9.9)	20 (23.0)	0 (0.0)
低アルブミン血症	44 (9.2)	4 (0.8)	38 (8.0)	2 (0.4)	14 (17.3)	3 (3.7)	8 (9.2)	0 (0.0)
低ナトリウム血症	23 (4.8)	20 (4.2)	9 (1.9)	9 (1.9)	4 (4.9)	4 (4.9)	1 (1.1)	1 (1.1)
脱水	17 (3.6)	4 (0.8)	5 (1.1)	0 (0.0)	9 (11.1)	2 (2.5)	3 (3.4)	0 (0.0)
低血糖	12 (2.5)	3 (0.6)	2 (0.4)	0 (0.0)	5 (6.2)	1 (1.2)	0 (0.0)	0 (0.0)
高カリウム血症	11 (2.3)	6 (1.3)	12 (2.5)	2 (0.4)	1 (1.2)	1 (1.2)	3 (3.4)	1 (1.1)
高アンモニア血症	9 (1.9)	0 (0.0)	3 (0.6)	0 (0.0)	8 (9.9)	0 (0.0)	3 (3.4)	0 (0.0)
低カリウム血症	8 (1.7)	5 (1.1)	25 (5.3)	12 (2.5)	3 (3.7)	2 (2.5)	3 (3.4)	2 (2.3)
低マグネシウム血症	5 (1.1)	1 (0.2)	2 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
低カルシウム血症	4 (0.8)	2 (0.4)	4 (0.8)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
低蛋白血症	4 (0.8)	1 (0.2)	3 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
高血糖	4 (0.8)	1 (0.2)	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
高尿酸血症	3 (0.6)	0 (0.0)	3 (0.6)	2 (0.4)	2 (2.5)	0 (0.0)	2 (2.3)	1 (1.1)
糖尿病	3 (0.6)	1 (0.2)	1 (0.2)	0 (0.0)	1 (1.2)	1 (1.2)	0 (0.0)	0 (0.0)
高脂血症	3 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
低リン酸血症	2 (0.4)	2 (0.4)	7 (1.5)	3 (0.6)	0 (0.0)	0 (0.0)	3 (3.4)	2 (2.3)

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付録 2.7.4.1
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 (%)
高カルシウム血症	2 (0.4)	0 (0.0)	2 (0.4)	1 (0.2)	1 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)
痛風	2 (0.4)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)
悪液質	2 (0.4)	2 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
過小食	2 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
高ナトリウム血症	1 (0.2)	0 (0.0)	1 (0.2)	0 (0.0)	1 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)
低クロール血症	1 (0.2)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
アシドーシス	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
糖尿病性代謝代償不全	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
高トリグリセリド血症	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
代謝性アシドーシス	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
高コレステロール血症	0 (0.0)	0 (0.0)	6 (1.3)	2 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
水分過負荷	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
高アミラーゼ血症	0 (0.0)	0 (0.0)	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	1 (1.1)	1 (1.1)
高リパーゼ血症	0 (0.0)	0 (0.0)	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	1 (1.1)	1 (1.1)
高蛋白血症	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
テタニー	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
筋骨格系および結合組織障害	180 (37.8)	18 (3.8)	132 (27.8)	14 (2.9)	30 (37.0)	0 (0.0)	20 (23.0)	1 (1.1)
背部痛	50 (10.5)	1 (0.2)	31 (6.5)	5 (1.1)	5 (6.2)	0 (0.0)	3 (3.4)	0 (0.0)
筋骨格痛	47 (9.9)	0 (0.0)	24 (5.1)	2 (0.4)	8 (9.9)	0 (0.0)	4 (4.6)	0 (0.0)
関節痛	42 (8.8)	0 (0.0)	20 (4.2)	1 (0.2)	7 (8.6)	0 (0.0)	4 (4.6)	0 (0.0)
四肢痛	37 (7.8)	3 (0.6)	18 (3.8)	1 (0.2)	3 (3.7)	0 (0.0)	2 (2.3)	0 (0.0)
筋肉痛	21 (4.4)	1 (0.2)	8 (1.7)	0 (0.0)	3 (3.7)	0 (0.0)	3 (3.4)	0 (0.0)
筋痙縮	13 (2.7)	0 (0.0)	18 (3.8)	1 (0.2)	4 (4.9)	0 (0.0)	4 (4.6)	0 (0.0)
筋力低下	13 (2.7)	2 (0.4)	6 (1.3)	1 (0.2)	2 (2.5)	0 (0.0)	1 (1.1)	0 (0.0)
筋骨格系胸痛	11 (2.3)	0 (0.0)	7 (1.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

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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 (%)
頚部痛	10 (2.1)	2 (0.4)	4 (0.8)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
側腹部痛	8 (1.7)	0 (0.0)	6 (1.3)	0 (0.0)	1 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)
骨痛	6 (1.3)	2 (0.4)	5 (1.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
変形性関節症	4 (0.8)	1 (0.2)	2 (0.4)	0 (0.0)	1 (1.2)	0 (0.0)	1 (1.1)	0 (0.0)
病的骨折	3 (0.6)	2 (0.4)	7 (1.5)	4 (0.8)	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)
筋骨格不快感	3 (0.6)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
骨粗鬆症	3 (0.6)	0 (0.0)	1 (0.2)	0 (0.0)	1 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)
関節腫脹	2 (0.4)	0 (0.0)	3 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
関節炎	2 (0.4)	0 (0.0)	1 (0.2)	0 (0.0)	1 (1.2)	0 (0.0)	1 (1.1)	0 (0.0)
尾骨痛	2 (0.4)	0 (0.0)	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
椎間板突出	2 (0.4)	2 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
腰部脊柱管狭窄症	2 (0.4)	1 (0.2)	0 (0.0)	0 (0.0)	1 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)
筋攣縮	2 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
脊柱管狭窄症	2 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
脊椎痛	2 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
脊椎すべり症	2 (0.4)	1 (0.2)	0 (0.0)	0 (0.0)	1 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)
関節可動域低下	1 (0.2)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
筋骨格硬直	1 (0.2)	0 (0.0)	1 (0.2)	0 (0.0)	1 (1.2)	0 (0.0)	1 (1.1)	0 (0.0)
滑液包炎	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
痛風性関節炎	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
運動性低下	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
筋萎縮	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
筋緊張	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
関節周囲炎	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)
横紋筋融解症	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

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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 (%)
肩回旋筋腱板症候群	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
変形性脊椎症	0 (0.0)	0 (0.0)	2 (0.4)	1 (0.2)	0 (0.0)	0 (0.0)	2 (2.3)	1 (1.1)
痛風結節	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
筋肉疲労	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
頚部腫瘤	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
顎痛	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
軟部組織腫瘤	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
滑膜炎	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
腱痛	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
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）	51 (10.7)	28 (5.9)	57 (12.0)	32 (6.7)	13 (16.0)	6 (7.4)	13 (14.9)	2 (2.3)
癌疼痛	17 (3.6)	4 (0.8)	15 (3.2)	6 (1.3)	7 (8.6)	3 (3.7)	8 (9.2)	1 (1.1)
悪性新生物進行	10 (2.1)	10 (2.1)	15 (3.2)	15 (3.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
腫瘍疼痛	4 (0.8)	1 (0.2)	5 (1.1)	2 (0.4)	2 (2.5)	0 (0.0)	3 (3.4)	1 (1.1)
悪性腹水	3 (0.6)	1 (0.2)	8 (1.7)	1 (0.2)	1 (1.2)	0 (0.0)	1 (1.1)	0 (0.0)
腫瘍出血	3 (0.6)	3 (0.6)	3 (0.6)	3 (0.6)	1 (1.2)	1 (1.2)	1 (1.1)	1 (1.1)
腫瘍熱	3 (0.6)	0 (0.0)	1 (0.2)	0 (0.0)	1 (1.2)	0 (0.0)	1 (1.1)	0 (0.0)
肝癌破裂	2 (0.4)	2 (0.4)	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
悪性胸水	2 (0.4)	0 (0.0)	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
脊椎転移	2 (0.4)	2 (0.4)	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
中枢神経系転移	2 (0.4)	2 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
骨転移	1 (0.2)	0 (0.0)	2 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
腫瘍壊死	1 (0.2)	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)
腫瘍破裂	1 (0.2)	1 (0.2)	1 (0.2)	1 (0.2)	0 (0.0)	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)	0 (0.0)	0 (0.0)	0 (0.0)	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 2.7.4.1
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 (%)
基底細胞癌	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
感染性新生物	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	1 (1.2)	1 (1.2)	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)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
髄膜腫	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
腫瘍随伴症候群	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	1 (1.2)	1 (1.2)	0 (0.0)	0 (0.0)
腎細胞癌	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
子宮頚部の良性新生物	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ケラトアカントーマ	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
口唇扁平上皮癌	0 (0.0)	0 (0.0)	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
肺の悪性新生物	0 (0.0)	0 (0.0)	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
菌状息肉症	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
口腔新生物	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
形質細胞性骨髄腫	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)
脂漏性角化症	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)
神経系障害	163 (34.2)	47 (9.9)	106 (22.3)	20 (4.2)	30 (37.0)	8 (9.9)	16 (18.4)	2 (2.3)
頭痛	46 (9.7)	3 (0.6)	38 (8.0)	0 (0.0)	3 (3.7)	0 (0.0)	5 (5.7)	0 (0.0)
肝性脳症	38 (8.0)	23 (4.8)	9 (1.9)	7 (1.5)	9 (11.1)	5 (6.2)	2 (2.3)	2 (2.3)
浮動性めまい	30 (6.3)	1 (0.2)	16 (3.4)	1 (0.2)	0 (0.0)	0 (0.0)	2 (2.3)	0 (0.0)
味覚異常	22 (4.6)	0 (0.0)	12 (2.5)	0 (0.0)	10 (12.3)	0 (0.0)	6 (6.9)	0 (0.0)
錯感覚	9 (1.9)	2 (0.4)	6 (1.3)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
傾眠	7 (1.5)	1 (0.2)	6 (1.3)	0 (0.0)	2 (2.5)	0 (0.0)	2 (2.3)	0 (0.0)
嗜眠	6 (1.3)	0 (0.0)	3 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
感覚鈍麻	6 (1.3)	0 (0.0)	2 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)
末梢性感覚ニューロパチー	4 (0.8)	0 (0.0)	7 (1.5)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
注意力障害	3 (0.6)	0 (0.0)	2 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

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付録 2.7.4.1
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 (%)
多発ニューロパチー	3 (0.6)	0 (0.0)	2 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
肝性昏睡	3 (0.6)	3 (0.6)	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
痙攣発作	3 (0.6)	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
脳出血	3 (0.6)	3 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
脳梗塞	3 (0.6)	2 (0.4)	0 (0.0)	0 (0.0)	2 (2.5)	1 (1.2)	0 (0.0)	0 (0.0)
失神	3 (0.6)	3 (0.6)	0 (0.0)	0 (0.0)	1 (1.2)	1 (1.2)	0 (0.0)	0 (0.0)
脳血管発作	2 (0.4)	2 (0.4)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
振戦	2 (0.4)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
失語症	2 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
固定姿勢保持困難	2 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
意識レベルの低下	2 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	2 (2.5)	0 (0.0)	0 (0.0)	0 (0.0)
過眠症	2 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)
睡眠の質低下	2 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
脊髄圧迫	2 (0.4)	2 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
認知障害	1 (0.2)	0 (0.0)	2 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)
脳症	1 (0.2)	1 (0.2)	2 (0.4)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
両麻痺	1 (0.2)	1 (0.2)	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
坐骨神経痛	1 (0.2)	0 (0.0)	1 (0.2)	1 (0.2)	1 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)
意識変容状態	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)
健忘	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
運動失調	1 (0.2)	0 (0.0)	0 (0.0)	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)
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)

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付録 2.7.4.1
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 (%)
測定障害	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
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)
第３脳神経麻痺	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
記憶障害	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
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)
反回神経麻痺	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	1 (1.2)	1 (1.2)	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)
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)
一過性脳虚血発作	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
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)
白質病変	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
失声症	0 (0.0)	0 (0.0)	3 (0.6)	2 (0.4)	0 (0.0)	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)
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)
脳虚血	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
頭部不快感	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
肋間神経痛	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
頭蓋内圧上昇	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
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)

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付録 2.7.4.1
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 (%)
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)
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)
ヘルペス後神経痛	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
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)
神経根障害	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
下肢静止不能症候群	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	56 (11.8)	6 (1.3)	46 (9.7)	1 (0.2)	10 (12.3)	0 (0.0)	6 (6.9)	0 (0.0)
不眠症	33 (6.9)	1 (0.2)	27 (5.7)	0 (0.0)	7 (8.6)	0 (0.0)	4 (4.6)	0 (0.0)
不安	9 (1.9)	0 (0.0)	5 (1.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
うつ病	7 (1.5)	1 (0.2)	6 (1.3)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)
錯乱状態	6 (1.3)	2 (0.4)	4 (0.8)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
譫妄	4 (0.8)	0 (0.0)	1 (0.2)	0 (0.0)	2 (2.5)	0 (0.0)	1 (1.1)	0 (0.0)
精神状態変化	3 (0.6)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
失見当識	2 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
睡眠障害	1 (0.2)	0 (0.0)	3 (0.6)	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)
大うつ病	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
精神運動制止遅滞	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
落ち着きのなさ	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)
自殺企図	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
激越	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
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 (%)
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)
神経過敏	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
人格変化	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	151 (31.7)	38 (8.0)	84 (17.7)	15 (3.2)	42 (51.9)	10 (12.3)	24 (27.6)	3 (3.4)
蛋白尿	117 (24.6)	27 (5.7)	54 (11.4)	8 (1.7)	38 (46.9)	7 (8.6)	19 (21.8)	1 (1.1)
血尿	25 (5.3)	1 (0.2)	10 (2.1)	0 (0.0)	6 (7.4)	0 (0.0)	4 (4.6)	0 (0.0)
急性腎障害	9 (1.9)	4 (0.8)	5 (1.1)	4 (0.8)	0 (0.0)	0 (0.0)	1 (1.1)	1 (1.1)
腎機能障害	5 (1.1)	1 (0.2)	6 (1.3)	2 (0.4)	5 (6.2)	1 (1.2)	5 (5.7)	1 (1.1)
排尿困難	4 (0.8)	0 (0.0)	3 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ビリルビン尿	3 (0.6)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
着色尿	3 (0.6)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
尿閉	3 (0.6)	1 (0.2)	0 (0.0)	0 (0.0)	3 (3.7)	1 (1.2)	0 (0.0)	0 (0.0)
慢性腎臓病	2 (0.4)	0 (0.0)	1 (0.2)	0 (0.0)	2 (2.5)	0 (0.0)	0 (0.0)	0 (0.0)
白血球尿	2 (0.4)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
夜間頻尿	2 (0.4)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
腎不全	2 (0.4)	2 (0.4)	1 (0.2)	0 (0.0)	1 (1.2)	1 (1.2)	0 (0.0)	0 (0.0)
腎仙痛	2 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
頻尿	1 (0.2)	0 (0.0)	6 (1.3)	0 (0.0)	1 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)
尿失禁	1 (0.2)	0 (0.0)	2 (0.4)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
乏尿	1 (0.2)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
尿流量減少	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)
高窒素血症	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
膀胱障害	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
膀胱腫瘤	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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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 2.7.4.1
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 (%)
尿路結石	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
非感染性膀胱炎	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
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)
ＩｇＡ腎症	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ケトン尿	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)
腎結石症	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)
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)
尿意切迫	0 (0.0)	0 (0.0)	1 (0.2)	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)
尿路の炎症	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
尿路痛	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
生殖系および乳房障害	26 (5.5)	2 (0.4)	19 (4.0)	0 (0.0)	6 (7.4)	0 (0.0)	2 (2.3)	0 (0.0)
女性化乳房	6 (1.3)	0 (0.0)	1 (0.2)	0 (0.0)	3 (3.7)	0 (0.0)	0 (0.0)	0 (0.0)
骨盤痛	4 (0.8)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
良性前立腺肥大症	2 (0.4)	0 (0.0)	2 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
乳房痛	2 (0.4)	0 (0.0)	2 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
陰嚢紅斑	2 (0.4)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
陰嚢潰瘍	2 (0.4)	0 (0.0)	1 (0.2)	0 (0.0)	1 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)
陰部そう痒症	2 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)
乳頭痛	1 (0.2)	0 (0.0)	1 (0.2)	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)	1 (0.2)	0 (0.0)	1 (1.2)	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)

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付録 2.7.4.1
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 (%)
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)
性器浮腫	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
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)
陰茎浮腫	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
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)
乳房分泌	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
線維嚢胞性乳腺疾患	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
性器びらん	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)
前立腺石灰化	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
前立腺炎	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)
陰嚢腫脹	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
膣出血	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
膣の炎症	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
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	213 (44.7)	25 (5.3)	148 (31.2)	16 (3.4)	47 (58.0)	4 (4.9)	29 (33.3)	0 (0.0)
発声障害	113 (23.7)	1 (0.2)	57 (12.0)	0 (0.0)	35 (43.2)	0 (0.0)	22 (25.3)	0 (0.0)
咳嗽	45 (9.5)	0 (0.0)	36 (7.6)	1 (0.2)	7 (8.6)	0 (0.0)	3 (3.4)	0 (0.0)
呼吸困難	36 (7.6)	9 (1.9)	18 (3.8)	3 (0.6)	5 (6.2)	2 (2.5)	0 (0.0)	0 (0.0)
鼻出血	34 (7.1)	1 (0.2)	15 (3.2)	0 (0.0)	7 (8.6)	0 (0.0)	3 (3.4)	0 (0.0)

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付録 2.7.4.1
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 (%)
口腔咽頭痛	21 (4.4)	0 (0.0)	16 (3.4)	0 (0.0)	2 (2.5)	0 (0.0)	1 (1.1)	0 (0.0)
喀血	9 (1.9)	1 (0.2)	7 (1.5)	0 (0.0)	1 (1.2)	0 (0.0)	1 (1.1)	0 (0.0)
胸水	9 (1.9)	0 (0.0)	6 (1.3)	2 (0.4)	3 (3.7)	0 (0.0)	2 (2.3)	0 (0.0)
しゃっくり	4 (0.8)	0 (0.0)	4 (0.8)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
肺塞栓症	4 (0.8)	4 (0.8)	4 (0.8)	4 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
湿性咳嗽	3 (0.6)	0 (0.0)	10 (2.1)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
鼻漏	3 (0.6)	0 (0.0)	4 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
呼吸不全	3 (0.6)	3 (0.6)	3 (0.6)	3 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
アレルギー性鼻炎	3 (0.6)	0 (0.0)	2 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
誤嚥性肺炎	3 (0.6)	3 (0.6)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
上気道の炎症	2 (0.4)	0 (0.0)	2 (0.4)	0 (0.0)	2 (2.5)	0 (0.0)	1 (1.1)	0 (0.0)
気胸	2 (0.4)	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
喘鳴	2 (0.4)	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
肝肺症候群	2 (0.4)	1 (0.2)	0 (0.0)	0 (0.0)	1 (1.2)	1 (1.2)	0 (0.0)	0 (0.0)
非心原性肺水腫	2 (0.4)	1 (0.2)	0 (0.0)	0 (0.0)	1 (1.2)	1 (1.2)	0 (0.0)	0 (0.0)
肺梗塞	2 (0.4)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
胸膜炎	1 (0.2)	0 (0.0)	2 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
胸膜痛	1 (0.2)	0 (0.0)	2 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
急性呼吸不全	1 (0.2)	1 (0.2)	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
慢性閉塞性肺疾患	1 (0.2)	0 (0.0)	1 (0.2)	0 (0.0)	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)
鼻閉	1 (0.2)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
鼻乾燥	1 (0.2)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
肺臓炎	1 (0.2)	0 (0.0)	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
呼吸抑制	1 (0.2)	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

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Eisai

Protocol: Lenvatinib (E7080) Integrated Summary of Safety

付録 2.7.4.1
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 (%)
呼吸窮迫	1 (0.2)	0 (0.0)	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	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)
無気肺	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	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)
気管支痙攣	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
気管支狭窄	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)
労作性呼吸困難	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
低酸素症	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
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)
上気道分泌増加	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)
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)
咽頭びらん	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)
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)
変色痰	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
喀痰増加	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
痰貯留	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)
上気道うっ血	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
上気道咳症候群	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
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)
ラ音	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
咽喉刺激感	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
皮膚および皮下組織障害	237 (49.8)	17 (3.6)	353 (74.3)	64 (13.5)	58 (71.6)	6 (7.4)	78 (89.7)	17 (19.5)
手掌・足底発赤知覚不全症候群	128 (26.9)	14 (2.9)	249 (52.4)	54 (11.4)	42 (51.9)	6 (7.4)	64 (73.6)	15 (17.2)
発疹	46 (9.7)	0 (0.0)	76 (16.0)	2 (0.4)	10 (12.3)	0 (0.0)	14 (16.1)	0 (0.0)

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付録 2.7.4.1
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 (%)
そう痒症	34 (7.1)	0 (0.0)	34 (7.2)	1 (0.2)	6 (7.4)	0 (0.0)	4 (4.6)	0 (0.0)
皮膚乾燥	21 (4.4)	0 (0.0)	19 (4.0)	0 (0.0)	4 (4.9)	0 (0.0)	1 (1.1)	0 (0.0)
脱毛症	14 (2.9)	0 (0.0)	119 (25.1)	0 (0.0)	5 (6.2)	0 (0.0)	32 (36.8)	0 (0.0)
過角化	9 (1.9)	0 (0.0)	11 (2.3)	0 (0.0)	4 (4.9)	0 (0.0)	3 (3.4)	0 (0.0)
紅斑	9 (1.9)	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)	19 (4.0)	4 (0.8)	1 (1.2)	0 (0.0)	5 (5.7)	2 (2.3)
蕁麻疹	6 (1.3)	0 (0.0)	6 (1.3)	0 (0.0)	2 (2.5)	0 (0.0)	0 (0.0)	0 (0.0)
皮膚剥脱	6 (1.3)	0 (0.0)	3 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
褥瘡性潰瘍	5 (1.1)	1 (0.2)	2 (0.4)	0 (0.0)	3 (3.7)	0 (0.0)	2 (2.3)	0 (0.0)
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)
湿疹	4 (0.8)	1 (0.2)	6 (1.3)	0 (0.0)	3 (3.7)	1 (1.2)	2 (2.3)	0 (0.0)
多汗症	4 (0.8)	0 (0.0)	2 (0.4)	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)	5 (1.1)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
皮膚炎	3 (0.6)	0 (0.0)	2 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)
寝汗	3 (0.6)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
丘疹性皮疹	2 (0.4)	0 (0.0)	6 (1.3)	2 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
水疱性皮膚炎	2 (0.4)	0 (0.0)	3 (0.6)	0 (0.0)	1 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)
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)
そう痒性皮疹	2 (0.4)	0 (0.0)	3 (0.6)	0 (0.0)	1 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)
皮膚潰瘍	2 (0.4)	0 (0.0)	3 (0.6)	0 (0.0)	2 (2.5)	0 (0.0)	3 (3.4)	0 (0.0)
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)
点状出血	2 (0.4)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
皮膚嚢腫	2 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)

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付録 2.7.4.1
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 (%)
皮膚びらん	2 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	2 (2.5)	0 (0.0)	0 (0.0)	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)
乾癬	1 (0.2)	0 (0.0)	4 (0.8)	1 (0.2)	1 (1.2)	0 (0.0)	1 (1.1)	0 (0.0)
皮膚刺激	1 (0.2)	0 (0.0)	2 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
皮膚病変	1 (0.2)	0 (0.0)	2 (0.4)	1 (0.2)	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)
斑状出血	1 (0.2)	0 (0.0)	1 (0.2)	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)
毛細血管拡張症	1 (0.2)	0 (0.0)	1 (0.2)	0 (0.0)	1 (1.2)	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)
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)
環状肉芽腫	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.2)	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)
爪床圧痛	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
爪の障害	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
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)
白色粃糠疹	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.2)	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)

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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 (%)
くも状母斑	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	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)
全身性そう痒症	0 (0.0)	0 (0.0)	2 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
痂皮	0 (0.0)	0 (0.0)	2 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	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)
糖尿病性足病変	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)
ヘノッホ・シェーンライン紫斑病	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
汗疹	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)
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)
皮膚腫瘤	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)
線状出血	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血管障害	214 (45.0)	116 (24.4)	152 (32.0)	73 (15.4)	43 (53.1)	28 (34.6)	42 (48.3)	23 (26.4)
高血圧	201 (42.2)	111 (23.3)	144 (30.3)	68 (14.3)	42 (51.9)	28 (34.6)	42 (48.3)	23 (26.4)
低血圧	6 (1.3)	2 (0.4)	5 (1.1)	2 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
起立性低血圧	3 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
潮紅	2 (0.4)	0 (0.0)	3 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

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	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 (%)
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)
静脈炎	1 (0.2)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
大静脈血栓症	1 (0.2)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
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)
動脈硬化症	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)
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)
ほてり	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
リンパ浮腫	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
起立性高血圧	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)
静脈瘤	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
大動脈狭窄	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.1)	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)
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)
表在性血栓性静脈炎	0 (0.0)	0 (0.0)	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	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.
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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 (%)
Subjects with Any Related TEAEs	447 (93.9)	270 (56.7)	452 (95.2)	231 (48.6)	81 (100.0)	51 (63.0)	87 (100.0)	60 (69.0)
血液およびリンパ系障害	59 (12.4)	21 (4.4)	49 (10.3)	11 (2.3)	8 (9.9)	3 (3.7)	9 (10.3)	4 (4.6)
血小板減少症	31 (6.5)	7 (1.5)	24 (5.1)	4 (0.8)	2 (2.5)	1 (1.2)	3 (3.4)	1 (1.1)
好中球減少症	18 (3.8)	6 (1.3)	6 (1.3)	0 (0.0)	1 (1.2)	1 (1.2)	1 (1.1)	0 (0.0)
貧血	14 (2.9)	4 (0.8)	25 (5.3)	7 (1.5)	4 (4.9)	1 (1.2)	5 (5.7)	3 (3.4)
白血球減少症	13 (2.7)	1 (0.2)	10 (2.1)	1 (0.2)	2 (2.5)	0 (0.0)	1 (1.1)	0 (0.0)
骨髄機能不全	2 (0.4)	2 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
リンパ球減少症	1 (0.2)	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
白血球増加症	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
リンパ節症	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
汎血球減少症	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
赤血球増加症	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)
ビタミンＢ１２欠乏性貧血	0 (0.0)	0 (0.0)	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
心臓障害	19 (4.0)	3 (0.6)	14 (2.9)	2 (0.4)	4 (4.9)	0 (0.0)	3 (3.4)	0 (0.0)
洞性徐脈	3 (0.6)	0 (0.0)	2 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
心筋梗塞	3 (0.6)	3 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
心房細動	2 (0.4)	0 (0.0)	4 (0.8)	1 (0.2)	2 (2.5)	0 (0.0)	2 (2.3)	0 (0.0)
心筋虚血	2 (0.4)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
動悸	2 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)
上室性期外収縮	2 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
左室肥大	1 (0.2)	0 (0.0)	2 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
頻脈	1 (0.2)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
心室性期外収縮	1 (0.2)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)

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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 (%)
第一度房室ブロック	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	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)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
期外収縮	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
プリンツメタル狭心症	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)
洞性不整脈	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
洞性頻脈	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
徐脈性不整脈	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
右脚ブロック	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
心不全	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
心臓弁狭窄	0 (0.0)	0 (0.0)	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
心室性不整脈	0 (0.0)	0 (0.0)	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
耳および迷路障害	10 (2.1)	0 (0.0)	4 (0.8)	1 (0.2)	2 (2.5)	0 (0.0)	1 (1.1)	0 (0.0)
耳鳴	4 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
回転性めまい	3 (0.6)	0 (0.0)	1 (0.2)	0 (0.0)	2 (2.5)	0 (0.0)	0 (0.0)	0 (0.0)
難聴	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
耳不快感	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
耳の障害	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
耳管開放	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)
聴覚過敏	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
聴力低下	0 (0.0)	0 (0.0)	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
内分泌障害	74 (15.5)	0 (0.0)	10 (2.1)	0 (0.0)	35 (43.2)	0 (0.0)	5 (5.7)	0 (0.0)
甲状腺機能低下症	70 (14.7)	0 (0.0)	8 (1.7)	0 (0.0)	33 (40.7)	0 (0.0)	4 (4.6)	0 (0.0)
甲状腺機能亢進症	4 (0.8)	0 (0.0)	2 (0.4)	0 (0.0)	3 (3.7)	0 (0.0)	0 (0.0)	0 (0.0)

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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 (%)
甲状腺炎	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
自己免疫性甲状腺炎	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)
眼障害	5 (1.1)	0 (0.0)	3 (0.6)	0 (0.0)	2 (2.5)	0 (0.0)	1 (1.1)	0 (0.0)
眼痛	1 (0.2)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
眼刺激	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
眼瞼浮腫	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)
眼瞼そう痒症	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)
眼充血	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
眼乾燥	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)
眼窩周囲浮腫	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
胃腸障害	281 (59.0)	38 (8.0)	291 (61.3)	42 (8.8)	57 (70.4)	6 (7.4)	54 (62.1)	5 (5.7)
下痢	143 (30.0)	20 (4.2)	197 (41.5)	17 (3.6)	30 (37.0)	3 (3.7)	32 (36.8)	2 (2.3)
悪心	65 (13.7)	2 (0.4)	54 (11.4)	3 (0.6)	12 (14.8)	0 (0.0)	8 (9.2)	0 (0.0)
口内炎	43 (9.0)	1 (0.2)	54 (11.4)	2 (0.4)	14 (17.3)	0 (0.0)	11 (12.6)	0 (0.0)
嘔吐	43 (9.0)	2 (0.4)	23 (4.8)	5 (1.1)	7 (8.6)	0 (0.0)	3 (3.4)	0 (0.0)
腹水	31 (6.5)	7 (1.5)	7 (1.5)	2 (0.4)	12 (14.8)	2 (2.5)	2 (2.3)	0 (0.0)
腹痛	30 (6.3)	2 (0.4)	32 (6.7)	5 (1.1)	3 (3.7)	0 (0.0)	4 (4.6)	1 (1.1)
上腹部痛	30 (6.3)	1 (0.2)	19 (4.0)	1 (0.2)	5 (6.2)	0 (0.0)	2 (2.3)	0 (0.0)
口内乾燥	28 (5.9)	0 (0.0)	8 (1.7)	0 (0.0)	4 (4.9)	0 (0.0)	0 (0.0)	0 (0.0)
便秘	26 (5.5)	0 (0.0)	19 (4.0)	0 (0.0)	7 (8.6)	0 (0.0)	2 (2.3)	0 (0.0)
消化不良	20 (4.2)	0 (0.0)	11 (2.3)	0 (0.0)	1 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)
腹部膨満	15 (3.2)	0 (0.0)	8 (1.7)	0 (0.0)	2 (2.5)	0 (0.0)	3 (3.4)	0 (0.0)
歯肉腫脹	8 (1.7)	0 (0.0)	2 (0.4)	0 (0.0)	1 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)

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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 (%)
歯肉出血	6 (1.3)	0 (0.0)	6 (1.3)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
歯肉痛	6 (1.3)	0 (0.0)	3 (0.6)	0 (0.0)	1 (1.2)	0 (0.0)	1 (1.1)	0 (0.0)
鼓腸	5 (1.1)	0 (0.0)	6 (1.3)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
痔核	4 (0.8)	0 (0.0)	5 (1.1)	1 (0.2)	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)
口腔内潰瘍形成	4 (0.8)	1 (0.2)	3 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
食道静脈瘤出血	4 (0.8)	4 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
歯痛	4 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
口腔内痛	3 (0.6)	0 (0.0)	3 (0.6)	0 (0.0)	1 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)
上部消化管出血	3 (0.6)	2 (0.4)	3 (0.6)	2 (0.4)	2 (2.5)	1 (1.2)	1 (1.1)	0 (0.0)
舌痛	3 (0.6)	0 (0.0)	2 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
口腔内出血	3 (0.6)	0 (0.0)	1 (0.2)	0 (0.0)	2 (2.5)	0 (0.0)	0 (0.0)	0 (0.0)
直腸炎	3 (0.6)	0 (0.0)	1 (0.2)	0 (0.0)	2 (2.5)	0 (0.0)	0 (0.0)	0 (0.0)
おくび	3 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
胃潰瘍	3 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)
歯周病	3 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)
胃炎	2 (0.4)	0 (0.0)	3 (0.6)	1 (0.2)	2 (2.5)	0 (0.0)	0 (0.0)	0 (0.0)
舌炎	2 (0.4)	0 (0.0)	3 (0.6)	0 (0.0)	1 (1.2)	0 (0.0)	2 (2.3)	0 (0.0)
排便回数増加	2 (0.4)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
消化器痛	2 (0.4)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
痔出血	2 (0.4)	0 (0.0)	1 (0.2)	0 (0.0)	2 (2.5)	0 (0.0)	0 (0.0)	0 (0.0)
嚥下痛	2 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
直腸出血	2 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
腹部不快感	1 (0.2)	0 (0.0)	4 (0.8)	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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	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 (%)
胃出血	1 (0.2)	0 (0.0)	2 (0.4)	2 (0.4)	1 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)
胃食道逆流性疾患	1 (0.2)	0 (0.0)	2 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)
食道静脈瘤	1 (0.2)	1 (0.2)	2 (0.4)	1 (0.2)	1 (1.2)	1 (1.2)	0 (0.0)	0 (0.0)
肛門の炎症	1 (0.2)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
出血性十二指腸潰瘍	1 (0.2)	0 (0.0)	1 (0.2)	1 (0.2)	1 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)
嚥下障害	1 (0.2)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
心窩部不快感	1 (0.2)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
軟便	1 (0.2)	0 (0.0)	1 (0.2)	0 (0.0)	1 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)
消化管運動障害	1 (0.2)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
裂肛	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)
口唇のひび割れ	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
十二指腸潰瘍	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
排便障害	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
糞塊	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
歯肉潰瘍	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
口唇痛	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
舌不快感	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
大腸炎	0 (0.0)	0 (0.0)	2 (0.4)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
口唇潰瘍	0 (0.0)	0 (0.0)	2 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
下部消化管出血	0 (0.0)	0 (0.0)	2 (0.4)	2 (0.4)	0 (0.0)	0 (0.0)	2 (2.3)	2 (2.3)
膵炎	0 (0.0)	0 (0.0)	2 (0.4)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
下腹部痛	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
肛門そう痒症	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

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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 (%)
アフタ性潰瘍	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
小腸炎	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
食中毒	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
胃穿孔	0 (0.0)	0 (0.0)	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
びらん性胃炎	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
胃十二指腸炎	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
胃腸出血	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
歯肉びらん	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血便排泄	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
胃酸過多	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
メレナ	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
口腔知覚不全	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
口腔扁平苔癬	0 (0.0)	0 (0.0)	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
口腔粘膜水疱形成	0 (0.0)	0 (0.0)	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
腹膜出血	0 (0.0)	0 (0.0)	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ひだ舌	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
門脈圧亢進性胃障害	0 (0.0)	0 (0.0)	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
レッチング	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
一般・全身障害および投与部位の状態	198 (41.6)	24 (5.0)	163 (34.3)	21 (4.4)	43 (53.1)	1 (1.2)	23 (26.4)	2 (2.3)
疲労	111 (23.3)	10 (2.1)	99 (20.8)	12 (2.5)	12 (14.8)	0 (0.0)	6 (6.9)	2 (2.3)
無力症	36 (7.6)	9 (1.9)	33 (6.9)	7 (1.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
末梢性浮腫	31 (6.5)	1 (0.2)	9 (1.9)	0 (0.0)	18 (22.2)	1 (1.2)	5 (5.7)	0 (0.0)
発熱	28 (5.9)	0 (0.0)	23 (4.8)	1 (0.2)	8 (9.9)	0 (0.0)	9 (10.3)	0 (0.0)

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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 (%)
倦怠感	21 (4.4)	0 (0.0)	6 (1.3)	0 (0.0)	15 (18.5)	0 (0.0)	6 (6.9)	0 (0.0)
悪寒	6 (1.3)	0 (0.0)	2 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
全身性浮腫	3 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	2 (2.5)	0 (0.0)	0 (0.0)	0 (0.0)
肝疾患による浮腫	3 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	3 (3.7)	0 (0.0)	0 (0.0)	0 (0.0)
口渇	2 (0.4)	0 (0.0)	3 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
疼痛	2 (0.4)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
全身健康状態低下	2 (0.4)	2 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
非心臓性胸痛	2 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
乾燥症	2 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
インフルエンザ様疾患	1 (0.2)	0 (0.0)	2 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
胸痛	1 (0.2)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
顔面浮腫	1 (0.2)	0 (0.0)	1 (0.2)	0 (0.0)	1 (1.2)	0 (0.0)	1 (1.1)	0 (0.0)
治癒不良	1 (0.2)	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)
薬物不耐性	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
早期満腹	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
冷感	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
高熱	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
小結節	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
温度変化不耐症	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
顔面痛	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
歩行障害	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
粘膜の炎症	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
活動状態低下	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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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 (%)
突然死	0 (0.0)	0 (0.0)	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
肝胆道系障害	38 (8.0)	23 (4.8)	26 (5.5)	16 (3.4)	10 (12.3)	5 (6.2)	10 (11.5)	7 (8.0)
肝機能異常	8 (1.7)	6 (1.3)	11 (2.3)	8 (1.7)	6 (7.4)	4 (4.9)	10 (11.5)	7 (8.0)
高ビリルビン血症	8 (1.7)	3 (0.6)	5 (1.1)	1 (0.2)	1 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)
肝不全	6 (1.3)	6 (1.3)	3 (0.6)	3 (0.6)	1 (1.2)	1 (1.2)	0 (0.0)	0 (0.0)
門脈血栓症	4 (0.8)	1 (0.2)	2 (0.4)	1 (0.2)	2 (2.5)	1 (1.2)	0 (0.0)	0 (0.0)
黄疸	2 (0.4)	1 (0.2)	2 (0.4)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
胆管炎	2 (0.4)	1 (0.2)	1 (0.2)	1 (0.2)	1 (1.2)	1 (1.2)	0 (0.0)	0 (0.0)
胆嚢炎	2 (0.4)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
肝臓痛	2 (0.4)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
胆汁うっ滞性黄疸	2 (0.4)	2 (0.4)	0 (0.0)	0 (0.0)	1 (1.2)	1 (1.2)	0 (0.0)	0 (0.0)
胆管結石	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	1 (1.2)	1 (1.2)	0 (0.0)	0 (0.0)
後天性胆管拡張症	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血性胆汁	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
肝硬変	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
肝腎症候群	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
肝障害	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)
門脈圧亢進症	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
肝毒性	0 (0.0)	0 (0.0)	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
肝損傷	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
免疫系障害	0 (0.0)	0 (0.0)	3 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)
薬物過敏症	0 (0.0)	0 (0.0)	2 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
季節性アレルギー	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)

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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 (%)
感染症および寄生虫症	36 (7.6)	7 (1.5)	28 (5.9)	5 (1.1)	9 (11.1)	0 (0.0)	8 (9.2)	1 (1.1)
咽頭炎	4 (0.8)	0 (0.0)	2 (0.4)	0 (0.0)	2 (2.5)	0 (0.0)	0 (0.0)	0 (0.0)
毛包炎	3 (0.6)	0 (0.0)	3 (0.6)	0 (0.0)	1 (1.2)	0 (0.0)	2 (2.3)	0 (0.0)
口角口唇炎	3 (0.6)	0 (0.0)	1 (0.2)	0 (0.0)	2 (2.5)	0 (0.0)	1 (1.1)	0 (0.0)
肺炎	2 (0.4)	1 (0.2)	2 (0.4)	1 (0.2)	1 (1.2)	0 (0.0)	1 (1.1)	0 (0.0)
歯肉炎	2 (0.4)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)
鼻咽頭炎	2 (0.4)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
膿疱性皮疹	2 (0.4)	0 (0.0)	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
胃腸炎	2 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	2 (2.5)	0 (0.0)	0 (0.0)	0 (0.0)
口腔カンジダ症	1 (0.2)	0 (0.0)	4 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)
上気道感染	1 (0.2)	0 (0.0)	2 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)
結膜炎	1 (0.2)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
爪囲炎	1 (0.2)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	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)	0 (0.0)	0 (0.0)	1 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)
膀胱炎	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
耳感染	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
細菌性胃腸炎	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
インフルエンザ	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
腎感染	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
肺感染	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
爪感染	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)
術後膿瘍	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
陰嚢感染	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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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 (%)
敗血症	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
副鼻腔炎	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
皮膚感染	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
歯感染	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
気管炎	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
尿路感染	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
蜂巣炎	0 (0.0)	0 (0.0)	2 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
鼻炎	0 (0.0)	0 (0.0)	2 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
気管支炎	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
医療機器関連感染	0 (0.0)	0 (0.0)	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	1 (1.1)	1 (1.1)
眼瞼毛包炎	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
帯状疱疹	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
麦粒腫	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
感染	0 (0.0)	0 (0.0)	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
食道カンジダ症	0 (0.0)	0 (0.0)	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
足部白癬	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)
癜風	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)
傷害、中毒および処置合併症	1 (0.2)	0 (0.0)	3 (0.6)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
サンバーン	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
転倒	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ストーマ部出血	0 (0.0)	0 (0.0)	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
創傷	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
臨床検査	228 (47.9)	92 (19.3)	196 (41.3)	74 (15.6)	47 (58.0)	19 (23.5)	38 (43.7)	20 (23.0)

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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 (%)
体重減少	86 (18.1)	19 (4.0)	66 (13.9)	6 (1.3)	16 (19.8)	4 (4.9)	13 (14.9)	0 (0.0)
血小板数減少	66 (13.9)	21 (4.4)	47 (9.9)	12 (2.5)	23 (28.4)	6 (7.4)	16 (18.4)	9 (10.3)
血中ビリルビン増加	44 (9.2)	14 (2.9)	32 (6.7)	9 (1.9)	8 (9.9)	2 (2.5)	4 (4.6)	1 (1.1)
アスパラギン酸アミノトランスフェラーゼ増加	40 (8.4)	10 (2.1)	53 (11.2)	22 (4.6)	5 (6.2)	2 (2.5)	7 (8.0)	5 (5.7)
好中球数減少	38 (8.0)	13 (2.7)	9 (1.9)	6 (1.3)	10 (12.3)	5 (6.2)	2 (2.3)	1 (1.1)
白血球数減少	36 (7.6)	8 (1.7)	16 (3.4)	6 (1.3)	5 (6.2)	2 (2.5)	4 (4.6)	3 (3.4)
アラニンアミノトランスフェラーゼ増加	33 (6.9)	9 (1.9)	37 (7.8)	11 (2.3)	2 (2.5)	1 (1.2)	5 (5.7)	2 (2.3)
血中甲状腺刺激ホルモン増加	22 (4.6)	0 (0.0)	4 (0.8)	0 (0.0)	7 (8.6)	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	19 (4.0)	13 (2.7)	13 (2.7)	9 (1.9)	2 (2.5)	1 (1.2)	1 (1.1)	1 (1.1)
血中アルカリホスファターゼ増加	18 (3.8)	3 (0.6)	12 (2.5)	1 (0.2)	1 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)
心電図ＱＴ延長	16 (3.4)	1 (0.2)	20 (4.2)	4 (0.8)	3 (3.7)	0 (0.0)	1 (1.1)	0 (0.0)
リパーゼ増加	12 (2.5)	7 (1.5)	16 (3.4)	9 (1.9)	2 (2.5)	2 (2.5)	4 (4.6)	4 (4.6)
血圧上昇	9 (1.9)	1 (0.2)	3 (0.6)	1 (0.2)	1 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)
尿中蛋白陽性	9 (1.9)	1 (0.2)	2 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
リンパ球数減少	8 (1.7)	4 (0.8)	9 (1.9)	5 (1.1)	1 (1.2)	0 (0.0)	3 (3.4)	1 (1.1)
血中アルブミン減少	8 (1.7)	0 (0.0)	5 (1.1)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)
血中乳酸脱水素酵素増加	8 (1.7)	0 (0.0)	5 (1.1)	1 (0.2)	1 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)
Ｃ－反応性蛋白増加	8 (1.7)	0 (0.0)	5 (1.1)	0 (0.0)	1 (1.2)	0 (0.0)	3 (3.4)	0 (0.0)
国際標準比増加	7 (1.5)	0 (0.0)	8 (1.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血中コレステロール増加	6 (1.3)	0 (0.0)	1 (0.2)	0 (0.0)	2 (2.5)	0 (0.0)	0 (0.0)	0 (0.0)

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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 (%)
アミラーゼ増加	5 (1.1)	2 (0.4)	3 (0.6)	1 (0.2)	2 (2.5)	0 (0.0)	0 (0.0)	0 (0.0)
血中クレアチニン増加	5 (1.1)	0 (0.0)	1 (0.2)	0 (0.0)	2 (2.5)	0 (0.0)	1 (1.1)	0 (0.0)
血中尿素増加	4 (0.8)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
プロトロンビン時間延長	3 (0.6)	0 (0.0)	2 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血中甲状腺刺激ホルモン減少	2 (0.4)	0 (0.0)	2 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
赤血球数減少	2 (0.4)	0 (0.0)	2 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
尿中ビリルビン増加	2 (0.4)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
抱合ビリルビン増加	2 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ヘモグロビン増加	2 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
体重増加	2 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)
尿中白血球陽性	2 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血中カルシウム減少	1 (0.2)	0 (0.0)	2 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
尿中ウロビリノーゲン増加	1 (0.2)	0 (0.0)	2 (0.4)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血中カリウム減少	1 (0.2)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血中ナトリウム減少	1 (0.2)	1 (0.2)	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
尿中ブドウ糖陽性	1 (0.2)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
肝酵素上昇	1 (0.2)	1 (0.2)	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
アンモニア増加	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)
血中クレアチニン減少	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
血中フィブリノゲン増加	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
拡張期血圧上昇	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
体温上昇	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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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 (%)
ＥＣＯＧパフォーマンスステータス悪化	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
心電図ＳＴ部分下降	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
心電図異常Ｔ波	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
尿中ブドウ糖	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
国際標準比減少	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
リパーゼ減少	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
リンパ球数増加	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
好中球数増加	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
総蛋白減少	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	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)	0 (0.0)	0 (0.0)	1 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)
トランスアミナーゼ上昇	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
トリヨードチロニン増加	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
トロポニンＴ増加	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	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)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
白血球数増加	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
ヘモグロビン減少	0 (0.0)	0 (0.0)	3 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)
血中クロール減少	0 (0.0)	0 (0.0)	2 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
膵酵素増加	0 (0.0)	0 (0.0)	2 (0.4)	2 (0.4)	0 (0.0)	0 (0.0)	2 (2.3)	2 (2.3)
血中リン減少	0 (0.0)	0 (0.0)	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	1 (1.1)	1 (1.1)
心電図Ｔ波逆転	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
肝機能検査値上昇	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)
遊離トリヨードチロニン増加	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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	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 (%)
代謝および栄養障害	149 (31.3)	33 (6.9)	124 (26.1)	14 (2.9)	47 (58.0)	9 (11.1)	23 (26.4)	3 (3.4)
食欲減退	122 (25.6)	16 (3.4)	100 (21.1)	4 (0.8)	39 (48.1)	6 (7.4)	15 (17.2)	0 (0.0)
低アルブミン血症	21 (4.4)	2 (0.4)	13 (2.7)	0 (0.0)	13 (16.0)	2 (2.5)	5 (5.7)	0 (0.0)
脱水	10 (2.1)	2 (0.4)	2 (0.4)	0 (0.0)	5 (6.2)	1 (1.2)	1 (1.1)	0 (0.0)
低ナトリウム血症	8 (1.7)	8 (1.7)	3 (0.6)	3 (0.6)	2 (2.5)	2 (2.5)	0 (0.0)	0 (0.0)
高アンモニア血症	8 (1.7)	0 (0.0)	2 (0.4)	0 (0.0)	8 (9.9)	0 (0.0)	2 (2.3)	0 (0.0)
高カリウム血症	4 (0.8)	1 (0.2)	3 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)
低マグネシウム血症	3 (0.6)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
低カリウム血症	2 (0.4)	1 (0.2)	10 (2.1)	6 (1.3)	1 (1.2)	0 (0.0)	2 (2.3)	2 (2.3)
低リン酸血症	2 (0.4)	2 (0.4)	5 (1.1)	2 (0.4)	0 (0.0)	0 (0.0)	3 (3.4)	2 (2.3)
高血糖	2 (0.4)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
低カルシウム血症	2 (0.4)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
低血糖	2 (0.4)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
高尿酸血症	1 (0.2)	0 (0.0)	1 (0.2)	0 (0.0)	1 (1.2)	0 (0.0)	1 (1.1)	0 (0.0)
糖尿病性代謝代償不全	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
痛風	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
高脂血症	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
過小食	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
低蛋白血症	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
高アミラーゼ血症	0 (0.0)	0 (0.0)	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	1 (1.1)	1 (1.1)
高コレステロール血症	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
高リパーゼ血症	0 (0.0)	0 (0.0)	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	1 (1.1)	1 (1.1)
高ナトリウム血症	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.

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 (%)
高蛋白血症	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
低クロール血症	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
筋骨格系および結合組織障害	74 (15.5)	1 (0.2)	47 (9.9)	2 (0.4)	10 (12.3)	0 (0.0)	7 (8.0)	0 (0.0)
関節痛	19 (4.0)	0 (0.0)	6 (1.3)	0 (0.0)	4 (4.9)	0 (0.0)	0 (0.0)	0 (0.0)
四肢痛	15 (3.2)	1 (0.2)	11 (2.3)	1 (0.2)	1 (1.2)	0 (0.0)	1 (1.1)	0 (0.0)
筋肉痛	14 (2.9)	0 (0.0)	5 (1.1)	0 (0.0)	3 (3.7)	0 (0.0)	1 (1.1)	0 (0.0)
筋骨格痛	10 (2.1)	0 (0.0)	3 (0.6)	0 (0.0)	1 (1.2)	0 (0.0)	1 (1.1)	0 (0.0)
背部痛	9 (1.9)	0 (0.0)	6 (1.3)	0 (0.0)	1 (1.2)	0 (0.0)	2 (2.3)	0 (0.0)
筋力低下	7 (1.5)	0 (0.0)	3 (0.6)	0 (0.0)	2 (2.5)	0 (0.0)	1 (1.1)	0 (0.0)
頚部痛	4 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
筋痙縮	3 (0.6)	0 (0.0)	8 (1.7)	1 (0.2)	1 (1.2)	0 (0.0)	1 (1.1)	0 (0.0)
側腹部痛	2 (0.4)	0 (0.0)	2 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
骨痛	1 (0.2)	0 (0.0)	2 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
関節腫脹	1 (0.2)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
筋骨格系胸痛	1 (0.2)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
筋緊張	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
筋骨格不快感	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
脊椎痛	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
関節可動域低下	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
筋肉疲労	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
筋骨格硬直	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)
顎痛	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
腱痛	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

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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 (%)
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）	2 (0.4)	1 (0.2)	7 (1.5)	3 (0.6)	2 (2.5)	1 (1.2)	4 (4.6)	1 (1.1)
腫瘍出血	1 (0.2)	1 (0.2)	2 (0.4)	2 (0.4)	1 (1.2)	1 (1.2)	1 (1.1)	1 (1.1)
腫瘍熱	1 (0.2)	0 (0.0)	1 (0.2)	0 (0.0)	1 (1.2)	0 (0.0)	1 (1.1)	0 (0.0)
ケラトアカントーマ	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
悪性腹水	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)
脂漏性角化症	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)
腫瘍壊死	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)
腫瘍破裂	0 (0.0)	0 (0.0)	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
神経系障害	104 (21.8)	18 (3.8)	67 (14.1)	9 (1.9)	21 (25.9)	3 (3.7)	12 (13.8)	1 (1.1)
頭痛	24 (5.0)	1 (0.2)	19 (4.0)	0 (0.0)	1 (1.2)	0 (0.0)	3 (3.4)	0 (0.0)
浮動性めまい	21 (4.4)	0 (0.0)	7 (1.5)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)
味覚異常	19 (4.0)	0 (0.0)	12 (2.5)	0 (0.0)	10 (12.3)	0 (0.0)	6 (6.9)	0 (0.0)
肝性脳症	18 (3.8)	8 (1.7)	3 (0.6)	2 (0.4)	6 (7.4)	2 (2.5)	1 (1.1)	1 (1.1)
末梢性感覚ニューロパチー	4 (0.8)	0 (0.0)	6 (1.3)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
嗜眠	4 (0.8)	0 (0.0)	2 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
傾眠	4 (0.8)	1 (0.2)	2 (0.4)	0 (0.0)	1 (1.2)	0 (0.0)	1 (1.1)	0 (0.0)
脳出血	3 (0.6)	3 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
感覚鈍麻	3 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
錯感覚	2 (0.4)	0 (0.0)	5 (1.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
多発ニューロパチー	2 (0.4)	0 (0.0)	2 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
失語症	2 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
脳梗塞	2 (0.4)	2 (0.4)	0 (0.0)	0 (0.0)	1 (1.2)	1 (1.2)	0 (0.0)	0 (0.0)

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