表 2.7.4-49　日本人集団及び外国人集団の主な感染症の副作用（安全性解析対象集団）

器官別大分類 基本語	日本人集団 （51 例）		外国人集団 [a] （353 例）		全体 （404 例）	
	全 Grade	Grade 3 以上	全 Grade	Grade 3 以上	全 Grade	Grade 3 以上
感染症および寄生虫症	17 (33.3)	2 (3.9)	38 (10.8)	10 (2.8)	55 (13.6)	12 (3.0)
膀胱炎	1 (2.0)	0	1 (0.3)	1 (0.3)	2 (0.5)	1 (0.2)
蓄膿	1 (2.0)	1 (2.0)	0	0	1 (0.2)	1 (0.2)
感染性腸炎	1 (2.0)	0	0	0	1 (0.2)	0
毛包炎	1 (2.0)	0	2 (0.6)	0	3 (0.7)	0
胃腸炎	1 (2.0)	0	0	0	1 (0.2)	0
歯肉炎	1 (2.0)	0	1 (0.3)	0	2 (0.5)	0
帯状疱疹	1 (2.0)	0	1 (0.3)	0	2 (0.5)	0
鼻咽頭炎	6 (11.8)	0	3 (0.8)	0	9 (2.2)	0
急性中耳炎	1 (2.0)	0	0	0	1 (0.2)	0
咽頭炎	1 (2.0)	0	3 (0.8)	2 (0.6)	4 (1.0)	2 (0.5)
肺炎	0	0	5 (1.4)	5 (1.4)	5 (1.2)	5 (1.2)
レンサ球菌感染	1 (2.0)	1 (2.0)	0	0	1 (0.2)	1 (0.2)
上気道感染	6 (11.8)	0	4 (1.1)	1 (0.3)	10 (2.5)	1 (0.2)
尿路感染	1 (2.0)	0	3 (0.8)	0	4 (1.0)	0

MedDRA Version 17.1
数字は例数，(　)内は発現率(%)
いずれかの集団で全 Grade の発現率が 1%以上の副作用を記載
a:　外国 207 試験及び外国 309 試験の本薬群の集計

（付録 2.7.4-5 を引用）

2.7.4.2.1.4.3.4 肝機能障害

悪性軟部腫瘍を対象とした臨床試験における日本人集団と外国人集団（外国 309 試験の本薬群）の肝機能障害の有害事象及び副作用を表 2.7.4-50 及び表 2.7.4-51 に示した。また，日本人集団及び外国人集団（外国 207 試験及び外国 309 試験の本薬群の合計）における ALT，ALP，AST 及び総ビリルビンの TEMAV を表 2.7.4-52 に示した（TEMAV の定義は 2.7.4.3 項参照）。なお，外国 207 試験では，臨床検査に関する事象が有害事象として収集されていなかったため，本項における外国人集団について，有害事象及び副作用発現率は外国 309 試験の本薬群の集計を用い，TEMAV は外国 207 試験及び外国 309 試験の本薬群の集計を用いた。

日本人集団における肝機能障害の有害事象及び副作用発現率はともに 11.8%であった。肝機能障害では，Grade 3 以上の有害事象はみられず，重篤な有害事象及び投与中止に至った有害事象もみられなかった。また，TEMAV について，ALT 7.8%及び AST 3.9%がみられ，ALP 及び総ビリルビンでは TEMAV は認められなかった。

外国人集団における肝機能障害の有害事象及び副作用発現率は，1.8%及び 1.3%であった。Grade 4 の有害事象として肝毒性が 1 例に認められ，本事象は重篤な有害事象であった。なお，Grade 4 の肝毒性が認められた 1 例では Grade 3 の肝毒性も認められており，本事象の治験薬との因果関係は否定されなかった。肝毒性以外に Grade 3 以上の肝機能障害の有害事象及び重篤な有害事象は認められず，投与中止に至った有害事象もみられなかった。TEMAV について，ALT 2.8%，ALP 及び AST 各 1.4%，総ビリルビン 1.1%が認められた。

また，日本人集団及び外国人集団において，Hy's law の基準に合致した被験者は認められなかった。

Hy's law の基準：肝障害を起こさない実対照薬又はプラセボよりも AST，ALT が基準値上限の 3 倍以上上昇し，投与開始時に胆汁うっ滞の所見（ALP の上昇）がないにもかかわらず総ビリルビンが基準値上限の 2 倍を超えて上昇し，これらを説明する他の理由（A，B 又は C 型肝炎ウィルス，既往又は急性の肝臓疾患，肝機能障害を引き起こす可能性のある他

の薬剤等）がみつけられない

表 2.7.4-50　日本人集団及び外国人集団の肝機能障害の有害事象（安全性解析対象集団）

まとめた事象名 基本語 CTCAE Grade	日本人集団 （51 例）	外国人集団 [a] （226 例）	全体 （277 例）
肝機能障害			
全 Grade	6 (11.8)	4 (1.8)	10 (3.6)
Grade 3 以上	0	1 (0.4)	1 (0.4)
Grade 3	0	0	0
Grade 4	0	1 (0.4)	1 (0.4)
Grade 5	0	0	0
トランスアミナーゼ上昇			
全 Grade	0	1 (0.4)	1 (0.4)
Grade 3 以上	0	0	0
黄疸			
全 Grade	0	1 (0.4)	1 (0.4)
Grade 3 以上	0	0	0
黄疸眼			
全 Grade	0	1 (0.4)	1 (0.4)
Grade 3 以上	0	0	0
肝機能異常			
全 Grade	5 (9.8)	0	5 (1.8)
Grade 3 以上	0	0	0
肝機能検査異常			
全 Grade	1 (2.0)	0	1 (0.4)
Grade 3 以上	0	0	0
肝細胞損傷			
全 Grade	0	1 (0.4)	1 (0.4)
Grade 3 以上	0	0	0
肝毒性			
全 Grade	0	1 (0.4)	1 (0.4)
Grade 3 以上	0	1 (0.4)	1 (0.4)
Grade 4	0	1 (0.4)	1 (0.4)

MedDRA Version 17.1
数字は例数，（　）内は発現率(%)
a:　外国 309 試験の本薬群の集計

（付録 2.7.4-20 を引用）

表 2.7.4-51　日本人集団及び外国人集団の肝機能障害の副作用（安全性解析対象集団）

まとめた事象名 基本語 CTCAE Grade	日本人集団 （51 例）	外国人集団 [a] （226 例）	全体 （277 例）
肝機能障害			
全 Grade	6 (11.8)	3 (1.3)	9 (3.2)
Grade 3 以上	0	1 (0.4)	1 (0.4)
Grade 3	0	1 (0.4)	1 (0.4)
Grade 4	0	0	0
Grade 5	0	0	0
トランスアミナーゼ上昇			
全 Grade	0	1 (0.4)	1 (0.4)
Grade 3 以上	0	0	0
黄疸			
全 Grade	0	1 (0.4)	1 (0.4)
Grade 3 以上	0	0	0
肝機能異常			
全 Grade	5 (9.8)	0	5 (1.8)
Grade 3 以上	0	0	0
肝機能検査異常			
全 Grade	1 (2.0)	0	1 (0.4)
Grade 3 以上	0	0	0
肝細胞損傷			
全 Grade	0	1 (0.4)	1 (0.4)
Grade 3 以上	0	0	0
肝毒性			
全 Grade	0	1 (0.4)	1 (0.4)
Grade 3 以上	0	1 (0.4)	1 (0.4)
Grade 3	0	1 (0.4)	1 (0.4)

MedDRA Version 17.1
数字は例数，（　）内は発現率(%)
a:　外国 309 試験の本薬群の集計

（付録 2.7.4-22 を引用）

表 2.7.4-52　日本人集団及び外国人集団における ALT，ALP，AST 及び総ビリルビンの TEMAV（安全性解析対象集団）

	日本人集団 （51 例）	外国人集団 [a] （353 例）	全体 （404 例）
ALT			
異常高値	4/51 (7.8)	10/351 (2.8)	14/402 (3.5)
ALP			
異常高値	0	5/351 (1.4)	5/402 (1.2)
AST			
異常高値	2/51 (3.9)	5/351 (1.4)	7/402 (1.7)
総ビリルビン			
異常高値	0	4/351 (1.1)	4/402 (1.0)

数字は該当例数/解析対象例数，（　）内は解析対象例数に対する割合(%)
ALP = alkaline phosphatase, ALT = alanine aminotransferase, AST = aspartate aminotransferase
a:　外国 207 試験及び外国 309 試験の本薬群の集計

（添付資料 5.3.5.3.2 の Table 6.2 を引用）

2.7.4.2.1.4.3.5 間質性肺炎

悪性軟部腫瘍を対象とした臨床試験における日本人集団と外国人集団（外国 207 試験及び外国 309 試験の本薬群の合計）の間質性肺炎に関する有害事象一覧を表 2.7.4-53 に示した。

日本人集団において，Grade 1 の間質性肺疾患が 1 例に認められ，本事象の因果関係は否定されなかった。本事象発現により本薬の投与を中止し，本薬最終投与から 30 日後の転帰では未回

復であった。なお，本事象は重篤な有害事象に該当しなかった。また，本事象以外に間質性肺炎に関する事象は国内外で認められなかった。

表 2.7.4-53　日本人集団及び外国人集団の間質性肺炎に関する有害事象一覧（安全性解析対象集団）

被験者識別コード	年齢[a] 性別 人種	発現日[b] （発現時用量）	有害事象 MedDRA（基本語） Version 17.1	CTCAE Grade	重篤性	転帰 持続期間	治験薬の処置	治験薬との因果関係
日本人集団								
20062004	5[redacted]歳 女性 Japanese	48 日目 (1.1 mg/m^2)	間質性肺疾患	1	非重篤	未回復 該当せず	投与中止	おそらく 関連あり
外国人集団[c]								
該当被験者なし								

a:　同意取得時の年齢
b:　発現日は投与開始日を 1 日目として起算
c:　外国 207 試験及び外国 309 試験の本薬群の合計

（付録 2.7.4-19，添付資料 5.3.5.2.2 の Table 41 を引用）

2.7.4.2.1.5 器官別又は症候群別有害事象の解析

本項では，MedDRA 器官別大分類別の有害事象を示した。

2.7.4.2.1.5.1 外国 309 試験

外国 309 試験の器官別大分類別の有害事象を表 2.7.4-54 に示した。

本薬群で有害事象発現率が 50%以上であった器官別大分類は，胃腸障害（78.8%），一般・全身障害および投与部位の状態（76.1%），血液およびリンパ系障害（60.6%）であり，本薬群で有害事象発現率が 10%以上であった Grade 3 以上の器官別大分類は，血液およびリンパ系障害（42.9%），臨床検査（15.5%）感染症および寄生虫症（10.2%），代謝および栄養障害（10.2%）であった。

一方，ダカルバジン群で有害事象発現率が 50%以上であった器官別大分類は，胃腸障害（72.3%），一般・全身障害および投与部位の状態（68.3%），血液およびリンパ系障害（55.4%）であり，ダカルバジン群で有害事象発現率が 10%以上であった Grade 3 以上の器官別大分類は，血液およびリンパ系障害（32.1%），臨床検査（13.8%）であった。

表 2.7.4-54　外国 309 試験の器官別大分類別の有害事象（安全性解析対象集団）

器官別大分類	本薬群（226 例）		ダカルバジン群（224 例）	
	全 Grade	Grade 3 以上	全 Grade	Grade 3 以上
有害事象発現例数及び発現率	224 (99.1)	152 (67.3)	218 (97.3)	126 (56.3)
血液およびリンパ系障害	137 (60.6)	97 (42.9)	124 (55.4)	72 (32.1)
心臓障害	14 (6.2)	1 (0.4)	20 (8.9)	3 (1.3)
耳および迷路障害	9 (4.0)	0	5 (2.2)	0
内分泌障害	1 (0.4)	0	0	0
眼障害	28 (12.4)	0	13 (5.8)	0
胃腸障害	178 (78.8)	18 (8.0)	162 (72.3)	21 (9.4)
一般・全身障害および投与部位の状態	172 (76.1)	15 (6.6)	153 (68.3)	16 (7.1)
肝胆道系障害	10 (4.4)	4 (1.8)	7 (3.1)	2 (0.9)
免疫系障害	3 (1.3)	0	2 (0.9)	1 (0.4)
感染症および寄生虫症	98 (43.4)	23 (10.2)	62 (27.7)	11 (4.9)
傷害，中毒および処置合併症	19 (8.4)	4 (1.8)	12 (5.4)	1 (0.4)
臨床検査	80 (35.4)	35 (15.5)	64 (28.6)	31 (13.8)
代謝および栄養障害	83 (36.7)	23 (10.2)	71 (31.7)	16 (7.1)
筋骨格系および結合組織障害	104 (46.0)	7 (3.1)	90 (40.2)	10 (4.5)
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）	19 (8.4)	10 (4.4)	18 (8.0)	6 (2.7)
神経系障害	112 (49.6)	13 (5.8)	75 (33.5)	5 (2.2)
精神障害	48 (21.2)	1 (0.4)	35 (15.6)	0
腎および尿路障害	20 (8.8)	1 (0.4)	17 (7.6)	1 (0.4)
生殖系および乳房障害	10 (4.4)	0	5 (2.2)	0
呼吸器，胸郭および縦隔障害	92 (40.7)	16 (7.1)	75 (33.5)	12 (5.4)
皮膚および皮下組織障害	109 (48.2)	1 (0.4)	45 (20.1)	1 (0.4)
血管障害	35 (15.5)	3 (1.3)	30 (13.4)	8 (3.6)

MedDRA Version 17.1
数字は例数，(　)内は発現率(%)

（付録 2.7.4-1 を引用）

2.7.4.2.1.5.2 日本人集団及び外国人集団

2.7.4.2.1.5.2.1 「血液およびリンパ系障害」及び「臨床検査」以外の器官別大分類

悪性軟部腫瘍を対象とした臨床試験における日本人集団と外国人集団（外国 207 試験及び外国 309 試験の本薬群の合計）の器官別大分類別の有害事象（血液およびリンパ系障害及び臨床検査を除く）を表 2.7.4-55 に示した。

日本人集団で有害事象発現率が 50%以上であった器官別大分類は，一般・全身障害および投与部位の状態（80.4%），胃腸障害（64.7%），代謝および栄養障害（58.8%），神経系障害（56.9%），感染症および寄生虫症（52.9%）であり，日本人集団で有害事象発現率が 10%以上であった Grade 3 以上の器官別大分類は，代謝および栄養障害（19.6%）であった。

外国人集団で有害事象発現率が 50%以上であった器官別大分類は，一般・全身障害および投与部位の状態（77.9%），胃腸障害（77.3%），神経系障害（53.0%）であり，外国人集団で有害事象発現率が 10%以上であった Grade 3 以上の器官別大分類はなかった。

表 2.7.4-55　日本人集団及び外国人集団の器官別大分類別の有害事象（血液およびリンパ系障害及び臨床検査を除く）（安全性解析対象集団）

器官別大分類	日本人集団（51 例）		外国人集団[a]（353 例）		全体（404 例）	
	全 Grade	Grade 3 以上	全 Grade	Grade 3 以上	全 Grade	Grade 3 以上
有害事象発現例数及び発現率	51 (100.0)	49 (96.1)	348 (98.6)	218 (61.8)	399 (98.8)	267 (66.1)
心臓障害	7 (13.7)	1 (2.0)	24 (6.8)	2 (0.6)	31 (7.7)	3 (0.7)
耳および迷路障害	2 (3.9)	0	16 (4.5)	0	18 (4.5)	0
内分泌障害	0	0	1 (0.3)	0	1 (0.2)	0
眼障害	4 (7.8)	1 (2.0)	36 (10.2)	0	40 (9.9)	1 (0.2)
胃腸障害	33 (64.7)	2 (3.9)	273 (77.3)	30 (8.5)	306 (75.7)	32 (7.9)
一般・全身障害および投与部位の状態	41 (80.4)	2 (3.9)	275 (77.9)	34 (9.6)	316 (78.2)	36 (8.9)
肝胆道系障害	6 (11.8)	1 (2.0)	13 (3.7)	6 (1.7)	19 (4.7)	7 (1.7)
免疫系障害	0	0	4 (1.1)	0	4 (1.0)	0
感染症および寄生虫症	27 (52.9)	3 (5.9)	142 (40.2)	33 (9.3)	169 (41.8)	36 (8.9)
傷害，中毒および処置合併症	10 (19.6)	0	24 (6.8)	6 (1.7)	34 (8.4)	6 (1.5)
代謝および栄養障害	30 (58.8)	10 (19.6)	127 (36.0)	29 (8.2)	157 (38.9)	39 (9.7)
筋骨格系および結合組織障害	15 (29.4)	1 (2.0)	169 (47.9)	12 (3.4)	184 (45.5)	13 (3.2)
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）	25 (49.0)	5 (9.8)	70 (19.8)	21 (5.9)	95 (23.5)	26 (6.4)
神経系障害	29 (56.9)	0	187 (53.0)	26 (7.4)	216 (53.5)	26 (6.4)
精神障害	7 (13.7)	1 (2.0)	81 (22.9)	3 (0.8)	88 (21.8)	4 (1.0)
腎および尿路障害	9 (17.6)	1 (2.0)	31 (8.8)	3 (0.8)	40 (9.9)	4 (1.0)
生殖系および乳房障害	1 (2.0)	1 (2.0)	17 (4.8)	0	18 (4.5)	1 (0.2)
呼吸器，胸郭および縦隔障害	22 (43.1)	2 (3.9)	162 (45.9)	27 (7.6)	184 (45.5)	29 (7.2)
皮膚および皮下組織障害	24 (47.1)	0	180 (51.0)	1 (0.3)	204 (50.5)	1 (0.2)
血管障害	7 (13.7)	1 (2.0)	59 (16.7)	6 (1.7)	66 (16.3)	7 (1.7)

MedDRA Version 17.1
数字は例数，( )内は発現率(%)
a:　外国 207 試験及び外国 309 試験の本薬群の集計

（付録 2.7.4-3 を引用）

2.7.4.2.1.5.2.2 「血液およびリンパ系障害」及び「臨床検査」

悪性軟部腫瘍を対象とした臨床試験における日本人集団と外国人集団（外国 309 試験の本薬群）の器官別大分類別の有害事象（血液およびリンパ系障害及び臨床検査）を表 2.7.4-56 に示した。

日本人集団では，血液およびリンパ系障害の有害事象は全ての被験者に認められ，臨床検査の有害事象は 64.7%の被験者に認められた。血液およびリンパ系障害の Grade 3 以上の有害事象は 94.1%の被験者に認められ，臨床検査の Grade 3 以上の有害事象は 9.8%の被験者に認められた。

外国人集団では，血液およびリンパ系障害の有害事象は 60.6%の被験者に認められ，臨床検査の有害事象は 35.4%の被験者に認められた。血液およびリンパ系障害の Grade 3 以上の有害事象は 42.9%の被験者に認められ，臨床検査の Grade 3 以上の有害事象は 15.5%の被験者に認められた。

表 2.7.4-56　日本人集団と外国人集団の器官別大分類別の有害事象（血液およびリンパ系障害，臨床検査）（安全性解析対象集団）

器官別大分類	日本人集団（51 例）		外国人集団[a]（226 例）		全体（277 例）	
	全 Grade	Grade 3 以上	全 Grade	Grade 3 以上	全 Grade	Grade 3 以上
有害事象発現例数及び発現率	51 (100.0)	48 (94.1)	159 (70.4)	115 (50.9)	210 (75.8)	163 (58.8)
血液およびリンパ系障害	51 (100.0)	48 (94.1)	137 (60.6)	97 (42.9)	188 (67.9)	145 (52.3)
臨床検査	33 (64.7)	5 (9.8)	80 (35.4)	35 (15.5)	113 (40.8)	40 (14.4)

MedDRA Version 17.1
数字は例数，(　)内は発現率(%)
a:　外国 309 試験の本薬群の集計

（付録 2.7.4-4 を引用）

2.7.4.2.2 個別有害事象の文章による説明

死亡，その他の重篤な有害事象の叙述は，各試験の総括報告書及び 2.7.6 項に記載した（表 2.7.4-57）。

表 2.7.4-57　死亡，その他の重篤な有害事象の叙述の記載箇所

試験名	添付資料番号	総括報告書等の記載箇所	2.7.6 項の記載箇所
外国 309 試験	5.3.5.1.1	14.3.6 項	付録 2.7.6-3
外国 207 試験	5.3.5.2.1	14.3.3 項	付録 2.7.6-6
国内 217 試験	5.3.5.2.2	14.3.3 項	付録 2.7.6-9

2.7.4.3 臨床検査値の評価

本項では，外国 309 試験並びに日本人集団及び外国人集団における臨床検査項目別の TEMAV を示し，本薬が投与されたときの臨床検査値を評価した。TEMAV は以下のとおり定義した。

- 投与前の測定値の Grade が欠測，0（正常値），1 又は 2 で，投与後の測定値の Grade が 3，4 又は 5 であった場合，あるいは投与前の測定値の Grade が 3 又は 4 で，投与後の測定値の Grade が投与前の Grade よりも悪化した場合

2.7.4.3.1 外国 309 試験

外国 309 試験の臨床検査項目別の TEMAV を表 2.7.4-58 に示した。

外国 309 試験の本薬群で発現率が 10%以上であった TEMAV は，好中球数（低値；42.9%［97/226 例］），白血球数（低値；28.8%［65/226 例］）及びリンパ球数（低値；19.5%［44/226 例］）であった。また，ダカルバジン群で発現率が 10%以上であった TEMAV は，好中球数（低値；21.3%［47/221 例］），血小板数（低値；20.8%［46/221 例］），リンパ球数（低値；19.9%［44/221 例］），白血球数（低値；14.9%［33/221 例］）及びヘモグロビン量（低値；14.5%［32/221 例］）であった。

表 2.7.4-58　外国 309 試験の臨床検査項目別の TEMAV（安全性解析対象集団）

	本薬群 (N=226) n (%)	ダカルバジン群 (N=224) n (%)
ヘモグロビン量		
異常高値	0	0
異常低値	16/226 (7.1)	32/221 (14.5)
白血球数		
異常低値	65/226 (28.8)	33/221 (14.9)
リンパ球数		
異常高値	0	0
異常低値	44/226 (19.5)	44/221 (19.9)
好中球数		
異常低値	97/226 (42.9)	47/221 (21.3)
血小板数		
異常低値	5/226 (2.2)	46/221 (20.8)
ALT		
異常高値	6/225 (2.7)	6/219 (2.7)
アルブミン		
異常低値	2/225 (0.9)	1/219 (0.5)
ALP		
異常高値	5/225 (2.2)	6/219 (2.7)
AST		
異常高値	4/225 (1.8)	2/219 (0.9)
Ca		
異常高値	1/225 (0.4)	5/220 (2.3)
異常低値	11/225 (4.9)	3/220 (1.4)
クレアチニン		
異常高値	0	0
血糖値		
異常高値	4/106 (3.8)	1/100 (1.0)
異常低値	0	0
Mg		
異常高値	0	4/219 (1.8)
異常低値	2/225 (0.9)	1/219 (0.5)
P		
異常低値	8/225 (3.6)	4/219 (1.8)
K		
異常高値	3/225 (1.3)	2/220 (0.9)
異常低値	18/225 (8.0)	6/220 (2.7)
Na		
異常高値	0	0
異常低値	10/225 (4.4)	9/220 (4.1)
総ビリルビン		
異常高値	4/225 (1.8)	1/219 (0.5)

数字は該当例数/解析対象例数，（ ）内は解析対象例数に対する割合(%)
ALP = alkaline phosphatase, ALT = alanine aminotransferase, AST = aspartate aminotransferase, Ca = calcium, K = potassium, Mg = magnesium, Na = sodium, P = phosphorus

（添付資料 5.3.5.3.1 の Table 6.9，Table 6.10 を引用）

2.7.4.3.2 日本人集団及び外国人集団

悪性軟部腫瘍を対象とした臨床試験における日本人集団と外国人集団（外国 207 試験及び外国 309 試験の本薬群の合計）の臨床検査項目別の TEMAV を表 2.7.4-59 に示した。

日本人集団で発現率が 10%以上であった TEMAV は，好中球数（低値；86.3%［44/51 例］），白血球数（低値；74.5%［38/51 例］），リンパ球数（低値；33.3%［17/51 例］）及びヘモグロビン量（低値；15.7%［8/51 例］）であった。また，外国人集団で発現率が 10%以上であった TEMAV は，好中球数（低値；46.3%［163/352 例］），白血球数（低値；30.9%［109/353 例］）及びリンパ球数（低値；21.0%［74/352 例］）であった。発現率の高い TEMAV の項目は同じであったが，その発現率は，外国人集団と比べ日本人集団のほうが高かった。

日本人集団及び外国人集団において TEMAV の発現率が最も高かった好中球数低値に関する詳細な分析は 2.7.4.2.1.4.3.1 項に示した。

表 2.7.4-59　日本人集団及び外国人集団の臨床検査項目別の TEMAV（安全性解析対象集団）

	日本人集団 （51 例）	外国人集団 [a] （353 例）	全体 （404 例）
ヘモグロビン量			
異常高値	0	1/353 (0.3)	1/404 (0.2)
異常低値	8/51 (15.7)	24/353 (6.8)	32/404 (7.9)
白血球数			
異常低値	38/51 (74.5)	109/353 (30.9)	147/404 (36.4)
リンパ球数			
異常高値	0	0	0
異常低値	17/51 (33.3)	74/352 (21.0)	91/403 (22.6)
好中球数			
異常低値	44/51 (86.3)	163/352 (46.3)	207/403 (51.4)
血小板数			
異常低値	0	7/353 (2.0)	7/404 (1.7)
ALT			
異常高値	4/51 (7.8)	10/351 (2.8)	14/402 (3.5)
アルブミン			
異常低値	2/51 (3.9)	7/350 (2.0)	9/401 (2.2)
ALP			
異常高値	0	5/351 (1.4)	5/402 (1.2)
AST			
異常高値	2/51 (3.9)	5/351 (1.4)	7/402 (1.7)
Ca			
異常高値	0	2/348 (0.6)	2/399 (0.5)
異常低値	0	15/348 (4.3)	15/399 (3.8)
クレアチニン			
異常高値	2/51 (3.9)	1/352 (0.3)	3/403 (0.7)
血糖値			
異常高値	3/51 (5.9)	4/106 (3.8)	7/157 (4.5)
異常低値	0	0	0
P			
異常低値	4/51 (7.8)	28/337 (8.3)	32/388 (8.2)
K			
異常高値	1/51 (2.0)	3/352 (0.9)	4/403 (1.0)
異常低値	3/51 (5.9)	25/352 (7.1)	28/403 (6.9)
Na			
異常高値	0	0	0
異常低値	2/51 (3.9)	19/352 (5.4)	21/403 (5.2)
総ビリルビン			
異常高値	0	4/351 (1.1)	4/402 (1.0)

数字は該当例数/解析対象例数，(　)内は解析対象例数に対する割合(%)
Mg は日本人集団（国内 217 試験）で測定していないため算出せず
ALP = alkaline phosphatase, ALT = alanine aminotransferase, AST = aspartate aminotransferase, Ca = calcium, K = potassium, Mg = magnesium, Na = sodium, P = phosphorus
a:　外国 207 試験及び外国 309 試験の本薬群の集計

（添付資料 5.3.5.3.2 の Table 6.1，Table 6.2 を引用）

2.7.4.4 バイタルサイン，身体的所見及び安全性に関連する他の観察項目

2.7.4.4.1 バイタルサイン

外国 309 試験の本薬群では，血圧（収縮期血圧，拡張期血圧），脈拍数の平均値について，臨床的に問題となる変動は認められなかった。

外国 207 試験では，血圧（収縮期血圧，拡張期血圧）及び脈拍数の平均値について，臨床的に問題となる変動は認められなかった。また，Grade 3 又は 4 のバイタルサインに関連する有害事象については，Grade 3 の発熱が 2 例に認められ，Grade 4 となった被験者は認められなかった。

国内 217 試験では，血圧（収縮期血圧，拡張期血圧），脈拍数及び体温の平均値について，臨床的に問題となる変動は認められなかった。Grade 3 又は 4 のバイタルサインに関連する有害事象については，Grade 3 の心不全，発熱，呼吸困難が各 1 例（2.0%）に認められ，Grade 4 となった被験者は認められなかった。ただし，Grade 3 の心不全（1 例）が認められた被験者は，Grade 3 に悪化した 35 日後に死亡した。

2.7.4.4.2 12 誘導心電図

外国 309 試験の本薬群では，投与前からの Fridercia 式による補正 QT 間隔（QTcF）の変化量が 60 msec を超えた被験者は 7 例（6.4%），投与後の QTcF が 501 msec 以上を示した被験者は 2 例（1.8%）であった。本薬群では，心臓障害又は心電図に関連する有害事象として，心電図 QT 延長 15 例（6.6%），頻脈 5 例（2.2%），洞性頻脈 3 例（1.3%），心房細動及び動悸 各 2 例（0.9%），心房粗動，徐脈，右脚ブロック，心嚢液貯留，上室性頻脈，心雑音及び心電図 T 波逆転 各 1 例（0.4%）が認められ，このうち Grade 3 以上は，心電図 QT 延長 5 例（2.2%），心嚢液貯留 1 例（0.4%）であった。

外国 207 試験では，QTcF 延長に関する集計はされていないが，心電図の異常所見から臨床的に問題となる変化は認められなかった。心臓障害又は心電図に関連する有害事象として，洞性頻脈 6 例（4.7%），動悸 2 例（1.6%），狭心症，第一度房室ブロック，心不全，心嚢液貯留及び上室性頻脈 各 1 例（0.8%）が認められ，このうち Grade 3 以上は心嚢液貯留 1 例（0.8%）のみであった。

国内 217 試験では，投与前からの QTcF の変化量が 60 msec を超えた被験者は 3 例（5.9%），投与後の QTcF が 500 msec を超えた被験者が 2 例（3.9%）であった。心臓障害又は心電図に関連する有害事象として，頻脈 3 例（5.9%），動悸 2 例（3.9%），心不全，洞性頻脈，心室性期外収縮及び心電図 QT 延長 各 1 例（2.0%）が認められ，このうち Grade 3 以上は心不全 1 例（2.0%）のみであった。

2.7.4.5 特別な患者集団及び状況下における安全性

2.7.4.5.1 内因性要因

日本人集団及び外国人集団の有害事象及び副作用について，下記の被験者背景の部分集団別に発現率を算出し，本薬の安全性に対する内因性要因の影響を検討した。

- 人種，性別，年齢，体表面積，末梢神経障害の投与前 Grade，ECOG PS，心血管疾患，クレアチニンクリアランス投与前値，ALT 投与前値，AST 投与前値，アルブミン投与前値，ヘモグロビン投与前値，悪性軟部腫瘍の組織型（併合）（脂肪肉腫及び平滑筋肉腫/その他の悪性軟部腫瘍），悪性軟部腫瘍の組織型（脂肪肉腫/平滑筋肉腫/滑膜肉腫/その他の悪性軟部腫瘍）

上記部分集団における，日本人集団及び外国人集団（外国 207 試験及び外国 309 試験の本薬群の合計）の主な有害事象及び副作用を添付資料 5.3.5.3.2 の Table 5.2.3.1.1～Table 5.2.3.1.15 及び Table 5.2.4.1.1～Table 5.2.4.1.15 に示し，日本人集団及び外国人集団（外国 309 試験の本薬群）の血液およびリンパ系障害，臨床検査における主な有害事象及び副作用を添付資料 5.3.5.3.2 の Table 5.2.3.2.1～Table 5.2.3.2.15 及び Table 5.2.4.2.1～Table 5.2.4.2.15 に示した。また，上記部分集団における，日本人集団及び外国人集団（外国 207 試験及び外国 309 試験の本薬群の合計）の特に関心のある有害事象及び副作用を添付資料 5.3.5.3.2 の Table 5.3.1.1～Table 5.3.1.15 及び Table 5.3.3.1～Table 5.3.3.15 に示し，日本人集団及び外国人集団（外国 309 試験の本薬群）の骨

髄抑制及び肝機能障害における特に関心のある有害事象及び副作用を添付資料 5.3.5.3.2 の Table 5.3.2.1～Table 5.3.2.15 及び Table 5.3.4.1～Table 5.3.4.15 に示した。

特に関心のある有害事象のうち，副作用発現率が高かった骨髄抑制（Grade 4 の好中球減少）及び末梢神経障害の発現率について部分集団解析した結果を表 2.7.4-60 に示した。

日本人集団では，被験者数の少ない集団（10 例未満）を除くと，体表面積（m^2）が 1.50 未満の集団は，1.50 以上 1.70 未満の集団と比べ，末梢神経障害の発現率が高く，アルブミン投与前値（g/L）が 30 以上 LLN の 1 倍未満の集団では末梢神経障害が認められなかった。また，その他の悪性軟部腫瘍（脂肪肉腫，平滑筋肉腫及び滑膜肉腫以外）の集団は，末梢神経障害の発現率が他の組織型と比べ低かった。しかし，体表面積（m^2）が 1.50 未満の集団は 12 例，アルブミン投与前値（g/L）が 30 以上 LLN の 1 倍未満の集団は 11 例，その他の悪性軟部腫瘍（脂肪肉腫，平滑筋肉腫及び滑膜肉腫以外）の集団は 13 例と少数例であり，これらの部分集団については明確なことは言えなかった。その他の部分集団の有害事象発現率に大きな違いはなく，日本人集団では本薬の安全性に対する内因性要因の影響は認められないと考えられた。

外国人集団では，被験者数の少ない集団（10 例未満）を除くと，人種が Asian or Pacific Islander の集団は，他の集団と比べ，Grade 4 の好中球減少がやや高く，末梢神経障害の投与前 Grade 1 の集団は，投与前 Grade 0 の集団と比べ，Grade 4 の好中球減少がやや高かった。また，アルブミン投与前値（g/L）が 30 未満の集団は，他の集団と比べ，末梢神経障害の発現率が低かった。しかし，その他の部分集団では有害事象発現率に大きな違いはないため，外国人集団では総じて本薬の安全性に対する内因性要因の影響は認められないと考えられた。

悪性軟部腫瘍の組織型（脂肪肉腫，平滑筋肉腫，滑膜肉腫及びその他の悪性軟部腫瘍）については，組織型別の日本人集団及び外国人集団の主な有害事象を表 2.7.4-61 に示した。

日本人集団及び外国人集団のそれぞれで，組織型別の有害事象発現率は総じて大きく異なることはなく，特記すべき違いは認められなかった。

表 2.7.4-60　被験者背景による有害事象発現率の部分集団解析（安全性解析対象集団）

対象集団		Grade 4 の好中球減少				末梢神経障害			
		日本人集団		外国人集団[a]		日本人集団		外国人集団[b]	
全体		39/51	(76.5)	43/226	(19.0)	19/51	(37.3)	116/353	(32.9)
人種	White	–		28/161	(17.4)	–		46/161	(28.6)
	Black or African American	–		4/6	(66.7)	–		1/6	(16.7)
	Asian or Pacific Islander	39/51	(76.5)	6/19	(31.6)	19/51	(37.3)	5/19	(26.3)
	Other	–		1/6	(16.7)	–		3/6	(50.0)
	Unknown	–		4/34	(11.8)	–		61/161	(37.9)
性別	男性	18/23	(78.3)	14/67	(20.9)	7/23	(30.4)	51/128	(39.8)
	女性	21/28	(75.0)	29/159	(18.2)	12/28	(42.9)	65/225	(28.9)
年齢	65 歳未満	34/45	(75.6)	31/176	(17.6)	18/45	(40.0)	89/269	(33.1)
	65 歳以上	5/6	(83.3)	12/50	(24.0)	1/6	(16.7)	27/84	(32.1)
体表面積（m^2）	1.50 未満	9/12	(75.0)	2/16	(12.5)	6/12	(50.0)	6/24	(25.0)
	1.50 以上 1.70 未満	19/24	(79.2)	12/61	(19.7)	7/24	(29.2)	27/96	(28.1)
	1.70 以上	11/15	(73.3)	29/149	(19.5)	6/15	(40.0)	83/233	(35.6)
末梢神経障害の投与前 Grade[c]	0	29/38	(76.3)	30/186	(16.1)	15/38	(39.5)	59/186	(31.7)
	1	7/10	(70.0)	13/40	(32.5)	2/10	(20.0)	7/40	(17.5)
	2	3/3	(100.0)	–		2/3	(66.7)	–	
ECOG PS[d]	0	21/27	(77.8)	22/110	(20.0)	11/27	(40.7)	63/172	(36.6)
	1	18/24	(75.0)	21/113	(18.6)	8/24	(33.3)	53/177	(29.9)
	2 以上	–		0/3		–		0/4	
心血管疾患	あり	6/8	(75.0)	8/36	(22.2)	0/8		12/46	(26.1)
	なし	33/43	(76.7)	35/190	(18.4)	19/43	(44.2)	104/307	(33.9)
クレアチニンクリアランス投与前値（mL/min）	80 以上	28/39	(71.8)	28/151	(18.5)	15/39	(38.5)	79/227	(34.8)
	50 以上 80 未満	10/11	(90.9)	15/70	(21.4)	3/11	(27.3)	31/109	(28.4)
	50 未満	1/1	(100.0)	0/5		1/1	(100.0)	6/17	(35.3)
ALT 投与前値	ULN の 1 倍以下	34/44	(77.3)	36/194	(18.6)	16/44	(36.4)	101/308	(32.8)
	ULN の 1 倍超～3 倍	5/7	(71.4)	7/32	(21.9)	3/7	(42.9)	15/44	(34.1)
	ULN の 3 倍超	–		–		–		0/1	
AST 投与前値	ULN の 1 倍以下	33/44	(75.0)	38/206	(18.4)	19/44	(43.2)	105/317	(33.1)
	ULN の 1 倍超～3 倍	6/7	(85.7)	5/20	(25.0)	0/7		11/35	(31.4)
	ULN の 3 倍超	–		–		–		0/1	
アルブミン投与前値（g/L）	30 未満	0/1		1/7	(14.3)	0/1		2/16	(12.5)
	30 以上 LLN の 1 倍未満	9/11	(81.8)	3/12	(25.0)	0/11		9/24	(37.5)
	LLN の 1 倍以上 ULN の 1 倍以下	30/39	(76.9)	39/207	(18.8)	19/39	(48.7)	101/304	(33.2)
	ULN の 1 倍超	–		–		–		0/1	
ヘモグロビン投与前値（g/dL）	10 未満	–		3/12	(25.0)	–		6/25	(24.0)
	10 以上	39/51	(76.5)	40/214	(18.7)	19/51	(37.3)	110/328	(33.5)
組織型（併合）	脂肪肉腫/平滑筋肉腫	26/35	(74.3)	43/226	(19.0)	15/35	(42.9)	101/303	(33.3)
	その他の悪性軟部腫瘍	13/16	(81.3)	–		4/16	(25.0)	15/50	(30.0)

数字は該当例数/各部分集団の例数，（ ）内は各部分集団の例数に対する割合(%)，－：該当被験者なし
ALT = alanine aminotransferase, AST = aspartate aminotransferase, ECOG PS = Eastern Cooperative Oncology Group Performance Status, LLN = lower limit of normal, ULN = upper limit of normal, WHO PS = World Health Organization Performance Status
a:　外国 309 試験の本薬群の集計
b:　外国 207 試験及び外国 309 試験の本薬群の集計
c:　外国 207 試験では，末梢神経障害の投与前 Grade を収集しなかったため，各部分集団の例数に含めず
d:　外国 207 試験では，WHO PS スコアをそのまま ECOG PS スコアに置き換えて集計
（付録 2.7.4-19，付録 2.7.4-20，添付資料 5.3.5.3.2 の Table 5.3.1.1～Table 5.3.1.3，Table 5.3.1.5～Table 5.3.1.15，Table 5.3.2.1～Table 5.3.2.3，Table 5.3.2.5～Table 5.3.2.15 を引用）

表 2.7.4-60　被験者背景による有害事象発現率の部分集団解析（安全性解析対象集団）（続き）

対象集団		Grade 4 の好中球減少				末梢神経障害			
		日本人集団		外国人集団 [a]		日本人集団		外国人集団 [b]	
組織型	脂肪肉腫	14/16	(87.5)	13/70	(18.6)	8/16	(50.0)	39/107	(36.4)
	平滑筋肉腫	12/19	(63.2)	30/156	(19.2)	7/19	(36.8)	62/196	(31.6)
	滑膜肉腫	2/3	(66.7)	－		2/3	(66.7)	7/19	(36.8)
	その他の悪性軟部腫瘍	11/13	(84.6)	－		2/13	(15.4)	8/31	(25.8)

数字は該当例数/各部分集団の例数，（　）内は各部分集団の例数に対する割合(%)，－：該当被験者なし
ALT = alanine aminotransferase, AST = aspartate aminotransferase, ECOG PS = Eastern Cooperative Oncology Group Performance Status, LLN = lower limit of normal, ULN = upper limit of normal, WHO PS = World Health Organization Performance Status
a:　外国 309 試験の本薬群の集計
b:　外国 207 試験及び外国 309 試験の本薬群の集計
c:　外国 207 試験では，末梢神経障害の投与前 Grade を収集しなかったため，各部分集団の例数に含めず
d:　外国 207 試験では，WHO PS スコアをそのまま ECOG PS スコアに置き換えて集計
（付録 2.7.4-19，付録 2.7.4-20，添付資料 5.3.5.3.2 の Table 5.3.1.1～Table 5.3.1.3，Table 5.3.1.5～Table 5.3.1.15，Table 5.3.2.1～Table 5.3.2.3，Table 5.3.2.5～Table 5.3.2.15 を引用）

表 2.7.4-61　組織型別の日本人集団及び外国人集団の主な有害事象（安全性解析対象集団）

器官別大分類 基本語	日本人部分集団							
	脂肪肉腫（16 例）		平滑筋肉腫（19 例）		滑膜肉腫（3 例）		その他の悪性軟部腫瘍（13 例）	
	全 Grade	Grade 3 以上	全 Grade	Grade 3 以上	全 Grade	Grade 3 以上	全 Grade	Grade 3 以上
有害事象発現例数及び発現率	16 (100.0)	16 (100.0)	19 (100.0)	17 (89.5)	3 (100.0)	3 (100.0)	13 (100.0)	13 (100.0)
血液およびリンパ系障害	16 (100.0)	16 (100.0)	19 (100.0)	17 (89.5)	3 (100.0)	3 (100.0)	13 (100.0)	12 (92.3)
貧血	9 (56.3)	3 (18.8)	8 (42.1)	1 (5.3)	1 (33.3)	1 (33.3)	6 (46.2)	2 (15.4)
白血球減少症	16 (100.0)	13 (81.3)	19 (100.0)	12 (63.2)	3 (100.0)	3 (100.0)	13 (100.0)	10 (76.9)
リンパ球減少症	15 (93.8)	6 (37.5)	14 (73.7)	7 (36.8)	2 (66.7)	2 (66.7)	9 (69.2)	2 (15.4)
好中球減少症	16 (100.0)	15 (93.8)	19 (100.0)	15 (78.9)	3 (100.0)	3 (100.0)	12 (92.3)	11 (84.6)
胃腸障害	8 (50.0)	1 (6.3)	14 (73.7)	0	2 (66.7)	0	9 (69.2)	1 (7.7)
腹痛	0	0	1 (5.3)	0	0	0	0	0
便秘	5 (31.3)	0	6 (31.6)	0	1 (33.3)	0	4 (30.8)	0
下痢	4 (25.0)	0	3 (15.8)	0	0	0	0	0
悪心	5 (31.3)	0	9 (47.4)	0	1 (33.3)	0	6 (46.2)	0
口内炎	5 (31.3)	0	4 (21.1)	0	2 (66.7)	0	2 (15.4)	0
嘔吐	2 (12.5)	0	1 (5.3)	0	0	0	1 (7.7)	0
一般・全身障害および投与部位の状態	10 (62.5)	2 (12.5)	15 (78.9)	0	3 (100.0)	0	13 (100.0)	0
無力症	0	0	0	0	0	0	0	0
疲労	2 (12.5)	0	3 (15.8)	0	1 (33.3)	0	3 (23.1)	0
倦怠感	2 (12.5)	0	10 (52.6)	0	1 (33.3)	0	7 (53.8)	0
末梢性浮腫	1 (6.3)	0	1 (5.3)	0	1 (33.3)	0	2 (15.4)	0
発熱	7 (43.8)	1 (6.3)	8 (42.1)	0	0	0	6 (46.2)	0
感染症および寄生虫症	12 (75.0)	2 (12.5)	11 (57.9)	0	1 (33.3)	1 (33.3)	3 (23.1)	0
鼻咽頭炎	7 (43.8)	0	3 (15.8)	0	0	0	1 (7.7)	0
上気道感染	5 (31.3)	0	5 (26.3)	0	0	0	1 (7.7)	0
臨床検査	11 (68.8)	2 (12.5)	12 (63.2)	1 (5.3)	3 (100.0)	2 (66.7)	7 (53.8)	0
アラニンアミノトランスフェラーゼ増加	6 (37.5)	1 (6.3)	4 (21.1)	1 (5.3)	2 (66.7)	1 (33.3)	2 (15.4)	0
アスパラギン酸アミノトランスフェラーゼ増加	5 (31.3)	2 (12.5)	5 (26.3)	0	1 (33.3)	0	2 (15.4)	0
血中クレアチンホスホキナーゼ増加	2 (12.5)	0	4 (21.1)	0	2 (66.7)	0	0	0
血中乳酸脱水素酵素増加	1 (6.3)	0	5 (26.3)	0	2 (66.7)	0	3 (23.1)	0
C一反応性蛋白増加	3 (18.8)	0	1 (5.3)	0	0	0	2 (15.4)	0
代謝および栄養障害	11 (68.8)	2 (12.5)	8 (42.1)	3 (15.8)	2 (66.7)	1 (33.3)	9 (69.2)	4 (30.8)
食欲減退	4 (25.0)	0	3 (15.8)	0	1 (33.3)	0	4 (30.8)	0
低アルブミン血症	5 (31.3)	1 (6.3)	1 (5.3)	0	1 (33.3)	0	3 (23.1)	1 (7.7)
低カリウム血症	1 (6.3)	0	2 (10.5)	1 (5.3)	0	0	3 (23.1)	2 (15.4)
低リン酸血症	2 (12.5)	1 (6.3)	1 (5.3)	1 (5.3)	1 (33.3)	0	4 (30.8)	3 (23.1)
筋骨格系および結合組織障害	5 (31.3)	1 (6.3)	6 (31.6)	0	1 (33.3)	0	3 (23.1)	0
背部痛	3 (18.8)	0	2 (10.5)	0	0	0	2 (15.4)	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）	6 (37.5)	0	8 (42.1)	1 (5.3)	0	0	11 (84.6)	4 (30.8)
癌疼痛	6 (37.5)	0	7 (36.8)	0	0	0	10 (76.9)	3 (23.1)
腫瘍疼痛	0	0	0	0	0	0	0	0

MedDRA Version 17.1
数字は例数，（　）内は発現率(%)
日本人集団又は外国人集団で全 Grade の発現率が 10%以上の有害事象を記載
a:　外国 207 試験及び外国 309 試験の本薬群の集計
b:　外国 309 試験の本薬群の集計

（添付資料 5.3.5.3.2 の Table 5.2.3.1.15，Table 5.2.3.2.15 を引用）

表 2.7.4-61　組織型別の日本人集団及び外国人集団の主な有害事象（安全性解析対象集団）（続き）

器官別大分類 基本語	日本人部分集団							
	脂肪肉腫（16 例）		平滑筋肉腫（19 例）		滑膜肉腫（3 例）		その他の悪性軟部腫瘍（13 例）	
	全 Grade	Grade 3 以上	全 Grade	Grade 3 以上	全 Grade	Grade 3 以上	全 Grade	Grade 3 以上
神経系障害	11 (68.8)	0	10 (52.6)	0	2 (66.7)	0	6 (46.2)	0
浮動性めまい	1 (6.3)	0	1 (5.3)	0	0	0	0	0
味覚異常	5 (31.3)	0	5 (26.3)	0	0	0	2 (15.4)	0
頭痛	3 (18.8)	0	1 (5.3)	0	0	0	2 (15.4)	0
末梢性ニューロパチー	7 (43.8)	0	7 (36.8)	0	0	0	2 (15.4)	0
末梢性感覚ニューロパチー	1 (6.3)	0	0	0	2 (66.7)	0	0	0
精神障害	1 (6.3)	0	2 (10.5)	0	0	0	4 (30.8)	1 (7.7)
不眠症	1 (6.3)	0	2 (10.5)	0	0	0	2 (15.4)	0
呼吸器，胸郭および縦隔障害	7 (43.8)	0	7 (36.8)	2 (10.5)	0	0	8 (61.5)	0
咳嗽	2 (12.5)	0	2 (10.5)	0	0	0	2 (15.4)	0
呼吸困難	0	0	2 (10.5)	1 (5.3)	0	0	1 (7.7)	0
皮膚および皮下組織障害	8 (50.0)	0	11 (57.9)	0	2 (66.7)	0	3 (23.1)	0
脱毛症	5 (31.3)	0	6 (31.6)	0	1 (33.3)	0	2 (15.4)	0
発疹	2 (12.5)	0	2 (10.5)	0	1 (33.3)	0	1 (7.7)	0

器官別大分類 基本語	外国人部分集団[a]							
	脂肪肉腫（107 例）		平滑筋肉腫（196 例）		滑膜肉腫（19 例）		その他の悪性軟部腫瘍（31 例）	
	全 Grade	Grade 3 以上	全 Grade	Grade 3 以上	全 Grade	Grade 3 以上	全 Grade	Grade 3 以上
有害事象発現例数及び発現率	106 (99.1)	64 (59.8)	192 (98.0)	127 (64.8)	19 (100.0)	9 (47.4)	31 (100.0)	18 (58.1)
胃腸障害	86 (80.4)	9 (8.4)	153 (78.1)	17 (8.7)	15 (78.9)	2 (10.5)	19 (61.3)	2 (6.5)
腹痛	19 (17.8)	0	28 (14.3)	4 (2.0)	0	0	0	0
便秘	26 (24.3)	0	65 (33.2)	4 (2.0)	6 (31.6)	0	8 (25.8)	0
下痢	22 (20.6)	1 (0.9)	37 (18.9)	0	4 (21.1)	1 (5.3)	5 (16.1)	0
悪心	43 (40.2)	2 (1.9)	76 (38.8)	1 (0.5)	9 (47.4)	0	8 (25.8)	0
口内炎	14 (13.1)	2 (1.9)	31 (15.8)	2 (1.0)	4 (21.1)	1 (5.3)	8 (25.8)	1 (3.2)
嘔吐	24 (22.4)	2 (1.9)	37 (18.9)	3 (1.5)	3 (15.8)	0	5 (16.1)	0
一般・全身障害および投与部位の状態	78 (72.9)	10 (9.3)	158 (80.6)	20 (10.2)	15 (78.9)	3 (15.8)	24 (77.4)	1 (3.2)
無力症	12 (11.2)	2 (1.9)	35 (17.9)	2 (1.0)	0	0	0	0
疲労	54 (50.5)	4 (3.7)	101 (51.5)	13 (6.6)	13 (68.4)	3 (15.8)	20 (64.5)	1 (3.2)
倦怠感	0	0	2 (1.0)	0	0	0	0	0
末梢性浮腫	12 (11.2)	0	30 (15.3)	0	2 (10.5)	0	5 (16.1)	0
発熱	25 (23.4)	0	55 (28.1)	4 (2.0)	6 (31.6)	0	4 (12.9)	0
感染症および寄生虫症	44 (41.1)	12 (11.2)	80 (40.8)	17 (8.7)	6 (31.6)	0	12 (38.7)	4 (12.9)
鼻咽頭炎	5 (4.7)	0	9 (4.6)	0	3 (15.8)	0	3 (9.7)	0
上気道感染	8 (7.5)	1 (0.9)	13 (6.6)	0	0	0	0	0
代謝および栄養障害	37 (34.6)	8 (7.5)	73 (37.2)	18 (9.2)	6 (31.6)	0	11 (35.5)	3 (9.7)
食欲減退	25 (23.4)	1 (0.9)	42 (21.4)	1 (0.5)	6 (31.6)	0	9 (29.0)	0
低アルブミン血症	2 (1.9)	1 (0.9)	10 (5.1)	2 (1.0)	0	0	0	0
低カリウム血症	6 (5.6)	2 (1.9)	17 (8.7)	4 (2.0)	0	0	1 (3.2)	1 (3.2)
低リン酸血症	2 (1.9)	1 (0.9)	4 (2.0)	1 (0.5)	0	0	0	0
筋骨格系および結合組織障害	47 (43.9)	4 (3.7)	93 (47.4)	5 (2.6)	13 (68.4)	0	16 (51.6)	3 (9.7)
背部痛	9 (8.4)	2 (1.9)	27 (13.8)	2 (1.0)	0	0	0	0

MedDRA Version 17.1
数字は例数，（　）内は発現率(%)
日本人集団又は外国人集団で全 Grade の発現率が 10%以上の有害事象を記載
a:　外国 207 試験及び外国 309 試験の本薬群の集計
b:　外国 309 試験の本薬群の集計

（添付資料 5.3.5.3.2 の Table 5.2.3.1.15，Table 5.2.3.2.15 を引用）

表 2.7.4-61　組織型別の日本人集団及び外国人集団の主な有害事象（安全性解析対象集団）（続き）

器官別大分類 基本語	外国人部分集団 [a]							
	脂肪肉腫（107 例）		平滑筋肉腫（196 例）		滑膜肉腫（19 例）		その他の悪性軟部腫瘍（31 例）	
	全 Grade	Grade 3 以上	全 Grade	Grade 3 以上	全 Grade	Grade 3 以上	全 Grade	Grade 3 以上
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）	15 (14.0)	2 (1.9)	25 (12.8)	9 (4.6)	11 (57.9)	1 (5.3)	19 (61.3)	9 (29.0)
癌疼痛	1 (0.9)	0	3 (1.5)	2 (1.0)	0	0	0	0
腫瘍疼痛	11 (10.3)	2 (1.9)	11 (5.6)	0	11 (57.9)	1 (5.3)	16 (51.6)	7 (22.6)
神経系障害	60 (56.1)	8 (7.5)	103 (52.6)	11 (5.6)	8 (42.1)	3 (15.8)	16 (51.6)	4 (12.9)
浮動性めまい	14 (13.1)	0	25 (12.8)	0	1 (5.3)	0	8 (25.8)	1 (3.2)
味覚異常	15 (14.0)	0	16 (8.2)	0	3 (15.8)	0	3 (9.7)	0
頭痛	16 (15.0)	0	40 (20.4)	0	1 (5.3)	0	7 (22.6)	0
末梢性ニューロパチー	0	0	1 (0.5)	0	0	0	0	0
末梢性感覚ニューロパチー	33 (30.8)	4 (3.7)	46 (23.5)	2 (1.0)	7 (36.8)	1 (5.3)	6 (19.4)	1 (3.2)
精神障害	26 (24.3)	1 (0.9)	44 (22.4)	2 (1.0)	4 (21.1)	0	7 (22.6)	0
不眠症	15 (14.0)	1 (0.9)	18 (9.2)	0	0	0	4 (12.9)	0
呼吸器，胸郭および縦隔障害	41 (38.3)	4 (3.7)	91 (46.4)	15 (7.7)	13 (68.4)	5 (26.3)	17 (54.8)	3 (9.7)
咳嗽	11 (10.3)	0	43 (21.9)	0	6 (31.6)	1 (5.3)	9 (29.0)	0
呼吸困難	19 (17.8)	1 (0.9)	38 (19.4)	6 (3.1)	10 (52.6)	3 (15.8)	10 (32.3)	1 (3.2)
皮膚および皮下組織障害	54 (50.5)	0	103 (52.6)	1 (0.5)	11 (57.9)	0	12 (38.7)	0
脱毛症	44 (41.1)	0	75 (38.3)	1 (0.5)	10 (52.6)	0	11 (35.5)	0
発疹	4 (3.7)	0	6 (3.1)	0	0	0	0	0

器官別大分類 基本語	外国人部分集団 [b]							
	脂肪肉腫（70 例）		平滑筋肉腫（156 例）		滑膜肉腫（0 例）		その他の悪性軟部腫瘍（0 例）	
	全 Grade	Grade 3 以上	全 Grade	Grade 3 以上	全 Grade	Grade 3 以上	全 Grade	Grade 3 以上
有害事象発現例数及び発現率	49 (70.0)	33 (47.1)	110 (70.5)	82 (52.6)	–	–	–	–
血液およびリンパ系障害	37 (52.9)	24 (34.3)	100 (64.1)	73 (46.8)	–	–	–	–
貧血	18 (25.7)	4 (5.7)	49 (31.4)	12 (7.7)	–	–	–	–
白血球減少症	11 (15.7)	7 (10.0)	25 (16.0)	16 (10.3)	–	–	–	–
リンパ球減少症	2 (2.9)	2 (2.9)	1 (0.6)	1 (0.6)	–	–	–	–
好中球減少症	27 (38.6)	19 (27.1)	72 (46.2)	61 (39.1)	–	–	–	–
臨床検査	25 (35.7)	12 (17.1)	55 (35.3)	23 (14.7)	–	–	–	–
アラニンアミノトランスフェラーゼ増加	5 (7.1)	1 (1.4)	13 (8.3)	2 (1.3)	–	–	–	–
アスパラギン酸アミノトランスフェラーゼ増加	5 (7.1)	0	16 (10.3)	1 (0.6)	–	–	–	–
血中クレアチンホスホキナーゼ増加	0	0	0	0	–	–	–	–
血中乳酸脱水素酵素増加	1 (1.4)	0	11 (7.1)	0	–	–	–	–
C－反応性蛋白増加	0	0	0	0	–	–	–	–

MedDRA Version 17.1
数字は例数，（ ）内は発現率(%)
日本人集団又は外国人集団で全 Grade の発現率が 10%以上の有害事象を記載
a:　外国 207 試験及び外国 309 試験の本薬群の集計
b:　外国 309 試験の本薬群の集計

（添付資料 5.3.5.3.2 の Table 5.2.3.1.15，Table 5.2.3.2.15 を引用）

2.7.4.5.2 外因性要因

日本人集団及び外国人集団の有害事象及び副作用について，下記の被験者背景の部分集団別に発現率を算出し，本薬の安全性に対する外因性要因の影響を検討した。

· 地理学的地域

地理学的地域の部分集団における，日本人集団及び外国人集団（外国 207 試験及び外国 309 試験の本薬群の合計）の主な有害事象及び副作用を添付資料 5.3.5.3.2 の Table 5.2.3.1.4 及び Table 5.2.4.1.4 に示し，日本人集団及び外国人集団（外国 309 試験の本薬群）の血液およびリンパ系障害，臨床検査における主な有害事象及び副作用を添付資料 5.3.5.3.2 の Table 5.2.3.2.4 及び Table 5.2.4.2.4 に示した。また，地理学的地域の部分集団における，日本人集団及び外国人集団（外国 207 試験及び外国 309 試験の本薬群の合計）の特に関心のある有害事象及び副作用を添付資料 5.3.5.3.2 の Table 5.3.1.4 及び Table 5.3.3.4 に示し，日本人集団及び外国人集団（外国 309 試験の本薬群）の骨髄抑制及び肝機能障害における特に関心のある有害事象及び副作用を添付資料 5.3.5.3.2 の Table 5.3.2.4 及び Table 5.3.4.4 に示した。

特に関心のある有害事象のうち，副作用発現率が高かった骨髄抑制（Grade 4 の好中球減少）及び末梢神経障害の発現率について部分集団解析した結果を表 2.7.4-62 に示した。

日本の Grade 4 の好中球減少の発現率は，他のどの地理学的地域と比べても高かった。末梢神経障害は，地理学的地域別でみても発現率に違いは認められなかった。

表 2.7.4-62　被験者背景による有害事象発現率の部分集団解析（安全性解析対象集団）

		Grade 4 の好中球減少		末梢神経障害	
対象集団		日本人集団	外国人集団 [a]	日本人集団	外国人集団 [b]
全体		39/51 (76.5)	43/226 (19.0)	19/51 (37.3)	116/353 (32.9)
地理学的地域	米国及びカナダ	–	22/86 (25.6)	–	28/86 (32.6)
	西欧，オーストラリア及びイスラエル	–	14/105 (13.3)	–	80/228 (35.1)
	東欧，ラテンアメリカ，南アフリカ及びアジア（日本を除く）	–	7/35 (20.0)	–	8/39 (20.5)
	日本	39/51 (76.5)	–	19/51 (37.3)	–

数字は該当例数/各部分集団の例数，( )内は各部分集団の例数に対する割合(%)，－：該当被験者なし
a:　外国 309 試験の本薬群の集計
b:　外国 207 試験及び外国 309 試験の本薬群の集計
（付録 2.7.4-19，付録 2.7.4-20，添付資料 5.3.5.3.2 の Table 5.3.1.4，Table 5.3.2.4 を引用）

2.7.4.5.3 薬物相互作用

In vitro 試験において，エリブリンは CYP3A4 に対して可逆的な競合阻害作用（Ki：3～17 μmol/L）を示したが，CYP1A2，CYP2C9，CYP2C19，CYP2D6 及び CYP2E1 に対してはほとんど阻害作用を示さなかった。また，ヒト肝細胞において CYP1A，CYP2C9，CYP2C19 及び CYP3A の酵素活性及びタンパク発現量に影響を及ぼさなかった。

外国人固形がん患者 10 例に，本薬と CYP3A の強力な阻害剤であるケトコナゾールを併用投与した結果，エリブリンの薬物動態パラメータはケトコナゾールの影響を受けなかった。

外国人固形がん患者 11 例に，CYP3A の誘導剤であるリファンピシンを反復投与した後に本薬と併用投与した結果，エリブリンの薬物動態パラメータはリファンピシンの影響を受けなかった。

2.7.4.5.4 妊娠及び授乳時の使用

動物実験（ラット）で胚致死作用及び催奇形作用が報告されているため，妊婦又は妊娠している可能性のある婦人には本薬を投与してはいけない。また，安全性が確立していなため，授乳中の婦人に本薬を投与する場合には，授乳を中止させる必要がある。

2.7.4.5.5 過量投与

本薬の過量投与に対する解毒剤は知られていない。国内及び外国第 1 相試験において骨髄抑制に関する用量制限毒性がみられたことから，過量投与の結果として好中球減少症等の血液毒性の発現が懸念される。過量投与が行われた場合には，観察を十分に行い，異常が認められた場合には，対症療法等の適切な処置を行う必要がある。

2.7.4.5.6 薬物乱用

悪性軟部腫瘍患者を対象とした臨床試験において，薬物乱用に関する報告はなかった。

2.7.4.5.7 離脱症状及び反跳現象

国内外において，離脱症状又は反跳現象の検討を目的とした臨床試験は実施していない。

2.7.4.5.8 自動車運転及び機械操作に対する影響又は精神機能の障害

国内外において，自動車運転及び機械操作に対する影響又は精神機能の障害の検討を目的とした臨床試験は実施していない。

2.7.4.6 市販後データ

ハラヴェン静注 1 mg（以下，本剤）は，2011 年 4 月 22 日に国内にて「手術不能又は再発乳癌」の適応で承認された。

本剤の安全性定期報告に基づき，市販後における安全性情報を要約した。

2.7.4.6.1 安全性定期報告

本剤の市販後における安全性情報を要約するため，第 6 回安全性定期報告の調査単位期間である 2013 年 11 月 15 日から 2014 年 11 月 14 日までに集積された使用成績調査の結果及び副作用等の発現状況を以下に記載した。また，本剤が 2010 年 11 月に米国にて初めて承認されて以降，定期的安全性最新報告（PSUR）が発行されおり，当該調査単位期間（2013 年 11 月 15 日から 2014 年 11 月 14 日）を対象とした PSUR の概要も以下に記載した。

なお，末梢神経障害の発現状況及び発現因子の検討を目的とした特定使用成績調査を実施しているが，当該調査単位期間では調査票の回収はなかった。また，当該調査単位期間において，製造販売後臨床試験は実施していなかった。

市販後データとして下記資料を添付した。

- 新医療用医薬品に関する安全性定期報告書（第 6 回 2013 年 11 月 15 日～2014 年 11 月 14 日）（添付資料 5.3.6.1）
- 使用成績調査に関する資料－手術不能又は再発乳癌における安全性及び有効性に関する調査－（添付資料 5.3.6.2）
- 定期的安全性最新報告（PSUR）（第 7 回 2013 年 11 月 15 日～2014 年 11 月 14 日）（添付資料 5.3.6.3）

2.7.4.6.1.1 使用成績調査

本剤が承認されたことにより，未知の副作用や副作用の発現状況等を把握することを目的として，手術不能又は再発乳癌患者を対象とした使用成績調査を実施した。

2011 年 7 月 19 日から使用成績調査を開始し，2013 年 11 月 14 日をデータロックポイントとして，調査を終了した。本調査では，953 例の調査票が回収され，安全性解析対象例数は 951 例であった。

副作用発現率は 88.43%（841/951 例）であり，承認時までの試験の副作用発現率 100.00

（81/81 例）に比べ，低かった。発現した主な副作用は好中球減少症，白血球減少症等を含む「血液およびリンパ系障害」が 77.18%（734/951 例）と最も多く，次いで，悪心，口内炎等を含む「胃腸障害」が 26.60%（253/951 例），末梢性ニューロパチー，味覚異常等を含む「神経系障害」が 23.66%（225/951 例），アスパラギン酸アミノトランスフェラーゼ増加，アラニンアミノトランスフェラーゼ増加等を含む「臨床検査」が 22.82%（217/951 例），発熱，倦怠感等を含む「一般・全身障害および投与部位の状態」が 22.08%（210/951 例）であった。これら副作用の種類は承認時までに認められたものであったが，承認時までの試験での発現率と比較すると，使用成績調査での発現率が低かった。

重篤な副作用は 146 例（事象として 324 件）に発現し，主な内訳は白血球減少症が 5.26%（50/951 例），発熱性好中球減少症が 4.94%（47/951 例），好中球減少症が 4.73%（45/951 例），肺炎が 1.05%（10/951 例），リンパ球減少症が 0.95%（9/951 例），血小板減少症及び口内炎が各 0.84%（8/951 例），発熱が 0.74%（7/951 例），食欲減退が 0.63%（6/951 例），貧血及び間質性肺疾患が各 0.53%（5/951 例）であった。

死亡に至った副作用が 6 例に 8 件認められた。内訳は，肺炎が 2 例，肝転移，間質性肺疾患，肺出血，敗血症，腫瘍崩壊症候群及び播種性血管内凝固が各 1 例であった。

本剤の中止に至った副作用の発現率は 9.78%（93/951 例）であり，主な内訳は好中球減少症，白血球減少症，末梢性ニューロパチー等であった。

本剤の減量，休薬又は延期に至った副作用の発現率は 55.84%（531/951 例）であり，主な内訳は好中球減少症及び白血球減少症であった。

重点調査事項として，骨髄抑制，重篤な感染症，末梢神経障害，肝機能障害及び間質性肺疾患の発現について検討した。

- 骨髄抑制に関する副作用は 737 例に発現した。このうち好中球減少症が 66.56%（633/951 例）及び白血球減少症が 62.36%（593/951 例）と発現率が高かった。
- 重篤な感染症に関する副作用は 18 例に発現した。このうち肺炎が 1.05%（10/951 例）と発現率が最も多く，次いで敗血症が 0.42%（4/951 例）であった。肺炎を発現した 10 例中 2 例，並びに敗血症を発現した 4 例中 1 例で死亡が認められた。
- 末梢神経障害に関する副作用は 174 例に発現した。このうち末梢性ニューロパチーが 16.82%（160/951 例）と最も多く，次いで末梢性感覚ニューロパチーが 1.47%（5/951 例）であった。
- 肝機能障害に関する副作用は 136 例に発現した。主なものはアスパラギン酸アミノトランスフェラーゼ増加が 7.99%（76/951 例）と最も多く，次いで,アラニンアミノトランスフェラーゼ増加が 5.47%（52/951 例）であった。
- 間質性肺疾患の副作用は 7 例に発現した。この 7 例中 4 例が重篤な副作用であった。また 1 例で死亡が認められた。

これら重点調査事項で検討した副作用は，添付文書の「使用上の注意，4. 副作用，(1) 重大な副作用」の項に記載しており，今後も引き続き注意喚起に努めることとした。

2.7.4.6.1.2 副作用等の発現状況

当該調査単位期間（2013 年年 11 月 15 日から 2014 年 11 月 14 日）内に独立行政法人医薬品医療機器総合機構（Pharmaceutical and Medical Devices Agency：PMDA）に報告を行った重篤な副作用は 87 例 118 件であった。なお，当該調査単位期間内において，PMDA に報告すべき感染症の報告はなかった。

2.7.4.6.1.2.1 未知・重篤な副作用

当該調査単位期間内に PMDA に報告した現行の本剤の添付文書「使用上の注意」の記載から予測できない重篤な副作用は 21 例 25 件であった。これらの副作用について，本剤の承認時か

らの累積で 3 件以上が報告されたものは，「播種性血管内凝固」（6 件），「肺炎」（5 件），「心不全」（5 件），「敗血症」（4 件），「間質性肺疾患」（4 件）及び「出血性膀胱炎」（3 件）であった。なお，肺炎及び敗血症などの感染症及び間質性肺炎について，現行の本剤の添付文書「使用上の注意」にて注意喚起を行っているが，報告された事象はいずれも致死的転帰であり，予測できない副作用と判断した。予測できない重篤な副作用が報告されたいずれの症例も，診断根拠が明確でないことや本剤が直接原因となって発症したとの根拠も明確でないものが多く，現時点で措置を実施する必要はないと判断した。

2.7.4.6.1.2.2 既知・重篤な副作用

当該調査単位期間内に PMDA に報告した現行の「使用上の注意」の記載から予測できる重篤な副作用は 71 例 93 件であった。器官別大分類別の内訳は，血液およびリンパ系障害が 38 例 44 件と最も多く，胃腸障害が 10 例 11 件，呼吸器，胸郭および縦隔障害が 10 例 11 件，感染症および寄生虫が 6 例 6 件，一般・全身障害および投与部位の状態が 5 例 5 件，代謝および栄養障害が 4 例 4 件，神経系障害が 3 例 4 件と次いで多く報告した。

これらの副作用は乳癌を対象とした国内臨床第 2 相試験においても重篤な副作用として報告されており，報告の頻度や傾向に大きな違いはみられてないことから，現時点での更なる注意喚起は不要と判断した。

2.7.4.6.1.3 定期的安全性最新報告（PSUR）

PSUR の当該調査単位期間（2013 年 11 月 15 日から 2014 年 11 月 14 日）の終了時点において，本剤は日本を含む 55 ヵ国で承認されていた。期間内に報告された自発報告は 814 例 1234 件であり，重篤な副作用は 163 例 253 件であった。また，2014 年 11 月 14 日までに本剤の臨床試験に登録された被験者は 5711 人であり，約 4129 人に本剤が投与された。5711 人のうち 3758 人が乳癌患者，1953 人が前立腺癌，非小細胞肺癌，軟部肉腫，転移性尿路上皮癌等の患者であった。また，重篤な副作用数は 1678 例 2441 件であった。

当該調査単位期間において企業中核データシート（CCDS）の 4.2 項「Posology and method of administration」に「中等度あるいは高度の腎機能障害患者への初回投与量について考慮すべき」が追加され（2014 年 4 月改訂），国内添付文書では「使用上の注意の慎重投与」に「腎機能障害のある患者」が追記されたが（2014 年 9 月改訂），当該調査単位期間内における副作用の評価では本剤の安全性プロファイルに変更は無く，安全性情報上の改訂は実施されなかった。

2.7.4.7 付録

付録 2.7.4-1　Treatment-Emergent Adverse Events by System Organ Class and Preferred Term – Study 309

付録 2.7.4-2　Treatment-Related Treatment-Emergent Adverse Events by System Organ Class and Preferred Term – Study 309

付録 2.7.4-3　Treatment-Emergent Adverse Events by System Organ Class and Preferred Term – Japanese and Non-Japanese

付録 2.7.4-4　Treatment-Emergent Adverse Events by System Organ Class and Preferred Term /血液およびリンパ系障害，臨床検査 – Japanese and Non-Japanese (Excluding Study 207)

付録 2.7.4-5　Treatment-Related Treatment-Emergent Adverse Events by System Organ Class and Preferred Term – Japanese and Non-Japanese

付録 2.7.4-6　Treatment-Related Treatment-Emergent Adverse Events by System Organ Class and Preferred Term /血液およびリンパ系障害，臨床検査 – Japanese and Non-Japanese (Excluding Study 207)

付録 2.7.4-7 Treatment-Emergent Adverse Events with Outcome of Death by System Organ Class and Preferred Term – Study 309
付録 2.7.4-8 Treatment-Related Treatment-Emergent Adverse Events with Outcome of Death by System Organ Class and Preferred Term – Study 309
付録 2.7.4-9 Treatment-Emergent Adverse Events with Outcome of Death by System Organ Class and Preferred Term – Japanese and Non-Japanese
付録 2.7.4-10 Treatment-Related Treatment-Emergent Adverse Events with Outcome of Death by System Organ Class and Preferred Term – Japanese and Non-Japanese
付録 2.7.4-11 Serious Treatment-Emergent Adverse Events by System Organ Class and Preferred Term – Study 309
付録 2.7.4-12 Treatment-Related Serious Treatment-Emergent Adverse Events by System Organ Class and Preferred Term – Study 309
付録 2.7.4-13 Serious Treatment-Emergent Adverse Events by System Organ Class and Preferred Term – Japanese and Non-Japanese
付録 2.7.4-14 Treatment-Related Serious Treatment-Emergent Adverse Events by System Organ Class and Preferred Term – Japanese and Non-Japanese
付録 2.7.4-15 Treatment-Emergent Adverse Events Leading to Study Drug Withdrawn by System Organ Class and Preferred Term – Study 309
付録 2.7.4-16 Treatment-Emergent Adverse Events Leading to Study Drug Withdrawn by System Organ Class and Preferred Term – Japanese and Non-Japanese (Excluding Study 207)
付録 2.7.4-17 Treatment-Emergent Adverse Events Leading to Drug Action Taken (Drug Withdrawn, Dose Reduction, or Drug Interruption) by System Organ Class and Preferred Term – Study 309
付録 2.7.4-18 Treatment-Emergent Adverse Events Leading to Drug Action Taken (Drug Withdrawn, Dose Reduction, or Drug Interruption) by System Organ Class and Preferred Term – Japanese and Non-Japanese (Excluding Study 207)
付録 2.7.4-19 Treatment-Emergent Adverse Events of Interest Specified in Japan by CTCAE Grade – Japanese and Non-Japanese
付録 2.7.4-20 Treatment-Emergent Adverse Events of Interest Specified in Japan by CTCAE Grade / 骨髄抑制，肝機能障害 – Japanese and Non-Japanese (Excluding Study 207)
付録 2.7.4-21 Treatment-Related Treatment-Emergent Adverse Events of Interest Specified in Japan by CTCAE Grade – Japanese and Non-Japanese
付録 2.7.4-22 Treatment-Related Treatment-Emergent Adverse Events of Interest Specified in Japan by CTCAE Grade /骨髄抑制，肝機能障害 – Japanese and Non-Japanese (Excluding Study 207)

付録 2.7.4-1
Study 309
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Safety Population

	Eribulin Study 309 (N=226)		Dacarbazine Study 309 (N=224)	
MedDRA System Organ Class Preferred Term	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)
Any TEAEs	224 (99.1)	152 (67.3)	218 (97.3)	126 (56.3)
血液およびリンパ系障害	137 (60.6)	97 (42.9)	124 (55.4)	72 (32.1)
貧血	67 (29.6)	16 (7.1)	69 (30.8)	27 (12.1)
発熱性好中球減少症	2 (0.9)	2 (0.9)	3 (1.3)	2 (0.9)
ヘモグロビン血症	3 (1.3)	2 (0.9)	1 (0.4)	0
内出血発生の増加傾向	0	0	1 (0.4)	0
白血球増加症	1 (0.4)	1 (0.4)	0	0
白血球減少症	36 (15.9)	23 (10.2)	23 (10.3)	10 (4.5)
リンパ節痛	1 (0.4)	0	0	0
リンパ節症	1 (0.4)	0	0	0
リンパ球減少症	3 (1.3)	3 (1.3)	6 (2.7)	3 (1.3)
好中球減少症	99 (43.8)	80 (35.4)	53 (23.7)	35 (15.6)
汎血球減少症	0	0	4 (1.8)	3 (1.3)
血小板減少症	13 (5.8)	1 (0.4)	62 (27.7)	34 (15.2)
血小板増加症	1 (0.4)	0	0	0

TEAE = treatment-emergent adverse event, Graded using Common Terminology Criteria for Adverse Events (CTCAE)
A subject with two or more adverse events in the same system organ class (or with the same preferred term) is counted once for that system organ class (or preferred term).
Adverse event terms are coded using Medical Dictionary for Regulatory Activities (MedDRA) version 17.1.

Program: V:¥projects¥e7389¥iss309¥csr¥dev¥pg¥tables¥T_2_7_4_1.sas 18JUN201513:32

付録 2.7.4-1
Study 309
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Safety Population

	Eribulin Study 309 (N=226)		Dacarbazine Study 309 (N=224)	
MedDRA System Organ Class Preferred Term	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)
心臓障害	14 (6.2)	1 (0.4)	20 (8.9)	3 (1.3)
心房細動	2 (0.9)	0	2 (0.9)	1 (0.4)
心房粗動	1 (0.4)	0	0	0
徐脈	1 (0.4)	0	0	0
右脚ブロック	1 (0.4)	0	0	0
心停止	0	0	1 (0.4)	1 (0.4)
うっ血性心不全	0	0	1 (0.4)	0
期外収縮	0	0	1 (0.4)	0
動悸	2 (0.9)	0	0	0
心嚢液貯留	1 (0.4)	1 (0.4)	1 (0.4)	0
洞性頻脈	3 (1.3)	0	7 (3.1)	0
上室性頻脈	1 (0.4)	0	1 (0.4)	0
頻脈	5 (2.2)	0	7 (3.1)	1 (0.4)
耳および迷路障害	9 (4.0)	0	5 (2.2)	0
難聴	1 (0.4)	0	0	0
耳閉	0	0	1 (0.4)	0

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A subject with two or more adverse events in the same system organ class (or with the same preferred term) is counted once for that system organ class (or preferred term).
Adverse event terms are coded using Medical Dictionary for Regulatory Activities (MedDRA) version 17.1.

Program: V:¥projects¥e7389¥iss309¥csr¥dev¥pg¥tables¥T_2_7_4_1.sas 18JUN201513:32

付録 2.7.4-1
Study 309
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Safety Population

	Eribulin Study 309 (N=226)		Dacarbazine Study 309 (N=224)	
MedDRA System Organ Class Preferred Term	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)
耳および迷路障害 (contd)				
耳痛	3 (1.3)	0	1 (0.4)	0
耳鳴	4 (1.8)	0	0	0
回転性めまい	1 (0.4)	0	2 (0.9)	0
前庭障害	0	0	1 (0.4)	0
内分泌障害	1 (0.4)	0	0	0
甲状腺機能低下症	1 (0.4)	0	0	0
眼障害	28 (12.4)	0	13 (5.8)	0
眼精疲労	0	0	1 (0.4)	0
眼瞼炎	2 (0.9)	0	0	0
失明	2 (0.9)	0	0	0
白内障	2 (0.9)	0	0	0
眼乾燥	3 (1.3)	0	0	0
眼刺激	3 (1.3)	0	0	0
眼痛	1 (0.4)	0	0	0

TEAE = treatment-emergent adverse event, Graded using Common Terminology Criteria for Adverse Events (CTCAE)
A subject with two or more adverse events in the same system organ class (or with the same preferred term) is counted once for that system organ class (or preferred term).
Adverse event terms are coded using Medical Dictionary for Regulatory Activities (MedDRA) version 17.1.

Program: V:¥projects¥e7389¥iss309¥csr¥dev¥pg¥tables¥T_2_7_4_1.sas 18JUN201513:32

付録 2.7.4-1
Study 309
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Safety Population

	Eribulin Study 309 (N=226)		Dacarbazine Study 309 (N=224)	
MedDRA System Organ Class Preferred Term	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)
眼障害 (contd)				
眼そう痒症	1 (0.4)	0	0	0
緑内障	0	0	1 (0.4)	0
流涙増加	18 (8.0)	0	1 (0.4)	0
黄斑線維症	0	0	1 (0.4)	0
眼充血	3 (1.3)	0	0	0
黄疸眼	1 (0.4)	0	0	0
霧視	4 (1.8)	0	8 (3.6)	0
視力障害	1 (0.4)	0	1 (0.4)	0
硝子体浮遊物	1 (0.4)	0	0	0
胃腸障害	178 (78.8)	18 (8.0)	162 (72.3)	21 (9.4)
腹部不快感	5 (2.2)	0	4 (1.8)	0
腹部膨満	16 (7.1)	0	12 (5.4)	0
腹痛	45 (19.9)	4 (1.8)	33 (14.7)	8 (3.6)
下腹部痛	0	0	3 (1.3)	0
上腹部痛	19 (8.4)	0	13 (5.8)	1 (0.4)

TEAE = treatment-emergent adverse event, Graded using Common Terminology Criteria for Adverse Events (CTCAE)
A subject with two or more adverse events in the same system organ class (or with the same preferred term) is counted once for that system organ class (or preferred term).
Adverse event terms are coded using Medical Dictionary for Regulatory Activities (MedDRA) version 17.1.

Program: V:¥projects¥e7389¥iss309¥csr¥dev¥pg¥tables¥T_2_7_4_1.sas 18JUN201513:32

付録 2.7.4-1
Study 309
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Safety Population

	Eribulin Study 309 (N=226)		Dacarbazine Study 309 (N=224)	
MedDRA System Organ Class Preferred Term	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)
胃腸障害 (contd)				
異常便	1 (0.4)	0	0	0
後天性巨舌症	1 (0.4)	0	0	0
肛門出血	1 (0.4)	0	0	0
肛門の炎症	0	0	1 (0.4)	0
アフタ性口内炎	3 (1.3)	0	0	0
便秘	71 (31.4)	2 (0.9)	58 (25.9)	1 (0.4)
下痢	38 (16.8)	1 (0.4)	36 (16.1)	2 (0.9)
憩室	0	0	1 (0.4)	1 (0.4)
口内乾燥	12 (5.3)	0	4 (1.8)	0
十二指腸瘻	0	0	1 (0.4)	1 (0.4)
消化不良	18 (8.0)	1 (0.4)	7 (3.1)	1 (0.4)
嚥下障害	3 (1.3)	0	0	0
心窩部不快感	1 (0.4)	0	0	0
便失禁	1 (0.4)	0	0	0
軟便	1 (0.4)	0	0	0
放屁	1 (0.4)	0	2 (0.9)	0

TEAE = treatment-emergent adverse event, Graded using Common Terminology Criteria for Adverse Events (CTCAE)
A subject with two or more adverse events in the same system organ class (or with the same preferred term) is counted once for that system organ class (or preferred term).
Adverse event terms are coded using Medical Dictionary for Regulatory Activities (MedDRA) version 17.1.

Program: V:¥projects¥e7389¥iss309¥csr¥dev¥pg¥tables¥T_2_7_4_1.sas 18JUN201513:32

付録 2.7.4-1
Study 309
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Safety Population

	Eribulin Study 309 (N=226)		Dacarbazine Study 309 (N=224)	
MedDRA System Organ Class Preferred Term	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)
胃腸障害 (contd)				
食中毒	0	0	1 (0.4)	1 (0.4)
排便回数増加	0	0	1 (0.4)	0
機能性胃腸障害	1 (0.4)	0	0	0
胃腸管瘻	1 (0.4)	0	0	0
胃腸出血	1 (0.4)	0	1 (0.4)	1 (0.4)
消化器痛	1 (0.4)	0	0	0
胃腸音異常	0	0	1 (0.4)	0
出血性胃腸潰瘍	0	0	1 (0.4)	1 (0.4)
胃食道逆流性疾患	9 (4.0)	0	4 (1.8)	0
歯肉出血	1 (0.4)	0	3 (1.3)	0
歯肉紅斑	0	0	1 (0.4)	1 (0.4)
歯肉痛	2 (0.9)	0	1 (0.4)	0
歯肉腫脹	1 (0.4)	0	0	0
舌炎	1 (0.4)	0	0	0
吐血	1 (0.4)	0	0	0
血便排泄	0	0	3 (1.3)	0

TEAE = treatment-emergent adverse event, Graded using Common Terminology Criteria for Adverse Events (CTCAE)
A subject with two or more adverse events in the same system organ class (or with the same preferred term) is counted once for that system organ class (or preferred term).
Adverse event terms are coded using Medical Dictionary for Regulatory Activities (MedDRA) version 17.1.

Program: V:¥projects¥e7389¥iss309¥csr¥dev¥pg¥tables¥T_2_7_4_1.sas 18JUN201513:32

付録 2.7.4-1
Study 309
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Safety Population

	Eribulin Study 309 (N=226)		Dacarbazine Study 309 (N=224)	
MedDRA System Organ Class Preferred Term	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)
胃腸障害 (contd)				
血性腹水	1 (0.4)	1 (0.4)	0	0
痔核	2 (0.9)	0	2 (0.9)	0
口の感覚鈍麻	3 (1.3)	0	0	0
イレウス	1 (0.4)	0	0	0
胃排出不全	1 (0.4)	0	0	0
単径ヘルニア	1 (0.4)	0	0	0
腸出血	0	0	1 (0.4)	1 (0.4)
腸管虚血	1 (0.4)	1 (0.4)	0	0
腸閉塞	5 (2.2)	4 (1.8)	5 (2.2)	4 (1.8)
大腸閉塞	0	0	1 (0.4)	1 (0.4)
大腸穿孔	1 (0.4)	1 (0.4)	0	0
口唇痛	1 (0.4)	0	0	0
弛緩歯	1 (0.4)	0	0	0
メレナ	0	0	1 (0.4)	0
口腔内潰瘍形成	3 (1.3)	0	1 (0.4)	0
悪心	91 (40.3)	2 (0.9)	106 (47.3)	1 (0.4)

TEAE = treatment-emergent adverse event, Graded using Common Terminology Criteria for Adverse Events (CTCAE)
A subject with two or more adverse events in the same system organ class (or with the same preferred term) is counted once for that system organ class (or preferred term).
Adverse event terms are coded using Medical Dictionary for Regulatory Activities (MedDRA) version 17.1.

Program: V:¥projects¥e7389¥iss309¥csr¥dev¥pg¥tables¥T_2_7_4_1.sas 18JUN201513:32

付録 2.7.4-1
Study 309
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Safety Population

	Eribulin Study 309 (N=226)		Dacarbazine Study 309 (N=224)	
MedDRA System Organ Class Preferred Term	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)
胃腸障害 (contd)				
嚥下痛	1 (0.4)	0	0	0
食道閉塞症	0	0	1 (0.4)	0
食道炎	1 (0.4)	1 (0.4)	0	0
口腔内分泌物	0	0	1 (0.4)	0
口腔障害	1 (0.4)	0	0	0
口腔知覚不全	1 (0.4)	0	0	0
口腔内痛	2 (0.9)	0	2 (0.9)	0
口の錯感覚	0	0	2 (0.9)	0
直腸出血	3 (1.3)	0	0	0
直腸しぶり	1 (0.4)	0	0	0
レッチング	1 (0.4)	0	0	0
後腹膜出血	1 (0.4)	1 (0.4)	0	0
流涎過多	0	0	1 (0.4)	0
小腸閉塞	3 (1.3)	2 (0.9)	3 (1.3)	2 (0.9)
口内炎	31 (13.7)	2 (0.9)	11 (4.9)	1 (0.4)
亜イレウス	1 (0.4)	1 (0.4)	0	0

TEAE = treatment-emergent adverse event, Graded using Common Terminology Criteria for Adverse Events (CTCAE)
A subject with two or more adverse events in the same system organ class (or with the same preferred term) is counted once for that system organ class (or preferred term).
Adverse event terms are coded using Medical Dictionary for Regulatory Activities (MedDRA) version 17.1.

Program: V:¥projects¥e7389¥iss309¥csr¥dev¥pg¥tables¥T_2_7_4_1.sas 18JUN201513:32

付録 2.7.4-1
Study 309
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Safety Population

	Eribulin Study 309 (N=226)		Dacarbazine Study 309 (N=224)	
MedDRA System Organ Class Preferred Term	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)
胃腸障害 (contd)				
舌腫脹	1 (0.4)	0	0	0
舌の運動障害	1 (0.4)	0	0	0
舌潰瘍	1 (0.4)	0	0	0
歯の脱落	1 (0.4)	0	0	0
歯痛	2 (0.9)	0	0	0
嘔吐	43 (19.0)	2 (0.9)	50 (22.3)	1 (0.4)
一般・全身障害および投与部位の状態	172 (76.1)	15 (6.6)	153 (68.3)	16 (7.1)
適用部位発疹	0	0	1 (0.4)	0
無力症	47 (20.8)	4 (1.8)	51 (22.8)	7 (3.1)
突出痛	0	0	1 (0.4)	1 (0.4)
カテーテル留置部位浮腫	1 (0.4)	0	0	0
カテーテル留置部位疼痛	3 (1.3)	0	1 (0.4)	0
カテーテル留置部位関連反応	0	0	1 (0.4)	0
胸部不快感	2 (0.9)	0	3 (1.3)	0
悪寒	11 (4.9)	0	2 (0.9)	0

TEAE = treatment-emergent adverse event, Graded using Common Terminology Criteria for Adverse Events (CTCAE)
A subject with two or more adverse events in the same system organ class (or with the same preferred term) is counted once for that system organ class (or preferred term).
Adverse event terms are coded using Medical Dictionary for Regulatory Activities (MedDRA) version 17.1.

Program: V:¥projects¥e7389¥iss309¥csr¥dev¥pg¥tables¥T_2_7_4_1.sas 18JUN201513:32

付録 2.7.4-1
Study 309
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Safety Population

	Eribulin Study 309 (N=226)		Dacarbazine Study 309 (N=224)	
MedDRA System Organ Class Preferred Term	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)
一般・全身障害および投与部位の状態 (contd)				
活動性低下	1 (0.4)	0	0	0
医療機器不具合	1 (0.4)	0	0	0
医療機器閉塞	0	0	1 (0.4)	1 (0.4)
早期満腹	0	0	1 (0.4)	0
顔面浮腫	3 (1.3)	0	0	0
疲労	99 (43.8)	7 (3.1)	86 (38.4)	3 (1.3)
歩行障害	4 (1.8)	0	1 (0.4)	1 (0.4)
全身健康状態低下	3 (1.3)	2 (0.9)	1 (0.4)	1 (0.4)
全身性浮腫	2 (0.9)	0	1 (0.4)	0
異常高熱	1 (0.4)	0	0	0
高熱	1 (0.4)	0	1 (0.4)	0
低体温	1 (0.4)	0	1 (0.4)	0
炎症	0	0	1 (0.4)	0
インフルエンザ様疾患	5 (2.2)	0	4 (1.8)	0
注入部位炎症	1 (0.4)	0	0	0
注入部位疼痛	0	0	2 (0.9)	0

TEAE = treatment-emergent adverse event, Graded using Common Terminology Criteria for Adverse Events (CTCAE)
A subject with two or more adverse events in the same system organ class (or with the same preferred term) is counted once for that system organ class (or preferred term).
Adverse event terms are coded using Medical Dictionary for Regulatory Activities (MedDRA) version 17.1.

Program: V:¥projects¥e7389¥iss309¥csr¥dev¥pg¥tables¥T_2_7_4_1.sas 18JUN201513:32

付録 2.7.4-1
Study 309
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Safety Population

	Eribulin Study 309 (N=226)		Dacarbazine Study 309 (N=224)	
MedDRA System Organ Class Preferred Term	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)
一般・全身障害および投与部位の状態 (contd)				
注射部位疼痛	1 (0.4)	0	0	0
注射部位反応	1 (0.4)	0	0	0
局所腫脹	0	0	1 (0.4)	0
倦怠感	2 (0.9)	0	2 (0.9)	0
非心臓性胸痛	5 (2.2)	0	3 (1.3)	1 (0.4)
末梢性浮腫	27 (11.9)	0	17 (7.6)	1 (0.4)
疼痛	0	0	1 (0.4)	0
末梢腫脹	4 (1.8)	0	4 (1.8)	1 (0.4)
発熱	63 (27.9)	2 (0.9)	31 (13.8)	1 (0.4)
肝胆道系障害	10 (4.4)	4 (1.8)	7 (3.1)	2 (0.9)
胆管拡張	1 (0.4)	1 (0.4)	0	0
胆管炎	1 (0.4)	0	1 (0.4)	1 (0.4)
胆嚢炎	1 (0.4)	0	1 (0.4)	1 (0.4)
胆汁うっ滞	0	0	2 (0.9)	0
肝不全	0	0	1 (0.4)	1 (0.4)

TEAE = treatment-emergent adverse event, Graded using Common Terminology Criteria for Adverse Events (CTCAE)
A subject with two or more adverse events in the same system organ class (or with the same preferred term) is counted once for that system organ class (or preferred term).
Adverse event terms are coded using Medical Dictionary for Regulatory Activities (MedDRA) version 17.1.

Program: V:¥projects¥e7389¥iss309¥csr¥dev¥pg¥tables¥T_2_7_4_1.sas 18JUN201513:32

付録 2.7.4-1
Study 309
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Safety Population

	Eribulin Study 309 (N=226)		Dacarbazine Study 309 (N=224)	
MedDRA System Organ Class Preferred Term	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)
肝胆道系障害 (contd)				
肝機能異常	0	0	1 (0.4)	0
肝臓痛	1 (0.4)	0	0	0
肝細胞損傷	1 (0.4)	0	0	0
肝腫大	1 (0.4)	0	0	0
肝毒性	1 (0.4)	1 (0.4)	0	0
高ビリルビン血症	5 (2.2)	3 (1.3)	2 (0.9)	0
黄疸	1 (0.4)	0	1 (0.4)	1 (0.4)
免疫系障害	3 (1.3)	0	2 (0.9)	1 (0.4)
化学物質アレルギー	0	0	1 (0.4)	0
造影剤アレルギー	0	0	1 (0.4)	0
薬物過敏症	2 (0.9)	0	1 (0.4)	1 (0.4)
過敏症	1 (0.4)	0	0	0
感染症および寄生虫症	98 (43.4)	23 (10.2)	62 (27.7)	11 (4.9)
腹部感染	1 (0.4)	0	0	0

TEAE = treatment-emergent adverse event, Graded using Common Terminology Criteria for Adverse Events (CTCAE)
A subject with two or more adverse events in the same system organ class (or with the same preferred term) is counted once for that system organ class (or preferred term).
Adverse event terms are coded using Medical Dictionary for Regulatory Activities (MedDRA) version 17.1.

Program: V:¥projects¥e7389¥iss309¥csr¥dev¥pg¥tables¥T_2_7_4_1.sas 18JUN201513:32

付録 2.7.4-1
Study 309
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Safety Population

	Eribulin Study 309 (N=226)		Dacarbazine Study 309 (N=224)	
MedDRA System Organ Class Preferred Term	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)
感染症および寄生虫症 (contd)				
腹部敗血症	1 (0.4)	0	0	0
細菌性関節炎	1 (0.4)	1 (0.4)	0	0
気管支炎	4 (1.8)	0	5 (2.2)	0
気管支肺炎	1 (0.4)	1 (0.4)	0	0
カンジダ尿	0	0	1 (0.4)	0
カテーテル留置部位蜂巣炎	1 (0.4)	0	0	0
カテーテル留置部位感染	1 (0.4)	1 (0.4)	0	0
蜂巣炎	2 (0.9)	0	2 (0.9)	1 (0.4)
クロストリジウム・ディフィシレ大腸炎	0	0	1 (0.4)	0
結膜炎	2 (0.9)	0	1 (0.4)	0
膀胱炎	1 (0.4)	1 (0.4)	2 (0.9)	0
医療機器関連感染	4 (1.8)	2 (0.9)	2 (0.9)	1 (0.4)
耳感染	3 (1.3)	0	2 (0.9)	0
丹毒	0	0	1 (0.4)	1 (0.4)
毛包炎	2 (0.9)	0	0	0
せつ	1 (0.4)	0	0	0

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Adverse event terms are coded using Medical Dictionary for Regulatory Activities (MedDRA) version 17.1.

Program: V:¥projects¥e7389¥iss309¥csr¥dev¥pg¥tables¥T_2_7_4_1.sas 18JUN201513:32

付録 2.7.4-1
Study 309
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Safety Population

	Eribulin Study 309 (N=226)		Dacarbazine Study 309 (N=224)	
MedDRA System Organ Class Preferred Term	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)
感染症および寄生虫症 (contd)				
胃腸炎	1 (0.4)	0	0	0
ウイルス性胃腸炎	0	0	1 (0.4)	0
尿径部感染	1 (0.4)	0	0	0
単純ヘルペス	0	0	1 (0.4)	0
帯状疱疹	3 (1.3)	0	2 (0.9)	0
感染性皮膚嚢腫	1 (0.4)	0	0	0
感染	2 (0.9)	0	2 (0.9)	1 (0.4)
インフルエンザ	6 (2.7)	0	2 (0.9)	0
迷路炎	0	0	1 (0.4)	0
肝膿瘍	1 (0.4)	0	0	0
限局性感染	1 (0.4)	0	0	0
下気道感染	1 (0.4)	0	1 (0.4)	0
真菌性下気道感染	1 (0.4)	1 (0.4)	0	0
肺感染	2 (0.9)	1 (0.4)	0	0
鼻咽頭炎	8 (3.5)	0	6 (2.7)	0
好中球減少性敗血症	1 (0.4)	1 (0.4)	0	0

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A subject with two or more adverse events in the same system organ class (or with the same preferred term) is counted once for that system organ class (or preferred term).
Adverse event terms are coded using Medical Dictionary for Regulatory Activities (MedDRA) version 17.1.

Program: V:¥projects¥e7389¥iss309¥csr¥dev¥pg¥tables¥T_2_7_4_1.sas 18JUN201513:32

付録 2.7.4-1
Study 309
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Safety Population

	Eribulin Study 309 (N=226)		Dacarbazine Study 309 (N=224)	
MedDRA System Organ Class Preferred Term	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)
感染症および寄生虫症 (contd)				
口腔細菌感染	1 (0.4)	0	0	0
口腔カンジダ症	5 (2.2)	0	2 (0.9)	0
口腔真菌感染	0	0	2 (0.9)	1 (0.4)
口腔ヘルペス	0	0	2 (0.9)	0
眼窩感染	1 (0.4)	0	0	0
外耳炎	0	0	1 (0.4)	0
腹膜炎	2 (0.9)	1 (0.4)	0	0
細菌性腹膜炎	2 (0.9)	2 (0.9)	0	0
咽頭炎	4 (1.8)	1 (0.4)	3 (1.3)	0
肺炎	8 (3.5)	4 (1.8)	3 (1.3)	3 (1.3)
術後創感染	0	0	1 (0.4)	0
シュードモナス性菌血症	1 (0.4)	1 (0.4)	0	0
腎盂腎炎	1 (0.4)	1 (0.4)	0	0
気道感染	1 (0.4)	0	2 (0.9)	1 (0.4)
鼻炎	4 (1.8)	0	2 (0.9)	0
敗血症	1 (0.4)	0	0	0

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A subject with two or more adverse events in the same system organ class (or with the same preferred term) is counted once for that system organ class (or preferred term).
Adverse event terms are coded using Medical Dictionary for Regulatory Activities (MedDRA) version 17.1.

Program: V:¥projects¥e7389¥iss309¥csr¥dev¥pg¥tables¥T_2_7_4_1.sas 18JUN201513:32

付録 2.7.4-1
Study 309
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Safety Population

	Eribulin Study 309 (N=226)		Dacarbazine Study 309 (N=224)	
MedDRA System Organ Class Preferred Term	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)
感染症および寄生虫症 (contd)				
敗血症性ショック	1 (0.4)	1 (0.4)	0	0
セラチア性菌血症	1 (0.4)	1 (0.4)	0	0
副鼻腔炎	3 (1.3)	0	0	0
軟部組織感染	1 (0.4)	0	0	0
ブドウ球菌性菌血症	1 (0.4)	1 (0.4)	0	0
ブドウ球菌感染	1 (0.4)	1 (0.4)	0	0
白癬感染	1 (0.4)	0	0	0
歯膿瘍	0	0	1 (0.4)	0
気管炎	0	0	1 (0.4)	0
上気道感染	20 (8.8)	1 (0.4)	9 (4.0)	0
尿路感染	25 (11.1)	5 (2.2)	12 (5.4)	1 (0.4)
尿路性敗血症	1 (0.4)	0	0	0
前庭神経炎	0	0	1 (0.4)	1 (0.4)
ウイルス性上気道感染	1 (0.4)	0	0	0
外陰腟真菌感染	1 (0.4)	0	1 (0.4)	0
創傷感染	0	0	1 (0.4)	0

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Program: V:¥projects¥e7389¥iss309¥csr¥dev¥pg¥tables¥T_2_7_4_1.sas 18JUN201513:32

付録 2.7.4-1
Study 309
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Safety Population

	Eribulin Study 309 (N=226)		Dacarbazine Study 309 (N=224)	
MedDRA System Organ Class Preferred Term	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)
傷害、中毒および処置合併症	19 (8.4)	4 (1.8)	12 (5.4)	1 (0.4)
投与に伴う反応	0	0	2 (0.9)	0
足関節部骨折	0	0	1 (0.4)	0
挫傷	1 (0.4)	0	1 (0.4)	0
焼痂	1 (0.4)	0	0	0
転倒	4 (1.8)	0	2 (0.9)	0
上腕骨骨折	1 (0.4)	1 (0.4)	0	0
切開部位紅斑	1 (0.4)	0	0	0
切開部位痛	1 (0.4)	0	0	0
注入に伴う反応	2 (0.9)	0	0	0
関節損傷	1 (0.4)	0	0	0
裂傷	1 (0.4)	0	0	0
靭帯捻挫	2 (0.9)	0	0	0
眼窩周囲出血	1 (0.4)	0	0	0
処置後出血	1 (0.4)	1 (0.4)	0	0
処置による出血	1 (0.4)	0	0	0
処置による疼痛	3 (1.3)	1 (0.4)	0	0

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Adverse event terms are coded using Medical Dictionary for Regulatory Activities (MedDRA) version 17.1.

Program: V:¥projects¥e7389¥iss309¥csr¥dev¥pg¥tables¥T_2_7_4_1.sas 18JUN201513:32

付録 2.7.4-1
Study 309
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Safety Population

	Eribulin Study 309 (N=226)		Dacarbazine Study 309 (N=224)	
MedDRA System Organ Class Preferred Term	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)
傷害、中毒および処置合併症 (contd)				
放射線性肺臓炎	1 (0.4)	1 (0.4)	0	0
脊椎圧迫骨折	0	0	1 (0.4)	1 (0.4)
ストーマ部疼痛	0	0	1 (0.4)	0
サンバーン	0	0	1 (0.4)	0
舌損傷	1 (0.4)	0	0	0
各種物質毒性	0	0	1 (0.4)	0
輸血反応	0	0	1 (0.4)	0
創傷	2 (0.9)	0	0	0
創離開	1 (0.4)	1 (0.4)	1 (0.4)	0
創部内臓脱出	1 (0.4)	0	0	0
誤薬投与	0	0	1 (0.4)	0
臨床検査	80 (35.4)	35 (15.5)	64 (28.6)	31 (13.8)
アラニンアミノトランスフェラーゼ増加	18 (8.0)	3 (1.3)	9 (4.0)	4 (1.8)
アスパラギン酸アミノトランスフェラーゼ増加	21 (9.3)	1 (0.4)	6 (2.7)	2 (0.9)
血中アルブミン減少	1 (0.4)	0	0	0

TEAE = treatment-emergent adverse event, Graded using Common Terminology Criteria for Adverse Events (CTCAE)
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Program: V:¥projects¥e7389¥iss309¥csr¥dev¥pg¥tables¥T_2_7_4_1.sas 18JUN201513:32

付録 2.7.4-1
Study 309
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Safety Population

	Eribulin Study 309 (N=226)		Dacarbazine Study 309 (N=224)	
MedDRA System Organ Class Preferred Term	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)
臨床検査 (contd)				
血中アルカリホスファターゼ増加	10 (4.4)	1 (0.4)	11 (4.9)	2 (0.9)
血中ビリルビン増加	1 (0.4)	1 (0.4)	2 (0.9)	0
血中カルシウム減少	1 (0.4)	0	0	0
血中クレアチニン増加	5 (2.2)	0	3 (1.3)	0
血中ブドウ糖増加	0	0	1 (0.4)	0
血中乳酸脱水素酵素増加	12 (5.3)	0	7 (3.1)	0
血中マグネシウム減少	1 (0.4)	0	0	0
血中リン減少	0	0	1 (0.4)	0
血中カリウム減少	1 (0.4)	1 (0.4)	0	0
血圧上昇	0	0	1 (0.4)	0
血中尿素増加	1 (0.4)	0	0	0
心雑音	1 (0.4)	0	0	0
腎クレアチニン・クリアランス減少	1 (0.4)	0	0	0
心電図ＱＴ延長	15 (6.6)	5 (2.2)	11 (4.9)	3 (1.3)
心電図Ｔ波逆転	1 (0.4)	0	0	0
γ－グルタミルトランスフェラーゼ増加	5 (2.2)	3 (1.3)	2 (0.9)	2 (0.9)

TEAE = treatment-emergent adverse event, Graded using Common Terminology Criteria for Adverse Events (CTCAE)
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Adverse event terms are coded using Medical Dictionary for Regulatory Activities (MedDRA) version 17.1.

Program: V:¥projects¥e7389¥iss309¥csr¥dev¥pg¥tables¥T_2_7_4_1.sas 18JUN201513:32

付録 2.7.4-1
Study 309
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Safety Population

	Eribulin Study 309 (N=226)		Dacarbazine Study 309 (N=224)	
MedDRA System Organ Class Preferred Term	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)
臨床検査 (contd)				
グリコヘモグロビン増加	1 (0.4)	0	0	0
ヘマトクリット減少	1 (0.4)	0	1 (0.4)	0
ヘモグロビン減少	7 (3.1)	0	3 (1.3)	3 (1.3)
心拍数増加	0	0	1 (0.4)	0
国際標準比増加	3 (1.3)	1 (0.4)	0	0
リパーゼ増加	1 (0.4)	1 (0.4)	0	0
リンパ球数減少	3 (1.3)	0	10 (4.5)	4 (1.8)
好中球数減少	19 (8.4)	16 (7.1)	12 (5.4)	6 (2.7)
便潜血陽性	0	0	1 (0.4)	0
血小板数減少	2 (0.9)	2 (0.9)	17 (7.6)	7 (3.1)
総蛋白減少	2 (0.9)	0	0	0
赤血球数減少	2 (0.9)	0	1 (0.4)	0
トランスアミナーゼ上昇	1 (0.4)	0	1 (0.4)	0
尿中ケトン体陽性	1 (0.4)	0	0	0
体重減少	7 (3.1)	0	8 (3.6)	0
体重増加	2 (0.9)	0	0	0

TEAE = treatment-emergent adverse event, Graded using Common Terminology Criteria for Adverse Events (CTCAE)
A subject with two or more adverse events in the same system organ class (or with the same preferred term) is counted once for that system organ class (or preferred term).
Adverse event terms are coded using Medical Dictionary for Regulatory Activities (MedDRA) version 17.1.

Program: V:¥projects¥e7389¥iss309¥csr¥dev¥pg¥tables¥T_2_7_4_1.sas 18JUN201513:32

付録 2.7.4-1
Study 309
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Safety Population

	Eribulin Study 309 (N=226)		Dacarbazine Study 309 (N=224)	
MedDRA System Organ Class Preferred Term	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)
臨床検査 (contd)				
白血球数減少	16 (7.1)	8 (3.5)	15 (6.7)	8 (3.6)
白血球数増加	0	0	1 (0.4)	1 (0.4)
尿中白血球陽性	1 (0.4)	0	0	0
代謝および栄養障害	83 (36.7)	23 (10.2)	71 (31.7)	16 (7.1)
悪液質	1 (0.4)	0	0	0
食欲減退	43 (19.0)	1 (0.4)	43 (19.2)	2 (0.9)
脱水	6 (2.7)	0	8 (3.6)	2 (0.9)
糖尿病	1 (0.4)	0	0	0
食物不耐性	1 (0.4)	0	0	0
高カルシウム血症	1 (0.4)	0	1 (0.4)	0
高コレステロール血症	0	0	1 (0.4)	0
高クレアチニン血症	1 (0.4)	0	1 (0.4)	0
高血糖	17 (7.5)	7 (3.1)	6 (2.7)	3 (1.3)
高カリウム血症	1 (0.4)	0	3 (1.3)	1 (0.4)
高脂血症	1 (0.4)	0	0	0

TEAE = treatment-emergent adverse event, Graded using Common Terminology Criteria for Adverse Events (CTCAE)
A subject with two or more adverse events in the same system organ class (or with the same preferred term) is counted once for that system organ class (or preferred term).
Adverse event terms are coded using Medical Dictionary for Regulatory Activities (MedDRA) version 17.1.

Program: V:¥projects¥e7389¥iss309¥csr¥dev¥pg¥tables¥T_2_7_4_1.sas 18JUN201513:32

付録 2.7.4-1
Study 309
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Safety Population

	Eribulin Study 309 (N=226)		Dacarbazine Study 309 (N=224)	
MedDRA System Organ Class Preferred Term	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)
代謝および栄養障害 (contd)				
高マグネシウム血症	1 (0.4)	0	1 (0.4)	0
高ナトリウム血症	0	0	1 (0.4)	0
高尿酸血症	1 (0.4)	0	1 (0.4)	0
低アルブミン血症	11 (4.9)	2 (0.9)	7 (3.1)	1 (0.4)
低カルシウム血症	10 (4.4)	3 (1.3)	10 (4.5)	0
低血糖症	2 (0.9)	0	2 (0.9)	0
低カリウム血症	23 (10.2)	6 (2.7)	9 (4.0)	4 (1.8)
低マグネシウム血症	7 (3.1)	1 (0.4)	3 (1.3)	0
低ナトリウム血症	6 (2.7)	4 (1.8)	8 (3.6)	4 (1.8)
低リン酸血症	6 (2.7)	2 (0.9)	4 (1.8)	1 (0.4)
鉄欠乏	1 (0.4)	0	1 (0.4)	0
乳酸アシドーシス	1 (0.4)	0	0	0
栄養障害	1 (0.4)	0	0	0
代謝性アシドーシス	1 (0.4)	0	0	0
筋骨格系および結合組織障害	104 (46.0)	7 (3.1)	90 (40.2)	10 (4.5)

TEAE = treatment-emergent adverse event, Graded using Common Terminology Criteria for Adverse Events (CTCAE)
A subject with two or more adverse events in the same system organ class (or with the same preferred term) is counted once for that system organ class (or preferred term).
Adverse event terms are coded using Medical Dictionary for Regulatory Activities (MedDRA) version 17.1.

Program: V:¥projects¥e7389¥iss309¥csr¥dev¥pg¥tables¥T_2_7_4_1.sas 18JUN201513:32

付録 2.7.4-1
Study 309
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Safety Population

	Eribulin Study 309 (N=226)		Dacarbazine Study 309 (N=224)	
MedDRA System Organ Class Preferred Term	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)
筋骨格系および結合組織障害 (contd)				
関節痛	19 (8.4)	0	13 (5.8)	0
関節炎	1 (0.4)	0	0	0
背部痛	35 (15.5)	4 (1.8)	31 (13.8)	3 (1.3)
骨痛	3 (1.3)	0	11 (4.9)	1 (0.4)
側腹部痛	4 (1.8)	0	4 (1.8)	0
肢径部痛	3 (1.3)	0	1 (0.4)	0
顎障害	1 (0.4)	0	0	0
関節腫脹	2 (0.9)	0	1 (0.4)	0
四肢不快感	1 (0.4)	0	1 (0.4)	0
咀嚼障害	1 (0.4)	0	0	0
筋肉疲労	1 (0.4)	0	0	0
筋痙縮	13 (5.8)	0	7 (3.1)	0
筋力低下	7 (3.1)	0	3 (1.3)	1 (0.4)
筋骨格系胸痛	11 (4.9)	0	6 (2.7)	1 (0.4)
筋骨格不快感	2 (0.9)	0	1 (0.4)	0
筋骨格痛	12 (5.3)	0	11 (4.9)	3 (1.3)

TEAE = treatment-emergent adverse event, Graded using Common Terminology Criteria for Adverse Events (CTCAE)
A subject with two or more adverse events in the same system organ class (or with the same preferred term) is counted once for that system organ class (or preferred term).
Adverse event terms are coded using Medical Dictionary for Regulatory Activities (MedDRA) version 17.1.

Program: V:¥projects¥e7389¥iss309¥csr¥dev¥pg¥tables¥T_2_7_4_1.sas 18JUN201513:32

付録 2.7.4-1
Study 309
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Safety Population

	Eribulin Study 309 (N=226)		Dacarbazine Study 309 (N=224)	
MedDRA System Organ Class Preferred Term	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)
筋骨格系および結合組織障害 (contd)				
筋骨格硬直	2 (0.9)	0	0	0
筋肉痛	23 (10.2)	0	17 (7.6)	0
ミオパチー	1 (0.4)	0	0	0
頚部痛	4 (1.8)	0	1 (0.4)	0
四肢痛	20 (8.8)	0	18 (8.0)	2 (0.9)
顎痛	2 (0.9)	0	0	0
病的骨折	2 (0.9)	2 (0.9)	1 (0.4)	1 (0.4)
肩回旋筋腱板症候群	2 (0.9)	0	0	0
軟部組織腫瘤	0	0	1 (0.4)	0
脊椎痛	1 (0.4)	1 (0.4)	2 (0.9)	1 (0.4)
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）	19 (8.4)	10 (4.4)	18 (8.0)	6 (2.7)
基底細胞癌	1 (0.4)	0	0	0
癌疼痛	4 (1.8)	2 (0.9)	1 (0.4)	0
頭蓋内腫瘍出血	0	0	1 (0.4)	1 (0.4)
平滑筋肉腫	0	0	1 (0.4)	1 (0.4)

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Program: V:¥projects¥e7389¥iss309¥csr¥dev¥pg¥tables¥T_2_7_4_1.sas 18JUN201513:32

付録 2.7.4-1
Study 309
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Safety Population

	Eribulin Study 309 (N=226)		Dacarbazine Study 309 (N=224)	
MedDRA System Organ Class Preferred Term	All Grades n(%)	Grade >= 3 n(%)	All Grades 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） (contd)				
悪性腹水	0	0	3 (1.3)	1 (0.4)
悪性新生物進行	2 (0.9)	1 (0.4)	0	0
悪性胸水	2 (0.9)	0	4 (1.8)	1 (0.4)
腹腔内転移	1 (0.4)	1 (0.4)	0	0
骨転移	1 (0.4)	1 (0.4)	0	0
肺転移	1 (0.4)	1 (0.4)	1 (0.4)	1 (0.4)
頚部転移	1 (0.4)	1 (0.4)	0	0
転移	0	0	1 (0.4)	0
転移部痛	2 (0.9)	1 (0.4)	2 (0.9)	0
骨髄異形成症候群	0	0	1 (0.4)	0
粘液型脂肪肉腫	1 (0.4)	0	0	0
腫瘍熱	1 (0.4)	0	0	0
腫瘍出血	1 (0.4)	1 (0.4)	1 (0.4)	0
腫瘍疼痛	1 (0.4)	1 (0.4)	5 (2.2)	1 (0.4)
腫瘍の潰瘍形成	1 (0.4)	1 (0.4)	0	0

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Program: V:¥projects¥e7389¥iss309¥csr¥dev¥pg¥tables¥T_2_7_4_1.sas 18JUN201513:32

付録 2.7.4-1
Study 309
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Safety Population

	Eribulin Study 309 (N=226)		Dacarbazine Study 309 (N=224)	
MedDRA System Organ Class Preferred Term	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)
神経系障害	112 (49.6)	13 (5.8)	75 (33.5)	5 (2.2)
味覚消失	1 (0.4)	0	0	0
意識変容状態	0	0	1 (0.4)	0
断端痛	0	0	1 (0.4)	0
失声症	1 (0.4)	1 (0.4)	0	0
平衡障害	1 (0.4)	0	1 (0.4)	0
灼熱感	1 (0.4)	0	6 (2.7)	0
頚腕症候群	1 (0.4)	0	0	0
痙攣	1 (0.4)	1 (0.4)	0	0
意識レベルの低下	0	0	1 (0.4)	0
注意力障害	4 (1.8)	0	0	0
浮動性めまい	21 (9.3)	0	16 (7.1)	0
異常感覚	1 (0.4)	0	2 (0.9)	0
味覚異常	18 (8.0)	0	5 (2.2)	0
頭痛	41 (18.1)	0	21 (9.4)	0
感覚鈍麻	5 (2.2)	1 (0.4)	3 (1.3)	0
嗅覚減退	1 (0.4)	0	0	0

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Program: V:¥projects¥e7389¥iss309¥csr¥dev¥pg¥tables¥T_2_7_4_1.sas 18JUN201513:32

付録 2.7.4-1
Study 309
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Safety Population

	Eribulin Study 309 (N=226)		Dacarbazine Study 309 (N=224)	
MedDRA System Organ Class Preferred Term	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)
神経系障害 (contd)				
嗜眠	6 (2.7)	1 (0.4)	0	0
固有感覚の欠如	1 (0.4)	0	0	0
記憶障害	1 (0.4)	0	1 (0.4)	0
精神的機能障害	0	0	1 (0.4)	0
片頭痛	2 (0.9)	0	0	0
前兆を伴う片頭痛	0	0	1 (0.4)	0
単麻痺	1 (0.4)	1 (0.4)	0	0
神経痛	1 (0.4)	0	2 (0.9)	1 (0.4)
末梢性ニューロパチー	1 (0.4)	0	0	0
神経毒性	0	0	1 (0.4)	0
錯感覚	20 (8.8)	1 (0.4)	7 (3.1)	0
嗅覚錯誤	0	0	1 (0.4)	0
末梢性運動ニューロパチー	5 (2.2)	2 (0.9)	1 (0.4)	1 (0.4)
末梢性感覚運動ニューロパチー	2 (0.9)	0	0	0
末梢性感覚ニューロパチー	46 (20.4)	4 (1.8)	8 (3.6)	0
幻痛	0	0	1 (0.4)	0

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Program: V:¥projects¥e7389¥iss309¥csr¥dev¥pg¥tables¥T_2_7_4_1.sas 18JUN201513:32

付録 2.7.4-1
Study 309
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Safety Population

	Eribulin Study 309 (N=226)		Dacarbazine Study 309 (N=224)	
MedDRA System Organ Class Preferred Term	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)
神経系障害 (contd)				
多発ニューロパチー	1 (0.4)	1 (0.4)	1 (0.4)	0
失神寸前の状態	1 (0.4)	1 (0.4)	1 (0.4)	0
神経根痛	0	0	1 (0.4)	0
下肢静止不能症候群	1 (0.4)	0	0	0
坐骨神経痛	2 (0.9)	0	0	0
感覚障害	1 (0.4)	0	1 (0.4)	0
副鼻腔炎に伴う頭痛	1 (0.4)	0	0	0
傾眠	7 (3.1)	0	5 (2.2)	0
脊髄圧迫	1 (0.4)	1 (0.4)	0	0
失神	0	0	3 (1.3)	3 (1.3)
緊張性頭痛	0	0	2 (0.9)	0
振戦	1 (0.4)	0	1 (0.4)	0
精神障害	48 (21.2)	1 (0.4)	35 (15.6)	0
感情障害	3 (1.3)	0	0	0
激越	3 (1.3)	1 (0.4)	1 (0.4)	0

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Program: V:¥projects¥e7389¥iss309¥csr¥dev¥pg¥tables¥T_2_7_4_1.sas 18JUN201513:32

付録 2.7.4-1
Study 309
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Safety Population

	Eribulin Study 309 (N=226)		Dacarbazine Study 309 (N=224)	
MedDRA System Organ Class Preferred Term	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)
精神障害 (contd)				
不安	12 (5.3)	0	14 (6.3)	0
精神緩慢	0	0	1 (0.4)	0
カタトニー	1 (0.4)	0	0	0
錯乱状態	3 (1.3)	0	0	0
譫妄	1 (0.4)	0	0	0
抑うつ気分	1 (0.4)	0	0	0
うつ病	4 (1.8)	0	6 (2.7)	0
多幸気分	0	0	2 (0.9)	0
幻覚	1 (0.4)	0	1 (0.4)	0
不眠症	22 (9.7)	0	10 (4.5)	0
易刺激性	2 (0.9)	0	0	0
気分変化	1 (0.4)	0	0	0
精神病性障害	0	0	1 (0.4)	0
落ち着きのなさ	0	0	1 (0.4)	0
睡眠障害	2 (0.9)	0	2 (0.9)	0

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付録 2.7.4-1
Study 309
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Safety Population

	Eribulin Study 309 (N=226)		Dacarbazine Study 309 (N=224)	
MedDRA System Organ Class Preferred Term	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)
腎および尿路障害	20 (8.8)	1 (0.4)	17 (7.6)	1 (0.4)
膀胱痛	1 (0.4)	0	0	0
黄疸尿	0	0	1 (0.4)	0
排尿困難	7 (3.1)	0	4 (1.8)	0
遺尿	0	0	1 (0.4)	0
糖尿	2 (0.9)	0	2 (0.9)	0
血尿	2 (0.9)	1 (0.4)	1 (0.4)	0
水腎症	2 (0.9)	0	1 (0.4)	0
尿意切迫	2 (0.9)	0	0	0
夜間頻尿	0	0	1 (0.4)	0
頻尿	3 (1.3)	0	4 (1.8)	0
多尿	1 (0.4)	0	0	0
蛋白尿	1 (0.4)	0	2 (0.9)	0
急性腎不全	2 (0.9)	0	2 (0.9)	0
排尿躊躇	0	0	1 (0.4)	0
尿失禁	0	0	1 (0.4)	1 (0.4)
尿閉	1 (0.4)	0	0	0

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Program: V:¥projects¥e7389¥iss309¥csr¥dev¥pg¥tables¥T_2_7_4_1.sas 18JUN201513:32

付録 2.7.4-1
Study 309
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Safety Population

	Eribulin Study 309 (N=226)		Dacarbazine Study 309 (N=224)	
MedDRA System Organ Class Preferred Term	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)
腎および尿路障害 (contd)				
尿路障害	0	0	1 (0.4)	0
尿路痛	1 (0.4)	0	0	0
生殖系および乳房障害	10 (4.4)	0	5 (2.2)	0
後天性包茎	1 (0.4)	0	0	0
勃起不全	2 (0.9)	0	0	0
卵管障害	1 (0.4)	0	0	0
不正子宮出血	0	0	1 (0.4)	0
乳頭痛	1 (0.4)	0	0	0
性器浮腫	1 (0.4)	0	0	0
骨盤不快感	0	0	1 (0.4)	0
骨盤痛	0	0	2 (0.9)	0
会陰痛	1 (0.4)	0	0	0
陰嚢浮腫	0	0	1 (0.4)	0
精巣浮腫	0	0	1 (0.4)	0
膣出血	1 (0.4)	0	0	0

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付録 2.7.4-1
Study 309
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Safety Population

	Eribulin Study 309 (N=226)		Dacarbazine Study 309 (N=224)	
MedDRA System Organ Class Preferred Term	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)
生殖系および乳房障害 (contd)				
膣の炎症	1 (0.4)	0	0	0
外陰膣乾燥	2 (0.9)	0	0	0
外陰膣そう痒症	1 (0.4)	0	0	0
呼吸器、胸郭および縦隔障害	92 (40.7)	16 (7.1)	75 (33.5)	12 (5.4)
急性呼吸不全	2 (0.9)	1 (0.4)	0	0
無気肺	1 (0.4)	0	1 (0.4)	1 (0.4)
気管支痙攣	0	0	1 (0.4)	0
咳嗽	39 (17.3)	0	28 (12.5)	0
発声障害	8 (3.5)	0	3 (1.3)	0
呼吸困難	36 (15.9)	5 (2.2)	36 (16.1)	5 (2.2)
労作性呼吸困難	2 (0.9)	0	5 (2.2)	1 (0.4)
鼻出血	4 (1.8)	0	3 (1.3)	1 (0.4)
喀血	0	0	3 (1.3)	0
しゃっくり	1 (0.4)	0	3 (1.3)	1 (0.4)
高炭酸ガス血症	1 (0.4)	0	0	0

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Program: V:¥projects¥e7389¥iss309¥csr¥dev¥pg¥tables¥T_2_7_4_1.sas 18JUN201513:32

付録 2.7.4-1
Study 309
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Safety Population

	Eribulin Study 309 (N=226)		Dacarbazine Study 309 (N=224)	
MedDRA System Organ Class Preferred Term	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)
呼吸器、胸郭および縦隔障害 (contd)				
鼻閉	5 (2.2)	0	4 (1.8)	0
鼻部不快感	0	0	1 (0.4)	0
鼻潰瘍	1 (0.4)	0	0	0
口腔咽頭痛	12 (5.3)	0	5 (2.2)	0
呼吸時疼痛	1 (0.4)	1 (0.4)	1 (0.4)	0
副鼻腔分泌過多	0	0	1 (0.4)	0
咽頭紅斑	2 (0.9)	0	0	0
胸水	4 (1.8)	1 (0.4)	5 (2.2)	1 (0.4)
誤嚥性肺炎	1 (0.4)	1 (0.4)	0	0
気胸	1 (0.4)	0	1 (0.4)	1 (0.4)
湿性咳嗽	3 (1.3)	0	2 (0.9)	0
肺塞栓症	4 (1.8)	4 (1.8)	3 (1.3)	1 (0.4)
肺水腫	1 (0.4)	0	0	0
肺血栓症	1 (0.4)	0	0	0
呼吸不全	4 (1.8)	4 (1.8)	2 (0.9)	2 (0.9)
鼻痛	1 (0.4)	0	0	0

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Program: V:¥projects¥e7389¥iss309¥csr¥dev¥pg¥tables¥T_2_7_4_1.sas 18JUN201513:32

付録 2.7.4-1
Study 309
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Safety Population

	Eribulin Study 309 (N=226)		Dacarbazine Study 309 (N=224)	
MedDRA System Organ Class Preferred Term	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)
呼吸器、胸郭および縦隔障害 (contd)				
アレルギー性鼻炎	1 (0.4)	0	0	0
鼻漏	10 (4.4)	0	3 (1.3)	0
副鼻腔うっ血	2 (0.9)	0	0	0
くしゃみ	0	0	1 (0.4)	0
咽喉刺激感	0	0	1 (0.4)	0
上気道咳症候群	2 (0.9)	0	1 (0.4)	0
喘鳴	0	0	2 (0.9)	0
皮膚および皮下組織障害	109 (48.2)	1 (0.4)	45 (20.1)	1 (0.4)
日光角化症	1 (0.4)	0	0	0
脱毛症	79 (35.0)	1 (0.4)	6 (2.7)	0
血性水疱	0	0	1 (0.4)	0
皮膚嚢腫	1 (0.4)	0	0	0
皮膚炎	1 (0.4)	0	0	0
ざ瘡様皮膚炎	1 (0.4)	0	0	0
アレルギー性皮膚炎	0	0	1 (0.4)	0

TEAE = treatment-emergent adverse event, Graded using Common Terminology Criteria for Adverse Events (CTCAE)
A subject with two or more adverse events in the same system organ class (or with the same preferred term) is counted once for that system organ class (or preferred term).
Adverse event terms are coded using Medical Dictionary for Regulatory Activities (MedDRA) version 17.1.

Program: V:¥projects¥e7389¥iss309¥csr¥dev¥pg¥tables¥T_2_7_4_1.sas 18JUN201513:32

付録 2.7.4-1
Study 309
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Safety Population

	Eribulin Study 309 (N=226)		Dacarbazine Study 309 (N=224)	
MedDRA System Organ Class Preferred Term	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)
皮膚および皮下組織障害 (contd)				
おむつ皮膚炎	1 (0.4)	0	0	0
皮膚乾燥	5 (2.2)	0	5 (2.2)	0
湿疹	1 (0.4)	0	0	0
紅斑	4 (1.8)	0	4 (1.8)	0
毛髪変色	1 (0.4)	0	0	0
多汗症	4 (1.8)	0	3 (1.3)	0
睫毛眉毛脱落症	1 (0.4)	0	0	0
爪床圧痛	0	0	1 (0.4)	0
爪の障害	1 (0.4)	0	1 (0.4)	0
爪線状隆起	0	0	1 (0.4)	0
爪毒性	1 (0.4)	0	0	0
寝汗	3 (1.3)	0	0	0
爪甲離床症	1 (0.4)	0	0	0
爪甲脱落症	1 (0.4)	0	0	0
皮膚疼痛	1 (0.4)	0	2 (0.9)	0
手掌・足底発赤知覚不全症候群	2 (0.9)	0	0	0

TEAE = treatment-emergent adverse event, Graded using Common Terminology Criteria for Adverse Events (CTCAE)
A subject with two or more adverse events in the same system organ class (or with the same preferred term) is counted once for that system organ class (or preferred term).
Adverse event terms are coded using Medical Dictionary for Regulatory Activities (MedDRA) version 17.1.

Program: V:¥projects¥e7389¥iss309¥csr¥dev¥pg¥tables¥T_2_7_4_1.sas 18JUN201513:32

付録 2.7.4-1
Study 309
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Safety Population

	Eribulin Study 309 (N=226)		Dacarbazine Study 309 (N=224)	
MedDRA System Organ Class Preferred Term	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)
皮膚および皮下組織障害 (contd)				
点状出血	0	0	3 (1.3)	1 (0.4)
光線過敏性反応	1 (0.4)	0	8 (3.6)	0
そう痒症	9 (4.0)	0	5 (2.2)	0
全身性そう痒症	1 (0.4)	0	0	0
発疹	9 (4.0)	0	7 (3.1)	0
斑状丘疹状皮疹	1 (0.4)	0	0	0
そう痒性皮疹	1 (0.4)	0	1 (0.4)	0
瘢痕痛	1 (0.4)	0	0	0
皮膚亀裂	2 (0.9)	0	1 (0.4)	0
皮膚色素過剰	1 (0.4)	0	0	0
皮膚病変	2 (0.9)	0	1 (0.4)	0
皮膚潰瘍	1 (0.4)	0	0	0
日光皮膚炎	0	0	1 (0.4)	0
皮膚のべとつき感	1 (0.4)	0	0	0
顔面腫脹	1 (0.4)	0	2 (0.9)	0
毛細血管拡張症	0	0	1 (0.4)	0

TEAE = treatment-emergent adverse event, Graded using Common Terminology Criteria for Adverse Events (CTCAE)
A subject with two or more adverse events in the same system organ class (or with the same preferred term) is counted once for that system organ class (or preferred term).
Adverse event terms are coded using Medical Dictionary for Regulatory Activities (MedDRA) version 17.1.

Program: V:¥projects¥e7389¥iss309¥csr¥dev¥pg¥tables¥T_2_7_4_1.sas 18JUN201513:32

付録 2.7.4-1
Study 309
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Safety Population

	Eribulin Study 309 (N=226)		Dacarbazine Study 309 (N=224)	
MedDRA System Organ Class Preferred Term	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)
皮膚および皮下組織障害 (contd)				
蕁麻疹	1 (0.4)	0	0	0
血管障害	35 (15.5)	3 (1.3)	30 (13.4)	8 (3.6)
深部静脈血栓症	1 (0.4)	0	4 (1.8)	3 (1.3)
潮紅	6 (2.7)	0	3 (1.3)	0
血腫	0	0	1 (0.4)	0
ほてり	5 (2.2)	0	3 (1.3)	0
高血圧	7 (3.1)	1 (0.4)	7 (3.1)	2 (0.9)
低血圧	13 (5.8)	1 (0.4)	6 (2.7)	2 (0.9)
頸静脈血栓症	0	0	1 (0.4)	0
リンパ浮腫	1 (0.4)	0	2 (0.9)	0
起立性低血圧	1 (0.4)	0	1 (0.4)	0
末梢静脈疾患	1 (0.4)	0	0	0
静脈炎	1 (0.4)	0	0	0
高血圧前症	1 (0.4)	0	0	0
ショック	0	0	1 (0.4)	1 (0.4)

TEAE = treatment-emergent adverse event, Graded using Common Terminology Criteria for Adverse Events (CTCAE)
A subject with two or more adverse events in the same system organ class (or with the same preferred term) is counted once for that system organ class (or preferred term).
Adverse event terms are coded using Medical Dictionary for Regulatory Activities (MedDRA) version 17.1.

Program: V:¥projects¥e7389¥iss309¥csr¥dev¥pg¥tables¥T_2_7_4_1.sas 18JUN201513:32

付録 2.7.4-1
Study 309
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Safety Population

	Eribulin Study 309 (N=226)		Dacarbazine Study 309 (N=224)	
MedDRA System Organ Class Preferred Term	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)
血管障害 (contd)				
上大静脈症候群	1 (0.4)	0	0	0
血管痛	0	0	1 (0.4)	0
大静脈血栓症	1 (0.4)	1 (0.4)	1 (0.4)	1 (0.4)
静脈血栓症	0	0	2 (0.9)	0

TEAE = treatment-emergent adverse event, Graded using Common Terminology Criteria for Adverse Events (CTCAE)
A subject with two or more adverse events in the same system organ class (or with the same preferred term) is counted once for that system organ class (or preferred term).
Adverse event terms are coded using Medical Dictionary for Regulatory Activities (MedDRA) version 17.1.

Program: V:¥projects¥e7389¥iss309¥csr¥dev¥pg¥tables¥T_2_7_4_1.sas 18JUN201513:32

付録 2.7.4-2
Study 309
Treatment-Related Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Safety Population

	Eribulin Study 309 (N=226)		Dacarbazine Study 309 (N=224)	
MedDRA System Organ Class Preferred Term	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)
Any treatment-related TEAEs	210 (92.9)	123 (54.4)	203 (90.6)	90 (40.2)
血液およびリンパ系障害	127 (56.2)	90 (39.8)	116 (51.8)	67 (29.9)
貧血	55 (24.3)	10 (4.4)	59 (26.3)	21 (9.4)
発熱性好中球減少症	2 (0.9)	2 (0.9)	2 (0.9)	2 (0.9)
ヘモグロビン血症	3 (1.3)	2 (0.9)	1 (0.4)	0
内出血発生の増加傾向	0	0	1 (0.4)	0
白血球増加症	1 (0.4)	1 (0.4)	0	0
白血球減少症	35 (15.5)	22 (9.7)	21 (9.4)	8 (3.6)
リンパ節症	1 (0.4)	0	0	0
リンパ球減少症	1 (0.4)	1 (0.4)	6 (2.7)	3 (1.3)
好中球減少症	96 (42.5)	76 (33.6)	53 (23.7)	35 (15.6)
汎血球減少症	0	0	3 (1.3)	2 (0.9)
血小板減少症	13 (5.8)	1 (0.4)	59 (26.3)	34 (15.2)
心臓障害	2 (0.9)	1 (0.4)	6 (2.7)	0

TEAE = treatment-emergent adverse event, Graded using Common Terminology Criteria for Adverse Events (CTCAE)
Treatment-related adverse events include adverse events that were considered by the investigator to be possibly or probably related to study drug and adverse events with missing relationship to study drug.
A subject with two or more adverse events in the same system organ class (or with the same preferred term) is counted once for that system organ class (or preferred term).
Adverse event terms are coded using Medical Dictionary for Regulatory Activities (MedDRA) version 17.1.

Program: V:¥projects¥e7389¥iss309¥csr¥dev¥pg¥tables¥T_2_7_4_2.sas 18JUN201513:32

付録 2.7.4-2
Study 309
Treatment-Related Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Safety Population

	Eribulin Study 309 (N=226)		Dacarbazine Study 309 (N=224)	
MedDRA System Organ Class Preferred Term	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)
心臓障害 (contd)				
心嚢液貯留	1 (0.4)	1 (0.4)	0	0
洞性頻脈	0	0	3 (1.3)	0
頻脈	1 (0.4)	0	3 (1.3)	0
耳および迷路障害	5 (2.2)	0	2 (0.9)	0
難聴	1 (0.4)	0	0	0
耳鳴	3 (1.3)	0	0	0
回転性めまい	1 (0.4)	0	1 (0.4)	0
前庭障害	0	0	1 (0.4)	0
眼障害	22 (9.7)	0	6 (2.7)	0
眼精疲労	0	0	1 (0.4)	0
眼瞼炎	2 (0.9)	0	0	0
失明	1 (0.4)	0	0	0
眼乾燥	2 (0.9)	0	0	0

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Treatment-related adverse events include adverse events that were considered by the investigator to be possibly or probably related to study drug and adverse events with missing relationship to study drug.
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Program: V:¥projects¥e7389¥iss309¥csr¥dev¥pg¥tables¥T_2_7_4_2.sas 18JUN201513:32

付録 2.7.4-2
Study 309
Treatment-Related Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Safety Population

	Eribulin Study 309 (N=226)		Dacarbazine Study 309 (N=224)	
MedDRA System Organ Class Preferred Term	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)
眼障害 (contd)				
眼刺激	3 (1.3)	0	0	0
眼痛	1 (0.4)	0	0	0
流涙増加	15 (6.6)	0	0	0
眼充血	3 (1.3)	0	0	0
霧視	3 (1.3)	0	4 (1.8)	0
視力障害	1 (0.4)	0	1 (0.4)	0
硝子体浮遊物	1 (0.4)	0	0	0
胃腸障害	132 (58.4)	9 (4.0)	133 (59.4)	5 (2.2)
腹部膨満	5 (2.2)	0	4 (1.8)	0
腹痛	9 (4.0)	0	1 (0.4)	0
下腹部痛	0	0	1 (0.4)	0
上腹部痛	5 (2.2)	0	5 (2.2)	0
後天性巨舌症	1 (0.4)	0	0	0
肛門の炎症	0	0	1 (0.4)	0

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Treatment-related adverse events include adverse events that were considered by the investigator to be possibly or probably related to study drug and adverse events with missing relationship to study drug.
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Adverse event terms are coded using Medical Dictionary for Regulatory Activities (MedDRA) version 17.1.

Program: V:¥projects¥e7389¥iss309¥csr¥dev¥pg¥tables¥T_2_7_4_2.sas 18JUN201513:32

付録 2.7.4-2
Study 309
Treatment-Related Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Safety Population

	Eribulin Study 309 (N=226)		Dacarbazine Study 309 (N=224)	
MedDRA System Organ Class Preferred Term	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)
胃腸障害 (contd)				
アフタ性口内炎	3 (1.3)	0	0	0
便秘	38 (16.8)	0	28 (12.5)	1 (0.4)
下痢	30 (13.3)	1 (0.4)	22 (9.8)	0
口内乾燥	9 (4.0)	0	3 (1.3)	0
消化不良	9 (4.0)	1 (0.4)	5 (2.2)	1 (0.4)
嚥下障害	1 (0.4)	0	0	0
放屁	1 (0.4)	0	0	0
食中毒	0	0	1 (0.4)	1 (0.4)
胃腸管瘻	1 (0.4)	0	0	0
胃腸出血	0	0	1 (0.4)	1 (0.4)
胃食道逆流性疾患	6 (2.7)	0	1 (0.4)	0
歯肉出血	0	0	2 (0.9)	0
歯肉紅斑	0	0	1 (0.4)	1 (0.4)
歯肉痛	1 (0.4)	0	0	0
歯肉腫脹	1 (0.4)	0	0	0

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Treatment-related adverse events include adverse events that were considered by the investigator to be possibly or probably related to study drug and adverse events with missing relationship to study drug.
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Adverse event terms are coded using Medical Dictionary for Regulatory Activities (MedDRA) version 17.1.

Program: V:¥projects¥e7389¥iss309¥csr¥dev¥pg¥tables¥T_2_7_4_2.sas 18JUN201513:32

付録 2.7.4-2
Study 309
Treatment-Related Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Safety Population

	Eribulin Study 309 (N=226)		Dacarbazine Study 309 (N=224)	
MedDRA System Organ Class Preferred Term	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)
胃腸障害 (contd)				
舌炎	1 (0.4)	0	0	0
口の感覚鈍麻	3 (1.3)	0	0	0
腸閉塞	1 (0.4)	1 (0.4)	0	0
口腔内潰瘍形成	3 (1.3)	0	1 (0.4)	0
悪心	75 (33.2)	2 (0.9)	101 (45.1)	0
嚥下痛	1 (0.4)	0	0	0
口腔知覚不全	1 (0.4)	0	0	0
口腔内痛	2 (0.9)	0	1 (0.4)	0
口の錯感覚	0	0	1 (0.4)	0
直腸出血	1 (0.4)	0	0	0
後腹膜出血	1 (0.4)	1 (0.4)	0	0
流涎過多	0	0	1 (0.4)	0
口内炎	26 (11.5)	2 (0.9)	9 (4.0)	1 (0.4)
舌の運動障害	1 (0.4)	0	0	0
舌潰瘍	1 (0.4)	0	0	0

TEAE = treatment-emergent adverse event, Graded using Common Terminology Criteria for Adverse Events (CTCAE)
Treatment-related adverse events include adverse events that were considered by the investigator to be possibly or probably related to study drug and adverse events with missing relationship to study drug.
A subject with two or more adverse events in the same system organ class (or with the same preferred term) is counted once for that system organ class (or preferred term).
Adverse event terms are coded using Medical Dictionary for Regulatory Activities (MedDRA) version 17.1.

Program: V:¥projects¥e7389¥iss309¥csr¥dev¥pg¥tables¥T_2_7_4_2.sas 18JUN201513:32

付録 2.7.4-2
Study 309
Treatment-Related Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Safety Population

	Eribulin Study 309 (N=226)		Dacarbazine Study 309 (N=224)	
MedDRA System Organ Class Preferred Term	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)
胃腸障害 (contd)				
嘔吐	27 (11.9)	1 (0.4)	38 (17.0)	0
一般・全身障害および投与部位の状態	136 (60.2)	9 (4.0)	121 (54.0)	7 (3.1)
無力症	36 (15.9)	2 (0.9)	41 (18.3)	4 (1.8)
胸部不快感	0	0	1 (0.4)	0
悪寒	8 (3.5)	0	1 (0.4)	0
活動性低下	1 (0.4)	0	0	0
顔面浮腫	2 (0.9)	0	0	0
疲労	83 (36.7)	6 (2.7)	76 (33.9)	1 (0.4)
歩行障害	3 (1.3)	0	0	0
全身性浮腫	1 (0.4)	0	0	0
低体温	1 (0.4)	0	0	0
インフルエンザ様疾患	3 (1.3)	0	3 (1.3)	0
注入部位疼痛	0	0	2 (0.9)	0
注射部位反応	1 (0.4)	0	0	0

TEAE = treatment-emergent adverse event, Graded using Common Terminology Criteria for Adverse Events (CTCAE)
Treatment-related adverse events include adverse events that were considered by the investigator to be possibly or probably related to study drug and adverse events with missing relationship to study drug.
A subject with two or more adverse events in the same system organ class (or with the same preferred term) is counted once for that system organ class (or preferred term).
Adverse event terms are coded using Medical Dictionary for Regulatory Activities (MedDRA) version 17.1.

Program: V:¥projects¥e7389¥iss309¥csr¥dev¥pg¥tables¥T_2_7_4_2.sas 18JUN201513:32

付録 2.7.4-2
Study 309
Treatment-Related Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Safety Population

	Eribulin Study 309 (N=226)		Dacarbazine Study 309 (N=224)	
MedDRA System Organ Class Preferred Term	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)
一般・全身障害および投与部位の状態 (contd)				
倦怠感	2 (0.9)	0	2 (0.9)	0
末梢性浮腫	9 (4.0)	0	5 (2.2)	1 (0.4)
末梢腫脹	0	0	1 (0.4)	0
発熱	33 (14.6)	1 (0.4)	10 (4.5)	1 (0.4)
肝胆道系障害	3 (1.3)	2 (0.9)	1 (0.4)	1 (0.4)
肝不全	0	0	1 (0.4)	1 (0.4)
肝細胞損傷	1 (0.4)	0	0	0
肝毒性	1 (0.4)	1 (0.4)	0	0
高ビリルビン血症	1 (0.4)	1 (0.4)	0	0
黄疸	1 (0.4)	0	0	0
免疫系障害	1 (0.4)	0	1 (0.4)	1 (0.4)
薬物過敏症	0	0	1 (0.4)	1 (0.4)
過敏症	1 (0.4)	0	0	0

TEAE = treatment-emergent adverse event, Graded using Common Terminology Criteria for Adverse Events (CTCAE)
Treatment-related adverse events include adverse events that were considered by the investigator to be possibly or probably related to study drug and adverse events with missing relationship to study drug.
A subject with two or more adverse events in the same system organ class (or with the same preferred term) is counted once for that system organ class (or preferred term).
Adverse event terms are coded using Medical Dictionary for Regulatory Activities (MedDRA) version 17.1.

Program: V:¥projects¥e7389¥iss309¥csr¥dev¥pg¥tables¥T_2_7_4_2.sas 18JUN201513:32

付録 2.7.4-2
Study 309
Treatment-Related Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Safety Population

	Eribulin Study 309 (N=226)		Dacarbazine Study 309 (N=224)	
MedDRA System Organ Class Preferred Term	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)
感染症および寄生虫症	24 (10.6)	7 (3.1)	16 (7.1)	4 (1.8)
気管支炎	1 (0.4)	0	0	0
気管支肺炎	1 (0.4)	1 (0.4)	0	0
カテーテル留置部位蜂巣炎	1 (0.4)	0	0	0
蜂巣炎	0	0	1 (0.4)	1 (0.4)
クロストリジウム・ディフィシレ大腸炎	0	0	1 (0.4)	0
耳感染	2 (0.9)	0	0	0
毛包炎	2 (0.9)	0	0	0
帯状疱疹	0	0	2 (0.9)	0
感染	0	0	1 (0.4)	1 (0.4)
真菌性下気道感染	1 (0.4)	1 (0.4)	0	0
鼻咽頭炎	0	0	1 (0.4)	0
好中球減少性敗血症	1 (0.4)	1 (0.4)	0	0
口腔カンジダ症	3 (1.3)	0	2 (0.9)	0
口腔真菌感染	0	0	1 (0.4)	0
外耳炎	0	0	1 (0.4)	0

TEAE = treatment-emergent adverse event, Graded using Common Terminology Criteria for Adverse Events (CTCAE)
Treatment-related adverse events include adverse events that were considered by the investigator to be possibly or probably related to study drug and adverse events with missing relationship to study drug.
A subject with two or more adverse events in the same system organ class (or with the same preferred term) is counted once for that system organ class (or preferred term).
Adverse event terms are coded using Medical Dictionary for Regulatory Activities (MedDRA) version 17.1.

Program: V:¥projects¥e7389¥iss309¥csr¥dev¥pg¥tables¥T_2_7_4_2.sas 18JUN201513:32

付録 2.7.4-2
Study 309
Treatment-Related Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Safety Population

	Eribulin Study 309 (N=226)		Dacarbazine Study 309 (N=224)	
MedDRA System Organ Class Preferred Term	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)
感染症および寄生虫症 (contd)				
咽頭炎	2 (0.9)	1 (0.4)	0	0
肺炎	3 (1.3)	3 (1.3)	2 (0.9)	2 (0.9)
気道感染	1 (0.4)	0	0	0
鼻炎	1 (0.4)	0	0	0
軟部組織感染	1 (0.4)	0	0	0
白癬感染	1 (0.4)	0	0	0
上気道感染	4 (1.8)	1 (0.4)	0	0
尿路感染	1 (0.4)	0	5 (2.2)	0
傷害、中毒および処置合併症	2 (0.9)	0	4 (1.8)	0
投与に伴う反応	0	0	2 (0.9)	0
挫傷	0	0	1 (0.4)	0
転倒	1 (0.4)	0	0	0
注入に伴う反応	1 (0.4)	0	0	0
サンバーン	0	0	1 (0.4)	0

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Treatment-related adverse events include adverse events that were considered by the investigator to be possibly or probably related to study drug and adverse events with missing relationship to study drug.
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Program: V:¥projects¥e7389¥iss309¥csr¥dev¥pg¥tables¥T_2_7_4_2.sas 18JUN201513:32

付録 2.7.4-2
Study 309
Treatment-Related Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Safety Population

	Eribulin Study 309 (N=226)		Dacarbazine Study 309 (N=224)	
MedDRA System Organ Class Preferred Term	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)
臨床検査	67 (29.6)	29 (12.8)	47 (21.0)	27 (12.1)
アラニンアミノトランスフェラーゼ増加	15 (6.6)	3 (1.3)	6 (2.7)	3 (1.3)
アスパラギン酸アミノトランスフェラーゼ増加	16 (7.1)	1 (0.4)	4 (1.8)	1 (0.4)
血中アルブミン減少	1 (0.4)	0	0	0
血中アルカリホスファターゼ増加	6 (2.7)	0	7 (3.1)	1 (0.4)
血中ビリルビン増加	0	0	2 (0.9)	0
血中カルシウム減少	1 (0.4)	0	0	0
血中クレアチニン増加	3 (1.3)	0	1 (0.4)	0
血中乳酸脱水素酵素増加	6 (2.7)	0	4 (1.8)	0
血中リン減少	0	0	1 (0.4)	0
血中カリウム減少	1 (0.4)	1 (0.4)	0	0
血中尿素増加	1 (0.4)	0	0	0
腎クレアチニン・クリアランス減少	1 (0.4)	0	0	0
心電図ＱＴ延長	14 (6.2)	5 (2.2)	7 (3.1)	1 (0.4)
γ－グルタミルトランスフェラーゼ増加	2 (0.9)	1 (0.4)	2 (0.9)	1 (0.4)
ヘマトクリット減少	1 (0.4)	0	1 (0.4)	0

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Program: V:¥projects¥e7389¥iss309¥csr¥dev¥pg¥tables¥T_2_7_4_2.sas 18JUN201513:32

付録 2.7.4-2
Study 309
Treatment-Related Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Safety Population

	Eribulin Study 309 (N=226)		Dacarbazine Study 309 (N=224)	
MedDRA System Organ Class Preferred Term	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)
臨床検査 (contd)				
ヘモグロビン減少	6 (2.7)	0	2 (0.9)	2 (0.9)
リンパ球数減少	2 (0.9)	0	10 (4.5)	4 (1.8)
好中球数減少	18 (8.0)	15 (6.6)	12 (5.4)	6 (2.7)
血小板数減少	1 (0.4)	1 (0.4)	16 (7.1)	7 (3.1)
総蛋白減少	2 (0.9)	0	0	0
赤血球数減少	2 (0.9)	0	1 (0.4)	0
トランスアミナーゼ上昇	1 (0.4)	0	0	0
尿中ケトン体陽性	1 (0.4)	0	0	0
体重減少	5 (2.2)	0	3 (1.3)	0
白血球数減少	16 (7.1)	7 (3.1)	15 (6.7)	8 (3.6)
白血球数増加	0	0	1 (0.4)	1 (0.4)
代謝および栄養障害	45 (19.9)	9 (4.0)	37 (16.5)	6 (2.7)
食欲減退	32 (14.2)	1 (0.4)	25 (11.2)	1 (0.4)
脱水	2 (0.9)	0	5 (2.2)	1 (0.4)

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Program: V:¥projects¥e7389¥iss309¥csr¥dev¥pg¥tables¥T_2_7_4_2.sas 18JUN201513:32

付録 2.7.4-2
Study 309
Treatment-Related Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Safety Population

	Eribulin Study 309 (N=226)		Dacarbazine Study 309 (N=224)	
MedDRA System Organ Class Preferred Term	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)
代謝および栄養障害 (contd)				
高コレステロール血症	0	0	1 (0.4)	0
高クレアチニン血症	0	0	1 (0.4)	0
高血糖	3 (1.3)	2 (0.9)	1 (0.4)	1 (0.4)
低アルブミン血症	3 (1.3)	0	0	0
低カルシウム血症	1 (0.4)	0	3 (1.3)	0
低カリウム血症	8 (3.5)	3 (1.3)	2 (0.9)	1 (0.4)
低マグネシウム血症	4 (1.8)	1 (0.4)	1 (0.4)	0
低ナトリウム血症	3 (1.3)	2 (0.9)	2 (0.9)	1 (0.4)
低リン酸血症	2 (0.9)	1 (0.4)	3 (1.3)	1 (0.4)
筋骨格系および結合組織障害	41 (18.1)	0	24 (10.7)	0
関節痛	10 (4.4)	0	4 (1.8)	0
関節炎	1 (0.4)	0	0	0
背部痛	5 (2.2)	0	2 (0.9)	0
骨痛	1 (0.4)	0	1 (0.4)	0

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Program: V:¥projects¥e7389¥iss309¥csr¥dev¥pg¥tables¥T_2_7_4_2.sas 18JUN201513:32

付録 2.7.4-2
Study 309
Treatment-Related Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Safety Population

	Eribulin Study 309 (N=226)		Dacarbazine Study 309 (N=224)	
MedDRA System Organ Class Preferred Term	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)
筋骨格系および結合組織障害 (contd)				
顎障害	1 (0.4)	0	0	0
咀嚼障害	1 (0.4)	0	0	0
筋肉疲労	1 (0.4)	0	0	0
筋痙縮	7 (3.1)	0	3 (1.3)	0
筋力低下	4 (1.8)	0	0	0
筋骨格系胸痛	2 (0.9)	0	1 (0.4)	0
筋骨格痛	2 (0.9)	0	3 (1.3)	0
筋骨格硬直	2 (0.9)	0	0	0
筋肉痛	15 (6.6)	0	13 (5.8)	0
四肢痛	5 (2.2)	0	3 (1.3)	0
顎痛	1 (0.4)	0	0	0
軟部組織腫瘤	0	0	1 (0.4)	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）	1 (0.4)	1 (0.4)	0	0
腫瘍疼痛	1 (0.4)	1 (0.4)	0	0

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Program: V:¥projects¥e7389¥iss309¥csr¥dev¥pg¥tables¥T_2_7_4_2.sas 18JUN201513:32

付録 2.7.4-2
Study 309
Treatment-Related Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Safety Population

	Eribulin Study 309 (N=226)		Dacarbazine Study 309 (N=224)	
MedDRA System Organ Class Preferred Term	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)
神経系障害	86 (38.1)	10 (4.4)	42 (18.8)	2 (0.9)
味覚消失	1 (0.4)	0	0	0
平衡障害	1 (0.4)	0	1 (0.4)	0
灼熱感	1 (0.4)	0	6 (2.7)	0
痙攣	1 (0.4)	1 (0.4)	0	0
意識レベルの低下	0	0	1 (0.4)	0
注意力障害	3 (1.3)	0	0	0
浮動性めまい	11 (4.9)	0	7 (3.1)	0
異常感覚	1 (0.4)	0	0	0
味覚異常	18 (8.0)	0	3 (1.3)	0
頭痛	23 (10.2)	0	15 (6.7)	0
感覚鈍麻	5 (2.2)	1 (0.4)	0	0
嗜眠	3 (1.3)	1 (0.4)	0	0
固有感覚の欠如	1 (0.4)	0	0	0
記憶障害	0	0	1 (0.4)	0
神経痛	0	0	1 (0.4)	0

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Program: V:¥projects¥e7389¥iss309¥csr¥dev¥pg¥tables¥T_2_7_4_2.sas 18JUN201513:32

付録 2.7.4-2
Study 309
Treatment-Related Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Safety Population

	Eribulin Study 309 (N=226)		Dacarbazine Study 309 (N=224)	
MedDRA System Organ Class Preferred Term	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)
神経系障害 (contd)				
末梢性ニューロパチー	1 (0.4)	0	0	0
錯感覚	17 (7.5)	1 (0.4)	4 (1.8)	0
嗅覚錯誤	0	0	1 (0.4)	0
末梢性運動ニューロパチー	5 (2.2)	2 (0.9)	0	0
末梢性感覚運動ニューロパチー	2 (0.9)	0	0	0
末梢性感覚ニューロパチー	43 (19.0)	4 (1.8)	5 (2.2)	0
多発ニューロパチー	1 (0.4)	1 (0.4)	0	0
失神寸前の状態	1 (0.4)	1 (0.4)	1 (0.4)	0
下肢静止不能症候群	1 (0.4)	0	0	0
感覚障害	1 (0.4)	0	1 (0.4)	0
傾眠	2 (0.9)	0	1 (0.4)	0
失神	0	0	2 (0.9)	2 (0.9)
緊張性頭痛	0	0	1 (0.4)	0
振戦	1 (0.4)	0	0	0

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Program: V:¥projects¥e7389¥iss309¥csr¥dev¥pg¥tables¥T_2_7_4_2.sas 18JUN201513:32

付録 2.7.4-2
Study 309
Treatment-Related Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Safety Population

	Eribulin Study 309 (N=226)		Dacarbazine Study 309 (N=224)	
MedDRA System Organ Class Preferred Term	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)
精神障害	11 (4.9)	1 (0.4)	6 (2.7)	0
感情障害	1 (0.4)	0	0	0
激越	1 (0.4)	1 (0.4)	0	0
不安	0	0	2 (0.9)	0
錯乱状態	1 (0.4)	0	0	0
うつ病	0	0	1 (0.4)	0
不眠症	7 (3.1)	0	2 (0.9)	0
易刺激性	1 (0.4)	0	0	0
落ち着きのなさ	0	0	1 (0.4)	0
睡眠障害	0	0	1 (0.4)	0
腎および尿路障害	5 (2.2)	0	3 (1.3)	0
排尿困難	1 (0.4)	0	0	0
血尿	0	0	1 (0.4)	0
頻尿	1 (0.4)	0	2 (0.9)	0
多尿	1 (0.4)	0	0	0

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Program: V:¥projects¥e7389¥iss309¥csr¥dev¥pg¥tables¥T_2_7_4_2.sas 18JUN201513:32

付録 2.7.4-2
Study 309
Treatment-Related Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Safety Population

	Eribulin Study 309 (N=226)		Dacarbazine Study 309 (N=224)	
MedDRA System Organ Class Preferred Term	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)
腎および尿路障害 (contd)				
蛋白尿	1 (0.4)	0	0	0
尿路痛	1 (0.4)	0	0	0
生殖系および乳房障害	6 (2.7)	0	0	0
勃起不全	2 (0.9)	0	0	0
乳頭痛	1 (0.4)	0	0	0
膣出血	1 (0.4)	0	0	0
膣の炎症	1 (0.4)	0	0	0
外陰膣乾燥	2 (0.9)	0	0	0
外陰膣そう痒症	1 (0.4)	0	0	0
呼吸器、胸郭および縦隔障害	37 (16.4)	0	14 (6.3)	2 (0.9)
咳嗽	15 (6.6)	0	1 (0.4)	0
発声障害	5 (2.2)	0	1 (0.4)	0
呼吸困難	10 (4.4)	0	6 (2.7)	0

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Program: V:¥projects¥e7389¥iss309¥csr¥dev¥pg¥tables¥T_2_7_4_2.sas 18JUN201513:32

付録 2.7.4-2
Study 309
Treatment-Related Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Safety Population

	Eribulin Study 309 (N=226)		Dacarbazine Study 309 (N=224)	
MedDRA System Organ Class Preferred Term	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)
呼吸器、胸郭および縦隔障害 (contd)				
労作性呼吸困難	1 (0.4)	0	1 (0.4)	0
鼻出血	3 (1.3)	0	1 (0.4)	1 (0.4)
しゃっくり	0	0	1 (0.4)	0
鼻閉	3 (1.3)	0	0	0
口腔咽頭痛	6 (2.7)	0	0	0
副鼻腔分泌過多	0	0	1 (0.4)	0
咽頭紅斑	1 (0.4)	0	0	0
気胸	0	0	1 (0.4)	1 (0.4)
湿性咳嗽	1 (0.4)	0	0	0
肺塞栓症	0	0	1 (0.4)	0
鼻痛	1 (0.4)	0	0	0
鼻漏	4 (1.8)	0	1 (0.4)	0
副鼻腔うっ血	1 (0.4)	0	0	0
上気道咳症候群	1 (0.4)	0	0	0

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Program: V:¥projects¥e7389¥iss309¥csr¥dev¥pg¥tables¥T_2_7_4_2.sas 18JUN201513:32

付録 2.7.4-2
Study 309
Treatment-Related Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Safety Population

	Eribulin Study 309 (N=226)		Dacarbazine Study 309 (N=224)	
MedDRA System Organ Class Preferred Term	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)
皮膚および皮下組織障害	93 (41.2)	1 (0.4)	31 (13.8)	1 (0.4)
脱毛症	78 (34.5)	1 (0.4)	6 (2.7)	0
ざ瘡様皮膚炎	1 (0.4)	0	0	0
アレルギー性皮膚炎	0	0	1 (0.4)	0
皮膚乾燥	5 (2.2)	0	2 (0.9)	0
紅斑	2 (0.9)	0	3 (1.3)	0
毛髪変色	1 (0.4)	0	0	0
多汗症	1 (0.4)	0	1 (0.4)	0
睫毛眉毛脱落症	1 (0.4)	0	0	0
爪の障害	1 (0.4)	0	1 (0.4)	0
爪線状隆起	0	0	1 (0.4)	0
爪毒性	1 (0.4)	0	0	0
爪甲離床症	1 (0.4)	0	0	0
爪甲脱落症	1 (0.4)	0	0	0
皮膚疼痛	0	0	1 (0.4)	0
手掌・足底発赤知覚不全症候群	2 (0.9)	0	0	0

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Program: V:¥projects¥e7389¥iss309¥csr¥dev¥pg¥tables¥T_2_7_4_2.sas 18JUN201513:32

付録 2.7.4-2
Study 309
Treatment-Related Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Safety Population

	Eribulin Study 309 (N=226)		Dacarbazine Study 309 (N=224)	
MedDRA System Organ Class Preferred Term	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)
皮膚および皮下組織障害 (contd)				
点状出血	0	0	1 (0.4)	1 (0.4)
光線過敏性反応	1 (0.4)	0	8 (3.6)	0
そう痒症	4 (1.8)	0	3 (1.3)	0
全身性そう痒症	1 (0.4)	0	0	0
発疹	5 (2.2)	0	4 (1.8)	0
瘢痕痛	1 (0.4)	0	0	0
皮膚亀裂	1 (0.4)	0	1 (0.4)	0
皮膚色素過剰	1 (0.4)	0	0	0
皮膚潰瘍	1 (0.4)	0	0	0
日光皮膚炎	0	0	1 (0.4)	0
皮膚のべとつき感	1 (0.4)	0	0	0
顔面腫脹	1 (0.4)	0	1 (0.4)	0
毛細血管拡張症	0	0	1 (0.4)	0
蕁麻疹	1 (0.4)	0	0	0

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Program: V:¥projects¥e7389¥iss309¥csr¥dev¥pg¥tables¥T_2_7_4_2.sas 18JUN201513:32

付録 2.7.4-2
Study 309
Treatment-Related Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Safety Population

	Eribulin Study 309 (N=226)		Dacarbazine Study 309 (N=224)	
MedDRA System Organ Class Preferred Term	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)
血管障害	15 (6.6)	0	11 (4.9)	1 (0.4)
深部静脈血栓症	0	0	1 (0.4)	0
潮紅	4 (1.8)	0	0	0
血腫	0	0	1 (0.4)	0
ほてり	3 (1.3)	0	2 (0.9)	0
高血圧	3 (1.3)	0	3 (1.3)	0
低血圧	4 (1.8)	0	2 (0.9)	1 (0.4)
起立性低血圧	1 (0.4)	0	0	0
血管痛	0	0	1 (0.4)	0
静脈血栓症	0	0	1 (0.4)	0

TEAE = treatment-emergent adverse event, Graded using Common Terminology Criteria for Adverse Events (CTCAE)
Treatment-related adverse events include adverse events that were considered by the investigator to be possibly or probably related to study drug and adverse events with missing relationship to study drug.
A subject with two or more adverse events in the same system organ class (or with the same preferred term) is counted once for that system organ class (or preferred term).
Adverse event terms are coded using Medical Dictionary for Regulatory Activities (MedDRA) version 17.1.

Program: V:¥projects¥e7389¥iss309¥csr¥dev¥pg¥tables¥T_2_7_4_2.sas 18JUN201513:32

付録 2.7.4-3
Japanese and Non-Japanese
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Eribulin Treated Safety Population

	日本人 Study 217 (N=51)		外国人 Studies 207+309 (N=353)		全体 Studies 217+207+309 (N=404)	
MedDRA System Organ Class Preferred Term	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)
Any TEAEs	51 (100.0)	49 (96.1)	348 (98.6)	218 (61.8)	399 (98.8)	267 (66.1)
血液およびリンパ系障害	51 (100.0)	48 (94.1)	148 (41.9)	107 (30.3)	199 (49.3)	155 (38.4)
貧血	24 (47.1)	7 (13.7)	68 (19.3)	17 (4.8)	92 (22.8)	24 (5.9)
発熱性好中球減少症	4 (7.8)	4 (7.8)	10 (2.8)	10 (2.8)	14 (3.5)	14 (3.5)
ヘモグロビン血症	0	0	3 (0.8)	2 (0.6)	3 (0.7)	2 (0.5)
白血球増加症	0	0	1 (0.3)	1 (0.3)	1 (0.2)	1 (0.2)
白血球減少症	51 (100.0)	38 (74.5)	36 (10.2)	23 (6.5)	87 (21.5)	61 (15.1)
リンパ節痛	0	0	2 (0.6)	0	2 (0.5)	0
リンパ節症	0	0	1 (0.3)	0	1 (0.2)	0
リンパ球減少症	40 (78.4)	17 (33.3)	3 (0.8)	3 (0.8)	43 (10.6)	20 (5.0)
好中球減少症	50 (98.0)	44 (86.3)	101 (28.6)	82 (23.2)	151 (37.4)	126 (31.2)
血小板減少症	3 (5.9)	0	13 (3.7)	1 (0.3)	16 (4.0)	1 (0.2)
血小板増加症	0	0	1 (0.3)	0	1 (0.2)	0
心臓障害	7 (13.7)	1 (2.0)	24 (6.8)	2 (0.6)	31 (7.7)	3 (0.7)
狭心症	0	0	1 (0.3)	0	1 (0.2)	0

TEAE = treatment-emergent adverse event, Graded using Common Terminology Criteria for Adverse Events (CTCAE)
A subject with two or more adverse events in the same system organ class (or with the same preferred term) is counted once for that system organ class (or preferred term).
Adverse event terms are coded using Medical Dictionary for Regulatory Activities (MedDRA) version 17.1.
This table is based on adverse events data as available. Study 207 did not record laboratory abnormalities into adverse events data.

Program: V:¥projects¥e7389¥iss309¥csr¥dev¥pg¥tables¥T_2_7_4_3.sas 18JUN201513:33

付録 2.7.4-3
Japanese and Non-Japanese
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Eribulin Treated Safety Population

	日本人 Study 217 (N=51)		外国人 Studies 207+309 (N=353)		全体 Studies 217+207+309 (N=404)	
MedDRA System Organ Class Preferred Term	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)
心臓障害 (contd)						
心房細動	0	0	2 (0.6)	0	2 (0.5)	0
心房粗動	0	0	1 (0.3)	0	1 (0.2)	0
第一度房室ブロック	0	0	1 (0.3)	0	1 (0.2)	0
徐脈	0	0	1 (0.3)	0	1 (0.2)	0
右脚ブロック	0	0	1 (0.3)	0	1 (0.2)	0
心不全	1 (2.0)	1 (2.0)	1 (0.3)	0	2 (0.5)	1 (0.2)
動悸	2 (3.9)	0	4 (1.1)	0	6 (1.5)	0
心嚢液貯留	0	0	2 (0.6)	2 (0.6)	2 (0.5)	2 (0.5)
洞性頻脈	1 (2.0)	0	9 (2.5)	0	10 (2.5)	0
上室性頻脈	0	0	2 (0.6)	0	2 (0.5)	0
頻脈	3 (5.9)	0	5 (1.4)	0	8 (2.0)	0
心室性期外収縮	1 (2.0)	0	0	0	1 (0.2)	0
耳および迷路障害	2 (3.9)	0	16 (4.5)	0	18 (4.5)	0
難聴	0	0	3 (0.8)	0	3 (0.7)	0
耳不快感	0	0	1 (0.3)	0	1 (0.2)	0

TEAE = treatment-emergent adverse event, Graded using Common Terminology Criteria for Adverse Events (CTCAE)
A subject with two or more adverse events in the same system organ class (or with the same preferred term) is counted once for that system organ class (or preferred term).
Adverse event terms are coded using Medical Dictionary for Regulatory Activities (MedDRA) version 17.1.
This table is based on adverse events data as available. Study 207 did not record laboratory abnormalities into adverse events data.

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付録 2.7.4-3
Japanese and Non-Japanese
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Eribulin Treated Safety Population

	日本人 Study 217 (N=51)		外国人 Studies 207+309 (N=353)		全体 Studies 217+207+309 (N=404)	
MedDRA System Organ Class Preferred Term	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)
耳および迷路障害 (contd)						
耳出血	0	0	1 (0.3)	0	1 (0.2)	0
耳痛	0	0	4 (1.1)	0	4 (1.0)	0
外耳痛	0	0	2 (0.6)	0	2 (0.5)	0
耳鳴	1 (2.0)	0	4 (1.1)	0	5 (1.2)	0
鼓膜穿孔	1 (2.0)	0	0	0	1 (0.2)	0
回転性めまい	0	0	1 (0.3)	0	1 (0.2)	0
内分泌障害	0	0	1 (0.3)	0	1 (0.2)	0
甲状腺機能低下症	0	0	1 (0.3)	0	1 (0.2)	0
眼障害	4 (7.8)	1 (2.0)	36 (10.2)	0	40 (9.9)	1 (0.2)
眼瞼炎	0	0	2 (0.6)	0	2 (0.5)	0
失明	0	0	2 (0.6)	0	2 (0.5)	0
白内障	2 (3.9)	1 (2.0)	3 (0.8)	0	5 (1.2)	1 (0.2)
結膜出血	1 (2.0)	0	0	0	1 (0.2)	0
眼乾燥	1 (2.0)	0	4 (1.1)	0	5 (1.2)	0

TEAE = treatment-emergent adverse event, Graded using Common Terminology Criteria for Adverse Events (CTCAE)
A subject with two or more adverse events in the same system organ class (or with the same preferred term) is counted once for that system organ class (or preferred term).
Adverse event terms are coded using Medical Dictionary for Regulatory Activities (MedDRA) version 17.1.
This table is based on adverse events data as available. Study 207 did not record laboratory abnormalities into adverse events data.

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付録 2.7.4-3
Japanese and Non-Japanese
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Eribulin Treated Safety Population

	日本人 Study 217 (N=51)		外国人 Studies 207+309 (N=353)		全体 Studies 217+207+309 (N=404)	
MedDRA System Organ Class Preferred Term	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)
眼障害 (contd)						
眼刺激	0	0	3 (0.8)	0	3 (0.7)	0
眼痛	0	0	2 (0.6)	0	2 (0.5)	0
眼そう痒症	0	0	1 (0.3)	0	1 (0.2)	0
流涙増加	0	0	19 (5.4)	0	19 (4.7)	0
黄斑変性	1 (2.0)	0	0	0	1 (0.2)	0
眼充血	0	0	3 (0.8)	0	3 (0.7)	0
黄疸眼	0	0	1 (0.3)	0	1 (0.2)	0
オキュラーサーフェス疾患	0	0	3 (0.8)	0	3 (0.7)	0
霧視	0	0	6 (1.7)	0	6 (1.5)	0
視力障害	0	0	1 (0.3)	0	1 (0.2)	0
硝子体浮遊物	0	0	1 (0.3)	0	1 (0.2)	0
胃腸障害	33 (64.7)	2 (3.9)	273 (77.3)	30 (8.5)	306 (75.7)	32 (7.9)
腹部癒着	0	0	1 (0.3)	1 (0.3)	1 (0.2)	1 (0.2)
腹部不快感	1 (2.0)	0	6 (1.7)	0	7 (1.7)	0
腹部膨満	0	0	22 (6.2)	0	22 (5.4)	0

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A subject with two or more adverse events in the same system organ class (or with the same preferred term) is counted once for that system organ class (or preferred term).
Adverse event terms are coded using Medical Dictionary for Regulatory Activities (MedDRA) version 17.1.
This table is based on adverse events data as available. Study 207 did not record laboratory abnormalities into adverse events data.

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付録 2.7.4-3
Japanese and Non-Japanese
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Eribulin Treated Safety Population

	日本人 Study 217 (N=51)		外国人 Studies 207+309 (N=353)		全体 Studies 217+207+309 (N=404)	
MedDRA System Organ Class Preferred Term	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)
胃腸障害 (contd)						
腹痛	1 (2.0)	0	47 (13.3)	4 (1.1)	48 (11.9)	4 (1.0)
下腹部痛	1 (2.0)	0	0	0	1 (0.2)	0
上腹部痛	3 (5.9)	0	23 (6.5)	0	26 (6.4)	0
異常便	0	0	1 (0.3)	0	1 (0.2)	0
後天性巨舌症	0	0	1 (0.3)	0	1 (0.2)	0
裂肛	1 (2.0)	0	1 (0.3)	0	2 (0.5)	0
肛門出血	0	0	2 (0.6)	0	2 (0.5)	0
肛門脱	1 (2.0)	0	0	0	1 (0.2)	0
肛門直腸静脈瘤出血	0	0	1 (0.3)	0	1 (0.2)	0
アフタ性口内炎	0	0	3 (0.8)	0	3 (0.7)	0
腹水	0	0	1 (0.3)	0	1 (0.2)	0
口唇炎	3 (5.9)	0	0	0	3 (0.7)	0
慢性胃炎	1 (2.0)	0	0	0	1 (0.2)	0
便秘	16 (31.4)	0	105 (29.7)	4 (1.1)	121 (30.0)	4 (1.0)
下痢	7 (13.7)	0	68 (19.3)	2 (0.6)	75 (18.6)	2 (0.5)
口内乾燥	1 (2.0)	0	17 (4.8)	0	18 (4.5)	0

TEAE = treatment-emergent adverse event, Graded using Common Terminology Criteria for Adverse Events (CTCAE)
A subject with two or more adverse events in the same system organ class (or with the same preferred term) is counted once for that system organ class (or preferred term).
Adverse event terms are coded using Medical Dictionary for Regulatory Activities (MedDRA) version 17.1.
This table is based on adverse events data as available. Study 207 did not record laboratory abnormalities into adverse events data.

Program: V:¥projects¥e7389¥iss309¥csr¥dev¥pg¥tables¥T_2_7_4_3.sas 18JUN201513:33

付録 2.7.4-3
Japanese and Non-Japanese
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Eribulin Treated Safety Population

	日本人 Study 217 (N=51)		外国人 Studies 207+309 (N=353)		全体 Studies 217+207+309 (N=404)	
MedDRA System Organ Class Preferred Term	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)
胃腸障害 (contd)						
十二指腸潰瘍	0	0	1 (0.3)	0	1 (0.2)	0
消化不良	1 (2.0)	0	31 (8.8)	2 (0.6)	32 (7.9)	2 (0.5)
嚥下障害	0	0	4 (1.1)	0	4 (1.0)	0
腸炎	1 (2.0)	0	0	0	1 (0.2)	0
心窩部不快感	0	0	1 (0.3)	0	1 (0.2)	0
便失禁	0	0	1 (0.3)	0	1 (0.2)	0
軟便	0	0	1 (0.3)	0	1 (0.2)	0
放屁	0	0	5 (1.4)	0	5 (1.2)	0
排便回数増加	0	0	1 (0.3)	0	1 (0.2)	0
機能性胃腸障害	0	0	1 (0.3)	0	1 (0.2)	0
胃障害	0	0	1 (0.3)	0	1 (0.2)	0
胃炎	1 (2.0)	0	0	0	1 (0.2)	0
胃腸障害	0	0	28 (7.9)	1 (0.3)	28 (6.9)	1 (0.2)
胃腸管瘻	0	0	2 (0.6)	0	2 (0.5)	0
胃腸出血	0	0	1 (0.3)	0	1 (0.2)	0
消化器痛	0	0	1 (0.3)	0	1 (0.2)	0

TEAE = treatment-emergent adverse event, Graded using Common Terminology Criteria for Adverse Events (CTCAE)
A subject with two or more adverse events in the same system organ class (or with the same preferred term) is counted once for that system organ class (or preferred term).
Adverse event terms are coded using Medical Dictionary for Regulatory Activities (MedDRA) version 17.1.
This table is based on adverse events data as available. Study 207 did not record laboratory abnormalities into adverse events data.

Program: V:¥projects¥e7389¥iss309¥csr¥dev¥pg¥tables¥T_2_7_4_3.sas 18JUN201513:33

付録 2.7.4-3
Japanese and Non-Japanese
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Eribulin Treated Safety Population

	日本人 Study 217 (N=51)		外国人 Studies 207+309 (N=353)		全体 Studies 217+207+309 (N=404)	
MedDRA System Organ Class Preferred Term	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)
胃腸障害 (contd)						
胃食道逆流性疾患	0	0	9 (2.5)	0	9 (2.2)	0
歯肉出血	0	0	1 (0.3)	0	1 (0.2)	0
歯肉痛	0	0	3 (0.8)	0	3 (0.7)	0
歯肉腫脹	0	0	1 (0.3)	0	1 (0.2)	0
舌炎	0	0	1 (0.3)	0	1 (0.2)	0
吐血	0	0	1 (0.3)	0	1 (0.2)	0
血性腹水	0	0	1 (0.3)	1 (0.3)	1 (0.2)	1 (0.2)
痔核	0	0	3 (0.8)	0	3 (0.7)	0
口の感覚鈍麻	0	0	3 (0.8)	0	3 (0.7)	0
イレウス	2 (3.9)	2 (3.9)	2 (0.6)	1 (0.3)	4 (1.0)	3 (0.7)
胃排出不全	0	0	1 (0.3)	0	1 (0.2)	0
単径ヘルニア	0	0	1 (0.3)	0	1 (0.2)	0
腸管虚血	0	0	1 (0.3)	1 (0.3)	1 (0.2)	1 (0.2)
腸閉塞	0	0	7 (2.0)	6 (1.7)	7 (1.7)	6 (1.5)
大腸穿孔	0	0	1 (0.3)	1 (0.3)	1 (0.2)	1 (0.2)
口唇痛	0	0	1 (0.3)	0	1 (0.2)	0

TEAE = treatment-emergent adverse event, Graded using Common Terminology Criteria for Adverse Events (CTCAE)
A subject with two or more adverse events in the same system organ class (or with the same preferred term) is counted once for that system organ class (or preferred term).
Adverse event terms are coded using Medical Dictionary for Regulatory Activities (MedDRA) version 17.1.
This table is based on adverse events data as available. Study 207 did not record laboratory abnormalities into adverse events data.

Program: V:¥projects¥e7389¥iss309¥csr¥dev¥pg¥tables¥T_2_7_4_3.sas 18JUN201513:33

付録 2.7.4-3
Japanese and Non-Japanese
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Eribulin Treated Safety Population

	日本人 Study 217 (N=51)		外国人 Studies 207+309 (N=353)		全体 Studies 217+207+309 (N=404)	
MedDRA System Organ Class Preferred Term	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)
胃腸障害 (contd)						
弛緩歯	0	0	1 (0.3)	0	1 (0.2)	0
口腔内出血	0	0	3 (0.8)	0	3 (0.7)	0
口腔内潰瘍形成	0	0	3 (0.8)	0	3 (0.7)	0
悪心	21 (41.2)	0	136 (38.5)	3 (0.8)	157 (38.9)	3 (0.7)
嚥下痛	0	0	2 (0.6)	0	2 (0.5)	0
食道痛	0	0	1 (0.3)	0	1 (0.2)	0
食道狭窄	1 (2.0)	0	0	0	1 (0.2)	0
食道炎	0	0	3 (0.8)	1 (0.3)	3 (0.7)	1 (0.2)
口腔障害	0	0	1 (0.3)	0	1 (0.2)	0
口腔知覚不全	0	0	1 (0.3)	0	1 (0.2)	0
口腔内痛	0	0	6 (1.7)	0	6 (1.5)	0
歯周病	0	0	1 (0.3)	0	1 (0.2)	0
直腸出血	0	0	3 (0.8)	0	3 (0.7)	0
直腸しぶり	0	0	1 (0.3)	0	1 (0.2)	0
レッチング	0	0	1 (0.3)	0	1 (0.2)	0
後腹膜出血	0	0	1 (0.3)	1 (0.3)	1 (0.2)	1 (0.2)

TEAE = treatment-emergent adverse event, Graded using Common Terminology Criteria for Adverse Events (CTCAE)
A subject with two or more adverse events in the same system organ class (or with the same preferred term) is counted once for that system organ class (or preferred term).
Adverse event terms are coded using Medical Dictionary for Regulatory Activities (MedDRA) version 17.1.
This table is based on adverse events data as available. Study 207 did not record laboratory abnormalities into adverse events data.

Program: V:¥projects¥e7389¥iss309¥csr¥dev¥pg¥tables¥T_2_7_4_3.sas 18JUN201513:33

付録 2.7.4-3
Japanese and Non-Japanese
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Eribulin Treated Safety Population

	日本人 Study 217 (N=51)		外国人 Studies 207+309 (N=353)		全体 Studies 217+207+309 (N=404)	
MedDRA System Organ Class Preferred Term	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)
胃腸障害 (contd)						
小腸出血	0	0	1 (0.3)	0	1 (0.2)	0
小腸閉塞	0	0	3 (0.8)	2 (0.6)	3 (0.7)	2 (0.5)
口内炎	13 (25.5)	0	57 (16.1)	6 (1.7)	70 (17.3)	6 (1.5)
亜イレウス	0	0	1 (0.3)	1 (0.3)	1 (0.2)	1 (0.2)
舌腫脹	0	0	1 (0.3)	0	1 (0.2)	0
舌の運動障害	0	0	1 (0.3)	0	1 (0.2)	0
舌潰瘍	0	0	1 (0.3)	0	1 (0.2)	0
歯の脱落	0	0	1 (0.3)	0	1 (0.2)	0
歯痛	2 (3.9)	0	4 (1.1)	0	6 (1.5)	0
臍ヘルニア	0	0	2 (0.6)	0	2 (0.5)	0
上部消化管出血	0	0	1 (0.3)	0	1 (0.2)	0
嘔吐	4 (7.8)	0	69 (19.5)	5 (1.4)	73 (18.1)	5 (1.2)
一般・全身障害および投与部位の状態	41 (80.4)	2 (3.9)	275 (77.9)	34 (9.6)	316 (78.2)	36 (8.9)
無力症	0	0	47 (13.3)	4 (1.1)	47 (11.6)	4 (1.0)
カテーテル留置部位浮腫	0	0	1 (0.3)	0	1 (0.2)	0

TEAE = treatment-emergent adverse event, Graded using Common Terminology Criteria for Adverse Events (CTCAE)
A subject with two or more adverse events in the same system organ class (or with the same preferred term) is counted once for that system organ class (or preferred term).
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Program: V:¥projects¥e7389¥iss309¥csr¥dev¥pg¥tables¥T_2_7_4_3.sas 18JUN201513:33

付録 2.7.4-3
Japanese and Non-Japanese
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Eribulin Treated Safety Population

	日本人 Study 217 (N=51)		外国人 Studies 207+309 (N=353)		全体 Studies 217+207+309 (N=404)	
MedDRA System Organ Class Preferred Term	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)
一般・全身障害および投与部位の状態 (contd)						
カテーテル留置部位疼痛	0	0	5 (1.4)	0	5 (1.2)	0
胸部不快感	0	0	2 (0.6)	0	2 (0.5)	0
胸痛	0	0	10 (2.8)	2 (0.6)	10 (2.5)	2 (0.5)
悪寒	0	0	17 (4.8)	0	17 (4.2)	0
活動性低下	0	0	1 (0.3)	0	1 (0.2)	0
医療機器不具合	0	0	1 (0.3)	0	1 (0.2)	0
顔面浮腫	0	0	5 (1.4)	0	5 (1.2)	0
顔面痛	0	0	1 (0.3)	0	1 (0.2)	0
疲労	9 (17.6)	0	188 (53.3)	21 (5.9)	197 (48.8)	21 (5.2)
歩行障害	0	0	4 (1.1)	0	4 (1.0)	0
全身健康状態低下	0	0	8 (2.3)	7 (2.0)	8 (2.0)	7 (1.7)
全身性浮腫	2 (3.9)	1 (2.0)	2 (0.6)	0	4 (1.0)	1 (0.2)
異常高熱	0	0	1 (0.3)	0	1 (0.2)	0
高熱	0	0	1 (0.3)	0	1 (0.2)	0
低体温	0	0	1 (0.3)	0	1 (0.2)	0
インフルエンザ様疾患	1 (2.0)	0	8 (2.3)	0	9 (2.2)	0

TEAE = treatment-emergent adverse event, Graded using Common Terminology Criteria for Adverse Events (CTCAE)
A subject with two or more adverse events in the same system organ class (or with the same preferred term) is counted once for that system organ class (or preferred term).
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付録 2.7.4-3
Japanese and Non-Japanese
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Eribulin Treated Safety Population

	日本人 Study 217 (N=51)		外国人 Studies 207+309 (N=353)		全体 Studies 217+207+309 (N=404)	
MedDRA System Organ Class Preferred Term	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)
一般・全身障害および投与部位の状態 (contd)						
注入部位炎症	0	0	1 (0.3)	0	1 (0.2)	0
注射部位漏出	2 (3.9)	0	0	0	2 (0.5)	0
注射部位疼痛	1 (2.0)	0	1 (0.3)	0	2 (0.5)	0
注射部位反応	0	0	1 (0.3)	0	1 (0.2)	0
限局性浮腫	0	0	2 (0.6)	0	2 (0.5)	0
倦怠感	20 (39.2)	0	2 (0.6)	0	22 (5.4)	0
非心臓性胸痛	0	0	5 (1.4)	0	5 (1.2)	0
末梢性浮腫	5 (9.8)	0	49 (13.9)	0	54 (13.4)	0
末梢腫脹	2 (3.9)	0	4 (1.1)	0	6 (1.5)	0
発熱	21 (41.2)	1 (2.0)	90 (25.5)	4 (1.1)	111 (27.5)	5 (1.2)
口渇	1 (2.0)	0	0	0	1 (0.2)	0
肝胆道系障害	6 (11.8)	1 (2.0)	13 (3.7)	6 (1.7)	19 (4.7)	7 (1.7)
胆管拡張	0	0	1 (0.3)	1 (0.3)	1 (0.2)	1 (0.2)
胆管炎	0	0	1 (0.3)	0	1 (0.2)	0
胆嚢炎	0	0	2 (0.6)	1 (0.3)	2 (0.5)	1 (0.2)

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付録 2.7.4-3
Japanese and Non-Japanese
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Eribulin Treated Safety Population

	日本人 Study 217 (N=51)		外国人 Studies 207+309 (N=353)		全体 Studies 217+207+309 (N=404)	
MedDRA System Organ Class Preferred Term	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)
肝胆道系障害 (contd)						
肝機能異常	5 (9.8)	0	0	0	5 (1.2)	0
肝出血	1 (2.0)	1 (2.0)	0	0	1 (0.2)	1 (0.2)
肝臓痛	0	0	2 (0.6)	0	2 (0.5)	0
肝静脈血栓症	0	0	1 (0.3)	1 (0.3)	1 (0.2)	1 (0.2)
肝細胞損傷	0	0	1 (0.3)	0	1 (0.2)	0
肝腫大	0	0	1 (0.3)	0	1 (0.2)	0
肝毒性	0	0	1 (0.3)	1 (0.3)	1 (0.2)	1 (0.2)
高ビリルビン血症	0	0	5 (1.4)	3 (0.8)	5 (1.2)	3 (0.7)
黄疸	0	0	1 (0.3)	0	1 (0.2)	0
免疫系障害	0	0	4 (1.1)	0	4 (1.0)	0
薬物過敏症	0	0	2 (0.6)	0	2 (0.5)	0
過敏症	0	0	2 (0.6)	0	2 (0.5)	0
感染症および寄生虫症	27 (52.9)	3 (5.9)	142 (40.2)	33 (9.3)	169 (41.8)	36 (8.9)
腹部感染	0	0	1 (0.3)	0	1 (0.2)	0

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付録 2.7.4-3
Japanese and Non-Japanese
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Eribulin Treated Safety Population

	日本人 Study 217 (N=51)		外国人 Studies 207+309 (N=353)		全体 Studies 217+207+309 (N=404)	
MedDRA System Organ Class Preferred Term	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)
感染症および寄生虫症 (contd)						
腹部敗血症	0	0	1 (0.3)	0	1 (0.2)	0
アメーバ症	0	0	1 (0.3)	0	1 (0.2)	0
細菌性関節炎	0	0	1 (0.3)	1 (0.3)	1 (0.2)	1 (0.2)
気管支炎	0	0	4 (1.1)	0	4 (1.0)	0
気管支肺炎	0	0	1 (0.3)	1 (0.3)	1 (0.2)	1 (0.2)
カテーテル留置部位蜂巣炎	0	0	1 (0.3)	0	1 (0.2)	0
カテーテル留置部位感染	0	0	1 (0.3)	1 (0.3)	1 (0.2)	1 (0.2)
蜂巣炎	0	0	4 (1.1)	0	4 (1.0)	0
結膜炎	0	0	3 (0.8)	0	3 (0.7)	0
膀胱炎	2 (3.9)	0	7 (2.0)	3 (0.8)	9 (2.2)	3 (0.7)
医療機器関連感染	0	0	7 (2.0)	5 (1.4)	7 (1.7)	5 (1.2)
耳感染	0	0	3 (0.8)	0	3 (0.7)	0
蓄膿	1 (2.0)	1 (2.0)	0	0	1 (0.2)	1 (0.2)
感染性腸炎	1 (2.0)	0	0	0	1 (0.2)	0
丹毒	0	0	1 (0.3)	0	1 (0.2)	0
毛包炎	1 (2.0)	0	3 (0.8)	0	4 (1.0)	0

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付録 2.7.4-3
Japanese and Non-Japanese
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Eribulin Treated Safety Population

	日本人 Study 217 (N=51)		外国人 Studies 207+309 (N=353)		全体 Studies 217+207+309 (N=404)	
MedDRA System Organ Class Preferred Term	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)
感染症および寄生虫症 (contd)						
せつ	0	0	1 (0.3)	0	1 (0.2)	0
胃腸炎	1 (2.0)	0	3 (0.8)	0	4 (1.0)	0
歯肉炎	3 (5.9)	0	1 (0.3)	0	4 (1.0)	0
単径部感染	0	0	1 (0.3)	0	1 (0.2)	0
帯状疱疹	1 (2.0)	0	5 (1.4)	0	6 (1.5)	0
感染性皮膚嚢腫	0	0	1 (0.3)	0	1 (0.2)	0
感染	0	0	2 (0.6)	0	2 (0.5)	0
インフルエンザ	1 (2.0)	0	6 (1.7)	0	7 (1.7)	0
喉頭炎	0	0	1 (0.3)	0	1 (0.2)	0
肝膿瘍	0	0	1 (0.3)	0	1 (0.2)	0
限局性感染	0	0	1 (0.3)	0	1 (0.2)	0
下気道感染	0	0	1 (0.3)	0	1 (0.2)	0
真菌性下気道感染	0	0	1 (0.3)	1 (0.3)	1 (0.2)	1 (0.2)
肺感染	0	0	2 (0.6)	1 (0.3)	2 (0.5)	1 (0.2)
リンパ節感染	0	0	1 (0.3)	1 (0.3)	1 (0.2)	1 (0.2)
脊髄炎	0	0	1 (0.3)	0	1 (0.2)	0

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付録 2.7.4-3
Japanese and Non-Japanese
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Eribulin Treated Safety Population

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MedDRA System Organ Class Preferred Term	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)
感染症および寄生虫症 (contd)						
鼻咽頭炎	11 (21.6)	0	20 (5.7)	0	31 (7.7)	0
好中球減少性敗血症	0	0	1 (0.3)	1 (0.3)	1 (0.2)	1 (0.2)
口腔細菌感染	0	0	1 (0.3)	0	1 (0.2)	0
口腔カンジダ症	0	0	5 (1.4)	0	5 (1.2)	0
口腔ヘルペス	0	0	1 (0.3)	0	1 (0.2)	0
口腔感染	0	0	1 (0.3)	0	1 (0.2)	0
眼窩感染	0	0	1 (0.3)	0	1 (0.2)	0
真菌性口腔咽頭炎	0	0	1 (0.3)	0	1 (0.2)	0
中耳炎	1 (2.0)	0	0	0	1 (0.2)	0
急性中耳炎	1 (2.0)	0	0	0	1 (0.2)	0
腹膜炎	0	0	2 (0.6)	1 (0.3)	2 (0.5)	1 (0.2)
細菌性腹膜炎	0	0	2 (0.6)	2 (0.6)	2 (0.5)	2 (0.5)
咽頭炎	2 (3.9)	0	9 (2.5)	3 (0.8)	11 (2.7)	3 (0.7)
肺炎	1 (2.0)	1 (2.0)	11 (3.1)	6 (1.7)	12 (3.0)	7 (1.7)
シュードモナス性菌血症	0	0	1 (0.3)	1 (0.3)	1 (0.2)	1 (0.2)
腎盂腎炎	0	0	1 (0.3)	1 (0.3)	1 (0.2)	1 (0.2)

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付録 2.7.4-3
Japanese and Non-Japanese
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Eribulin Treated Safety Population

	日本人 Study 217 (N=51)		外国人 Studies 207+309 (N=353)		全体 Studies 217+207+309 (N=404)	
MedDRA System Organ Class Preferred Term	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)
感染症および寄生虫症 (contd)						
膿尿	0	0	1 (0.3)	0	1 (0.2)	0
気道感染	0	0	1 (0.3)	0	1 (0.2)	0
鼻炎	1 (2.0)	0	6 (1.7)	1 (0.3)	7 (1.7)	1 (0.2)
敗血症	0	0	2 (0.6)	1 (0.3)	2 (0.5)	1 (0.2)
敗血症性ショック	0	0	1 (0.3)	1 (0.3)	1 (0.2)	1 (0.2)
セラチア性菌血症	0	0	1 (0.3)	1 (0.3)	1 (0.2)	1 (0.2)
副鼻腔炎	0	0	3 (0.8)	0	3 (0.7)	0
皮膚カンジダ	0	0	1 (0.3)	0	1 (0.2)	0
軟部組織感染	0	0	1 (0.3)	0	1 (0.2)	0
ブドウ球菌性菌血症	0	0	1 (0.3)	1 (0.3)	1 (0.2)	1 (0.2)
ブドウ球菌感染	0	0	1 (0.3)	1 (0.3)	1 (0.2)	1 (0.2)
レンサ球菌感染	1 (2.0)	1 (2.0)	0	0	1 (0.2)	1 (0.2)
皮下組織膿瘍	0	0	1 (0.3)	0	1 (0.2)	0
白癬感染	0	0	1 (0.3)	0	1 (0.2)	0
歯感染	0	0	1 (0.3)	1 (0.3)	1 (0.2)	1 (0.2)
上気道感染	11 (21.6)	0	21 (5.9)	1 (0.3)	32 (7.9)	1 (0.2)

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付録 2.7.4-3
Japanese and Non-Japanese
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Eribulin Treated Safety Population

	日本人 Study 217 (N=51)		外国人 Studies 207+309 (N=353)		全体 Studies 217+207+309 (N=404)	
MedDRA System Organ Class Preferred Term	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)
感染症および寄生虫症 (contd)						
尿路感染	3 (5.9)	0	30 (8.5)	5 (1.4)	33 (8.2)	5 (1.2)
尿路性敗血症	0	0	1 (0.3)	0	1 (0.2)	0
ウイルス性上気道感染	0	0	1 (0.3)	0	1 (0.2)	0
外陰膣真菌感染	0	0	1 (0.3)	0	1 (0.2)	0
創傷感染	1 (2.0)	0	0	0	1 (0.2)	0
傷害、中毒および処置合併症	10 (19.6)	0	24 (6.8)	6 (1.7)	34 (8.4)	6 (1.5)
剥離骨折	1 (2.0)	0	0	0	1 (0.2)	0
挫傷	2 (3.9)	0	2 (0.6)	0	4 (1.0)	0
焼痂	0	0	1 (0.3)	0	1 (0.2)	0
転倒	3 (5.9)	0	4 (1.1)	0	7 (1.7)	0
大腿骨骨折	0	0	1 (0.3)	0	1 (0.2)	0
足骨折	2 (3.9)	0	0	0	2 (0.5)	0
胃腸吻合部漏出	0	0	1 (0.3)	0	1 (0.2)	0
熱中症	1 (2.0)	0	0	0	1 (0.2)	0
股関節部骨折	0	0	1 (0.3)	1 (0.3)	1 (0.2)	1 (0.2)

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Japanese and Non-Japanese
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
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MedDRA System Organ Class Preferred Term	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)
傷害、中毒および処置合併症 (contd)						
上腕骨骨折	0	0	1 (0.3)	1 (0.3)	1 (0.2)	1 (0.2)
切開部位紅斑	0	0	1 (0.3)	0	1 (0.2)	0
切開部位痛	0	0	1 (0.3)	0	1 (0.2)	0
注入に伴う反応	0	0	2 (0.6)	0	2 (0.5)	0
関節損傷	0	0	1 (0.3)	0	1 (0.2)	0
裂傷	0	0	1 (0.3)	0	1 (0.2)	0
靭帯捻挫	1 (2.0)	0	2 (0.6)	0	3 (0.7)	0
眼窩周囲出血	0	0	1 (0.3)	0	1 (0.2)	0
処置後出血	0	0	1 (0.3)	1 (0.3)	1 (0.2)	1 (0.2)
処置による出血	0	0	1 (0.3)	0	1 (0.2)	0
処置による疼痛	1 (2.0)	0	3 (0.8)	1 (0.3)	4 (1.0)	1 (0.2)
放射線性肺臓炎	0	0	1 (0.3)	1 (0.3)	1 (0.2)	1 (0.2)
肋骨骨折	1 (2.0)	0	0	0	1 (0.2)	0
皮膚擦過傷	1 (2.0)	0	0	0	1 (0.2)	0
ストーマ部紅斑	1 (2.0)	0	0	0	1 (0.2)	0
舌損傷	0	0	1 (0.3)	0	1 (0.2)	0

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This table is based on adverse events data as available. Study 207 did not record laboratory abnormalities into adverse events data.

Program: V:¥projects¥e7389¥iss309¥csr¥dev¥pg¥tables¥T_2_7_4_3.sas 18JUN201513:33

付録 2.7.4-3
Japanese and Non-Japanese
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Eribulin Treated Safety Population

	日本人 Study 217 (N=51)		外国人 Studies 207+309 (N=353)		全体 Studies 217+207+309 (N=404)	
MedDRA System Organ Class Preferred Term	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)
傷害、中毒および処置合併症 (contd)						
尿管吻合合併症	0	0	1 (0.3)	1 (0.3)	1 (0.2)	1 (0.2)
創傷	1 (2.0)	0	2 (0.6)	0	3 (0.7)	0
創離開	0	0	1 (0.3)	1 (0.3)	1 (0.2)	1 (0.2)
創部内臓脱出	0	0	1 (0.3)	0	1 (0.2)	0
臨床検査	33 (64.7)	5 (9.8)	126 (35.7)	38 (10.8)	159 (39.4)	43 (10.6)
活性化部分トロンボプラスチン時間延長	1 (2.0)	0	0	0	1 (0.2)	0
アラニンアミノトランスフェラーゼ増加	14 (27.5)	3 (5.9)	18 (5.1)	3 (0.8)	32 (7.9)	6 (1.5)
アスパラギン酸アミノトランスフェラーゼ増加	13 (25.5)	2 (3.9)	21 (5.9)	1 (0.3)	34 (8.4)	3 (0.7)
血中アルブミン減少	2 (3.9)	0	1 (0.3)	0	3 (0.7)	0
血中アルカリホスファターゼ	0	0	1 (0.3)	0	1 (0.2)	0
血中アルカリホスファターゼ増加	5 (9.8)	0	10 (2.8)	1 (0.3)	15 (3.7)	1 (0.2)
血中ビリルビン増加	1 (2.0)	0	1 (0.3)	1 (0.3)	2 (0.5)	1 (0.2)
血中カルシウム減少	0	0	1 (0.3)	0	1 (0.2)	0
血中クレアチンホスホキナーゼ増加	8 (15.7)	0	0	0	8 (2.0)	0
血中クレアチニン増加	2 (3.9)	0	5 (1.4)	0	7 (1.7)	0

TEAE = treatment-emergent adverse event, Graded using Common Terminology Criteria for Adverse Events (CTCAE)
A subject with two or more adverse events in the same system organ class (or with the same preferred term) is counted once for that system organ class (or preferred term).
Adverse event terms are coded using Medical Dictionary for Regulatory Activities (MedDRA) version 17.1.
This table is based on adverse events data as available. Study 207 did not record laboratory abnormalities into adverse events data.

Program: V:¥projects¥e7389¥iss309¥csr¥dev¥pg¥tables¥T_2_7_4_3.sas 18JUN201513:33

付録 2.7.4-3
Japanese and Non-Japanese
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Eribulin Treated Safety Population

	日本人 Study 217 (N=51)		外国人 Studies 207+309 (N=353)		全体 Studies 217+207+309 (N=404)	
MedDRA System Organ Class Preferred Term	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)
臨床検査 (contd)						
血中乳酸脱水素酵素増加	11 (21.6)	0	12 (3.4)	0	23 (5.7)	0
血中マグネシウム減少	0	0	1 (0.3)	0	1 (0.2)	0
血中カリウム減少	0	0	1 (0.3)	1 (0.3)	1 (0.2)	1 (0.2)
血圧低下	1 (2.0)	0	0	0	1 (0.2)	0
血中尿素増加	0	0	1 (0.3)	0	1 (0.2)	0
尿中血陽性	2 (3.9)	0	0	0	2 (0.5)	0
Ｃ－反応性蛋白増加	6 (11.8)	0	0	0	6 (1.5)	0
心雑音	0	0	1 (0.3)	0	1 (0.2)	0
腎クレアチニン・クリアランス減少	0	0	1 (0.3)	0	1 (0.2)	0
心電図ＱＴ延長	1 (2.0)	0	15 (4.2)	5 (1.4)	16 (4.0)	5 (1.2)
心電図Ｔ波逆転	0	0	1 (0.3)	0	1 (0.2)	0
γ－グルタミルトランスフェラーゼ	0	0	2 (0.6)	2 (0.6)	2 (0.5)	2 (0.5)
γ－グルタミルトランスフェラーゼ増加	1 (2.0)	0	5 (1.4)	3 (0.8)	6 (1.5)	3 (0.7)
グリコヘモグロビン増加	0	0	1 (0.3)	0	1 (0.2)	0
ヘマトクリット減少	0	0	1 (0.3)	0	1 (0.2)	0
ヘモグロビン減少	2 (3.9)	0	7 (2.0)	0	9 (2.2)	0

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A subject with two or more adverse events in the same system organ class (or with the same preferred term) is counted once for that system organ class (or preferred term).
Adverse event terms are coded using Medical Dictionary for Regulatory Activities (MedDRA) version 17.1.
This table is based on adverse events data as available. Study 207 did not record laboratory abnormalities into adverse events data.

Program: V:¥projects¥e7389¥iss309¥csr¥dev¥pg¥tables¥T_2_7_4_3.sas 18JUN201513:33

付録 2.7.4-3
Japanese and Non-Japanese
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Eribulin Treated Safety Population

MedDRA System Organ Class Preferred Term	日本人 Study 217 (N=51) All Grades n(%)	 Grade >= 3 n(%)	外国人 Studies 207+309 (N=353) All Grades n(%)	 Grade >= 3 n(%)	全体 Studies 217+207+309 (N=404) All Grades n(%)	 Grade >= 3 n(%)
臨床検査 (contd)						
国際標準比増加	0	0	3 (0.8)	1 (0.3)	3 (0.7)	1 (0.2)
リパーゼ増加	0	0	1 (0.3)	1 (0.3)	1 (0.2)	1 (0.2)
肝機能検査異常	1 (2.0)	0	0	0	1 (0.2)	0
リンパ球数減少	0	0	3 (0.8)	0	3 (0.7)	0
好中球数減少	0	0	19 (5.4)	16 (4.5)	19 (4.7)	16 (4.0)
血小板数減少	0	0	2 (0.6)	2 (0.6)	2 (0.5)	2 (0.5)
総蛋白減少	1 (2.0)	0	2 (0.6)	0	3 (0.7)	0
尿蛋白	2 (3.9)	0	0	0	2 (0.5)	0
プロトロンビン時間比増加	1 (2.0)	0	0	0	1 (0.2)	0
赤血球数減少	0	0	2 (0.6)	0	2 (0.5)	0
トランスアミナーゼ上昇	0	0	1 (0.3)	0	1 (0.2)	0
尿中ケトン体陽性	0	0	1 (0.3)	0	1 (0.2)	0
体重減少	4 (7.8)	0	41 (11.6)	1 (0.3)	45 (11.1)	1 (0.2)
体重増加	1 (2.0)	1 (2.0)	13 (3.7)	0	14 (3.5)	1 (0.2)
白血球数減少	0	0	16 (4.5)	8 (2.3)	16 (4.0)	8 (2.0)
尿中白血球陽性	1 (2.0)	0	1 (0.3)	0	2 (0.5)	0

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A subject with two or more adverse events in the same system organ class (or with the same preferred term) is counted once for that system organ class (or preferred term).
Adverse event terms are coded using Medical Dictionary for Regulatory Activities (MedDRA) version 17.1.
This table is based on adverse events data as available. Study 207 did not record laboratory abnormalities into adverse events data.

Program: V:¥projects¥e7389¥iss309¥csr¥dev¥pg¥tables¥T_2_7_4_3.sas 18JUN201513:33

付録 2.7.4-3
Japanese and Non-Japanese
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Eribulin Treated Safety Population

MedDRA System Organ Class Preferred Term	日本人 Study 217 (N=51) All Grades n(%)	 Grade >= 3 n(%)	外国人 Studies 207+309 (N=353) All Grades n(%)	 Grade >= 3 n(%)	全体 Studies 217+207+309 (N=404) All Grades n(%)	 Grade >= 3 n(%)
代謝および栄養障害	30 (58.8)	10 (19.6)	127 (36.0)	29 (8.2)	157 (38.9)	39 (9.7)
悪液質	0	0	1 (0.3)	0	1 (0.2)	0
食欲減退	12 (23.5)	0	82 (23.2)	2 (0.6)	94 (23.3)	2 (0.5)
脱水	0	0	10 (2.8)	0	10 (2.5)	0
糖尿病	1 (2.0)	0	1 (0.3)	0	2 (0.5)	0
食物不耐性	0	0	1 (0.3)	0	1 (0.2)	0
高カルシウム血症	0	0	2 (0.6)	0	2 (0.5)	0
高クレアチニン血症	0	0	1 (0.3)	0	1 (0.2)	0
高血糖	0	0	18 (5.1)	7 (2.0)	18 (4.5)	7 (1.7)
高カリウム血症	0	0	1 (0.3)	0	1 (0.2)	0
高脂血症	4 (7.8)	0	1 (0.3)	0	5 (1.2)	0
高マグネシウム血症	0	0	2 (0.6)	0	2 (0.5)	0
高トリグリセリド血症	5 (9.8)	1 (2.0)	1 (0.3)	0	6 (1.5)	1 (0.2)
高尿酸血症	2 (3.9)	1 (2.0)	1 (0.3)	0	3 (0.7)	1 (0.2)
低アルブミン血症	10 (19.6)	2 (3.9)	12 (3.4)	3 (0.8)	22 (5.4)	5 (1.2)
低カルシウム血症	4 (7.8)	0	10 (2.8)	3 (0.8)	14 (3.5)	3 (0.7)
低血糖症	1 (2.0)	0	2 (0.6)	0	3 (0.7)	0

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A subject with two or more adverse events in the same system organ class (or with the same preferred term) is counted once for that system organ class (or preferred term).
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This table is based on adverse events data as available. Study 207 did not record laboratory abnormalities into adverse events data.

Program: V:¥projects¥e7389¥iss309¥csr¥dev¥pg¥tables¥T_2_7_4_3.sas 18JUN201513:33

付録 2.7.4-3
Japanese and Non-Japanese
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Eribulin Treated Safety Population

	日本人 Study 217 (N=51)		外国人 Studies 207+309 (N=353)		全体 Studies 217+207+309 (N=404)	
MedDRA System Organ Class Preferred Term	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)
代謝および栄養障害 (contd)						
低カリウム血症	6 (11.8)	3 (5.9)	24 (6.8)	7 (2.0)	30 (7.4)	10 (2.5)
低マグネシウム血症	0	0	8 (2.3)	2 (0.6)	8 (2.0)	2 (0.5)
低ナトリウム血症	0	0	6 (1.7)	4 (1.1)	6 (1.5)	4 (1.0)
低リン酸血症	8 (15.7)	5 (9.8)	6 (1.7)	2 (0.6)	14 (3.5)	7 (1.7)
低蛋白血症	3 (5.9)	0	0	0	3 (0.7)	0
鉄欠乏	0	0	1 (0.3)	0	1 (0.2)	0
乳酸アシドーシス	0	0	1 (0.3)	0	1 (0.2)	0
栄養障害	0	0	1 (0.3)	0	1 (0.2)	0
代謝性アシドーシス	0	0	1 (0.3)	0	1 (0.2)	0
肥満	0	0	2 (0.6)	2 (0.6)	2 (0.5)	2 (0.5)
筋骨格系および結合組織障害	15 (29.4)	1 (2.0)	169 (47.9)	12 (3.4)	184 (45.5)	13 (3.2)
関節痛	5 (9.8)	0	21 (5.9)	0	26 (6.4)	0
関節炎	0	0	1 (0.3)	0	1 (0.2)	0
関節障害	0	0	17 (4.8)	0	17 (4.2)	0
背部障害	0	0	21 (5.9)	1 (0.3)	21 (5.2)	1 (0.2)

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付録 2.7.4-3
Japanese and Non-Japanese
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Eribulin Treated Safety Population

	日本人 Study 217 (N=51)		外国人 Studies 207+309 (N=353)		全体 Studies 217+207+309 (N=404)	
MedDRA System Organ Class Preferred Term	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)
筋骨格系および結合組織障害 (contd)						
背部痛	7 (13.7)	0	36 (10.2)	4 (1.1)	43 (10.6)	4 (1.0)
骨痛	1 (2.0)	0	3 (0.8)	0	4 (1.0)	0
側腹部痛	0	0	4 (1.1)	0	4 (1.0)	0
鼡径部痛	0	0	4 (1.1)	0	4 (1.0)	0
顎障害	0	0	1 (0.3)	0	1 (0.2)	0
関節腫脹	0	0	2 (0.6)	0	2 (0.5)	0
四肢不快感	0	0	1 (0.3)	0	1 (0.2)	0
咀嚼障害	0	0	1 (0.3)	0	1 (0.2)	0
筋障害	0	0	26 (7.4)	2 (0.6)	26 (6.4)	2 (0.5)
筋肉疲労	0	0	1 (0.3)	0	1 (0.2)	0
筋痙縮	0	0	16 (4.5)	0	16 (4.0)	0
筋力低下	0	0	10 (2.8)	1 (0.3)	10 (2.5)	1 (0.2)
筋骨格系胸痛	0	0	16 (4.5)	0	16 (4.0)	0
筋骨格不快感	0	0	2 (0.6)	0	2 (0.5)	0
筋骨格痛	0	0	17 (4.8)	0	17 (4.2)	0
筋骨格硬直	0	0	3 (0.8)	0	3 (0.7)	0

TEAE = treatment-emergent adverse event, Graded using Common Terminology Criteria for Adverse Events (CTCAE)
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付録 2.7.4-3
Japanese and Non-Japanese
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Eribulin Treated Safety Population

	日本人 Study 217 (N=51)		外国人 Studies 207+309 (N=353)		全体 Studies 217+207+309 (N=404)	
MedDRA System Organ Class Preferred Term	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)
筋骨格系および結合組織障害 (contd)						
筋肉痛	2 (3.9)	0	23 (6.5)	0	25 (6.2)	0
ミオパチー	0	0	1 (0.3)	0	1 (0.2)	0
筋炎	0	0	1 (0.3)	1 (0.3)	1 (0.2)	1 (0.2)
頚部痛	0	0	4 (1.1)	0	4 (1.0)	0
変形性関節症	3 (5.9)	0	0	0	3 (0.7)	0
四肢痛	4 (7.8)	1 (2.0)	31 (8.8)	1 (0.3)	35 (8.7)	2 (0.5)
顎痛	0	0	2 (0.6)	0	2 (0.5)	0
病的骨折	0	0	2 (0.6)	2 (0.6)	2 (0.5)	2 (0.5)
肩回旋筋腱板症候群	0	0	2 (0.6)	0	2 (0.5)	0
脊椎痛	0	0	1 (0.3)	1 (0.3)	1 (0.2)	1 (0.2)
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）	25 (49.0)	5 (9.8)	70 (19.8)	21 (5.9)	95 (23.5)	26 (6.4)
基底細胞癌	0	0	1 (0.3)	0	1 (0.2)	0
癌疼痛	23 (45.1)	3 (5.9)	4 (1.1)	2 (0.6)	27 (6.7)	5 (1.2)
口唇および口腔内癌	0	0	1 (0.3)	1 (0.3)	1 (0.2)	1 (0.2)
悪性新生物進行	0	0	2 (0.6)	1 (0.3)	2 (0.5)	1 (0.2)

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Program: V:¥projects¥e7389¥iss309¥csr¥dev¥pg¥tables¥T_2_7_4_3.sas 18JUN201513:33

付録 2.7.4-3
Japanese and Non-Japanese
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Eribulin Treated Safety Population

	日本人 Study 217 (N=51)		外国人 Studies 207+309 (N=353)		全体 Studies 217+207+309 (N=404)	
MedDRA System Organ Class Preferred Term	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)	All Grades 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） (contd)						
悪性胸水	0	0	3 (0.8)	1 (0.3)	3 (0.7)	1 (0.2)
腹腔内転移	0	0	1 (0.3)	1 (0.3)	1 (0.2)	1 (0.2)
骨転移	0	0	1 (0.3)	1 (0.3)	1 (0.2)	1 (0.2)
肺転移	0	0	1 (0.3)	1 (0.3)	1 (0.2)	1 (0.2)
頚部転移	0	0	1 (0.3)	1 (0.3)	1 (0.2)	1 (0.2)
転移部痛	0	0	2 (0.6)	1 (0.3)	2 (0.5)	1 (0.2)
粘液型脂肪肉腫	0	0	1 (0.3)	0	1 (0.2)	0
悪性新生物	0	0	1 (0.3)	0	1 (0.2)	0
腫瘍熱	1 (2.0)	0	1 (0.3)	0	2 (0.5)	0
腫瘍性塞栓症	1 (2.0)	1 (2.0)	0	0	1 (0.2)	1 (0.2)
腫瘍出血	1 (2.0)	1 (2.0)	3 (0.8)	2 (0.6)	4 (1.0)	3 (0.7)
腫瘍疼痛	0	0	49 (13.9)	10 (2.8)	49 (12.1)	10 (2.5)
腫瘍の潰瘍形成	0	0	1 (0.3)	1 (0.3)	1 (0.2)	1 (0.2)
神経系障害	29 (56.9)	0	187 (53.0)	26 (7.4)	216 (53.5)	26 (6.4)
味覚消失	0	0	1 (0.3)	0	1 (0.2)	0

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Program: V:¥projects¥e7389¥iss309¥csr¥dev¥pg¥tables¥T_2_7_4_3.sas 18JUN201513:33

付録 2.7.4-3
Japanese and Non-Japanese
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Eribulin Treated Safety Population

	日本人 Study 217 (N=51)		外国人 Studies 207+309 (N=353)		全体 Studies 217+207+309 (N=404)	
MedDRA System Organ Class Preferred Term	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)
神経系障害 (contd)						
前脊髄動脈症候群	0	0	1 (0.3)	1 (0.3)	1 (0.2)	1 (0.2)
失声症	0	0	1 (0.3)	1 (0.3)	1 (0.2)	1 (0.2)
平衡障害	0	0	1 (0.3)	0	1 (0.2)	0
灼熱感	0	0	1 (0.3)	0	1 (0.2)	0
脳虚血	0	0	2 (0.6)	2 (0.6)	2 (0.5)	2 (0.5)
頚腕症候群	0	0	1 (0.3)	0	1 (0.2)	0
痙攣	0	0	1 (0.3)	1 (0.3)	1 (0.2)	1 (0.2)
注意力障害	0	0	4 (1.1)	0	4 (1.0)	0
浮動性めまい	2 (3.9)	0	48 (13.6)	1 (0.3)	50 (12.4)	1 (0.2)
異常感覚	0	0	1 (0.3)	0	1 (0.2)	0
味覚異常	12 (23.5)	0	37 (10.5)	0	49 (12.1)	0
ジスキネジア	0	0	1 (0.3)	0	1 (0.2)	0
頭痛	6 (11.8)	0	64 (18.1)	0	70 (17.3)	0
感覚鈍麻	2 (3.9)	0	5 (1.4)	1 (0.3)	7 (1.7)	1 (0.2)
嗅覚減退	0	0	1 (0.3)	0	1 (0.2)	0
肋間神経痛	1 (2.0)	0	0	0	1 (0.2)	0

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Program: V:¥projects¥e7389¥iss309¥csr¥dev¥pg¥tables¥T_2_7_4_3.sas 18JUN201513:33

付録 2.7.4-3
Japanese and Non-Japanese
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Eribulin Treated Safety Population

	日本人 Study 217 (N=51)		外国人 Studies 207+309 (N=353)		全体 Studies 217+207+309 (N=404)	
MedDRA System Organ Class Preferred Term	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)
神経系障害 (contd)						
嗜眠	0	0	6 (1.7)	1 (0.3)	6 (1.5)	1 (0.2)
固有感覚の欠如	0	0	1 (0.3)	0	1 (0.2)	0
記憶障害	0	0	3 (0.8)	0	3 (0.7)	0
片頭痛	0	0	2 (0.6)	0	2 (0.5)	0
単麻痺	0	0	1 (0.3)	1 (0.3)	1 (0.2)	1 (0.2)
神経痛	0	0	4 (1.1)	0	4 (1.0)	0
末梢性ニューロパチー	16 (31.4)	0	1 (0.3)	0	17 (4.2)	0
起立不耐性	0	0	1 (0.3)	0	1 (0.2)	0
錯感覚	0	0	20 (5.7)	1 (0.3)	20 (5.0)	1 (0.2)
嗅覚錯誤	0	0	1 (0.3)	0	1 (0.2)	0
末梢性運動ニューロパチー	0	0	16 (4.5)	7 (2.0)	16 (4.0)	7 (1.7)
末梢性感覚運動ニューロパチー	0	0	2 (0.6)	0	2 (0.5)	0
末梢性感覚ニューロパチー	3 (5.9)	0	92 (26.1)	8 (2.3)	95 (23.5)	8 (2.0)
多発ニューロパチー	0	0	1 (0.3)	1 (0.3)	1 (0.2)	1 (0.2)
ヘルペス後神経痛	1 (2.0)	0	0	0	1 (0.2)	0
失神寸前の状態	0	0	1 (0.3)	1 (0.3)	1 (0.2)	1 (0.2)

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Program: V:¥projects¥e7389¥iss309¥csr¥dev¥pg¥tables¥T_2_7_4_3.sas 18JUN201513:33

付録 2.7.4-3
Japanese and Non-Japanese
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Eribulin Treated Safety Population

	日本人 Study 217 (N=51)		外国人 Studies 207+309 (N=353)		全体 Studies 217+207+309 (N=404)	
MedDRA System Organ Class Preferred Term	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)
神経系障害 (contd)						
下肢静止不能症候群	0	0	1 (0.3)	0	1 (0.2)	0
坐骨神経痛	1 (2.0)	0	2 (0.6)	0	3 (0.7)	0
感覚障害	2 (3.9)	0	1 (0.3)	0	3 (0.7)	0
副鼻腔炎に伴う頭痛	0	0	1 (0.3)	0	1 (0.2)	0
傾眠	2 (3.9)	0	10 (2.8)	0	12 (3.0)	0
脊髄圧迫	0	0	1 (0.3)	1 (0.3)	1 (0.2)	1 (0.2)
失神	0	0	1 (0.3)	1 (0.3)	1 (0.2)	1 (0.2)
振戦	0	0	1 (0.3)	0	1 (0.2)	0
声帯麻痺	1 (2.0)	0	0	0	1 (0.2)	0
精神障害	7 (13.7)	1 (2.0)	81 (22.9)	3 (0.8)	88 (21.8)	4 (1.0)
感情障害	0	0	3 (0.8)	0	3 (0.7)	0
激越	0	0	4 (1.1)	1 (0.3)	4 (1.0)	1 (0.2)
不安	1 (2.0)	0	24 (6.8)	0	25 (6.2)	0
カタトニー	0	0	1 (0.3)	0	1 (0.2)	0
錯乱状態	0	0	7 (2.0)	1 (0.3)	7 (1.7)	1 (0.2)

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付録 2.7.4-3
Japanese and Non-Japanese
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Eribulin Treated Safety Population

	日本人 Study 217 (N=51)		外国人 Studies 207+309 (N=353)		全体 Studies 217+207+309 (N=404)	
MedDRA System Organ Class Preferred Term	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)
精神障害 (contd)						
譫妄	1 (2.0)	1 (2.0)	1 (0.3)	0	2 (0.5)	1 (0.2)
抑うつ気分	0	0	12 (3.4)	0	12 (3.0)	0
うつ病	0	0	4 (1.1)	0	4 (1.0)	0
幻覚	0	0	1 (0.3)	0	1 (0.2)	0
不眠症	5 (9.8)	0	37 (10.5)	1 (0.3)	42 (10.4)	1 (0.2)
易刺激性	0	0	2 (0.6)	0	2 (0.5)	0
気分変化	0	0	1 (0.3)	0	1 (0.2)	0
神経症	0	0	1 (0.3)	0	1 (0.2)	0
精神病性障害	0	0	1 (0.3)	0	1 (0.2)	0
睡眠障害	0	0	2 (0.6)	0	2 (0.5)	0
腎および尿路障害	9 (17.6)	1 (2.0)	31 (8.8)	3 (0.8)	40 (9.9)	4 (1.0)
膀胱痛	0	0	3 (0.8)	0	3 (0.7)	0
排尿困難	1 (2.0)	0	9 (2.5)	1 (0.3)	10 (2.5)	1 (0.2)
糖尿	0	0	2 (0.6)	0	2 (0.5)	0
血尿	1 (2.0)	0	4 (1.1)	1 (0.3)	5 (1.2)	1 (0.2)

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付録 2.7.4-3
Japanese and Non-Japanese
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Eribulin Treated Safety Population

	日本人 Study 217 (N=51)		外国人 Studies 207+309 (N=353)		全体 Studies 217+207+309 (N=404)	
MedDRA System Organ Class Preferred Term	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)
腎および尿路障害 (contd)						
水腎症	1 (2.0)	1 (2.0)	2 (0.6)	0	3 (0.7)	1 (0.2)
尿意切迫	0	0	3 (0.8)	0	3 (0.7)	0
乏尿	0	0	1 (0.3)	0	1 (0.2)	0
頻尿	1 (2.0)	0	4 (1.1)	0	5 (1.2)	0
多尿	0	0	1 (0.3)	0	1 (0.2)	0
蛋白尿	5 (9.8)	0	1 (0.3)	0	6 (1.5)	0
腎盂腎杯拡張症	0	0	2 (0.6)	0	2 (0.5)	0
腎障害	1 (2.0)	0	0	0	1 (0.2)	0
腎不全	0	0	3 (0.8)	1 (0.3)	3 (0.7)	1 (0.2)
急性腎不全	0	0	2 (0.6)	0	2 (0.5)	0
慢性腎不全	1 (2.0)	0	0	0	1 (0.2)	0
尿閉	0	0	3 (0.8)	0	3 (0.7)	0
尿路痛	0	0	1 (0.3)	0	1 (0.2)	0
生殖系および乳房障害	1 (2.0)	1 (2.0)	17 (4.8)	0	18 (4.5)	1 (0.2)
後天性包茎	0	0	1 (0.3)	0	1 (0.2)	0

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付録 2.7.4-3
Japanese and Non-Japanese
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Eribulin Treated Safety Population

	日本人 Study 217 (N=51)		外国人 Studies 207+309 (N=353)		全体 Studies 217+207+309 (N=404)	
MedDRA System Organ Class Preferred Term	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)
生殖系および乳房障害 (contd)						
乳房痛	0	0	2 (0.6)	0	2 (0.5)	0
勃起不全	0	0	2 (0.6)	0	2 (0.5)	0
卵管障害	0	0	1 (0.3)	0	1 (0.2)	0
不規則月経	1 (2.0)	1 (2.0)	1 (0.3)	0	2 (0.5)	1 (0.2)
乳頭痛	0	0	1 (0.3)	0	1 (0.2)	0
性器浮腫	0	0	1 (0.3)	0	1 (0.2)	0
骨盤不快感	0	0	1 (0.3)	0	1 (0.2)	0
会陰痛	0	0	1 (0.3)	0	1 (0.2)	0
腟出血	0	0	5 (1.4)	0	5 (1.2)	0
腟の炎症	0	0	1 (0.3)	0	1 (0.2)	0
外陰腟乾燥	0	0	2 (0.6)	0	2 (0.5)	0
外陰腟そう痒症	0	0	1 (0.3)	0	1 (0.2)	0
呼吸器、胸郭および縦隔障害	22 (43.1)	2 (3.9)	162 (45.9)	27 (7.6)	184 (45.5)	29 (7.2)
急性呼吸不全	0	0	2 (0.6)	1 (0.3)	2 (0.5)	1 (0.2)
無気肺	0	0	1 (0.3)	0	1 (0.2)	0

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付録 2.7.4-3
Japanese and Non-Japanese
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Eribulin Treated Safety Population

	日本人 Study 217 (N=51)		外国人 Studies 207+309 (N=353)		全体 Studies 217+207+309 (N=404)	
MedDRA System Organ Class Preferred Term	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)
呼吸器、胸郭および縦隔障害 (contd)						
慢性閉塞性肺疾患	0	0	1 (0.3)	1 (0.3)	1 (0.2)	1 (0.2)
咳嗽	6 (11.8)	0	69 (19.5)	1 (0.3)	75 (18.6)	1 (0.2)
発声障害	1 (2.0)	0	12 (3.4)	1 (0.3)	13 (3.2)	1 (0.2)
呼吸困難	3 (5.9)	1 (2.0)	77 (21.8)	11 (3.1)	80 (19.8)	12 (3.0)
労作性呼吸困難	0	0	2 (0.6)	0	2 (0.5)	0
鼻出血	2 (3.9)	0	10 (2.8)	0	12 (3.0)	0
喀血	1 (2.0)	0	0	0	1 (0.2)	0
しゃっくり	0	0	2 (0.6)	0	2 (0.5)	0
高炭酸ガス血症	0	0	1 (0.3)	0	1 (0.2)	0
低酸素症	1 (2.0)	0	0	0	1 (0.2)	0
間質性肺疾患	1 (2.0)	0	0	0	1 (0.2)	0
肺障害	0	0	1 (0.3)	0	1 (0.2)	0
鼻閉	1 (2.0)	0	5 (1.4)	0	6 (1.5)	0
鼻部障害	0	0	1 (0.3)	0	1 (0.2)	0
鼻潰瘍	0	0	1 (0.3)	0	1 (0.2)	0
閉塞性気道障害	0	0	1 (0.3)	0	1 (0.2)	0

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付録 2.7.4-3
Japanese and Non-Japanese
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Eribulin Treated Safety Population

	日本人 Study 217 (N=51)		外国人 Studies 207+309 (N=353)		全体 Studies 217+207+309 (N=404)	
MedDRA System Organ Class Preferred Term	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)
呼吸器、胸郭および縦隔障害 (contd)						
口腔咽頭不快感	2 (3.9)	0	0	0	2 (0.5)	0
口腔咽頭痛	5 (9.8)	0	18 (5.1)	0	23 (5.7)	0
呼吸時疼痛	0	0	1 (0.3)	1 (0.3)	1 (0.2)	1 (0.2)
咽頭紅斑	0	0	3 (0.8)	0	3 (0.7)	0
胸水	1 (2.0)	0	6 (1.7)	2 (0.6)	7 (1.7)	2 (0.5)
胸膜痛	0	0	2 (0.6)	0	2 (0.5)	0
誤嚥性肺炎	0	0	1 (0.3)	1 (0.3)	1 (0.2)	1 (0.2)
気胸	0	0	1 (0.3)	0	1 (0.2)	0
湿性咳嗽	0	0	4 (1.1)	0	4 (1.0)	0
肺塞栓症	1 (2.0)	1 (2.0)	6 (1.7)	6 (1.7)	7 (1.7)	7 (1.7)
肺水腫	0	0	1 (0.3)	0	1 (0.2)	0
肺血栓症	0	0	1 (0.3)	0	1 (0.2)	0
呼吸不全	0	0	4 (1.1)	4 (1.1)	4 (1.0)	4 (1.0)
気道出血	0	0	1 (0.3)	0	1 (0.2)	0
鼻痛	0	0	1 (0.3)	0	1 (0.2)	0
アレルギー性鼻炎	0	0	1 (0.3)	0	1 (0.2)	0

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付録 2.7.4-3
Japanese and Non-Japanese
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Eribulin Treated Safety Population

	日本人 Study 217 (N=51)		外国人 Studies 207+309 (N=353)		全体 Studies 217+207+309 (N=404)	
MedDRA System Organ Class Preferred Term	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)
呼吸器、胸郭および縦隔障害 (contd)						
鼻漏	0	0	11 (3.1)	0	11 (2.7)	0
副鼻腔うっ血	0	0	2 (0.6)	0	2 (0.5)	0
上気道の炎症	1 (2.0)	0	0	0	1 (0.2)	0
上気道咳症候群	0	0	2 (0.6)	0	2 (0.5)	0
皮膚および皮下組織障害	24 (47.1)	0	180 (51.0)	1 (0.3)	204 (50.5)	1 (0.2)
ざ瘡	0	0	1 (0.3)	0	1 (0.2)	0
日光角化症	0	0	1 (0.3)	0	1 (0.2)	0
脱毛症	14 (27.5)	0	140 (39.7)	1 (0.3)	154 (38.1)	1 (0.2)
水疱	1 (2.0)	0	0	0	1 (0.2)	0
褥瘡性潰瘍	1 (2.0)	0	0	0	1 (0.2)	0
皮膚嚢腫	0	0	1 (0.3)	0	1 (0.2)	0
皮膚炎	1 (2.0)	0	1 (0.3)	0	2 (0.5)	0
ざ瘡様皮膚炎	0	0	1 (0.3)	0	1 (0.2)	0
おむつ皮膚炎	0	0	1 (0.3)	0	1 (0.2)	0
皮膚筋炎	1 (2.0)	0	0	0	1 (0.2)	0

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付録 2.7.4-3
Japanese and Non-Japanese
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Eribulin Treated Safety Population

	日本人 Study 217 (N=51)		外国人 Studies 207+309 (N=353)		全体 Studies 217+207+309 (N=404)	
MedDRA System Organ Class Preferred Term	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)
皮膚および皮下組織障害 (contd)						
皮膚乾燥	2 (3.9)	0	8 (2.3)	0	10 (2.5)	0
湿疹	3 (5.9)	0	2 (0.6)	0	5 (1.2)	0
紅斑	2 (3.9)	0	4 (1.1)	0	6 (1.5)	0
剥脱性発疹	0	0	10 (2.8)	0	10 (2.5)	0
毛髪変色	0	0	1 (0.3)	0	1 (0.2)	0
多汗症	0	0	14 (4.0)	0	14 (3.5)	0
睫毛眉毛脱落症	0	0	1 (0.3)	0	1 (0.2)	0
爪の障害	0	0	6 (1.7)	0	6 (1.5)	0
爪毒性	0	0	1 (0.3)	0	1 (0.2)	0
寝汗	0	0	3 (0.8)	0	3 (0.7)	0
爪甲離床症	0	0	1 (0.3)	0	1 (0.2)	0
爪甲脱落症	0	0	1 (0.3)	0	1 (0.2)	0
皮膚疼痛	0	0	1 (0.3)	0	1 (0.2)	0
手掌・足底発赤知覚不全症候群	0	0	4 (1.1)	0	4 (1.0)	0
光線過敏性反応	0	0	1 (0.3)	0	1 (0.2)	0
そう痒症	2 (3.9)	0	14 (4.0)	0	16 (4.0)	0

TEAE = treatment-emergent adverse event, Graded using Common Terminology Criteria for Adverse Events (CTCAE)
A subject with two or more adverse events in the same system organ class (or with the same preferred term) is counted once for that system organ class (or preferred term).
Adverse event terms are coded using Medical Dictionary for Regulatory Activities (MedDRA) version 17.1.
This table is based on adverse events data as available. Study 207 did not record laboratory abnormalities into adverse events data.

Program: V:¥projects¥e7389¥iss309¥csr¥dev¥pg¥tables¥T_2_7_4_3.sas 18JUN201513:33

付録 2.7.4-3
Japanese and Non-Japanese
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Eribulin Treated Safety Population

	日本人 Study 217 (N=51)		外国人 Studies 207+309 (N=353)		全体 Studies 217+207+309 (N=404)	
MedDRA System Organ Class Preferred Term	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)
皮膚および皮下組織障害 (contd)						
全身性そう痒症	0	0	1 (0.3)	0	1 (0.2)	0
紫斑	1 (2.0)	0	0	0	1 (0.2)	0
発疹	6 (11.8)	0	10 (2.8)	0	16 (4.0)	0
斑状丘疹状皮疹	2 (3.9)	0	1 (0.3)	0	3 (0.7)	0
そう痒性皮疹	0	0	1 (0.3)	0	1 (0.2)	0
瘢痕痛	0	0	1 (0.3)	0	1 (0.2)	0
皮膚障害	0	0	1 (0.3)	0	1 (0.2)	0
皮膚亀裂	0	0	3 (0.8)	0	3 (0.7)	0
皮膚色素過剰	1 (2.0)	0	1 (0.3)	0	2 (0.5)	0
皮膚病変	0	0	2 (0.6)	0	2 (0.5)	0
皮膚のつっぱり感	0	0	1 (0.3)	0	1 (0.2)	0
皮膚潰瘍	0	0	1 (0.3)	0	1 (0.2)	0
皮膚のべとつき感	0	0	1 (0.3)	0	1 (0.2)	0
顔面腫脹	0	0	1 (0.3)	0	1 (0.2)	0
蕁麻疹	1 (2.0)	0	3 (0.8)	0	4 (1.0)	0

TEAE = treatment-emergent adverse event, Graded using Common Terminology Criteria for Adverse Events (CTCAE)
A subject with two or more adverse events in the same system organ class (or with the same preferred term) is counted once for that system organ class (or preferred term).
Adverse event terms are coded using Medical Dictionary for Regulatory Activities (MedDRA) version 17.1.
This table is based on adverse events data as available. Study 207 did not record laboratory abnormalities into adverse events data.

Program: V:¥projects¥e7389¥iss309¥csr¥dev¥pg¥tables¥T_2_7_4_3.sas 18JUN201513:33

付録 2.7.4-3
Japanese and Non-Japanese
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Eribulin Treated Safety Population

	日本人 Study 217 (N=51)		外国人 Studies 207+309 (N=353)		全体 Studies 217+207+309 (N=404)	
MedDRA System Organ Class Preferred Term	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)
外科および内科処置	0	0	1 (0.3)	1 (0.3)	1 (0.2)	1 (0.2)
癌手術	0	0	1 (0.3)	1 (0.3)	1 (0.2)	1 (0.2)
血管障害	7 (13.7)	1 (2.0)	59 (16.7)	6 (1.7)	66 (16.3)	7 (1.7)
深部静脈血栓症	1 (2.0)	0	2 (0.6)	1 (0.3)	3 (0.7)	1 (0.2)
塞栓症	0	0	3 (0.8)	0	3 (0.7)	0
潮紅	0	0	9 (2.5)	0	9 (2.2)	0
血腫	0	0	1 (0.3)	0	1 (0.2)	0
ほてり	0	0	5 (1.4)	0	5 (1.2)	0
高血圧	3 (5.9)	1 (2.0)	14 (4.0)	1 (0.3)	17 (4.2)	2 (0.5)
低血圧	0	0	18 (5.1)	1 (0.3)	18 (4.5)	1 (0.2)
リンパ浮腫	2 (3.9)	0	1 (0.3)	0	3 (0.7)	0
起立性低血圧	0	0	1 (0.3)	0	1 (0.2)	0
蒼白	0	0	1 (0.3)	0	1 (0.2)	0
骨盤静脈血栓症	1 (2.0)	0	0	0	1 (0.2)	0
末梢静脈疾患	0	0	1 (0.3)	0	1 (0.2)	0
静脈炎	0	0	2 (0.6)	0	2 (0.5)	0

TEAE = treatment-emergent adverse event, Graded using Common Terminology Criteria for Adverse Events (CTCAE)
A subject with two or more adverse events in the same system organ class (or with the same preferred term) is counted once for that system organ class (or preferred term).
Adverse event terms are coded using Medical Dictionary for Regulatory Activities (MedDRA) version 17.1.
This table is based on adverse events data as available. Study 207 did not record laboratory abnormalities into adverse events data.

Program: V:¥projects¥e7389¥iss309¥csr¥dev¥pg¥tables¥T_2_7_4_3.sas 18JUN201513:33

付録 2.7.4-3
Japanese and Non-Japanese
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Eribulin Treated Safety Population

	日本人 Study 217 (N=51)		外国人 Studies 207+309 (N=353)		全体 Studies 217+207+309 (N=404)	
MedDRA System Organ Class Preferred Term	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)
血管障害 (contd)						
高血圧前症	0	0	1 (0.3)	0	1 (0.2)	0
上大静脈症候群	0	0	1 (0.3)	0	1 (0.2)	0
血栓症	0	0	1 (0.3)	1 (0.3)	1 (0.2)	1 (0.2)
血管炎	1 (2.0)	0	0	0	1 (0.2)	0
大静脈塞栓症	0	0	1 (0.3)	1 (0.3)	1 (0.2)	1 (0.2)
大静脈血栓症	0	0	1 (0.3)	1 (0.3)	1 (0.2)	1 (0.2)

TEAE = treatment-emergent adverse event, Graded using Common Terminology Criteria for Adverse Events (CTCAE)
A subject with two or more adverse events in the same system organ class (or with the same preferred term) is counted once for that system organ class (or preferred term).
Adverse event terms are coded using Medical Dictionary for Regulatory Activities (MedDRA) version 17.1.
This table is based on adverse events data as available. Study 207 did not record laboratory abnormalities into adverse events data.

Program: V:¥projects¥e7389¥iss309¥csr¥dev¥pg¥tables¥T_2_7_4_3.sas 18JUN201513:33

付録 2.7.4-4
Japanese and Non-Japanese (Excluding Study 207)/血液およびリンパ系障害，臨床検査
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Eribulin Treated Safety Population

	日本人 Study 217 (N=51)		外国人 Study 309 (N=226)		全体 Studies 217+309 (N=277)	
MedDRA System Organ Class Preferred Term	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)
Any TEAEs	51 (100.0)	48 (94.1)	159 (70.4)	115 (50.9)	210 (75.8)	163 (58.8)
血液およびリンパ系障害	51 (100.0)	48 (94.1)	137 (60.6)	97 (42.9)	188 (67.9)	145 (52.3)
貧血	24 (47.1)	7 (13.7)	67 (29.6)	16 (7.1)	91 (32.9)	23 (8.3)
発熱性好中球減少症	4 (7.8)	4 (7.8)	2 (0.9)	2 (0.9)	6 (2.2)	6 (2.2)
ヘモグロビン血症	0	0	3 (1.3)	2 (0.9)	3 (1.1)	2 (0.7)
白血球増加症	0	0	1 (0.4)	1 (0.4)	1 (0.4)	1 (0.4)
白血球減少症	51 (100.0)	38 (74.5)	36 (15.9)	23 (10.2)	87 (31.4)	61 (22.0)
リンパ節痛	0	0	1 (0.4)	0	1 (0.4)	0
リンパ節症	0	0	1 (0.4)	0	1 (0.4)	0
リンパ球減少症	40 (78.4)	17 (33.3)	3 (1.3)	3 (1.3)	43 (15.5)	20 (7.2)
好中球減少症	50 (98.0)	44 (86.3)	99 (43.8)	80 (35.4)	149 (53.8)	124 (44.8)
血小板減少症	3 (5.9)	0	13 (5.8)	1 (0.4)	16 (5.8)	1 (0.4)
血小板増加症	0	0	1 (0.4)	0	1 (0.4)	0
臨床検査	33 (64.7)	5 (9.8)	80 (35.4)	35 (15.5)	113 (40.8)	40 (14.4)
活性化部分トロンボプラスチン時間延長	1 (2.0)	0	0	0	1 (0.4)	0

TEAE = treatment-emergent adverse event, Graded using Common Terminology Criteria for Adverse Events (CTCAE)
A subject with two or more adverse events in the same system organ class (or with the same preferred term) is counted once for that system organ class (or preferred term).
Adverse event terms are coded using Medical Dictionary for Regulatory Activities (MedDRA) version 17.1.

Program: V:¥projects¥e7389¥iss309¥csr¥dev¥pg¥tables¥T_2_7_4_4.sas 18JUN201513:33

付録 2.7.4-4
Japanese and Non-Japanese (Excluding Study 207)/血液およびリンパ系障害，臨床検査
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Eribulin Treated Safety Population

	日本人 Study 217 (N=51)		外国人 Study 309 (N=226)		全体 Studies 217+309 (N=277)	
MedDRA System Organ Class Preferred Term	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)
臨床検査 (contd)						
アラニンアミノトランスフェラーゼ増加	14 (27.5)	3 (5.9)	18 (8.0)	3 (1.3)	32 (11.6)	6 (2.2)
アスパラギン酸アミノトランスフェラーゼ増加	13 (25.5)	2 (3.9)	21 (9.3)	1 (0.4)	34 (12.3)	3 (1.1)
血中アルブミン減少	2 (3.9)	0	1 (0.4)	0	3 (1.1)	0
血中アルカリホスファターゼ増加	5 (9.8)	0	10 (4.4)	1 (0.4)	15 (5.4)	1 (0.4)
血中ビリルビン増加	1 (2.0)	0	1 (0.4)	1 (0.4)	2 (0.7)	1 (0.4)
血中カルシウム減少	0	0	1 (0.4)	0	1 (0.4)	0
血中クレアチンホスホキナーゼ増加	8 (15.7)	0	0	0	8 (2.9)	0
血中クレアチニン増加	2 (3.9)	0	5 (2.2)	0	7 (2.5)	0
血中乳酸脱水素酵素増加	11 (21.6)	0	12 (5.3)	0	23 (8.3)	0
血中マグネシウム減少	0	0	1 (0.4)	0	1 (0.4)	0
血中カリウム減少	0	0	1 (0.4)	1 (0.4)	1 (0.4)	1 (0.4)
血圧低下	1 (2.0)	0	0	0	1 (0.4)	0
血中尿素増加	0	0	1 (0.4)	0	1 (0.4)	0
尿中血陽性	2 (3.9)	0	0	0	2 (0.7)	0
Ｃ－反応性蛋白増加	6 (11.8)	0	0	0	6 (2.2)	0
心雑音	0	0	1 (0.4)	0	1 (0.4)	0

TEAE = treatment-emergent adverse event, Graded using Common Terminology Criteria for Adverse Events (CTCAE)
A subject with two or more adverse events in the same system organ class (or with the same preferred term) is counted once for that system organ class (or preferred term).
Adverse event terms are coded using Medical Dictionary for Regulatory Activities (MedDRA) version 17.1.

Program: V:¥projects¥e7389¥iss309¥csr¥dev¥pg¥tables¥T_2_7_4_4.sas 18JUN201513:33

付録 2.7.4-4
Japanese and Non-Japanese (Excluding Study 207)/血液およびリンパ系障害，臨床検査
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Eribulin Treated Safety Population

	日本人 Study 217 (N=51)		外国人 Study 309 (N=226)		全体 Studies 217+309 (N=277)	
MedDRA System Organ Class Preferred Term	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)
臨床検査 (contd)						
腎クレアチニン・クリアランス減少	0	0	1 (0.4)	0	1 (0.4)	0
心電図ＱＴ延長	1 (2.0)	0	15 (6.6)	5 (2.2)	16 (5.8)	5 (1.8)
心電図Ｔ波逆転	0	0	1 (0.4)	0	1 (0.4)	0
γ－グルタミルトランスフェラーゼ増加	1 (2.0)	0	5 (2.2)	3 (1.3)	6 (2.2)	3 (1.1)
グリコヘモグロビン増加	0	0	1 (0.4)	0	1 (0.4)	0
ヘマトクリット減少	0	0	1 (0.4)	0	1 (0.4)	0
ヘモグロビン減少	2 (3.9)	0	7 (3.1)	0	9 (3.2)	0
国際標準比増加	0	0	3 (1.3)	1 (0.4)	3 (1.1)	1 (0.4)
リパーゼ増加	0	0	1 (0.4)	1 (0.4)	1 (0.4)	1 (0.4)
肝機能検査異常	1 (2.0)	0	0	0	1 (0.4)	0
リンパ球数減少	0	0	3 (1.3)	0	3 (1.1)	0
好中球数減少	0	0	19 (8.4)	16 (7.1)	19 (6.9)	16 (5.8)
血小板数減少	0	0	2 (0.9)	2 (0.9)	2 (0.7)	2 (0.7)
総蛋白減少	1 (2.0)	0	2 (0.9)	0	3 (1.1)	0
尿蛋白	2 (3.9)	0	0	0	2 (0.7)	0
プロトロンビン時間比増加	1 (2.0)	0	0	0	1 (0.4)	0

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A subject with two or more adverse events in the same system organ class (or with the same preferred term) is counted once for that system organ class (or preferred term).
Adverse event terms are coded using Medical Dictionary for Regulatory Activities (MedDRA) version 17.1.

Program: V:¥projects¥e7389¥iss309¥csr¥dev¥pg¥tables¥T_2_7_4_4.sas 18JUN201513:33

付録 2.7.4-4
Japanese and Non-Japanese (Excluding Study 207)/血液およびリンパ系障害，臨床検査
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Eribulin Treated Safety Population

	日本人 Study 217 (N=51)		外国人 Study 309 (N=226)		全体 Studies 217+309 (N=277)	
MedDRA System Organ Class Preferred Term	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)
臨床検査 (contd)						
赤血球数減少	0	0	2 (0.9)	0	2 (0.7)	0
トランスアミナーゼ上昇	0	0	1 (0.4)	0	1 (0.4)	0
尿中ケトン体陽性	0	0	1 (0.4)	0	1 (0.4)	0
体重減少	4 (7.8)	0	7 (3.1)	0	11 (4.0)	0
体重増加	1 (2.0)	1 (2.0)	2 (0.9)	0	3 (1.1)	1 (0.4)
白血球数減少	0	0	16 (7.1)	8 (3.5)	16 (5.8)	8 (2.9)
尿中白血球陽性	1 (2.0)	0	1 (0.4)	0	2 (0.7)	0

TEAE = treatment-emergent adverse event, Graded using Common Terminology Criteria for Adverse Events (CTCAE)
A subject with two or more adverse events in the same system organ class (or with the same preferred term) is counted once for that system organ class (or preferred term).
Adverse event terms are coded using Medical Dictionary for Regulatory Activities (MedDRA) version 17.1.

Program: V:¥projects¥e7389¥iss309¥csr¥dev¥pg¥tables¥T_2_7_4_4.sas 18JUN201513:33

付録 2.7.4-5
Japanese and Non-Japanese
Treatment-Related Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Eribulin Treated Safety Population

	日本人 Study 217 (N=51)		外国人 Studies 207+309 (N=353)		全体 Studies 217+207+309 (N=404)	
MedDRA System Organ Class Preferred Term	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)
Any treatment-related TEAEs	51 (100.0)	48 (94.1)	324 (91.8)	156 (44.2)	375 (92.8)	204 (50.5)
血液およびリンパ系障害	51 (100.0)	48 (94.1)	137 (38.8)	99 (28.0)	188 (46.5)	147 (36.4)
貧血	24 (47.1)	6 (11.8)	55 (15.6)	10 (2.8)	79 (19.6)	16 (4.0)
発熱性好中球減少症	4 (7.8)	4 (7.8)	9 (2.5)	9 (2.5)	13 (3.2)	13 (3.2)
ヘモグロビン血症	0	0	3 (0.8)	2 (0.6)	3 (0.7)	2 (0.5)
白血球増加症	0	0	1 (0.3)	1 (0.3)	1 (0.2)	1 (0.2)
白血球減少症	51 (100.0)	38 (74.5)	35 (9.9)	22 (6.2)	86 (21.3)	60 (14.9)
リンパ節痛	0	0	1 (0.3)	0	1 (0.2)	0
リンパ節症	0	0	1 (0.3)	0	1 (0.2)	0
リンパ球減少症	40 (78.4)	16 (31.4)	1 (0.3)	1 (0.3)	41 (10.1)	17 (4.2)
好中球減少症	50 (98.0)	44 (86.3)	98 (27.8)	78 (22.1)	148 (36.6)	122 (30.2)
血小板減少症	3 (5.9)	0	13 (3.7)	1 (0.3)	16 (4.0)	1 (0.2)
心臓障害	4 (7.8)	0	5 (1.4)	1 (0.3)	9 (2.2)	1 (0.2)

TEAE = treatment-emergent adverse event, Graded using Common Terminology Criteria for Adverse Events (CTCAE)
Treatment-related adverse events include adverse events that were considered by the investigator to be possibly or probably related to study drug and adverse events with missing relationship to study drug.
A subject with two or more adverse events in the same system organ class (or with the same preferred term) is counted once for that system organ class (or preferred term).
Adverse event terms are coded using Medical Dictionary for Regulatory Activities (MedDRA) version 17.1.
This table is based on adverse events data as available. Study 207 did not record laboratory abnormalities into adverse events data.

Program: V:¥projects¥e7389¥iss309¥csr¥dev¥pg¥tables¥T_2_7_4_5.sas 18JUN201513:33

付録 2.7.4-5
Japanese and Non-Japanese
Treatment-Related Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Eribulin Treated Safety Population

	日本人 Study 217 (N=51)		外国人 Studies 207+309 (N=353)		全体 Studies 217+207+309 (N=404)	
MedDRA System Organ Class Preferred Term	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)
心臓障害 (contd)						
狭心症	0	0	1 (0.3)	0	1 (0.2)	0
第一度房室ブロック	0	0	1 (0.3)	0	1 (0.2)	0
動悸	1 (2.0)	0	1 (0.3)	0	2 (0.5)	0
心嚢液貯留	0	0	1 (0.3)	1 (0.3)	1 (0.2)	1 (0.2)
頻脈	2 (3.9)	0	1 (0.3)	0	3 (0.7)	0
心室性期外収縮	1 (2.0)	0	0	0	1 (0.2)	0
耳および迷路障害	0	0	6 (1.7)	0	6 (1.5)	0
難聴	0	0	1 (0.3)	0	1 (0.2)	0
耳痛	0	0	1 (0.3)	0	1 (0.2)	0
耳鳴	0	0	3 (0.8)	0	3 (0.7)	0
回転性めまい	0	0	1 (0.3)	0	1 (0.2)	0
眼障害	0	0	27 (7.6)	0	27 (6.7)	0

TEAE = treatment-emergent adverse event, Graded using Common Terminology Criteria for Adverse Events (CTCAE)
Treatment-related adverse events include adverse events that were considered by the investigator to be possibly or probably related to study drug and adverse events with missing relationship to study drug.
A subject with two or more adverse events in the same system organ class (or with the same preferred term) is counted once for that system organ class (or preferred term).
Adverse event terms are coded using Medical Dictionary for Regulatory Activities (MedDRA) version 17.1.
This table is based on adverse events data as available. Study 207 did not record laboratory abnormalities into adverse events data.

Program: V:¥projects¥e7389¥iss309¥csr¥dev¥pg¥tables¥T_2_7_4_5.sas 18JUN201513:33

付録 2.7.4-5
Japanese and Non-Japanese
Treatment-Related Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Eribulin Treated Safety Population

	日本人 Study 217 (N=51)		外国人 Studies 207+309 (N=353)		全体 Studies 217+207+309 (N=404)	
MedDRA System Organ Class Preferred Term	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)
眼障害 (contd)						
眼瞼炎	0	0	2 (0.6)	0	2 (0.5)	0
失明	0	0	1 (0.3)	0	1 (0.2)	0
眼乾燥	0	0	3 (0.8)	0	3 (0.7)	0
眼刺激	0	0	3 (0.8)	0	3 (0.7)	0
眼痛	0	0	1 (0.3)	0	1 (0.2)	0
流涙増加	0	0	16 (4.5)	0	16 (4.0)	0
眼充血	0	0	3 (0.8)	0	3 (0.7)	0
オキュラーサーフェス疾患	0	0	1 (0.3)	0	1 (0.2)	0
霧視	0	0	5 (1.4)	0	5 (1.2)	0
視力障害	0	0	1 (0.3)	0	1 (0.2)	0
硝子体浮遊物	0	0	1 (0.3)	0	1 (0.2)	0
胃腸障害	29 (56.9)	0	215 (60.9)	15 (4.2)	244 (60.4)	15 (3.7)
腹部不快感	1 (2.0)	0	0	0	1 (0.2)	0

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Program: V:¥projects¥e7389¥iss309¥csr¥dev¥pg¥tables¥T_2_7_4_5.sas 18JUN201513:33

付録 2.7.4-5
Japanese and Non-Japanese
Treatment-Related Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Eribulin Treated Safety Population

	日本人 Study 217 (N=51)		外国人 Studies 207+309 (N=353)		全体 Studies 217+207+309 (N=404)	
MedDRA System Organ Class Preferred Term	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)
胃腸障害 (contd)						
腹部膨満	0	0	10 (2.8)	0	10 (2.5)	0
腹痛	0	0	9 (2.5)	0	9 (2.2)	0
下腹部痛	1 (2.0)	0	0	0	1 (0.2)	0
上腹部痛	2 (3.9)	0	8 (2.3)	0	10 (2.5)	0
後天性巨舌症	0	0	1 (0.3)	0	1 (0.2)	0
肛門出血	0	0	1 (0.3)	0	1 (0.2)	0
アフタ性口内炎	0	0	3 (0.8)	0	3 (0.7)	0
口唇炎	2 (3.9)	0	0	0	2 (0.5)	0
慢性胃炎	1 (2.0)	0	0	0	1 (0.2)	0
便秘	8 (15.7)	0	54 (15.3)	0	62 (15.3)	0
下痢	5 (9.8)	0	53 (15.0)	2 (0.6)	58 (14.4)	2 (0.5)
口内乾燥	1 (2.0)	0	13 (3.7)	0	14 (3.5)	0
消化不良	0	0	13 (3.7)	1 (0.3)	13 (3.2)	1 (0.2)
嚥下障害	0	0	1 (0.3)	0	1 (0.2)	0

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付録 2.7.4-5
Japanese and Non-Japanese
Treatment-Related Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Eribulin Treated Safety Population

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MedDRA System Organ Class Preferred Term	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)
胃腸障害 (contd)						
放屁	0	0	4 (1.1)	0	4 (1.0)	0
排便回数増加	0	0	1 (0.3)	0	1 (0.2)	0
胃腸障害	0	0	7 (2.0)	0	7 (1.7)	0
胃腸管瘻	0	0	1 (0.3)	0	1 (0.2)	0
胃食道逆流性疾患	0	0	6 (1.7)	0	6 (1.5)	0
歯肉痛	0	0	1 (0.3)	0	1 (0.2)	0
歯肉腫脹	0	0	1 (0.3)	0	1 (0.2)	0
舌炎	0	0	1 (0.3)	0	1 (0.2)	0
口の感覚鈍麻	0	0	3 (0.8)	0	3 (0.7)	0
腸閉塞	0	0	1 (0.3)	1 (0.3)	1 (0.2)	1 (0.2)
口腔内潰瘍形成	0	0	3 (0.8)	0	3 (0.7)	0
悪心	19 (37.3)	0	118 (33.4)	3 (0.8)	137 (33.9)	3 (0.7)
嚥下痛	0	0	1 (0.3)	0	1 (0.2)	0
食道痛	0	0	1 (0.3)	0	1 (0.2)	0

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付録 2.7.4-5
Japanese and Non-Japanese
Treatment-Related Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Eribulin Treated Safety Population

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MedDRA System Organ Class Preferred Term	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)
胃腸障害 (contd)						
食道炎	0	0	1 (0.3)	0	1 (0.2)	0
口腔知覚不全	0	0	1 (0.3)	0	1 (0.2)	0
口腔内痛	0	0	5 (1.4)	0	5 (1.2)	0
歯周病	0	0	1 (0.3)	0	1 (0.2)	0
直腸出血	0	0	1 (0.3)	0	1 (0.2)	0
後腹膜出血	0	0	1 (0.3)	1 (0.3)	1 (0.2)	1 (0.2)
口内炎	13 (25.5)	0	52 (14.7)	6 (1.7)	65 (16.1)	6 (1.5)
舌の運動障害	0	0	1 (0.3)	0	1 (0.2)	0
舌潰瘍	0	0	1 (0.3)	0	1 (0.2)	0
上部消化管出血	0	0	1 (0.3)	0	1 (0.2)	0
嘔吐	1 (2.0)	0	47 (13.3)	2 (0.6)	48 (11.9)	2 (0.5)
一般・全身障害および投与部位の状態	40 (78.4)	2 (3.9)	216 (61.2)	17 (4.8)	256 (63.4)	19 (4.7)
無力症	0	0	36 (10.2)	2 (0.6)	36 (8.9)	2 (0.5)

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付録 2.7.4-5
Japanese and Non-Japanese
Treatment-Related Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Eribulin Treated Safety Population

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MedDRA System Organ Class Preferred Term	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)
一般・全身障害および投与部位の状態 (contd)						
カテーテル留置部位疼痛	0	0	1 (0.3)	0	1 (0.2)	0
胸痛	0	0	4 (1.1)	0	4 (1.0)	0
悪寒	0	0	14 (4.0)	0	14 (3.5)	0
活動性低下	0	0	1 (0.3)	0	1 (0.2)	0
顔面浮腫	0	0	3 (0.8)	0	3 (0.7)	0
疲労	9 (17.6)	0	153 (43.3)	14 (4.0)	162 (40.1)	14 (3.5)
歩行障害	0	0	3 (0.8)	0	3 (0.7)	0
全身健康状態低下	0	0	1 (0.3)	1 (0.3)	1 (0.2)	1 (0.2)
全身性浮腫	1 (2.0)	1 (2.0)	1 (0.3)	0	2 (0.5)	1 (0.2)
低体温	0	0	1 (0.3)	0	1 (0.2)	0
インフルエンザ様疾患	1 (2.0)	0	4 (1.1)	0	5 (1.2)	0
注射部位漏出	2 (3.9)	0	0	0	2 (0.5)	0
注射部位反応	0	0	1 (0.3)	0	1 (0.2)	0
倦怠感	20 (39.2)	0	2 (0.6)	0	22 (5.4)	0

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Eribulin Treated Safety Population

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MedDRA System Organ Class Preferred Term	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)
一般・全身障害および投与部位の状態 (contd)						
末梢性浮腫	3 (5.9)	0	15 (4.2)	0	18 (4.5)	0
発熱	21 (41.2)	1 (2.0)	49 (13.9)	1 (0.3)	70 (17.3)	2 (0.5)
肝胆道系障害	6 (11.8)	1 (2.0)	4 (1.1)	2 (0.6)	10 (2.5)	3 (0.7)
肝機能異常	5 (9.8)	0	0	0	5 (1.2)	0
肝出血	1 (2.0)	1 (2.0)	0	0	1 (0.2)	1 (0.2)
肝臓痛	0	0	1 (0.3)	0	1 (0.2)	0
肝細胞損傷	0	0	1 (0.3)	0	1 (0.2)	0
肝毒性	0	0	1 (0.3)	1 (0.3)	1 (0.2)	1 (0.2)
高ビリルビン血症	0	0	1 (0.3)	1 (0.3)	1 (0.2)	1 (0.2)
黄疸	0	0	1 (0.3)	0	1 (0.2)	0
免疫系障害	0	0	2 (0.6)	0	2 (0.5)	0
過敏症	0	0	2 (0.6)	0	2 (0.5)	0

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Japanese and Non-Japanese
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Eribulin Treated Safety Population

	日本人 Study 217 (N=51)		外国人 Studies 207+309 (N=353)		全体 Studies 217+207+309 (N=404)	
MedDRA System Organ Class Preferred Term	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)
感染症および寄生虫症	17 (33.3)	2 (3.9)	38 (10.8)	10 (2.8)	55 (13.6)	12 (3.0)
気管支炎	0	0	1 (0.3)	0	1 (0.2)	0
気管支肺炎	0	0	1 (0.3)	1 (0.3)	1 (0.2)	1 (0.2)
カテーテル留置部位蜂巣炎	0	0	1 (0.3)	0	1 (0.2)	0
蜂巣炎	0	0	1 (0.3)	0	1 (0.2)	0
膀胱炎	1 (2.0)	0	1 (0.3)	1 (0.3)	2 (0.5)	1 (0.2)
耳感染	0	0	2 (0.6)	0	2 (0.5)	0
蓄膿	1 (2.0)	1 (2.0)	0	0	1 (0.2)	1 (0.2)
感染性腸炎	1 (2.0)	0	0	0	1 (0.2)	0
丹毒	0	0	1 (0.3)	0	1 (0.2)	0
毛包炎	1 (2.0)	0	2 (0.6)	0	3 (0.7)	0
胃腸炎	1 (2.0)	0	0	0	1 (0.2)	0
歯肉炎	1 (2.0)	0	1 (0.3)	0	2 (0.5)	0
帯状疱疹	1 (2.0)	0	1 (0.3)	0	2 (0.5)	0
真菌性下気道感染	0	0	1 (0.3)	1 (0.3)	1 (0.2)	1 (0.2)

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付録 2.7.4-5
Japanese and Non-Japanese
Treatment-Related Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Eribulin Treated Safety Population

	日本人 Study 217 (N=51)		外国人 Studies 207+309 (N=353)		全体 Studies 217+207+309 (N=404)	
MedDRA System Organ Class Preferred Term	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)
感染症および寄生虫症 (contd)						
腎髄炎	0	0	1 (0.3)	0	1 (0.2)	0
鼻咽頭炎	6 (11.8)	0	3 (0.8)	0	9 (2.2)	0
好中球減少性敗血症	0	0	1 (0.3)	1 (0.3)	1 (0.2)	1 (0.2)
口腔カンジダ症	0	0	3 (0.8)	0	3 (0.7)	0
口腔ヘルペス	0	0	1 (0.3)	0	1 (0.2)	0
急性中耳炎	1 (2.0)	0	0	0	1 (0.2)	0
咽頭炎	1 (2.0)	0	3 (0.8)	2 (0.6)	4 (1.0)	2 (0.5)
肺炎	0	0	5 (1.4)	5 (1.4)	5 (1.2)	5 (1.2)
膿尿	0	0	1 (0.3)	0	1 (0.2)	0
気道感染	0	0	1 (0.3)	0	1 (0.2)	0
鼻炎	0	0	1 (0.3)	0	1 (0.2)	0
軟部組織感染	0	0	1 (0.3)	0	1 (0.2)	0
レンサ球菌感染	1 (2.0)	1 (2.0)	0	0	1 (0.2)	1 (0.2)
白癬感染	0	0	1 (0.3)	0	1 (0.2)	0

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Japanese and Non-Japanese
Treatment-Related Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Eribulin Treated Safety Population

	日本人 Study 217 (N=51)		外国人 Studies 207+309 (N=353)		全体 Studies 217+207+309 (N=404)	
MedDRA System Organ Class Preferred Term	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)
感染症および寄生虫症 (contd)						
上気道感染	6 (11.8)	0	4 (1.1)	1 (0.3)	10 (2.5)	1 (0.2)
尿路感染	1 (2.0)	0	3 (0.8)	0	4 (1.0)	0
傷害、中毒および処置合併症	0	0	2 (0.6)	0	2 (0.5)	0
転倒	0	0	1 (0.3)	0	1 (0.2)	0
注入に伴う反応	0	0	1 (0.3)	0	1 (0.2)	0
臨床検査	27 (52.9)	4 (7.8)	88 (24.9)	31 (8.8)	115 (28.5)	35 (8.7)
アラニンアミノトランスフェラーゼ増加	12 (23.5)	3 (5.9)	15 (4.2)	3 (0.8)	27 (6.7)	6 (1.5)
アスパラギン酸アミノトランスフェラーゼ増加	12 (23.5)	2 (3.9)	16 (4.5)	1 (0.3)	28 (6.9)	3 (0.7)
血中アルブミン減少	2 (3.9)	0	1 (0.3)	0	3 (0.7)	0
血中アルカリホスファターゼ	0	0	1 (0.3)	0	1 (0.2)	0
血中アルカリホスファターゼ増加	2 (3.9)	0	6 (1.7)	0	8 (2.0)	0
血中ビリルビン増加	1 (2.0)	0	0	0	1 (0.2)	0

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付録 2.7.4-5
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Treatment-Related Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Eribulin Treated Safety Population

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MedDRA System Organ Class Preferred Term	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)
臨床検査 (contd)						
血中カルシウム減少	0	0	1 (0.3)	0	1 (0.2)	0
血中クレアチンホスホキナーゼ増加	7 (13.7)	0	0	0	7 (1.7)	0
血中クレアチニン増加	1 (2.0)	0	3 (0.8)	0	4 (1.0)	0
血中乳酸脱水素酵素増加	8 (15.7)	0	6 (1.7)	0	14 (3.5)	0
血中カリウム減少	0	0	1 (0.3)	1 (0.3)	1 (0.2)	1 (0.2)
血中尿素増加	0	0	1 (0.3)	0	1 (0.2)	0
尿中血陽性	2 (3.9)	0	0	0	2 (0.5)	0
Ｃ－反応性蛋白増加	4 (7.8)	0	0	0	4 (1.0)	0
腎クレアチニン・クリアランス減少	0	0	1 (0.3)	0	1 (0.2)	0
心電図ＱＴ延長	1 (2.0)	0	14 (4.0)	5 (1.4)	15 (3.7)	5 (1.2)
γ－グルタミルトランスフェラーゼ	0	0	2 (0.6)	2 (0.6)	2 (0.5)	2 (0.5)
γ－グルタミルトランスフェラーゼ増加	1 (2.0)	0	2 (0.6)	1 (0.3)	3 (0.7)	1 (0.2)
ヘマトクリット減少	0	0	1 (0.3)	0	1 (0.2)	0
ヘモグロビン減少	2 (3.9)	0	6 (1.7)	0	8 (2.0)	0

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Program: V:¥projects¥e7389¥iss309¥csr¥dev¥pg¥tables¥T_2_7_4_5.sas 18JUN201513:33

付録 2.7.4-5
Japanese and Non-Japanese
Treatment-Related Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Eribulin Treated Safety Population

	日本人 Study 217 (N=51)		外国人 Studies 207+309 (N=353)		全体 Studies 217+207+309 (N=404)	
MedDRA System Organ Class Preferred Term	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)
臨床検査 (contd)						
肝機能検査異常	1 (2.0)	0	0	0	1 (0.2)	0
リンパ球数減少	0	0	2 (0.6)	0	2 (0.5)	0
好中球数減少	0	0	18 (5.1)	15 (4.2)	18 (4.5)	15 (3.7)
血小板数減少	0	0	1 (0.3)	1 (0.3)	1 (0.2)	1 (0.2)
総蛋白減少	1 (2.0)	0	2 (0.6)	0	3 (0.7)	0
尿蛋白	2 (3.9)	0	0	0	2 (0.5)	0
赤血球数減少	0	0	2 (0.6)	0	2 (0.5)	0
トランスアミナーゼ上昇	0	0	1 (0.3)	0	1 (0.2)	0
尿中ケトン体陽性	0	0	1 (0.3)	0	1 (0.2)	0
体重減少	1 (2.0)	0	22 (6.2)	0	23 (5.7)	0
体重増加	0	0	2 (0.6)	0	2 (0.5)	0
白血球数減少	0	0	16 (4.5)	7 (2.0)	16 (4.0)	7 (1.7)
代謝および栄養障害	23 (45.1)	6 (11.8)	76 (21.5)	11 (3.1)	99 (24.5)	17 (4.2)

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付録 2.7.4-5
Japanese and Non-Japanese
Treatment-Related Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Eribulin Treated Safety Population

	日本人 Study 217 (N=51)		外国人 Studies 207+309 (N=353)		全体 Studies 217+207+309 (N=404)	
MedDRA System Organ Class Preferred Term	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)
代謝および栄養障害 (contd)						
食欲減退	11 (21.6)	0	60 (17.0)	1 (0.3)	71 (17.6)	1 (0.2)
脱水	0	0	2 (0.6)	0	2 (0.5)	0
高血糖	0	0	3 (0.8)	2 (0.6)	3 (0.7)	2 (0.5)
高脂血症	3 (5.9)	0	0	0	3 (0.7)	0
高トリグリセリド血症	5 (9.8)	1 (2.0)	1 (0.3)	0	6 (1.5)	1 (0.2)
低アルブミン血症	6 (11.8)	2 (3.9)	4 (1.1)	1 (0.3)	10 (2.5)	3 (0.7)
低カルシウム血症	3 (5.9)	0	1 (0.3)	0	4 (1.0)	0
低カリウム血症	3 (5.9)	1 (2.0)	9 (2.5)	4 (1.1)	12 (3.0)	5 (1.2)
低マグネシウム血症	0	0	4 (1.1)	1 (0.3)	4 (1.0)	1 (0.2)
低ナトリウム血症	0	0	3 (0.8)	2 (0.6)	3 (0.7)	2 (0.5)
低リン酸血症	6 (11.8)	3 (5.9)	2 (0.6)	1 (0.3)	8 (2.0)	4 (1.0)
低蛋白血症	1 (2.0)	0	0	0	1 (0.2)	0
筋骨格系および結合組織障害	7 (13.7)	0	67 (19.0)	1 (0.3)	74 (18.3)	1 (0.2)

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付録 2.7.4-5
Japanese and Non-Japanese
Treatment-Related Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Eribulin Treated Safety Population

	日本人 Study 217 (N=51)		外国人 Studies 207+309 (N=353)		全体 Studies 217+207+309 (N=404)	
MedDRA System Organ Class Preferred Term	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)
筋骨格系および結合組織障害 (contd)						
関節痛	2 (3.9)	0	10 (2.8)	0	12 (3.0)	0
関節炎	0	0	1 (0.3)	0	1 (0.2)	0
関節障害	0	0	7 (2.0)	0	7 (1.7)	0
背部障害	0	0	5 (1.4)	0	5 (1.2)	0
背部痛	2 (3.9)	0	5 (1.4)	0	7 (1.7)	0
骨痛	0	0	1 (0.3)	0	1 (0.2)	0
顎障害	0	0	1 (0.3)	0	1 (0.2)	0
咀嚼障害	0	0	1 (0.3)	0	1 (0.2)	0
筋障害	0	0	12 (3.4)	1 (0.3)	12 (3.0)	1 (0.2)
筋肉疲労	0	0	1 (0.3)	0	1 (0.2)	0
筋痙縮	0	0	10 (2.8)	0	10 (2.5)	0
筋力低下	0	0	6 (1.7)	0	6 (1.5)	0
筋骨格系胸痛	0	0	2 (0.6)	0	2 (0.5)	0
筋骨格痛	0	0	3 (0.8)	0	3 (0.7)	0

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付録 2.7.4-5
Japanese and Non-Japanese
Treatment-Related Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Eribulin Treated Safety Population

	日本人 Study 217 (N=51)		外国人 Studies 207+309 (N=353)		全体 Studies 217+207+309 (N=404)	
MedDRA System Organ Class Preferred Term	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)
筋骨格系および結合組織障害 (contd)						
筋骨格硬直	0	0	3 (0.8)	0	3 (0.7)	0
筋肉痛	1 (2.0)	0	15 (4.2)	0	16 (4.0)	0
筋炎	0	0	1 (0.3)	1 (0.3)	1 (0.2)	1 (0.2)
変形性関節症	1 (2.0)	0	0	0	1 (0.2)	0
四肢痛	3 (5.9)	0	8 (2.3)	0	11 (2.7)	0
顎痛	0	0	1 (0.3)	0	1 (0.2)	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）	1 (2.0)	1 (2.0)	6 (1.7)	1 (0.3)	7 (1.7)	2 (0.5)
腫瘍出血	1 (2.0)	1 (2.0)	0	0	1 (0.2)	1 (0.2)
腫瘍疼痛	0	0	6 (1.7)	1 (0.3)	6 (1.5)	1 (0.2)
神経系障害	27 (52.9)	0	147 (41.6)	18 (5.1)	174 (43.1)	18 (4.5)
味覚消失	0	0	1 (0.3)	0	1 (0.2)	0
平衡障害	0	0	1 (0.3)	0	1 (0.2)	0

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付録 2.7.4-5
Japanese and Non-Japanese
Treatment-Related Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Eribulin Treated Safety Population

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MedDRA System Organ Class Preferred Term	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)
神経系障害 (contd)						
灼熱感	0	0	1 (0.3)	0	1 (0.2)	0
脳虚血	0	0	1 (0.3)	1 (0.3)	1 (0.2)	1 (0.2)
痙攣	0	0	1 (0.3)	1 (0.3)	1 (0.2)	1 (0.2)
注意力障害	0	0	3 (0.8)	0	3 (0.7)	0
浮動性めまい	1 (2.0)	0	29 (8.2)	0	30 (7.4)	0
異常感覚	0	0	1 (0.3)	0	1 (0.2)	0
味覚異常	12 (23.5)	0	34 (9.6)	0	46 (11.4)	0
頭痛	6 (11.8)	0	37 (10.5)	0	43 (10.6)	0
感覚鈍麻	1 (2.0)	0	5 (1.4)	1 (0.3)	6 (1.5)	1 (0.2)
嗜眠	0	0	3 (0.8)	1 (0.3)	3 (0.7)	1 (0.2)
固有感覚の欠如	0	0	1 (0.3)	0	1 (0.2)	0
神経痛	0	0	3 (0.8)	0	3 (0.7)	0
末梢性ニューロパチー	15 (29.4)	0	1 (0.3)	0	16 (4.0)	0
起立不耐性	0	0	1 (0.3)	0	1 (0.2)	0

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Eribulin Treated Safety Population

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MedDRA System Organ Class Preferred Term	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)
神経系障害 (contd)						
錯感覚	0	0	17 (4.8)	1 (0.3)	17 (4.2)	1 (0.2)
末梢性運動ニューロパチー	0	0	14 (4.0)	6 (1.7)	14 (3.5)	6 (1.5)
末梢性感覚運動ニューロパチー	0	0	2 (0.6)	0	2 (0.5)	0
末梢性感覚ニューロパチー	2 (3.9)	0	87 (24.6)	8 (2.3)	89 (22.0)	8 (2.0)
多発ニューロパチー	0	0	1 (0.3)	1 (0.3)	1 (0.2)	1 (0.2)
ヘルペス後神経痛	1 (2.0)	0	0	0	1 (0.2)	0
失神寸前の状態	0	0	1 (0.3)	1 (0.3)	1 (0.2)	1 (0.2)
下肢静止不能症候群	0	0	1 (0.3)	0	1 (0.2)	0
感覚障害	2 (3.9)	0	1 (0.3)	0	3 (0.7)	0
傾眠	1 (2.0)	0	2 (0.6)	0	3 (0.7)	0
振戦	0	0	1 (0.3)	0	1 (0.2)	0
精神障害	1 (2.0)	0	15 (4.2)	1 (0.3)	16 (4.0)	1 (0.2)
感情障害	0	0	1 (0.3)	0	1 (0.2)	0

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付録 2.7.4-5
Japanese and Non-Japanese
Treatment-Related Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Eribulin Treated Safety Population

	日本人 Study 217 (N=51)		外国人 Studies 207+309 (N=353)		全体 Studies 217+207+309 (N=404)	
MedDRA System Organ Class Preferred Term	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)
精神障害 (contd)						
激越	0	0	1 (0.3)	1 (0.3)	1 (0.2)	1 (0.2)
錯乱状態	0	0	1 (0.3)	0	1 (0.2)	0
不眠症	1 (2.0)	0	10 (2.8)	0	11 (2.7)	0
易刺激性	0	0	1 (0.3)	0	1 (0.2)	0
神経症	0	0	1 (0.3)	0	1 (0.2)	0
腎および尿路障害	7 (13.7)	0	8 (2.3)	0	15 (3.7)	0
排尿困難	1 (2.0)	0	1 (0.3)	0	2 (0.5)	0
尿意切迫	0	0	1 (0.3)	0	1 (0.2)	0
乏尿	0	0	1 (0.3)	0	1 (0.2)	0
頻尿	1 (2.0)	0	2 (0.6)	0	3 (0.7)	0
多尿	0	0	1 (0.3)	0	1 (0.2)	0
蛋白尿	5 (9.8)	0	1 (0.3)	0	6 (1.5)	0
腎不全	0	0	1 (0.3)	0	1 (0.2)	0

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Treatment-Related Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Eribulin Treated Safety Population

	日本人 Study 217 (N=51)		外国人 Studies 207+309 (N=353)		全体 Studies 217+207+309 (N=404)	
MedDRA System Organ Class Preferred Term	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)
腎および尿路障害 (contd)						
慢性腎不全	1 (2.0)	0	0	0	1 (0.2)	0
尿路痛	0	0	1 (0.3)	0	1 (0.2)	0
生殖系および乳房障害	1 (2.0)	1 (2.0)	8 (2.3)	0	9 (2.2)	1 (0.2)
乳房痛	0	0	1 (0.3)	0	1 (0.2)	0
勃起不全	0	0	2 (0.6)	0	2 (0.5)	0
不規則月経	1 (2.0)	1 (2.0)	0	0	1 (0.2)	1 (0.2)
乳頭痛	0	0	1 (0.3)	0	1 (0.2)	0
膣出血	0	0	3 (0.8)	0	3 (0.7)	0
膣の炎症	0	0	1 (0.3)	0	1 (0.2)	0
外陰膣乾燥	0	0	2 (0.6)	0	2 (0.5)	0
外陰膣そう痒症	0	0	1 (0.3)	0	1 (0.2)	0
呼吸器、胸郭および縦隔障害	14 (27.5)	1 (2.0)	64 (18.1)	3 (0.8)	78 (19.3)	4 (1.0)

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MedDRA System Organ Class Preferred Term	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)
呼吸器、胸郭および縦隔障害 (contd)						
咳嗽	3 (5.9)	0	24 (6.8)	1 (0.3)	27 (6.7)	1 (0.2)
発声障害	1 (2.0)	0	7 (2.0)	1 (0.3)	8 (2.0)	1 (0.2)
呼吸困難	1 (2.0)	0	24 (6.8)	2 (0.6)	25 (6.2)	2 (0.5)
労作性呼吸困難	0	0	1 (0.3)	0	1 (0.2)	0
鼻出血	1 (2.0)	0	6 (1.7)	0	7 (1.7)	0
喀血	1 (2.0)	0	0	0	1 (0.2)	0
しゃっくり	0	0	1 (0.3)	0	1 (0.2)	0
間質性肺疾患	1 (2.0)	0	0	0	1 (0.2)	0
鼻閉	0	0	3 (0.8)	0	3 (0.7)	0
鼻部障害	0	0	1 (0.3)	0	1 (0.2)	0
閉塞性気道障害	0	0	1 (0.3)	0	1 (0.2)	0
口腔咽頭不快感	2 (3.9)	0	0	0	2 (0.5)	0
口腔咽頭痛	3 (5.9)	0	8 (2.3)	0	11 (2.7)	0
咽頭紅斑	0	0	2 (0.6)	0	2 (0.5)	0

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付録 2.7.4-5
Japanese and Non-Japanese
Treatment-Related Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Eribulin Treated Safety Population

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MedDRA System Organ Class Preferred Term	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)
呼吸器、胸郭および縦隔障害 (contd)						
胸水	1 (2.0)	0	0	0	1 (0.2)	0
胸膜痛	0	0	1 (0.3)	0	1 (0.2)	0
湿性咳嗽	0	0	1 (0.3)	0	1 (0.2)	0
肺塞栓症	1 (2.0)	1 (2.0)	0	0	1 (0.2)	1 (0.2)
鼻痛	0	0	1 (0.3)	0	1 (0.2)	0
鼻漏	0	0	4 (1.1)	0	4 (1.0)	0
副鼻腔うっ血	0	0	1 (0.3)	0	1 (0.2)	0
上気道の炎症	1 (2.0)	0	0	0	1 (0.2)	0
上気道咳症候群	0	0	1 (0.3)	0	1 (0.2)	0
皮膚および皮下組織障害	23 (45.1)	0	159 (45.0)	1 (0.3)	182 (45.0)	1 (0.2)
ざ瘡	0	0	1 (0.3)	0	1 (0.2)	0
脱毛症	14 (27.5)	0	135 (38.2)	1 (0.3)	149 (36.9)	1 (0.2)
ざ瘡様皮膚炎	0	0	1 (0.3)	0	1 (0.2)	0

TEAE = treatment-emergent adverse event, Graded using Common Terminology Criteria for Adverse Events (CTCAE)
Treatment-related adverse events include adverse events that were considered by the investigator to be possibly or probably related to study drug and adverse events with missing relationship to study drug.
A subject with two or more adverse events in the same system organ class (or with the same preferred term) is counted once for that system organ class (or preferred term).
Adverse event terms are coded using Medical Dictionary for Regulatory Activities (MedDRA) version 17.1.
This table is based on adverse events data as available. Study 207 did not record laboratory abnormalities into adverse events data.

Program: V:¥projects¥e7389¥iss309¥csr¥dev¥pg¥tables¥T_2_7_4_5.sas 18JUN201513:33

付録 2.7.4-5
Japanese and Non-Japanese
Treatment-Related Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Eribulin Treated Safety Population

	日本人 Study 217 (N=51)		外国人 Studies 207+309 (N=353)		全体 Studies 217+207+309 (N=404)	
MedDRA System Organ Class Preferred Term	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)
皮膚および皮下組織障害 (contd)						
皮膚筋炎	1 (2.0)	0	0	0	1 (0.2)	0
皮膚乾燥	1 (2.0)	0	8 (2.3)	0	9 (2.2)	0
湿疹	2 (3.9)	0	0	0	2 (0.5)	0
紅斑	1 (2.0)	0	2 (0.6)	0	3 (0.7)	0
剥脱性発疹	0	0	10 (2.8)	0	10 (2.5)	0
毛髪変色	0	0	1 (0.3)	0	1 (0.2)	0
多汗症	0	0	6 (1.7)	0	6 (1.5)	0
睫毛眉毛脱落症	0	0	1 (0.3)	0	1 (0.2)	0
爪の障害	0	0	6 (1.7)	0	6 (1.5)	0
爪毒性	0	0	1 (0.3)	0	1 (0.2)	0
爪甲離床症	0	0	1 (0.3)	0	1 (0.2)	0
爪甲脱落症	0	0	1 (0.3)	0	1 (0.2)	0
手掌・足底発赤知覚不全症候群	0	0	4 (1.1)	0	4 (1.0)	0
光線過敏性反応	0	0	1 (0.3)	0	1 (0.2)	0

TEAE = treatment-emergent adverse event, Graded using Common Terminology Criteria for Adverse Events (CTCAE)
Treatment-related adverse events include adverse events that were considered by the investigator to be possibly or probably related to study drug and adverse events with missing relationship to study drug.
A subject with two or more adverse events in the same system organ class (or with the same preferred term) is counted once for that system organ class (or preferred term).
Adverse event terms are coded using Medical Dictionary for Regulatory Activities (MedDRA) version 17.1.
This table is based on adverse events data as available. Study 207 did not record laboratory abnormalities into adverse events data.

Program: V:¥projects¥e7389¥iss309¥csr¥dev¥pg¥tables¥T_2_7_4_5.sas 18JUN201513:33

付録 2.7.4-5
Japanese and Non-Japanese
Treatment-Related Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Eribulin Treated Safety Population

	日本人 Study 217 (N=51)		外国人 Studies 207+309 (N=353)		全体 Studies 217+207+309 (N=404)	
MedDRA System Organ Class Preferred Term	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)
皮膚および皮下組織障害 (contd)						
そう痒症	0	0	8 (2.3)	0	8 (2.0)	0
全身性そう痒症	0	0	1 (0.3)	0	1 (0.2)	0
発疹	5 (9.8)	0	6 (1.7)	0	11 (2.7)	0
斑状丘疹状皮疹	2 (3.9)	0	0	0	2 (0.5)	0
瘢痕痛	0	0	1 (0.3)	0	1 (0.2)	0
皮膚亀裂	0	0	2 (0.6)	0	2 (0.5)	0
皮膚色素過剰	0	0	1 (0.3)	0	1 (0.2)	0
皮膚のつっぱり感	0	0	1 (0.3)	0	1 (0.2)	0
皮膚潰瘍	0	0	1 (0.3)	0	1 (0.2)	0
皮膚のべとつき感	0	0	1 (0.3)	0	1 (0.2)	0
顔面腫脹	0	0	1 (0.3)	0	1 (0.2)	0
蕁麻疹	1 (2.0)	0	2 (0.6)	0	3 (0.7)	0
血管障害	4 (7.8)	0	21 (5.9)	0	25 (6.2)	0

TEAE = treatment-emergent adverse event, Graded using Common Terminology Criteria for Adverse Events (CTCAE)
Treatment-related adverse events include adverse events that were considered by the investigator to be possibly or probably related to study drug and adverse events with missing relationship to study drug.
A subject with two or more adverse events in the same system organ class (or with the same preferred term) is counted once for that system organ class (or preferred term).
Adverse event terms are coded using Medical Dictionary for Regulatory Activities (MedDRA) version 17.1.
This table is based on adverse events data as available. Study 207 did not record laboratory abnormalities into adverse events data.

Program: V:¥projects¥e7389¥iss309¥csr¥dev¥pg¥tables¥T_2_7_4_5.sas 18JUN201513:33

付録 2.7.4-5
Japanese and Non-Japanese
Treatment-Related Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Eribulin Treated Safety Population

	日本人 Study 217 (N=51)		外国人 Studies 207+309 (N=353)		全体 Studies 217+207+309 (N=404)	
MedDRA System Organ Class Preferred Term	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)
血管障害 (contd)						
潮紅	0	0	4 (1.1)	0	4 (1.0)	0
ほてり	0	0	3 (0.8)	0	3 (0.7)	0
高血圧	2 (3.9)	0	5 (1.4)	0	7 (1.7)	0
低血圧	0	0	6 (1.7)	0	6 (1.5)	0
リンパ浮腫	1 (2.0)	0	0	0	1 (0.2)	0
起立性低血圧	0	0	1 (0.3)	0	1 (0.2)	0
蒼白	0	0	1 (0.3)	0	1 (0.2)	0
静脈炎	0	0	1 (0.3)	0	1 (0.2)	0
血管炎	1 (2.0)	0	0	0	1 (0.2)	0

TEAE = treatment-emergent adverse event, Graded using Common Terminology Criteria for Adverse Events (CTCAE)
Treatment-related adverse events include adverse events that were considered by the investigator to be possibly or probably related to study drug and adverse events with missing relationship to study drug.
A subject with two or more adverse events in the same system organ class (or with the same preferred term) is counted once for that system organ class (or preferred term).
Adverse event terms are coded using Medical Dictionary for Regulatory Activities (MedDRA) version 17.1.
This table is based on adverse events data as available. Study 207 did not record laboratory abnormalities into adverse events data.

Program: V:¥projects¥e7389¥iss309¥csr¥dev¥pg¥tables¥T_2_7_4_5.sas 18JUN201513:33

付録 2.7.4-6

Japanese and Non-Japanese (Excluding Study 207)/血液およびリンパ系障害，臨床検査

Treatment-Related Treatment-Emergent Adverse Events by System Organ Class and Preferred Term

Eribulin Treated Safety Population

	日本人 Study 217 (N=51)		外国人 Study 309 (N=226)		全体 Studies 217+309 (N=277)	
MedDRA System Organ Class Preferred Term	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)
Any treatment-related TEAEs	51 (100.0)	48 (94.1)	150 (66.4)	108 (47.8)	201 (72.6)	156 (56.3)
血液およびリンパ系障害	51 (100.0)	48 (94.1)	127 (56.2)	90 (39.8)	178 (64.3)	138 (49.8)
貧血	24 (47.1)	6 (11.8)	55 (24.3)	10 (4.4)	79 (28.5)	16 (5.8)
発熱性好中球減少症	4 (7.8)	4 (7.8)	2 (0.9)	2 (0.9)	6 (2.2)	6 (2.2)
ヘモグロビン血症	0	0	3 (1.3)	2 (0.9)	3 (1.1)	2 (0.7)
白血球増加症	0	0	1 (0.4)	1 (0.4)	1 (0.4)	1 (0.4)
白血球減少症	51 (100.0)	38 (74.5)	35 (15.5)	22 (9.7)	86 (31.0)	60 (21.7)
リンパ節症	0	0	1 (0.4)	0	1 (0.4)	0
リンパ球減少症	40 (78.4)	16 (31.4)	1 (0.4)	1 (0.4)	41 (14.8)	17 (6.1)
好中球減少症	50 (98.0)	44 (86.3)	96 (42.5)	76 (33.6)	146 (52.7)	120 (43.3)
血小板減少症	3 (5.9)	0	13 (5.8)	1 (0.4)	16 (5.8)	1 (0.4)
臨床検査	27 (52.9)	4 (7.8)	67 (29.6)	29 (12.8)	94 (33.9)	33 (11.9)
アラニンアミノトランスフェラーゼ増加	12 (23.5)	3 (5.9)	15 (6.6)	3 (1.3)	27 (9.7)	6 (2.2)
アスパラギン酸アミノトランスフェラーゼ増加	12 (23.5)	2 (3.9)	16 (7.1)	1 (0.4)	28 (10.1)	3 (1.1)
血中アルブミン減少	2 (3.9)	0	1 (0.4)	0	3 (1.1)	0

TEAE = treatment-emergent adverse event, Graded using Common Terminology Criteria for Adverse Events (CTCAE)
Treatment-related adverse events include adverse events that were considered by the investigator to be possibly or probably related to study drug and adverse events with missing relationship to study drug.
A subject with two or more adverse events in the same system organ class (or with the same preferred term) is counted once for that system organ class (or preferred term).
Adverse event terms are coded using Medical Dictionary for Regulatory Activities (MedDRA) version 17.1.

Program: V:¥projects¥e7389¥iss309¥csr¥dev¥pg¥tables¥T_2_7_4_6.sas 18JUN201513:34

付録 2.7.4-6

Japanese and Non-Japanese (Excluding Study 207)/血液およびリンパ系障害，臨床検査

Treatment-Related Treatment-Emergent Adverse Events by System Organ Class and Preferred Term

Eribulin Treated Safety Population

	日本人 Study 217 (N=51)		外国人 Study 309 (N=226)		全体 Studies 217+309 (N=277)	
MedDRA System Organ Class Preferred Term	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)
臨床検査 (contd)						
血中アルカリホスファターゼ増加	2 (3.9)	0	6 (2.7)	0	8 (2.9)	0
血中ビリルビン増加	1 (2.0)	0	0	0	1 (0.4)	0
血中カルシウム減少	0	0	1 (0.4)	0	1 (0.4)	0
血中クレアチンホスホキナーゼ増加	7 (13.7)	0	0	0	7 (2.5)	0
血中クレアチニン増加	1 (2.0)	0	3 (1.3)	0	4 (1.4)	0
血中乳酸脱水素酵素増加	8 (15.7)	0	6 (2.7)	0	14 (5.1)	0
血中カリウム減少	0	0	1 (0.4)	1 (0.4)	1 (0.4)	1 (0.4)
血中尿素増加	0	0	1 (0.4)	0	1 (0.4)	0
尿中血陽性	2 (3.9)	0	0	0	2 (0.7)	0
Ｃ－反応性蛋白増加	4 (7.8)	0	0	0	4 (1.4)	0
腎クレアチニン・クリアランス減少	0	0	1 (0.4)	0	1 (0.4)	0
心電図ＱＴ延長	1 (2.0)	0	14 (6.2)	5 (2.2)	15 (5.4)	5 (1.8)
γ－グルタミルトランスフェラーゼ増加	1 (2.0)	0	2 (0.9)	1 (0.4)	3 (1.1)	1 (0.4)
ヘマトクリット減少	0	0	1 (0.4)	0	1 (0.4)	0
ヘモグロビン減少	2 (3.9)	0	6 (2.7)	0	8 (2.9)	0
肝機能検査異常	1 (2.0)	0	0	0	1 (0.4)	0

TEAE = treatment-emergent adverse event, Graded using Common Terminology Criteria for Adverse Events (CTCAE)
Treatment-related adverse events include adverse events that were considered by the investigator to be possibly or probably related to study drug and adverse events with missing relationship to study drug.
A subject with two or more adverse events in the same system organ class (or with the same preferred term) is counted once for that system organ class (or preferred term).
Adverse event terms are coded using Medical Dictionary for Regulatory Activities (MedDRA) version 17.1.

Program: V:¥projects¥e7389¥iss309¥csr¥dev¥pg¥tables¥T_2_7_4_6.sas 18JUN201513:34

付録 2.7.4-6

Japanese and Non-Japanese (Excluding Study 207)/血液およびリンパ系障害，臨床検査

Treatment-Related Treatment-Emergent Adverse Events by System Organ Class and Preferred Term

Eribulin Treated Safety Population

	日本人 Study 217 (N=51)		外国人 Study 309 (N=226)		全体 Studies 217+309 (N=277)	
MedDRA System Organ Class Preferred Term	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)	All Grades n(%)	Grade >= 3 n(%)
臨床検査 (contd)						
リンパ球数減少	0	0	2 (0.9)	0	2 (0.7)	0
好中球数減少	0	0	18 (8.0)	15 (6.6)	18 (6.5)	15 (5.4)
血小板数減少	0	0	1 (0.4)	1 (0.4)	1 (0.4)	1 (0.4)
総蛋白減少	1 (2.0)	0	2 (0.9)	0	3 (1.1)	0
尿蛋白	2 (3.9)	0	0	0	2 (0.7)	0
赤血球数減少	0	0	2 (0.9)	0	2 (0.7)	0
トランスアミナーゼ上昇	0	0	1 (0.4)	0	1 (0.4)	0
尿中ケトン体陽性	0	0	1 (0.4)	0	1 (0.4)	0
体重減少	1 (2.0)	0	5 (2.2)	0	6 (2.2)	0
白血球数減少	0	0	16 (7.1)	7 (3.1)	16 (5.8)	7 (2.5)

TEAE = treatment-emergent adverse event, Graded using Common Terminology Criteria for Adverse Events (CTCAE)
Treatment-related adverse events include adverse events that were considered by the investigator to be possibly or probably related to study drug and adverse events with missing relationship to study drug.
A subject with two or more adverse events in the same system organ class (or with the same preferred term) is counted once for that system organ class (or preferred term).
Adverse event terms are coded using Medical Dictionary for Regulatory Activities (MedDRA) version 17.1.

Program: V:¥projects¥e7389¥iss309¥csr¥dev¥pg¥tables¥T_2_7_4_6.sas 18JUN201513:34

付録 2.7.4-7
Study 309
Treatment-Emergent Adverse Events with Outcome of Death by System Organ Class and Preferred Term
Safety Population

MedDRA System Organ Class Preferred Term	Eribulin Study 309 (N=226) n(%)	Dacarbazine Study 309 (N=224) n(%)
Any TEAEs with outcome of death	10 (4.4)	3 (1.3)
心臓障害	0	1 (0.4)
心停止	0	1 (0.4)
胃腸障害	2 (0.9)	0
腸閉塞	1 (0.4)	0
大腸穿孔	1 (0.4)	0
一般・全身障害および投与部位の状態	1 (0.4)	1 (0.4)
全身健康状態低下	1 (0.4)	1 (0.4)
感染症および寄生虫症	2 (0.9)	0
好中球減少性敗血症	1 (0.4)	0
敗血症性ショック	1 (0.4)	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）	1 (0.4)	0

TEAE = treatment-emergent adverse event
A subject with two or more adverse events in the same system organ class (or with the same preferred term) is counted only once for that system organ class (or preferred term).
Adverse event terms are coded using Medical Dictionary for Regulatory Activities (MedDRA) version 17.1.

Program: V:¥projects¥e7389¥iss309¥csr¥dev¥pg¥tables¥T_2_7_4_7.sas 18JUN201513:34

付録 2.7.4-7
Study 309
Treatment-Emergent Adverse Events with Outcome of Death by System Organ Class and Preferred Term
Safety Population

MedDRA System Organ Class Preferred Term	Eribulin Study 309 (N=226) n(%)	Dacarbazine Study 309 (N=224) 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） (contd)		
肺転移	1 (0.4)	0
呼吸器、胸郭および縦隔障害	4 (1.8)	1 (0.4)
急性呼吸不全	1 (0.4)	0
誤嚥性肺炎	1 (0.4)	0
呼吸不全	2 (0.9)	1 (0.4)

TEAE = treatment-emergent adverse event
A subject with two or more adverse events in the same system organ class (or with the same preferred term) is counted only once for that system organ class (or preferred term).
Adverse event terms are coded using Medical Dictionary for Regulatory Activities (MedDRA) version 17.1.

Program: V:¥projects¥e7389¥iss309¥csr¥dev¥pg¥tables¥T_2_7_4_7.sas 18JUN201513:34

付録 2.7.4-8
Study 309
Treatment-Related Treatment-Emergent Adverse Events with Outcome of Death by System Organ Class and Preferred Term
Safety Population

MedDRA System Organ Class Preferred Term	Eribulin Study 309 (N=226) n(%)	Dacarbazine Study 309 (N=224) n(%)
Any Treatment-Related TEAEs with outcome of death	1 (0.4)	0
感染症および寄生虫症	1 (0.4)	0
好中球減少性敗血症	1 (0.4)	0

TEAE = treatment-emergent adverse event
Treatment-related adverse events include adverse events that were considered by the investigator to be possibly or probably related to study drug and adverse events with missing relationship to study drug.
A subject with two or more adverse events in the same system organ class (or with the same preferred term) is counted only once for that system organ class (or preferred term).
Adverse event terms are coded using Medical Dictionary for Regulatory Activities (MedDRA) version 17.1.

Program: V:¥projects¥e7389¥iss309¥csr¥dev¥pg¥tables¥T_2_7_4_8.sas 18JUN201513:34

付録 2.7.4-9
Japanese and Non-Japanese
Treatment-Emergent Adverse Events with Outcome of Death by System Organ Class and Preferred Term
Eribulin Treated Safety Population

MedDRA System Organ Class Preferred Term	日本人 Study 217 (N=51) n(%)	外国人 Studies 207+309 (N=353) n(%)	全体 Studies 217+207+309 (N=404) n(%)
Any TEAEs with outcome of death	1 (2.0)	13 (3.7)	14 (3.5)
心臓障害	1 (2.0)	0	1 (0.2)
心不全	1 (2.0)	0	1 (0.2)
胃腸障害	0	2 (0.6)	2 (0.5)
腸閉塞	0	1 (0.3)	1 (0.2)
大腸穿孔	0	1 (0.3)	1 (0.2)
一般・全身障害および投与部位の状態	0	2 (0.6)	2 (0.5)
全身健康状態低下	0	2 (0.6)	2 (0.5)
感染症および寄生虫症	0	2 (0.6)	2 (0.5)
好中球減少性敗血症	0	1 (0.3)	1 (0.2)
敗血症性ショック	0	1 (0.3)	1 (0.2)
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）	0	2 (0.6)	2 (0.5)

TEAE = treatment-emergent adverse event
A subject with two or more adverse events in the same system organ class (or with the same preferred term) is counted only once for that system organ class (or preferred term).
Adverse event terms are coded using Medical Dictionary for Regulatory Activities (MedDRA) version 17.1.
This table is based on adverse events data as available. Study 207 did not record laboratory abnormalities into adverse events data.

Program: V:¥projects¥e7389¥iss309¥csr¥dev¥pg¥tables¥T_2_7_4_9.sas 18JUN201513:34

付録 2.7.4-9
Japanese and Non-Japanese
Treatment-Emergent Adverse Events with Outcome of Death by System Organ Class and Preferred Term
Eribulin Treated Safety Population

MedDRA System Organ Class Preferred Term	日本人 Study 217 (N=51) n(%)	外国人 Studies 207+309 (N=353) n(%)	全体 Studies 217+207+309 (N=404) 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） (contd)			
悪性胸水	0	1 (0.3)	1 (0.2)
肺転移	0	1 (0.3)	1 (0.2)
神経系障害	0	1 (0.3)	1 (0.2)
脳虚血	0	1 (0.3)	1 (0.2)
呼吸器、胸郭および縦隔障害	0	4 (1.1)	4 (1.0)
急性呼吸不全	0	1 (0.3)	1 (0.2)
誤嚥性肺炎	0	1 (0.3)	1 (0.2)
呼吸不全	0	2 (0.6)	2 (0.5)

TEAE = treatment-emergent adverse event
A subject with two or more adverse events in the same system organ class (or with the same preferred term) is counted only once for that system organ class (or preferred term).
Adverse event terms are coded using Medical Dictionary for Regulatory Activities (MedDRA) version 17.1.
This table is based on adverse events data as available. Study 207 did not record laboratory abnormalities into adverse events data.

Program: V:¥projects¥e7389¥iss309¥csr¥dev¥pg¥tables¥T_2_7_4_9.sas 18JUN201513:34

付録 2.7.4-10
Japanese and Non-Japanese
Treatment-Related Treatment-Emergent Adverse Events with Outcome of Death by System Organ Class and Preferred Term
Eribulin Treated Safety Population

MedDRA System Organ Class Preferred Term	日本人 Study 217 (N=51) n(%)	外国人 Studies 207+309 (N=353) n(%)	全体 Studies 217+207+309 (N=404) n(%)
Any Treatment-Related TEAEs with outcome of death	0	2 (0.6)	2 (0.5)
感染症および寄生虫症	0	1 (0.3)	1 (0.2)
好中球減少性敗血症	0	1 (0.3)	1 (0.2)
神経系障害	0	1 (0.3)	1 (0.2)
脳虚血	0	1 (0.3)	1 (0.2)

TEAE = treatment-emergent adverse event
Treatment-related adverse events include adverse events that were considered by the investigator to be possibly or probably related to study drug and adverse events with missing relationship to study drug.
A subject with two or more adverse events in the same system organ class (or with the same preferred term) is counted only once for that system organ class (or preferred term).
Adverse event terms are coded using Medical Dictionary for Regulatory Activities (MedDRA) version 17.1.
This table is based on adverse events data as available. Study 207 did not record laboratory abnormalities into adverse events data.

Program: V:¥projects¥e7389¥iss309¥csr¥dev¥pg¥tables¥T_2_7_4_10.sas 18JUN201513:35

付録 2.7.4-11
Study 309
Serious Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Safety Population

MedDRA System Organ Class Preferred Term	Eribulin Study 309 (N=226) n(%)	Dacarbazine Study 309 (N=224) n(%)
Any serious TEAEs	76 (33.6)	71 (31.7)
血液およびリンパ系障害	17 (7.5)	26 (11.6)
貧血	5 (2.2)	9 (4.0)
発熱性好中球減少症	2 (0.9)	2 (0.9)
白血球減少症	3 (1.3)	3 (1.3)
リンパ球減少症	1 (0.4)	0
好中球減少症	11 (4.9)	10 (4.5)
汎血球減少症	0	3 (1.3)
血小板減少症	0	13 (5.8)
心臓障害	2 (0.9)	2 (0.9)
心房細動	1 (0.4)	1 (0.4)
心停止	0	1 (0.4)
心嚢液貯留	1 (0.4)	0
胃腸障害	16 (7.1)	18 (8.0)

A subject with two or more serious adverse events in the same system organ class (or with the same preferred term) is counted only once for that system organ class (or preferred term).
Adverse event terms are coded using Medical Dictionary for Regulatory Activities (MedDRA) version 17.1.

Program: V:¥projects¥e7389¥iss309¥csr¥dev¥pg¥tables¥T_2_7_4_11.sas 18JUN201513:36

付録 2.7.4-11
Study 309
Serious Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Safety Population

MedDRA System Organ Class Preferred Term	Eribulin Study 309 (N=226) n(%)	Dacarbazine Study 309 (N=224) n(%)
胃腸障害 (contd)		
腹部膨満	0	1 (0.4)
腹痛	4 (1.8)	4 (1.8)
上腹部痛	0	1 (0.4)
便秘	1 (0.4)	0
下痢	2 (0.9)	2 (0.9)
憩室	0	1 (0.4)
十二指腸潰瘍	0	1 (0.4)
胃腸出血	0	1 (0.4)
出血性胃腸潰瘍	0	1 (0.4)
イレウス	1 (0.4)	0
腸出血	0	1 (0.4)
腸管虚血	1 (0.4)	0
腸閉塞	4 (1.8)	5 (2.2)
大腸閉塞	0	1 (0.4)
大腸穿孔	1 (0.4)	0
食道炎	1 (0.4)	0

A subject with two or more serious adverse events in the same system organ class (or with the same preferred term) is counted only once for that system organ class (or preferred term).
Adverse event terms are coded using Medical Dictionary for Regulatory Activities (MedDRA) version 17.1.

Program: V:¥projects¥e7389¥iss309¥csr¥dev¥pg¥tables¥T_2_7_4_11.sas 18JUN201513:36

付録 2.7.4-11
Study 309
Serious Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Safety Population

MedDRA System Organ Class Preferred Term	Eribulin Study 309 (N=226) n(%)	Dacarbazine Study 309 (N=224) n(%)
胃腸障害 (contd)		
後腹膜出血	1 (0.4)	0
小腸閉塞	2 (0.9)	3 (1.3)
亜イレウス	1 (0.4)	0
一般・全身障害および投与部位の状態	16 (7.1)	7 (3.1)
無力症	3 (1.3)	1 (0.4)
疲労	1 (0.4)	0
全身健康状態低下	2 (0.9)	1 (0.4)
非心臓性胸痛	0	1 (0.4)
発熱	10 (4.4)	4 (1.8)
肝胆道系障害	3 (1.3)	1 (0.4)
胆管拡張	1 (0.4)	0
胆管炎	0	1 (0.4)
胆嚢炎	0	1 (0.4)
肝毒性	1 (0.4)	0

A subject with two or more serious adverse events in the same system organ class (or with the same preferred term) is counted only once for that system organ class (or preferred term).
Adverse event terms are coded using Medical Dictionary for Regulatory Activities (MedDRA) version 17.1.

Program: V:¥projects¥e7389¥iss309¥csr¥dev¥pg¥tables¥T_2_7_4_11.sas 18JUN201513:36

付録 2.7.4-11
Study 309
Serious Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Safety Population

MedDRA System Organ Class Preferred Term	Eribulin Study 309 (N=226) n(%)	Dacarbazine Study 309 (N=224) n(%)
肝胆道系障害 (contd)		
高ビリルビン血症	2 (0.9)	0
免疫系障害	1 (0.4)	1 (0.4)
薬物過敏症	0	1 (0.4)
過敏症	1 (0.4)	0
感染症および寄生虫症	20 (8.8)	8 (3.6)
細菌性関節炎	1 (0.4)	0
気管支肺炎	1 (0.4)	0
カテーテル留置部位感染	1 (0.4)	0
蜂巣炎	0	1 (0.4)
医療機器関連感染	1 (0.4)	1 (0.4)
丹毒	0	1 (0.4)
真菌性下気道感染	1 (0.4)	0
肺感染	2 (0.9)	0
好中球減少性敗血症	1 (0.4)	0

A subject with two or more serious adverse events in the same system organ class (or with the same preferred term) is counted only once for that system organ class (or preferred term).
Adverse event terms are coded using Medical Dictionary for Regulatory Activities (MedDRA) version 17.1.

Program: V:¥projects¥e7389¥iss309¥csr¥dev¥pg¥tables¥T_2_7_4_11.sas 18JUN201513:36

付録 2.7.4-11
Study 309
Serious Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Safety Population

MedDRA System Organ Class Preferred Term	Eribulin Study 309 (N=226) n(%)	Dacarbazine Study 309 (N=224) n(%)
感染症および寄生虫症 (contd)		
腹膜炎	1 (0.4)	0
細菌性腹膜炎	2 (0.9)	0
肺炎	3 (1.3)	2 (0.9)
シュードモナス性菌血症	1 (0.4)	0
腎盂腎炎	1 (0.4)	0
気道感染	0	1 (0.4)
敗血症性ショック	1 (0.4)	0
セラチア性菌血症	1 (0.4)	0
ブドウ球菌性菌血症	1 (0.4)	0
ブドウ球菌感染	1 (0.4)	0
尿路感染	4 (1.8)	1 (0.4)
前庭神経炎	0	1 (0.4)
傷害、中毒および処置合併症	4 (1.8)	1 (0.4)
上腕骨骨折	1 (0.4)	0
処置後出血	1 (0.4)	0

A subject with two or more serious adverse events in the same system organ class (or with the same preferred term) is counted only once for that system organ class (or preferred term).
Adverse event terms are coded using Medical Dictionary for Regulatory Activities (MedDRA) version 17.1.

Program: V:¥projects¥e7389¥iss309¥csr¥dev¥pg¥tables¥T_2_7_4_11.sas 18JUN201513:36

付録 2.7.4-11
Study 309
Serious Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Safety Population

MedDRA System Organ Class Preferred Term	Eribulin Study 309 (N=226) n(%)	Dacarbazine Study 309 (N=224) n(%)
傷害、中毒および処置合併症 (contd)		
放射線性肺臓炎	1 (0.4)	0
各種物質毒性	0	1 (0.4)
創離開	1 (0.4)	0
臨床検査	4 (1.8)	5 (2.2)
アラニンアミノトランスフェラーゼ増加	1 (0.4)	1 (0.4)
アスパラギン酸アミノトランスフェラーゼ増加	1 (0.4)	1 (0.4)
心電図ＱＴ延長	1 (0.4)	0
ヘモグロビン減少	0	2 (0.9)
国際標準比増加	1 (0.4)	0
好中球数減少	1 (0.4)	1 (0.4)
血小板数減少	0	1 (0.4)
白血球数減少	1 (0.4)	0
代謝および栄養障害	3 (1.3)	0
低カリウム血症	1 (0.4)	0

A subject with two or more serious adverse events in the same system organ class (or with the same preferred term) is counted only once for that system organ class (or preferred term).
Adverse event terms are coded using Medical Dictionary for Regulatory Activities (MedDRA) version 17.1.

Program: V:¥projects¥e7389¥iss309¥csr¥dev¥pg¥tables¥T_2_7_4_11.sas 18JUN201513:36

付録 2.7.4-11
Study 309
Serious Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Safety Population

MedDRA System Organ Class Preferred Term	Eribulin Study 309 (N=226) n(%)	Dacarbazine Study 309 (N=224) n(%)
代謝および栄養障害 (contd)		
低ナトリウム血症	1 (0.4)	0
低リン酸血症	1 (0.4)	0
筋骨格系および結合組織障害	4 (1.8)	3 (1.3)
背部痛	2 (0.9)	0
筋骨格痛	0	1 (0.4)
病的骨折	2 (0.9)	1 (0.4)
脊椎痛	0	1 (0.4)
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）	8 (3.5)	7 (3.1)
癌疼痛	2 (0.9)	0
頭蓋内腫瘍出血	0	1 (0.4)
平滑筋肉腫	0	1 (0.4)
悪性腹水	0	1 (0.4)
悪性胸水	0	2 (0.9)
骨転移	1 (0.4)	0

A subject with two or more serious adverse events in the same system organ class (or with the same preferred term) is counted only once for that system organ class (or preferred term).
Adverse event terms are coded using Medical Dictionary for Regulatory Activities (MedDRA) version 17.1.

Program: V:¥projects¥e7389¥iss309¥csr¥dev¥pg¥tables¥T_2_7_4_11.sas 18JUN201513:36

付録 2.7.4-11
Study 309
Serious Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Safety Population

MedDRA System Organ Class Preferred Term	Eribulin Study 309 (N=226) n(%)	Dacarbazine Study 309 (N=224) 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） (contd)		
肺転移	1 (0.4)	1 (0.4)
頚部転移	1 (0.4)	0
転移部痛	1 (0.4)	0
粘液型脂肪肉腫	1 (0.4)	0
腫瘍熱	1 (0.4)	0
腫瘍出血	1 (0.4)	0
腫瘍疼痛	0	1 (0.4)
神経系障害	3 (1.3)	2 (0.9)
痙攣	1 (0.4)	0
単麻痺	1 (0.4)	0
神経痛	0	1 (0.4)
末梢性運動ニューロパチー	0	1 (0.4)
脊髄圧迫	1 (0.4)	0
腎および尿路障害	1 (0.4)	1 (0.4)

A subject with two or more serious adverse events in the same system organ class (or with the same preferred term) is counted only once for that system organ class (or preferred term).
Adverse event terms are coded using Medical Dictionary for Regulatory Activities (MedDRA) version 17.1.

Program: V:¥projects¥e7389¥iss309¥csr¥dev¥pg¥tables¥T_2_7_4_11.sas 18JUN201513:36

付録 2.7.4-11
Study 309
Serious Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Safety Population

MedDRA System Organ Class Preferred Term	Eribulin Study 309 (N=226) n(%)	Dacarbazine Study 309 (N=224) n(%)
腎および尿路障害 (contd)		
急性腎不全	1 (0.4)	1 (0.4)
呼吸器、胸郭および縦隔障害	12 (5.3)	13 (5.8)
急性呼吸不全	1 (0.4)	0
無気肺	0	1 (0.4)
呼吸困難	2 (0.9)	4 (1.8)
労作性呼吸困難	0	1 (0.4)
鼻出血	0	1 (0.4)
しゃっくり	0	1 (0.4)
胸水	0	2 (0.9)
誤嚥性肺炎	1 (0.4)	0
気胸	1 (0.4)	1 (0.4)
肺塞栓症	4 (1.8)	1 (0.4)
呼吸不全	4 (1.8)	2 (0.9)
血管障害	2 (0.9)	5 (2.2)

A subject with two or more serious adverse events in the same system organ class (or with the same preferred term) is counted only once for that system organ class (or preferred term).
Adverse event terms are coded using Medical Dictionary for Regulatory Activities (MedDRA) version 17.1.

Program: V:¥projects¥e7389¥iss309¥csr¥dev¥pg¥tables¥T_2_7_4_11.sas 18JUN201513:36

付録 2.7.4-11
Study 309
Serious Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Safety Population

MedDRA System Organ Class Preferred Term	Eribulin Study 309 (N=226) n(%)	Dacarbazine Study 309 (N=224) n(%)
血管障害 (contd)		
深部静脈血栓症	0	3 (1.3)
低血圧	0	2 (0.9)
上大静脈症候群	1 (0.4)	0
大静脈血栓症	1 (0.4)	0

A subject with two or more serious adverse events in the same system organ class (or with the same preferred term) is counted only once for that system organ class (or preferred term).
Adverse event terms are coded using Medical Dictionary for Regulatory Activities (MedDRA) version 17.1.

Program: V:¥projects¥e7389¥iss309¥csr¥dev¥pg¥tables¥T_2_7_4_11.sas 18JUN201513:36

付録 2.7.4-12
Study 309
Treatment-Related Serious Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Safety Population

MedDRA System Organ Class Preferred Term	Eribulin Study 309 (N=226) n(%)	Dacarbazine Study 309 (N=224) n(%)
Any treatment-related serious TEAE	31 (13.7)	31 (13.8)
血液およびリンパ系障害	16 (7.1)	23 (10.3)
貧血	4 (1.8)	7 (3.1)
発熱性好中球減少症	2 (0.9)	2 (0.9)
白血球減少症	3 (1.3)	3 (1.3)
リンパ球減少症	1 (0.4)	0
好中球減少症	11 (4.9)	10 (4.5)
汎血球減少症	0	2 (0.9)
血小板減少症	0	13 (5.8)
心臓障害	1 (0.4)	0
心嚢液貯留	1 (0.4)	0
胃腸障害	3 (1.3)	2 (0.9)
下痢	1 (0.4)	1 (0.4)
胃腸出血	0	1 (0.4)

Treatment-related adverse events include adverse events that were considered by the investigator to be possibly or probably related to study drug and adverse events with missing relationship to study drug.
A subject with two or more serious adverse events in the same system organ class (or with the same preferred term) is counted only once for that system organ class (or preferred term).
Adverse event terms are coded using Medical Dictionary for Regulatory Activities (MedDRA) version 17.1.

Program: V:¥projects¥e7389¥iss309¥csr¥dev¥pg¥tables¥T_2_7_4_12.sas 18JUN201513:36

付録 2.7.4-12
Study 309
Treatment-Related Serious Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Safety Population

MedDRA System Organ Class Preferred Term	Eribulin Study 309 (N=226) n(%)	Dacarbazine Study 309 (N=224) n(%)
胃腸障害 (contd)		
腸閉塞	1 (0.4)	0
後腹膜出血	1 (0.4)	0
一般・全身障害および投与部位の状態	7 (3.1)	2 (0.9)
無力症	2 (0.9)	0
疲労	1 (0.4)	0
発熱	4 (1.8)	2 (0.9)
免疫系障害	1 (0.4)	1 (0.4)
薬物過敏症	0	1 (0.4)
過敏症	1 (0.4)	0
感染症および寄生虫症	4 (1.8)	3 (1.3)
気管支肺炎	1 (0.4)	0
蜂巣炎	0	1 (0.4)
真菌性下気道感染	1 (0.4)	0

Treatment-related adverse events include adverse events that were considered by the investigator to be possibly or probably related to study drug and adverse events with missing relationship to study drug.
A subject with two or more serious adverse events in the same system organ class (or with the same preferred term) is counted only once for that system organ class (or preferred term).
Adverse event terms are coded using Medical Dictionary for Regulatory Activities (MedDRA) version 17.1.

Program: V:¥projects¥e7389¥iss309¥csr¥dev¥pg¥tables¥T_2_7_4_12.sas 18JUN201513:36

付録 2.7.4-12
Study 309
Treatment-Related Serious Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Safety Population

MedDRA System Organ Class Preferred Term	Eribulin Study 309 (N=226) n(%)	Dacarbazine Study 309 (N=224) n(%)
感染症および寄生虫症 (contd)		
好中球減少性敗血症	1 (0.4)	0
肺炎	1 (0.4)	2 (0.9)
臨床検査	2 (0.9)	3 (1.3)
心電図ＱＴ延長	1 (0.4)	0
ヘモグロビン減少	0	1 (0.4)
好中球数減少	1 (0.4)	1 (0.4)
血小板数減少	0	1 (0.4)
白血球数減少	1 (0.4)	0
代謝および栄養障害	3 (1.3)	0
低カリウム血症	1 (0.4)	0
低ナトリウム血症	1 (0.4)	0
低リン酸血症	1 (0.4)	0
神経系障害	1 (0.4)	0

Treatment-related adverse events include adverse events that were considered by the investigator to be possibly or probably related to study drug and adverse events with missing relationship to study drug.
A subject with two or more serious adverse events in the same system organ class (or with the same preferred term) is counted only once for that system organ class (or preferred term).
Adverse event terms are coded using Medical Dictionary for Regulatory Activities (MedDRA) version 17.1.

Program: V:¥projects¥e7389¥iss309¥csr¥dev¥pg¥tables¥T_2_7_4_12.sas 18JUN201513:36

付録 2.7.4-12
Study 309
Treatment-Related Serious Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Safety Population

MedDRA System Organ Class Preferred Term	Eribulin Study 309 (N=226) n(%)	Dacarbazine Study 309 (N=224) n(%)
神経系障害 (contd)		
痙攣	1 (0.4)	0
呼吸器、胸郭および縦隔障害	0	3 (1.3)
呼吸困難	0	1 (0.4)
鼻出血	0	1 (0.4)
気胸	0	1 (0.4)
血管障害	0	1 (0.4)
低血圧	0	1 (0.4)

Treatment-related adverse events include adverse events that were considered by the investigator to be possibly or probably related to study drug and adverse events with missing relationship to study drug.
A subject with two or more serious adverse events in the same system organ class (or with the same preferred term) is counted only once for that system organ class (or preferred term).
Adverse event terms are coded using Medical Dictionary for Regulatory Activities (MedDRA) version 17.1.

Program: V:¥projects¥e7389¥iss309¥csr¥dev¥pg¥tables¥T_2_7_4_12.sas 18JUN201513:36

付録 2.7.4-13
Japanese and Non-Japanese
Serious Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Eribulin Treated Safety Population

MedDRA System Organ Class Preferred Term	日本人 Study 217 (N=51) n(%)	外国人 Studies 207+309 (N=353) n(%)	全体 Studies 217+207+309 (N=404) n(%)
Any serious TEAEs	15 (29.4)	123 (34.8)	138 (34.2)
血液およびリンパ系障害	1 (2.0)	24 (6.8)	25 (6.2)
貧血	0	6 (1.7)	6 (1.5)
発熱性好中球減少症	1 (2.0)	6 (1.7)	7 (1.7)
白血球減少症	0	3 (0.8)	3 (0.7)
リンパ球減少症	0	1 (0.3)	1 (0.2)
好中球減少症	0	13 (3.7)	13 (3.2)
心臓障害	1 (2.0)	3 (0.8)	4 (1.0)
心房細動	0	1 (0.3)	1 (0.2)
心不全	1 (2.0)	0	1 (0.2)
心嚢液貯留	0	2 (0.6)	2 (0.5)
眼障害	1 (2.0)	0	1 (0.2)
白内障	1 (2.0)	0	1 (0.2)

A subject with two or more serious adverse events in the same system organ class (or with the same preferred term) is counted only once for that system organ class (or preferred term).
Adverse event terms are coded using Medical Dictionary for Regulatory Activities (MedDRA) version 17.1.
This table is based on adverse events data as available. Study 207 did not record laboratory abnormalities into adverse events data.

Program: V:¥projects¥e7389¥iss309¥csr¥dev¥pg¥tables¥T_2_7_4_13.sas 18JUN201513:36

付録 2.7.4-13
Japanese and Non-Japanese
Serious Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Eribulin Treated Safety Population

MedDRA System Organ Class Preferred Term	日本人 Study 217 (N=51) n(%)	外国人 Studies 207+309 (N=353) n(%)	全体 Studies 217+207+309 (N=404) n(%)
胃腸障害	2 (3.9)	21 (5.9)	23 (5.7)
腹部癒着	0	1 (0.3)	1 (0.2)
腹痛	0	4 (1.1)	4 (1.0)
便秘	0	2 (0.6)	2 (0.5)
下痢	0	2 (0.6)	2 (0.5)
十二指腸潰瘍	0	1 (0.3)	1 (0.2)
胃腸障害	0	1 (0.3)	1 (0.2)
イレウス	2 (3.9)	2 (0.6)	4 (1.0)
腸管虚血	0	1 (0.3)	1 (0.2)
腸閉塞	0	6 (1.7)	6 (1.5)
大腸穿孔	0	1 (0.3)	1 (0.2)
食道炎	0	1 (0.3)	1 (0.2)
後腹膜出血	0	1 (0.3)	1 (0.2)
小腸閉塞	0	2 (0.6)	2 (0.5)
口内炎	0	1 (0.3)	1 (0.2)
亜イレウス	0	1 (0.3)	1 (0.2)
嘔吐	0	1 (0.3)	1 (0.2)

A subject with two or more serious adverse events in the same system organ class (or with the same preferred term) is counted only once for that system organ class (or preferred term).
Adverse event terms are coded using Medical Dictionary for Regulatory Activities (MedDRA) version 17.1.
This table is based on adverse events data as available. Study 207 did not record laboratory abnormalities into adverse events data.

Program: V:¥projects¥e7389¥iss309¥csr¥dev¥pg¥tables¥T_2_7_4_13.sas 18JUN201513:36

付録 2.7.4-13
Japanese and Non-Japanese
Serious Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Eribulin Treated Safety Population

MedDRA System Organ Class Preferred Term	日本人 Study 217 (N=51) n(%)	外国人 Studies 207+309 (N=353) n(%)	全体 Studies 217+207+309 (N=404) n(%)
一般・全身障害および投与部位の状態	0	26 (7.4)	26 (6.4)
無力症	0	3 (0.8)	3 (0.7)
胸痛	0	1 (0.3)	1 (0.2)
悪寒	0	1 (0.3)	1 (0.2)
疲労	0	2 (0.6)	2 (0.5)
全身健康状態低下	0	6 (1.7)	6 (1.5)
末梢性浮腫	0	1 (0.3)	1 (0.2)
発熱	0	14 (4.0)	14 (3.5)
肝胆道系障害	1 (2.0)	3 (0.8)	4 (1.0)
胆管拡張	0	1 (0.3)	1 (0.2)
肝出血	1 (2.0)	0	1 (0.2)
肝毒性	0	1 (0.3)	1 (0.2)
高ビリルビン血症	0	2 (0.6)	2 (0.5)
免疫系障害	0	1 (0.3)	1 (0.2)
過敏症	0	1 (0.3)	1 (0.2)

A subject with two or more serious adverse events in the same system organ class (or with the same preferred term) is counted only once for that system organ class (or preferred term).
Adverse event terms are coded using Medical Dictionary for Regulatory Activities (MedDRA) version 17.1.
This table is based on adverse events data as available. Study 207 did not record laboratory abnormalities into adverse events data.

Program: V:¥projects¥e7389¥iss309¥csr¥dev¥pg¥tables¥T_2_7_4_13.sas 18JUN201513:36

付録 2.7.4-13
Japanese and Non-Japanese
Serious Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Eribulin Treated Safety Population

MedDRA System Organ Class Preferred Term	日本人 Study 217 (N=51) n(%)	外国人 Studies 207+309 (N=353) n(%)	全体 Studies 217+207+309 (N=404) n(%)
感染症および寄生虫症	3 (5.9)	28 (7.9)	31 (7.7)
細菌性関節炎	0	1 (0.3)	1 (0.2)
気管支肺炎	0	1 (0.3)	1 (0.2)
カテーテル留置部位感染	0	1 (0.3)	1 (0.2)
医療機器関連感染	0	3 (0.8)	3 (0.7)
蓄膿	1 (2.0)	0	1 (0.2)
真菌性下気道感染	0	1 (0.3)	1 (0.2)
肺感染	0	2 (0.6)	2 (0.5)
好中球減少性敗血症	0	1 (0.3)	1 (0.2)
腹膜炎	0	1 (0.3)	1 (0.2)
細菌性腹膜炎	0	2 (0.6)	2 (0.5)
咽頭炎	0	1 (0.3)	1 (0.2)
肺炎	1 (2.0)	6 (1.7)	7 (1.7)
シュードモナス性菌血症	0	1 (0.3)	1 (0.2)
腎盂腎炎	0	1 (0.3)	1 (0.2)
敗血症	0	1 (0.3)	1 (0.2)
敗血症性ショック	0	1 (0.3)	1 (0.2)

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Adverse event terms are coded using Medical Dictionary for Regulatory Activities (MedDRA) version 17.1.
This table is based on adverse events data as available. Study 207 did not record laboratory abnormalities into adverse events data.

Program: V:¥projects¥e7389¥iss309¥csr¥dev¥pg¥tables¥T_2_7_4_13.sas 18JUN201513:36

付録 2.7.4-13
Japanese and Non-Japanese
Serious Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Eribulin Treated Safety Population

MedDRA System Organ Class Preferred Term	日本人 Study 217 (N=51) n(%)	外国人 Studies 207+309 (N=353) n(%)	全体 Studies 217+207+309 (N=404) n(%)
感染症および寄生虫症 (contd)			
セラチア性菌血症	0	1 (0.3)	1 (0.2)
ブドウ球菌性菌血症	0	1 (0.3)	1 (0.2)
ブドウ球菌感染	0	1 (0.3)	1 (0.2)
レンサ球菌感染	1 (2.0)	0	1 (0.2)
皮下組織膿瘍	0	1 (0.3)	1 (0.2)
尿路感染	0	4 (1.1)	4 (1.0)
傷害、中毒および処置合併症	0	7 (2.0)	7 (1.7)
大腿骨骨折	0	1 (0.3)	1 (0.2)
股関節部骨折	0	1 (0.3)	1 (0.2)
上腕骨骨折	0	1 (0.3)	1 (0.2)
処置後出血	0	1 (0.3)	1 (0.2)
放射線性肺臓炎	0	1 (0.3)	1 (0.2)
尿管吻合合併症	0	1 (0.3)	1 (0.2)
創離開	0	1 (0.3)	1 (0.2)

A subject with two or more serious adverse events in the same system organ class (or with the same preferred term) is counted only once for that system organ class (or preferred term).
Adverse event terms are coded using Medical Dictionary for Regulatory Activities (MedDRA) version 17.1.
This table is based on adverse events data as available. Study 207 did not record laboratory abnormalities into adverse events data.

Program: V:¥projects¥e7389¥iss309¥csr¥dev¥pg¥tables¥T_2_7_4_13.sas 18JUN201513:36

付録 2.7.4-13
Japanese and Non-Japanese
Serious Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Eribulin Treated Safety Population

MedDRA System Organ Class Preferred Term	日本人 Study 217 (N=51) n(%)	外国人 Studies 207+309 (N=353) n(%)	全体 Studies 217+207+309 (N=404) n(%)
臨床検査	0	5 (1.4)	5 (1.2)
アラニンアミノトランスフェラーゼ増加	0	1 (0.3)	1 (0.2)
アスパラギン酸アミノトランスフェラーゼ増加	0	1 (0.3)	1 (0.2)
血中アルカリホスファターゼ	0	1 (0.3)	1 (0.2)
心電図ＱＴ延長	0	1 (0.3)	1 (0.2)
γ－グルタミルトランスフェラーゼ	0	1 (0.3)	1 (0.2)
国際標準比増加	0	1 (0.3)	1 (0.2)
好中球数減少	0	1 (0.3)	1 (0.2)
白血球数減少	0	1 (0.3)	1 (0.2)
代謝および栄養障害	0	8 (2.3)	8 (2.0)
脱水	0	1 (0.3)	1 (0.2)
高カルシウム血症	0	1 (0.3)	1 (0.2)
高血糖	0	1 (0.3)	1 (0.2)
低アルブミン血症	0	1 (0.3)	1 (0.2)
低カリウム血症	0	2 (0.6)	2 (0.5)
低マグネシウム血症	0	1 (0.3)	1 (0.2)

A subject with two or more serious adverse events in the same system organ class (or with the same preferred term) is counted only once for that system organ class (or preferred term).
Adverse event terms are coded using Medical Dictionary for Regulatory Activities (MedDRA) version 17.1.
This table is based on adverse events data as available. Study 207 did not record laboratory abnormalities into adverse events data.

Program: V:¥projects¥e7389¥iss309¥csr¥dev¥pg¥tables¥T_2_7_4_13.sas 18JUN201513:36

付録 2.7.4-13
Japanese and Non-Japanese
Serious Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Eribulin Treated Safety Population

MedDRA System Organ Class Preferred Term	日本人 Study 217 (N=51) n(%)	外国人 Studies 207+309 (N=353) n(%)	全体 Studies 217+207+309 (N=404) n(%)
代謝および栄養障害 (contd)			
低ナトリウム血症	0	1 (0.3)	1 (0.2)
低リン酸血症	0	1 (0.3)	1 (0.2)
筋骨格系および結合組織障害	0	6 (1.7)	6 (1.5)
関節痛	0	1 (0.3)	1 (0.2)
背部痛	0	2 (0.6)	2 (0.5)
四肢痛	0	1 (0.3)	1 (0.2)
病的骨折	0	2 (0.6)	2 (0.5)
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）	5 (9.8)	15 (4.2)	20 (5.0)
癌疼痛	3 (5.9)	2 (0.6)	5 (1.2)
口唇および口腔内癌	0	1 (0.3)	1 (0.2)
悪性胸水	0	1 (0.3)	1 (0.2)
骨転移	0	1 (0.3)	1 (0.2)
肺転移	0	1 (0.3)	1 (0.2)
頸部転移	0	1 (0.3)	1 (0.2)

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Adverse event terms are coded using Medical Dictionary for Regulatory Activities (MedDRA) version 17.1.
This table is based on adverse events data as available. Study 207 did not record laboratory abnormalities into adverse events data.

Program: V:¥projects¥e7389¥iss309¥csr¥dev¥pg¥tables¥T_2_7_4_13.sas 18JUN201513:36

付録 2.7.4-13
Japanese and Non-Japanese
Serious Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Eribulin Treated Safety Population

MedDRA System Organ Class Preferred Term	日本人 Study 217 (N=51) n(%)	外国人 Studies 207+309 (N=353) n(%)	全体 Studies 217+207+309 (N=404) 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） (contd)			
転移部痛	0	1 (0.3)	1 (0.2)
粘液型脂肪肉腫	0	1 (0.3)	1 (0.2)
腫瘍熱	0	1 (0.3)	1 (0.2)
腫瘍性塞栓症	1 (2.0)	0	1 (0.2)
腫瘍出血	1 (2.0)	2 (0.6)	3 (0.7)
腫瘍疼痛	0	4 (1.1)	4 (1.0)
神経系障害	0	9 (2.5)	9 (2.2)
前脊髄動脈症候群	0	1 (0.3)	1 (0.2)
脳虚血	0	2 (0.6)	2 (0.5)
痙攣	0	1 (0.3)	1 (0.2)
単麻痺	0	1 (0.3)	1 (0.2)
末梢性運動ニューロパチー	0	1 (0.3)	1 (0.2)
末梢性感覚ニューロパチー	0	1 (0.3)	1 (0.2)
傾眠	0	1 (0.3)	1 (0.2)
脊髄圧迫	0	1 (0.3)	1 (0.2)

A subject with two or more serious adverse events in the same system organ class (or with the same preferred term) is counted only once for that system organ class (or preferred term).
Adverse event terms are coded using Medical Dictionary for Regulatory Activities (MedDRA) version 17.1.
This table is based on adverse events data as available. Study 207 did not record laboratory abnormalities into adverse events data.

Program: V:¥projects¥e7389¥iss309¥csr¥dev¥pg¥tables¥T_2_7_4_13.sas 18JUN201513:36

付録 2.7.4-13
Japanese and Non-Japanese
Serious Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Eribulin Treated Safety Population

MedDRA System Organ Class Preferred Term	日本人 Study 217 (N=51) n(%)	外国人 Studies 207+309 (N=353) n(%)	全体 Studies 217+207+309 (N=404) n(%)
神経系障害 (contd)			
失神	0	1 (0.3)	1 (0.2)
精神障害	0	1 (0.3)	1 (0.2)
錯乱状態	0	1 (0.3)	1 (0.2)
腎および尿路障害	1 (2.0)	2 (0.6)	3 (0.7)
排尿困難	0	1 (0.3)	1 (0.2)
水腎症	1 (2.0)	0	1 (0.2)
急性腎不全	0	1 (0.3)	1 (0.2)
生殖系および乳房障害	0	1 (0.3)	1 (0.2)
膣出血	0	1 (0.3)	1 (0.2)
呼吸器、胸郭および縦隔障害	2 (3.9)	19 (5.4)	21 (5.2)
急性呼吸不全	0	1 (0.3)	1 (0.2)
咳嗽	0	1 (0.3)	1 (0.2)

A subject with two or more serious adverse events in the same system organ class (or with the same preferred term) is counted only once for that system organ class (or preferred term).
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This table is based on adverse events data as available. Study 207 did not record laboratory abnormalities into adverse events data.

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付録 2.7.4-13
Japanese and Non-Japanese
Serious Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Eribulin Treated Safety Population

MedDRA System Organ Class Preferred Term	日本人 Study 217 (N=51) n(%)	外国人 Studies 207+309 (N=353) n(%)	全体 Studies 217+207+309 (N=404) n(%)
呼吸器、胸郭および縦隔障害 (contd)			
呼吸困難	1 (2.0)	5 (1.4)	6 (1.5)
胸水	0	1 (0.3)	1 (0.2)
誤嚥性肺炎	0	1 (0.3)	1 (0.2)
気胸	0	1 (0.3)	1 (0.2)
肺塞栓症	1 (2.0)	6 (1.7)	7 (1.7)
呼吸不全	0	4 (1.1)	4 (1.0)
気道出血	0	1 (0.3)	1 (0.2)
血管障害	0	4 (1.1)	4 (1.0)
深部静脈血栓症	0	1 (0.3)	1 (0.2)
上大静脈症候群	0	1 (0.3)	1 (0.2)
血栓症	0	1 (0.3)	1 (0.2)
大静脈血栓症	0	1 (0.3)	1 (0.2)

A subject with two or more serious adverse events in the same system organ class (or with the same preferred term) is counted only once for that system organ class (or preferred term).
Adverse event terms are coded using Medical Dictionary for Regulatory Activities (MedDRA) version 17.1.
This table is based on adverse events data as available. Study 207 did not record laboratory abnormalities into adverse events data.

Program: V:¥projects¥e7389¥iss309¥csr¥dev¥pg¥tables¥T_2_7_4_13.sas 18JUN201513:36

付録 2.7.4-14
Japanese and Non-Japanese
Treatment-Related Serious Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Eribulin Treated Safety Population

MedDRA System Organ Class Preferred Term	日本人 Study 217 (N=51) n(%)	外国人 Studies 207+309 (N=353) n(%)	全体 Studies 217+207+309 (N=404) n(%)
Any treatment-related serious TEAE	5 (9.8)	45 (12.7)	50 (12.4)
血液およびリンパ系障害	1 (2.0)	22 (6.2)	23 (5.7)
貧血	0	4 (1.1)	4 (1.0)
発熱性好中球減少症	1 (2.0)	6 (1.7)	7 (1.7)
白血球減少症	0	3 (0.8)	3 (0.7)
リンパ球減少症	0	1 (0.3)	1 (0.2)
好中球減少症	0	13 (3.7)	13 (3.2)
心臓障害	0	1 (0.3)	1 (0.2)
心嚢液貯留	0	1 (0.3)	1 (0.2)
胃腸障害	0	4 (1.1)	4 (1.0)
下痢	0	1 (0.3)	1 (0.2)
腸閉塞	0	1 (0.3)	1 (0.2)
後腹膜出血	0	1 (0.3)	1 (0.2)
口内炎	0	1 (0.3)	1 (0.2)

Treatment-related adverse events include adverse events that were considered by the investigator to be possibly or probably related to study drug and adverse events with missing relationship to study drug.
A subject with two or more serious adverse events in the same system organ class (or with the same preferred term) is counted only once for that system organ class (or preferred term).
Adverse event terms are coded using Medical Dictionary for Regulatory Activities (MedDRA) version 17.1.
This table is based on adverse events data as available. Study 207 did not record laboratory abnormalities into adverse events data.

Program: V:¥projects¥e7389¥iss309¥csr¥dev¥pg¥tables¥T_2_7_4_14.sas 18JUN201513:37

付録 2.7.4-14
Japanese and Non-Japanese
Treatment-Related Serious Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Eribulin Treated Safety Population

MedDRA System Organ Class Preferred Term	日本人 Study 217 (N=51) n(%)	外国人 Studies 207+309 (N=353) n(%)	全体 Studies 217+207+309 (N=404) n(%)
一般・全身障害および投与部位の状態	0	9 (2.5)	9 (2.2)
無力症	0	2 (0.6)	2 (0.5)
悪寒	0	1 (0.3)	1 (0.2)
疲労	0	1 (0.3)	1 (0.2)
発熱	0	6 (1.7)	6 (1.5)
肝胆道系障害	1 (2.0)	0	1 (0.2)
肝出血	1 (2.0)	0	1 (0.2)
免疫系障害	0	1 (0.3)	1 (0.2)
過敏症	0	1 (0.3)	1 (0.2)
感染症および寄生虫症	2 (3.9)	7 (2.0)	9 (2.2)
気管支肺炎	0	1 (0.3)	1 (0.2)
蓄膿	1 (2.0)	0	1 (0.2)
真菌性下気道感染	0	1 (0.3)	1 (0.2)
好中球減少性敗血症	0	1 (0.3)	1 (0.2)

Treatment-related adverse events include adverse events that were considered by the investigator to be possibly or probably related to study drug and adverse events with missing relationship to study drug.
A subject with two or more serious adverse events in the same system organ class (or with the same preferred term) is counted only once for that system organ class (or preferred term).
Adverse event terms are coded using Medical Dictionary for Regulatory Activities (MedDRA) version 17.1.
This table is based on adverse events data as available. Study 207 did not record laboratory abnormalities into adverse events data.

Program: V:¥projects¥e7389¥iss309¥csr¥dev¥pg¥tables¥T_2_7_4_14.sas 18JUN201513:37

付録 2.7.4-14
Japanese and Non-Japanese
Treatment-Related Serious Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Eribulin Treated Safety Population

MedDRA System Organ Class Preferred Term	日本人 Study 217 (N=51) n(%)	外国人 Studies 207+309 (N=353) n(%)	全体 Studies 217+207+309 (N=404) n(%)
感染症および寄生虫症 (contd)			
咽頭炎	0	1 (0.3)	1 (0.2)
肺炎	0	3 (0.8)	3 (0.7)
レンサ球菌感染	1 (2.0)	0	1 (0.2)
臨床検査	0	3 (0.8)	3 (0.7)
血中アルカリホスファターゼ	0	1 (0.3)	1 (0.2)
心電図ＱＴ延長	0	1 (0.3)	1 (0.2)
γ－グルタミルトランスフェラーゼ	0	1 (0.3)	1 (0.2)
好中球数減少	0	1 (0.3)	1 (0.2)
白血球数減少	0	1 (0.3)	1 (0.2)
代謝および栄養障害	0	5 (1.4)	5 (1.2)
低アルブミン血症	0	1 (0.3)	1 (0.2)
低カリウム血症	0	2 (0.6)	2 (0.5)
低ナトリウム血症	0	1 (0.3)	1 (0.2)
低リン酸血症	0	1 (0.3)	1 (0.2)

Treatment-related adverse events include adverse events that were considered by the investigator to be possibly or probably related to study drug and adverse events with missing relationship to study drug.
A subject with two or more serious adverse events in the same system organ class (or with the same preferred term) is counted only once for that system organ class (or preferred term).
Adverse event terms are coded using Medical Dictionary for Regulatory Activities (MedDRA) version 17.1.
This table is based on adverse events data as available. Study 207 did not record laboratory abnormalities into adverse events data.

Program: V:¥projects¥e7389¥iss309¥csr¥dev¥pg¥tables¥T_2_7_4_14.sas 18JUN201513:37

付録 2.7.4-14
Japanese and Non-Japanese
Treatment-Related Serious Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
Eribulin Treated Safety Population

MedDRA System Organ Class Preferred Term	日本人 Study 217 (N=51) n(%)	外国人 Studies 207+309 (N=353) n(%)	全体 Studies 217+207+309 (N=404) 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）	1 (2.0)	0	1 (0.2)
腫瘍出血	1 (2.0)	0	1 (0.2)
神経系障害	0	3 (0.8)	3 (0.7)
脳虚血	0	1 (0.3)	1 (0.2)
痙攣	0	1 (0.3)	1 (0.2)
末梢性運動ニューロパチー	0	1 (0.3)	1 (0.2)
末梢性感覚ニューロパチー	0	1 (0.3)	1 (0.2)
呼吸器、胸郭および縦隔障害	1 (2.0)	1 (0.3)	2 (0.5)
咳嗽	0	1 (0.3)	1 (0.2)
呼吸困難	0	1 (0.3)	1 (0.2)
肺塞栓症	1 (2.0)	0	1 (0.2)

Treatment-related adverse events include adverse events that were considered by the investigator to be possibly or probably related to study drug and adverse events with missing relationship to study drug.
A subject with two or more serious adverse events in the same system organ class (or with the same preferred term) is counted only once for that system organ class (or preferred term).
Adverse event terms are coded using Medical Dictionary for Regulatory Activities (MedDRA) version 17.1.
This table is based on adverse events data as available. Study 207 did not record laboratory abnormalities into adverse events data.

Program: V:¥projects¥e7389¥iss309¥csr¥dev¥pg¥tables¥T_2_7_4_14.sas 18JUN201513:37

付録 2.7.4-15
Study 309
Treatment-Emergent Adverse Events Leading to Study Drug Withdrawn by System Organ Class and Preferred Term
Safety Population

MedDRA System Organ Class Preferred Term	Eribulin Study 309 (N=226) n(%)	Dacarbazine Study 309 (N=224) n(%)
Any TEAEs leading to study drug withdrawn	17 (7.5)	11 (4.9)
血液およびリンパ系障害	2 (0.9)	4 (1.8)
貧血	0	1 (0.4)
血小板減少症	2 (0.9)	3 (1.3)
心臓障害	1 (0.4)	0
心嚢液貯留	1 (0.4)	0
胃腸障害	1 (0.4)	0
腸管虚血	1 (0.4)	0
一般・全身障害および投与部位の状態	3 (1.3)	2 (0.9)
疲労	2 (0.9)	2 (0.9)
発熱	1 (0.4)	0
免疫系障害	0	1 (0.4)

TEAE = treatment-emergent adverse event
A subject with two or more adverse events in the same system organ class (or with the same preferred term) is counted only once for that system organ class (or preferred term).
Adverse event terms are coded using Medical Dictionary for Regulatory Activities (MedDRA) version 17.1.

Program: V:¥projects¥e7389¥iss309¥csr¥dev¥pg¥tables¥T_2_7_4_15.sas 18JUN201513:37

付録 2.7.4-15
Study 309
Treatment-Emergent Adverse Events Leading to Study Drug Withdrawn by System Organ Class and Preferred Term
Safety Population

MedDRA System Organ Class Preferred Term	Eribulin Study 309 (N=226) n(%)	Dacarbazine Study 309 (N=224) n(%)
免疫系障害 (contd)		
薬物過敏症	0	1 (0.4)
感染症および寄生虫症	3 (1.3)	0
好中球減少性敗血症	1 (0.4)	0
敗血症性ショック	1 (0.4)	0
尿路感染	1 (0.4)	0
臨床検査	1 (0.4)	0
心電図ＱＴ延長	1 (0.4)	0
筋骨格系および結合組織障害	1 (0.4)	0
背部痛	1 (0.4)	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）	0	2 (0.9)
悪性胸水	0	1 (0.4)
骨髄異形成症候群	0	1 (0.4)

TEAE = treatment-emergent adverse event
A subject with two or more adverse events in the same system organ class (or with the same preferred term) is counted only once for that system organ class (or preferred term).
Adverse event terms are coded using Medical Dictionary for Regulatory Activities (MedDRA) version 17.1.

Program: V:¥projects¥e7389¥iss309¥csr¥dev¥pg¥tables¥T_2_7_4_15.sas 18JUN201513:37

付録 2.7.4-15
Study 309
Treatment-Emergent Adverse Events Leading to Study Drug Withdrawn by System Organ Class and Preferred Term
Safety Population

MedDRA System Organ Class Preferred Term	Eribulin Study 309 (N=226) n(%)	Dacarbazine Study 309 (N=224) n(%)
神経系障害	3 (1.3)	1 (0.4)
末梢性運動ニューロパチー	0	1 (0.4)
末梢性感覚ニューロパチー	1 (0.4)	0
多発ニューロパチー	1 (0.4)	0
脊髄圧迫	1 (0.4)	0
呼吸器、胸郭および縦隔障害	2 (0.9)	1 (0.4)
急性呼吸不全	1 (0.4)	0
誤嚥性肺炎	1 (0.4)	0
気胸	0	1 (0.4)

TEAE = treatment-emergent adverse event
A subject with two or more adverse events in the same system organ class (or with the same preferred term) is counted only once for that system organ class (or preferred term).
Adverse event terms are coded using Medical Dictionary for Regulatory Activities (MedDRA) version 17.1.

Program: V:¥projects¥e7389¥iss309¥csr¥dev¥pg¥tables¥T_2_7_4_15.sas 18JUN201513:37

付録 2.7.4-16
Japanese and Non-Japanese (Excluding Study 207)
Treatment-Emergent Adverse Events Leading to Study Drug Withdrawn by System Organ Class and Preferred Term
Eribulin Treated Safety Population

MedDRA System Organ Class Preferred Term	日本人 Study 217 (N=51) n(%)	外国人 Study 309 (N=226) n(%)	全体 Studies 217+309 (N=277) n(%)
Any TEAEs leading to study drug withdrawn	4 (7.8)	17 (7.5)	21 (7.6)
血液およびリンパ系障害	0	2 (0.9)	2 (0.7)
血小板減少症	0	2 (0.9)	2 (0.7)
心臓障害	1 (2.0)	1 (0.4)	2 (0.7)
心不全	1 (2.0)	0	1 (0.4)
心嚢液貯留	0	1 (0.4)	1 (0.4)
胃腸障害	0	1 (0.4)	1 (0.4)
腸管虚血	0	1 (0.4)	1 (0.4)
一般・全身障害および投与部位の状態	0	3 (1.3)	3 (1.1)
疲労	0	2 (0.9)	2 (0.7)
発熱	0	1 (0.4)	1 (0.4)
感染症および寄生虫症	2 (3.9)	3 (1.3)	5 (1.8)

TEAE = treatment-emergent adverse event
A subject with two or more adverse events in the same system organ class (or with the same preferred term) is counted only once for that system organ class (or preferred term).
Adverse event terms are coded using Medical Dictionary for Regulatory Activities (MedDRA) version 17.1.

Program: V:¥projects¥e7389¥iss309¥csr¥dev¥pg¥tables¥T_2_7_4_16.sas 18JUN201513:37

付録 2.7.4-16
Japanese and Non-Japanese (Excluding Study 207)
Treatment-Emergent Adverse Events Leading to Study Drug Withdrawn by System Organ Class and Preferred Term
Eribulin Treated Safety Population

MedDRA System Organ Class Preferred Term	日本人 Study 217 (N=51) n(%)	外国人 Study 309 (N=226) n(%)	全体 Studies 217+309 (N=277) n(%)
感染症および寄生虫症 (contd)			
蓄膿	1 (2.0)	0	1 (0.4)
好中球減少性敗血症	0	1 (0.4)	1 (0.4)
肺炎	1 (2.0)	0	1 (0.4)
敗血症性ショック	0	1 (0.4)	1 (0.4)
尿路感染	0	1 (0.4)	1 (0.4)
臨床検査	0	1 (0.4)	1 (0.4)
心電図ＱＴ延長	0	1 (0.4)	1 (0.4)
筋骨格系および結合組織障害	0	1 (0.4)	1 (0.4)
背部痛	0	1 (0.4)	1 (0.4)
神経系障害	0	3 (1.3)	3 (1.1)
末梢性感覚ニューロパチー	0	1 (0.4)	1 (0.4)
多発ニューロパチー	0	1 (0.4)	1 (0.4)
脊髄圧迫	0	1 (0.4)	1 (0.4)

TEAE = treatment-emergent adverse event
A subject with two or more adverse events in the same system organ class (or with the same preferred term) is counted only once for that system organ class (or preferred term).
Adverse event terms are coded using Medical Dictionary for Regulatory Activities (MedDRA) version 17.1.

Program: V:¥projects¥e7389¥iss309¥csr¥dev¥pg¥tables¥T_2_7_4_16.sas 18JUN201513:37

付録 2.7.4-16
Japanese and Non-Japanese (Excluding Study 207)
Treatment-Emergent Adverse Events Leading to Study Drug Withdrawn by System Organ Class and Preferred Term
Eribulin Treated Safety Population

MedDRA System Organ Class Preferred Term	日本人 Study 217 (N=51) n(%)	外国人 Study 309 (N=226) n(%)	全体 Studies 217+309 (N=277) n(%)
呼吸器、胸郭および縦隔障害	1 (2.0)	2 (0.9)	3 (1.1)
急性呼吸不全	0	1 (0.4)	1 (0.4)
間質性肺疾患	1 (2.0)	0	1 (0.4)
誤嚥性肺炎	0	1 (0.4)	1 (0.4)

TEAE = treatment-emergent adverse event
A subject with two or more adverse events in the same system organ class (or with the same preferred term) is counted only once for that system organ class (or preferred term).
Adverse event terms are coded using Medical Dictionary for Regulatory Activities (MedDRA) version 17.1.

Program: V:¥projects¥e7389¥iss309¥csr¥dev¥pg¥tables¥T_2_7_4_16.sas 18JUN201513:37

付録 2.7.4-17
Study 309
Treatment-Emergent Adverse Events Leading to Drug Action Taken (Drug Withdrawn, Dose Reduction, or Drug Interruption) by System Organ Class and Preferred Term
Safety Population

	Eribulin Study 309 (N=226) n(%)	Dacarbazine Study 309 (N=224) n(%)
Any TEAEs leading to Drug Action Taken (drug withdrawn, dose reduction,or drug interruption)	107 (47.3)	89 (39.7)
TEAE leading to drug withdrawn	17 (7.5)	11 (4.9)
TEAE leading to dose reduction	58 (25.7)	32 (14.3)
TEAE leading to drug interruption	74 (32.7)	72 (32.1)
血液およびリンパ系障害	57 (25.2)	64 (28.6)
貧血	5 (2.2)	7 (3.1)
発熱性好中球減少症	0	1 (0.4)
ヘモグロビン血症	2 (0.9)	0
白血球減少症	6 (2.7)	8 (3.6)
好中球減少症	48 (21.2)	30 (13.4)
汎血球減少症	0	2 (0.9)
血小板減少症	5 (2.2)	39 (17.4)
心臓障害	1 (0.4)	1 (0.4)
心嚢液貯留	1 (0.4)	0
頻脈	0	1 (0.4)

TEAE = treatment-emergent adverse event
A subject with two or more adverse events in the same system organ class (or with the same preferred term) is counted only once for that system organ class (or preferred term).
Adverse event terms are coded using Medical Dictionary for Regulatory Activities (MedDRA) version 17.1.

Program: V:¥projects¥e7389¥iss309¥csr¥dev¥pg¥tables¥T_2_7_4_17.sas 18JUN201513:37

付録 2.7.4-17
Study 309
Treatment-Emergent Adverse Events Leading to Drug Action Taken (Drug Withdrawn, Dose Reduction, or Drug Interruption) by System Organ Class and Preferred Term
Safety Population

	Eribulin Study 309 (N=226) n(%)	Dacarbazine Study 309 (N=224) n(%)
眼障害	0	1 (0.4)
眼精疲労	0	1 (0.4)
胃腸障害	12 (5.3)	12 (5.4)
腹痛	1 (0.4)	1 (0.4)
便秘	0	1 (0.4)
下痢	1 (0.4)	1 (0.4)
十二指腸潰	0	1 (0.4)
消化不良	1 (0.4)	1 (0.4)
食中毒	0	1 (0.4)
胃腸管瘻	1 (0.4)	0
単径ヘルニア	1 (0.4)	0
腸出血	0	1 (0.4)
腸管虚血	1 (0.4)	0
腸閉塞	1 (0.4)	1 (0.4)
大腸閉塞	0	1 (0.4)
弛緩歯	1 (0.4)	0

TEAE = treatment-emergent adverse event
A subject with two or more adverse events in the same system organ class (or with the same preferred term) is counted only once for that system organ class (or preferred term).
Adverse event terms are coded using Medical Dictionary for Regulatory Activities (MedDRA) version 17.1.

Program: V:¥projects¥e7389¥iss309¥csr¥dev¥pg¥tables¥T_2_7_4_17.sas 18JUN201513:37

付録 2.7.4-17
Study 309
Treatment-Emergent Adverse Events Leading to Drug Action Taken (Drug Withdrawn, Dose Reduction, or Drug Interruption) by System Organ Class and Preferred Term
Safety Population

	Eribulin Study 309 (N=226) n(%)	Dacarbazine Study 309 (N=224) n(%)
胃腸障害 (contd)		
メレナ	0	1 (0.4)
悪心	0	2 (0.9)
口の錯感覚	0	1 (0.4)
後腹膜出血	1 (0.4)	0
口内炎	2 (0.9)	2 (0.9)
嘔吐	2 (0.9)	2 (0.9)
一般・全身障害および投与部位の状態	20 (8.8)	5 (2.2)
無力症	2 (0.9)	1 (0.4)
疲労	8 (3.5)	3 (1.3)
全身健康状態低下	1 (0.4)	0
高熱	1 (0.4)	0
インフルエンザ様疾患	1 (0.4)	0
発熱	8 (3.5)	1 (0.4)
肝胆道系障害	1 (0.4)	1 (0.4)

TEAE = treatment-emergent adverse event
A subject with two or more adverse events in the same system organ class (or with the same preferred term) is counted only once for that system organ class (or preferred term).
Adverse event terms are coded using Medical Dictionary for Regulatory Activities (MedDRA) version 17.1.

Program: V:¥projects¥e7389¥iss309¥csr¥dev¥pg¥tables¥T_2_7_4_17.sas 18JUN201513:37

付録 2.7.4-17
Study 309
Treatment-Emergent Adverse Events Leading to Drug Action Taken (Drug Withdrawn, Dose Reduction, or Drug Interruption) by System Organ Class and Preferred Term
Safety Population

	Eribulin Study 309 (N=226) n(%)	Dacarbazine Study 309 (N=224) n(%)
肝胆道系障害 (contd)		
肝毒性	1 (0.4)	0
高ビリルビン血症	1 (0.4)	1 (0.4)
黄疸	1 (0.4)	0
免疫系障害	0	1 (0.4)
薬物過敏症	0	1 (0.4)
感染症および寄生虫症	23 (10.2)	6 (2.7)
腹部敗血症	1 (0.4)	0
細菌性関節炎	1 (0.4)	0
気管支肺炎	1 (0.4)	0
カテーテル留置部位感染	1 (0.4)	0
医療機器関連感染	1 (0.4)	0
耳感染	0	1 (0.4)
帯状疱疹	0	1 (0.4)
感染	1 (0.4)	1 (0.4)

TEAE = treatment-emergent adverse event
A subject with two or more adverse events in the same system organ class (or with the same preferred term) is counted only once for that system organ class (or preferred term).
Adverse event terms are coded using Medical Dictionary for Regulatory Activities (MedDRA) version 17.1.

Program: V:¥projects¥e7389¥iss309¥csr¥dev¥pg¥tables¥T_2_7_4_17.sas 18JUN201513:37

付録 2.7.4-17
Study 309
Treatment-Emergent Adverse Events Leading to Drug Action Taken (Drug Withdrawn, Dose Reduction, or Drug Interruption) by System Organ Class and Preferred Term
Safety Population

	Eribulin Study 309 (N=226) n(%)	Dacarbazine Study 309 (N=224) n(%)
感染症および寄生虫症 (contd)		
インフルエンザ	1 (0.4)	0
真菌性下気道感染	1 (0.4)	0
肺感染	2 (0.9)	0
好中球減少性敗血症	1 (0.4)	0
細菌性腹膜炎	2 (0.9)	0
咽頭炎	0	1 (0.4)
肺炎	1 (0.4)	0
シュードモナス性菌血症	1 (0.4)	0
気道感染	1 (0.4)	1 (0.4)
鼻炎	1 (0.4)	0
敗血症性ショック	1 (0.4)	0
ブドウ球菌性菌血症	1 (0.4)	0
上気道感染	2 (0.9)	2 (0.9)
尿路感染	4 (1.8)	0
ウイルス性上気道感染	1 (0.4)	0

TEAE = treatment-emergent adverse event
A subject with two or more adverse events in the same system organ class (or with the same preferred term) is counted only once for that system organ class (or preferred term).
Adverse event terms are coded using Medical Dictionary for Regulatory Activities (MedDRA) version 17.1.

Program: V:¥projects¥e7389¥iss309¥csr¥dev¥pg¥tables¥T_2_7_4_17.sas 18JUN201513:37

付録 2.7.4-17
Study 309
Treatment-Emergent Adverse Events Leading to Drug Action Taken (Drug Withdrawn, Dose Reduction, or Drug Interruption) by System Organ Class and Preferred Term
Safety Population

	Eribulin Study 309 (N=226) n(%)	Dacarbazine Study 309 (N=224) n(%)
傷害、中毒および処置合併症	2 (0.9)	2 (0.9)
挫傷	0	1 (0.4)
放射線性肺臓炎	1 (0.4)	0
創傷	1 (0.4)	0
創離開	0	1 (0.4)
臨床検査	18 (8.0)	13 (5.8)
アラニンアミノトランスフェラーゼ増加	3 (1.3)	0
アスパラギン酸アミノトランスフェラーゼ増加	3 (1.3)	0
血中アルカリホスファターゼ増加	1 (0.4)	1 (0.4)
血中ビリルビン増加	1 (0.4)	0
心電図ＱＴ延長	2 (0.9)	1 (0.4)
心電図Ｔ波逆転	1 (0.4)	0
γ－グルタミルトランスフェラーゼ増加	1 (0.4)	0
リンパ球数減少	0	1 (0.4)
好中球数減少	10 (4.4)	7 (3.1)
血小板数減少	1 (0.4)	7 (3.1)

TEAE = treatment-emergent adverse event
A subject with two or more adverse events in the same system organ class (or with the same preferred term) is counted only once for that system organ class (or preferred term).
Adverse event terms are coded using Medical Dictionary for Regulatory Activities (MedDRA) version 17.1.

Program: V:¥projects¥e7389¥iss309¥csr¥dev¥pg¥tables¥T_2_7_4_17.sas 18JUN201513:37

付録 2.7.4-17
Study 309
Treatment-Emergent Adverse Events Leading to Drug Action Taken (Drug Withdrawn, Dose Reduction, or Drug Interruption) by System Organ Class and Preferred Term
Safety Population

	Eribulin Study 309 (N=226) n(%)	Dacarbazine Study 309 (N=224) n(%)
臨床検査 (contd)		
白血球数減少	3 (1.3)	9 (4.0)
代謝および栄養障害	6 (2.7)	4 (1.8)
食欲減退	1 (0.4)	0
脱水	0	2 (0.9)
高クレアチニン血症	0	1 (0.4)
高血糖	3 (1.3)	0
低カルシウム血症	0	1 (0.4)
低カリウム血症	1 (0.4)	0
低ナトリウム血症	1 (0.4)	1 (0.4)
筋骨格系および結合組織障害	2 (0.9)	3 (1.3)
背部痛	1 (0.4)	2 (0.9)
関節腫脹	0	1 (0.4)
筋骨格系胸痛	1 (0.4)	0

TEAE = treatment-emergent adverse event
A subject with two or more adverse events in the same system organ class (or with the same preferred term) is counted only once for that system organ class (or preferred term).
Adverse event terms are coded using Medical Dictionary for Regulatory Activities (MedDRA) version 17.1.

Program: V:¥projects¥e7389¥iss309¥csr¥dev¥pg¥tables¥T_2_7_4_17.sas 18JUN201513:37

付録 2.7.4-17
Study 309
Treatment-Emergent Adverse Events Leading to Drug Action Taken (Drug Withdrawn, Dose Reduction, or Drug Interruption) by System Organ Class and Preferred Term
Safety Population

	Eribulin Study 309 (N=226) n(%)	Dacarbazine Study 309 (N=224) 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 (0.9)	4 (1.8)
悪性腹水	0	2 (0.9)
悪性胸水	0	1 (0.4)
骨転移	1 (0.4)	0
骨髄異形成症候群	0	1 (0.4)
腫瘍出血	1 (0.4)	0
神経系障害	17 (7.5)	1 (0.4)
浮動性めまい	1 (0.4)	0
頭痛	1 (0.4)	0
感覚鈍麻	1 (0.4)	0
嗜眠	1 (0.4)	0
単麻痺	1 (0.4)	0
錯感覚	1 (0.4)	0
末梢性運動ニューロパチー	2 (0.9)	1 (0.4)
末梢性感覚運動ニューロパチー	1 (0.4)	0
末梢性感覚ニューロパチー	10 (4.4)	0

TEAE = treatment-emergent adverse event
A subject with two or more adverse events in the same system organ class (or with the same preferred term) is counted only once for that system organ class (or preferred term).
Adverse event terms are coded using Medical Dictionary for Regulatory Activities (MedDRA) version 17.1.

Program: V:¥projects¥e7389¥iss309¥csr¥dev¥pg¥tables¥T_2_7_4_17.sas 18JUN201513:37

付録 2.7.4-17
Study 309
Treatment-Emergent Adverse Events Leading to Drug Action Taken (Drug Withdrawn, Dose Reduction, or Drug Interruption) by System Organ Class and Preferred Term
Safety Population

	Eribulin Study 309 (N=226) n(%)	Dacarbazine Study 309 (N=224) n(%)
神経系障害 (contd)		
多発ニューロパチー	1 (0.4)	0
脊髄圧迫	1 (0.4)	0
精神障害	1 (0.4)	1 (0.4)
激越	1 (0.4)	0
不安	0	1 (0.4)
腎および尿路障害	1 (0.4)	1 (0.4)
排尿困難	1 (0.4)	0
血尿	0	1 (0.4)
呼吸器、胸郭および縦隔障害	5 (2.2)	7 (3.1)
急性呼吸不全	1 (0.4)	0
咳嗽	0	2 (0.9)
呼吸困難	1 (0.4)	0
労作性呼吸困難	0	1 (0.4)

TEAE = treatment-emergent adverse event
A subject with two or more adverse events in the same system organ class (or with the same preferred term) is counted only once for that system organ class (or preferred term).
Adverse event terms are coded using Medical Dictionary for Regulatory Activities (MedDRA) version 17.1.

Program: V:¥projects¥e7389¥iss309¥csr¥dev¥pg¥tables¥T_2_7_4_17.sas 18JUN201513:37

付録 2.7.4-17
Study 309
Treatment-Emergent Adverse Events Leading to Drug Action Taken (Drug Withdrawn, Dose Reduction, or Drug Interruption) by System Organ Class and Preferred Term
Safety Population

	Eribulin Study 309 (N=226) n(%)	Dacarbazine Study 309 (N=224) n(%)
呼吸器、胸郭および縦隔障害 (contd)		
鼻出血	0	1 (0.4)
喀血	0	1 (0.4)
鼻閉	0	1 (0.4)
誤嚥性肺炎	1 (0.4)	0
気胸	0	1 (0.4)
肺塞栓症	2 (0.9)	0
呼吸不全	0	1 (0.4)
皮膚および皮下組織障害	2 (0.9)	0
紅斑	1 (0.4)	0
そう痒症	1 (0.4)	0
血管障害	1 (0.4)	0
起立性低血圧	1 (0.4)	0

TEAE = treatment-emergent adverse event
A subject with two or more adverse events in the same system organ class (or with the same preferred term) is counted only once for that system organ class (or preferred term).
Adverse event terms are coded using Medical Dictionary for Regulatory Activities (MedDRA) version 17.1.

Program: V:¥projects¥e7389¥iss309¥csr¥dev¥pg¥tables¥T_2_7_4_17.sas 18JUN201513:37

付録 2.7.4-18
Japanese and Non-Japanese (Excluding Study 207)
Treatment-Emergent Adverse Events Leading to Drug Action Taken (Drug Withdrawn, Dose Reduction, or Drug Interruption) by System Organ Class and Preferred Term
Eribulin Treated Safety Population

	日本人 Study 217 (N=51) n(%)	外国人 Study 309 (N=226) n(%)	全体 Studies 217+309 (N=277) n(%)
Any TEAEs leading to Drug Action Taken (drug withdrawn, dose reduction,or drug interruption)	18 (35.3)	107 (47.3)	125 (45.1)
TEAE leading to drug withdrawn	4 (7.8)	17 (7.5)	21 (7.6)
TEAE leading to dose reduction	16 (31.4)	58 (25.7)	74 (26.7)
TEAE leading to drug interruption	0	74 (32.7)	74 (26.7)
血液およびリンパ系障害	13 (25.5)	57 (25.2)	70 (25.3)
貧血	1 (2.0)	5 (2.2)	6 (2.2)
発熱性好中球減少症	1 (2.0)	0	1 (0.4)
ヘモグロビン血症	0	2 (0.9)	2 (0.7)
白血球減少症	1 (2.0)	6 (2.7)	7 (2.5)
好中球減少症	13 (25.5)	48 (21.2)	61 (22.0)
血小板減少症	0	5 (2.2)	5 (1.8)
心臓障害	1 (2.0)	1 (0.4)	2 (0.7)
心不全	1 (2.0)	0	1 (0.4)
心嚢液貯留	0	1 (0.4)	1 (0.4)

TEAE = treatment-emergent adverse event
A subject with two or more adverse events in the same system organ class (or with the same preferred term) is counted only once for that system organ class (or preferred term).
Adverse event terms are coded using Medical Dictionary for Regulatory Activities (MedDRA) version 17.1.

Program: V:¥projects¥e7389¥iss309¥csr¥dev¥pg¥tables¥T_2_7_4_18.sas 18JUN201513:38

付録 2.7.4-18
Japanese and Non-Japanese (Excluding Study 207)
Treatment-Emergent Adverse Events Leading to Drug Action Taken (Drug Withdrawn, Dose Reduction, or Drug Interruption) by System Organ Class and Preferred Term
Eribulin Treated Safety Population

	日本人 Study 217 (N=51) n(%)	外国人 Study 309 (N=226) n(%)	全体 Studies 217+309 (N=277) n(%)
胃腸障害	1 (2.0)	12 (5.3)	13 (4.7)
腹痛	0	1 (0.4)	1 (0.4)
下痢	0	1 (0.4)	1 (0.4)
消化不良	0	1 (0.4)	1 (0.4)
胃腸管瘻	0	1 (0.4)	1 (0.4)
鼠径ヘルニア	0	1 (0.4)	1 (0.4)
腸管虚血	0	1 (0.4)	1 (0.4)
腸閉塞	0	1 (0.4)	1 (0.4)
弛緩歯	0	1 (0.4)	1 (0.4)
後腹膜出血	0	1 (0.4)	1 (0.4)
口内炎	0	2 (0.9)	2 (0.7)
嘔吐	1 (2.0)	2 (0.9)	3 (1.1)
一般・全身障害および投与部位の状態	0	20 (8.8)	20 (7.2)
無力症	0	2 (0.9)	2 (0.7)
疲労	0	8 (3.5)	8 (2.9)
全身健康状態低下	0	1 (0.4)	1 (0.4)

TEAE = treatment-emergent adverse event
A subject with two or more adverse events in the same system organ class (or with the same preferred term) is counted only once for that system organ class (or preferred term).
Adverse event terms are coded using Medical Dictionary for Regulatory Activities (MedDRA) version 17.1.

Program: V:¥projects¥e7389¥iss309¥csr¥dev¥pg¥tables¥T_2_7_4_18.sas 18JUN201513:38

付録 2.7.4-18
Japanese and Non-Japanese (Excluding Study 207)
Treatment-Emergent Adverse Events Leading to Drug Action Taken (Drug Withdrawn, Dose Reduction, or Drug Interruption) by System Organ Class and Preferred Term
Eribulin Treated Safety Population

	日本人 Study 217 (N=51) n(%)	外国人 Study 309 (N=226) n(%)	全体 Studies 217+309 (N=277) n(%)
一般・全身障害および投与部位の状態 (contd)			
高熱	0	1 (0.4)	1 (0.4)
インフルエンザ様疾患	0	1 (0.4)	1 (0.4)
発熱	0	8 (3.5)	8 (2.9)
肝胆道系障害	1 (2.0)	1 (0.4)	2 (0.7)
肝出血	1 (2.0)	0	1 (0.4)
肝毒性	0	1 (0.4)	1 (0.4)
高ビリルビン血症	0	1 (0.4)	1 (0.4)
黄疸	0	1 (0.4)	1 (0.4)
感染症および寄生虫症	3 (5.9)	23 (10.2)	26 (9.4)
腹部敗血症	0	1 (0.4)	1 (0.4)
細菌性関節炎	0	1 (0.4)	1 (0.4)
気管支肺炎	0	1 (0.4)	1 (0.4)
カテーテル留置部位感染	0	1 (0.4)	1 (0.4)
医療機器関連感染	0	1 (0.4)	1 (0.4)

TEAE = treatment-emergent adverse event
A subject with two or more adverse events in the same system organ class (or with the same preferred term) is counted only once for that system organ class (or preferred term).
Adverse event terms are coded using Medical Dictionary for Regulatory Activities (MedDRA) version 17.1.

Program: V:¥projects¥e7389¥iss309¥csr¥dev¥pg¥tables¥T_2_7_4_18.sas 18JUN201513:38

付録 2.7.4-18
Japanese and Non-Japanese (Excluding Study 207)
Treatment-Emergent Adverse Events Leading to Drug Action Taken (Drug Withdrawn, Dose Reduction, or Drug Interruption) by System Organ Class and Preferred Term
Eribulin Treated Safety Population

	日本人 Study 217 (N=51) n(%)	外国人 Study 309 (N=226) n(%)	全体 Studies 217+309 (N=277) n(%)
感染症および寄生虫症 (contd)			
蓄膿	1 (2.0)	0	1 (0.4)
感染	0	1 (0.4)	1 (0.4)
インフルエンザ	0	1 (0.4)	1 (0.4)
真菌性下気道感染	0	1 (0.4)	1 (0.4)
肺感染	0	2 (0.9)	2 (0.7)
好中球減少性敗血症	0	1 (0.4)	1 (0.4)
細菌性腹膜炎	0	2 (0.9)	2 (0.7)
肺炎	1 (2.0)	1 (0.4)	2 (0.7)
シュードモナス性菌血症	0	1 (0.4)	1 (0.4)
気道感染	0	1 (0.4)	1 (0.4)
鼻炎	0	1 (0.4)	1 (0.4)
敗血症性ショック	0	1 (0.4)	1 (0.4)
ブドウ球菌性菌血症	0	1 (0.4)	1 (0.4)
レンサ球菌感染	1 (2.0)	0	1 (0.4)
上気道感染	0	2 (0.9)	2 (0.7)
尿路感染	0	4 (1.8)	4 (1.4)

TEAE = treatment-emergent adverse event
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Adverse event terms are coded using Medical Dictionary for Regulatory Activities (MedDRA) version 17.1.

Program: V:¥projects¥e7389¥iss309¥csr¥dev¥pg¥tables¥T_2_7_4_18.sas 18JUN201513:38

付録 2.7.4-18
Japanese and Non-Japanese (Excluding Study 207)
Treatment-Emergent Adverse Events Leading to Drug Action Taken (Drug Withdrawn, Dose Reduction, or Drug Interruption) by System Organ Class and Preferred Term
Eribulin Treated Safety Population

	日本人 Study 217 (N=51) n(%)	外国人 Study 309 (N=226) n(%)	全体 Studies 217+309 (N=277) n(%)
感染症および寄生虫症 (contd)			
ウイルス性上気道感染	0	1 (0.4)	1 (0.4)
傷害、中毒および処置合併症	0	2 (0.9)	2 (0.7)
放射線性肺臓炎	0	1 (0.4)	1 (0.4)
創傷	0	1 (0.4)	1 (0.4)
臨床検査	0	18 (8.0)	18 (6.5)
アラニンアミノトランスフェラーゼ増加	0	3 (1.3)	3 (1.1)
アスパラギン酸アミノトランスフェラーゼ増加	0	3 (1.3)	3 (1.1)
血中アルカリホスファターゼ増加	0	1 (0.4)	1 (0.4)
血中ビリルビン増加	0	1 (0.4)	1 (0.4)
心電図ＱＴ延長	0	2 (0.9)	2 (0.7)
心電図Ｔ波逆転	0	1 (0.4)	1 (0.4)
γ－グルタミルトランスフェラーゼ増加	0	1 (0.4)	1 (0.4)
好中球数減少	0	10 (4.4)	10 (3.6)
血小板数減少	0	1 (0.4)	1 (0.4)

TEAE = treatment-emergent adverse event
A subject with two or more adverse events in the same system organ class (or with the same preferred term) is counted only once for that system organ class (or preferred term).
Adverse event terms are coded using Medical Dictionary for Regulatory Activities (MedDRA) version 17.1.

Program: V:¥projects¥e7389¥iss309¥csr¥dev¥pg¥tables¥T_2_7_4_18.sas 18JUN201513:38

付録 2.7.4-18
Japanese and Non-Japanese (Excluding Study 207)
Treatment-Emergent Adverse Events Leading to Drug Action Taken (Drug Withdrawn, Dose Reduction, or Drug Interruption) by System Organ Class and Preferred Term
Eribulin Treated Safety Population

	日本人 Study 217 (N=51) n(%)	外国人 Study 309 (N=226) n(%)	全体 Studies 217+309 (N=277) n(%)
臨床検査 (contd)			
白血球数減少	0	3 (1.3)	3 (1.1)
代謝および栄養障害	0	6 (2.7)	6 (2.2)
食欲減退	0	1 (0.4)	1 (0.4)
高血糖	0	3 (1.3)	3 (1.1)
低カリウム血症	0	1 (0.4)	1 (0.4)
低ナトリウム血症	0	1 (0.4)	1 (0.4)
筋骨格系および結合組織障害	0	2 (0.9)	2 (0.7)
背部痛	0	1 (0.4)	1 (0.4)
筋骨格系胸痛	0	1 (0.4)	1 (0.4)
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）	0	2 (0.9)	2 (0.7)
骨転移	0	1 (0.4)	1 (0.4)
腫瘍出血	0	1 (0.4)	1 (0.4)

TEAE = treatment-emergent adverse event
A subject with two or more adverse events in the same system organ class (or with the same preferred term) is counted only once for that system organ class (or preferred term).
Adverse event terms are coded using Medical Dictionary for Regulatory Activities (MedDRA) version 17.1.

Program: V:¥projects¥e7389¥iss309¥csr¥dev¥pg¥tables¥T_2_7_4_18.sas 18JUN201513:38

付録 2.7.4-18
Japanese and Non-Japanese (Excluding Study 207)
Treatment-Emergent Adverse Events Leading to Drug Action Taken (Drug Withdrawn, Dose Reduction, or Drug Interruption) by System Organ Class and Preferred Term
Eribulin Treated Safety Population

	日本人 Study 217 (N=51) n(%)	外国人 Study 309 (N=226) n(%)	全体 Studies 217+309 (N=277) n(%)
神経系障害	1 (2.0)	17 (7.5)	18 (6.5)
浮動性めまい	0	1 (0.4)	1 (0.4)
頭痛	0	1 (0.4)	1 (0.4)
感覚鈍麻	0	1 (0.4)	1 (0.4)
嗜眠	0	1 (0.4)	1 (0.4)
単麻痺	0	1 (0.4)	1 (0.4)
末梢性ニューロパチー	1 (2.0)	0	1 (0.4)
錯感覚	0	1 (0.4)	1 (0.4)
末梢性運動ニューロパチー	0	2 (0.9)	2 (0.7)
末梢性感覚運動ニューロパチー	0	1 (0.4)	1 (0.4)
末梢性感覚ニューロパチー	0	10 (4.4)	10 (3.6)
多発ニューロパチー	0	1 (0.4)	1 (0.4)
脊髄圧迫	0	1 (0.4)	1 (0.4)
精神障害	0	1 (0.4)	1 (0.4)
激越	0	1 (0.4)	1 (0.4)

TEAE = treatment-emergent adverse event
A subject with two or more adverse events in the same system organ class (or with the same preferred term) is counted only once for that system organ class (or preferred term).
Adverse event terms are coded using Medical Dictionary for Regulatory Activities (MedDRA) version 17.1.

Program: V:¥projects¥e7389¥iss309¥csr¥dev¥pg¥tables¥T_2_7_4_18.sas 18JUN201513:38

付録 2.7.4-18
Japanese and Non-Japanese (Excluding Study 207)
Treatment-Emergent Adverse Events Leading to Drug Action Taken (Drug Withdrawn, Dose Reduction, or Drug Interruption) by System Organ Class and Preferred Term
Eribulin Treated Safety Population

	日本人 Study 217 (N=51) n(%)	外国人 Study 309 (N=226) n(%)	全体 Studies 217+309 (N=277) n(%)
腎および尿路障害	0	1 (0.4)	1 (0.4)
排尿困難	0	1 (0.4)	1 (0.4)
呼吸器、胸郭および縦隔障害	1 (2.0)	5 (2.2)	6 (2.2)
急性呼吸不全	0	1 (0.4)	1 (0.4)
呼吸困難	0	1 (0.4)	1 (0.4)
間質性肺疾患	1 (2.0)	0	1 (0.4)
誤嚥性肺炎	0	1 (0.4)	1 (0.4)
肺塞栓症	0	2 (0.9)	2 (0.7)
皮膚および皮下組織障害	0	2 (0.9)	2 (0.7)
紅斑	0	1 (0.4)	1 (0.4)
そう痒症	0	1 (0.4)	1 (0.4)
血管障害	0	1 (0.4)	1 (0.4)
起立性低血圧	0	1 (0.4)	1 (0.4)

TEAE = treatment-emergent adverse event
A subject with two or more adverse events in the same system organ class (or with the same preferred term) is counted only once for that system organ class (or preferred term).
Adverse event terms are coded using Medical Dictionary for Regulatory Activities (MedDRA) version 17.1.

Program: V:¥projects¥e7389¥iss309¥csr¥dev¥pg¥tables¥T_2_7_4_18.sas 18JUN201513:38

付録 2.7.4-19
Japanese and Non-Japanese
Treatment-Emergent Adverse Events of Interest Specified in Japan by CTCAE Grade
Eribulin Treated Safety Population

Event class Package insert term or preferred term Preferred term CTCAE grade	日本人 Study 217 (N=51) n(%)	外国人 Studies 207+309 (N=353) n(%)	全体 Studies 217+207+309 (N=404) n(%)
骨髄抑制			
Any preferred term	51 (100.0)	158 (44.8)	209 (51.7)
1	0	5 (1.4)	5 (1.2)
2	3 (5.9)	37 (10.5)	40 (9.9)
3	9 (17.6)	67 (19.0)	76 (18.8)
4	39 (76.5)	49 (13.9)	88 (21.8)
5	0	0	0
>=3	48 (94.1)	116 (32.9)	164 (40.6)
ヘマトクリット減少	0	1 (0.3)	1 (0.2)
1	0	1 (0.3)	1 (0.2)
2	0	0	0
3	0	0	0
4	0	0	0
5	0	0	0
>=3	0	0	0

CTCAE = Common Terminology Criteria for Adverse Events. Adverse events of interest are presented in pre-defined event classes; each class is based on pre-specified preferred terms.
A subject with two or more adverse events in the same event class (or with same package insert term/preferred term) is counted only once for that event class (or package insert term/preferred term).
A subject is counted once by the highest non-missing CTCAE grade as applicable for preferred term and event class respectively.
Adverse event terms are coded using Medical Dictionary for Regulatory Activities (MedDRA) version 17.1.
This table is based on adverse events data as available. Study 207 did not record laboratory abnormalities into adverse events data.

Program: V:¥projects¥e7389¥iss309¥csr¥dev¥pg¥tables¥T_2_7_4_19.sas 18JUN201513:38

付録 2.7.4-19
Japanese and Non-Japanese
Treatment-Emergent Adverse Events of Interest Specified in Japan by CTCAE Grade
Eribulin Treated Safety Population

Event class Package insert term or preferred term Preferred term CTCAE grade	日本人 Study 217 (N=51) n(%)	外国人 Studies 207+309 (N=353) n(%)	全体 Studies 217+207+309 (N=404) n(%)
骨髄抑制			
ヘマトクリット減少	0	1 (0.3)	1 (0.2)
1	0	1 (0.3)	1 (0.2)
2	0	0	0
3	0	0	0
4	0	0	0
5	0	0	0
>=3	0	0	0
ヘモグロビン減少	2 (3.9)	7 (2.0)	9 (2.2)
1	2 (3.9)	2 (0.6)	4 (1.0)
2	0	5 (1.4)	5 (1.2)
3	0	0	0
4	0	0	0
5	0	0	0
>=3	0	0	0

CTCAE = Common Terminology Criteria for Adverse Events. Adverse events of interest are presented in pre-defined event classes; each class is based on pre-specified preferred terms.
A subject with two or more adverse events in the same event class (or with same package insert term/preferred term) is counted only once for that event class (or package insert term/preferred term).
A subject is counted once by the highest non-missing CTCAE grade as applicable for preferred term and event class respectively.
Adverse event terms are coded using Medical Dictionary for Regulatory Activities (MedDRA) version 17.1.
This table is based on adverse events data as available. Study 207 did not record laboratory abnormalities into adverse events data.

Program: V:¥projects¥e7389¥iss309¥csr¥dev¥pg¥tables¥T_2_7_4_19.sas 18JUN201513:38

付録 2.7.4-19
Japanese and Non-Japanese
Treatment-Emergent Adverse Events of Interest Specified in Japan by CTCAE Grade
Eribulin Treated Safety Population

Event class Package insert term or preferred term Preferred term CTCAE grade	日本人 Study 217 (N=51) n(%)	外国人 Studies 207+309 (N=353) n(%)	全体 Studies 217+207+309 (N=404) n(%)
骨髄抑制			
ヘモグロビン減少	2 (3.9)	7 (2.0)	9 (2.2)
1	2 (3.9)	2 (0.6)	4 (1.0)
2	0	5 (1.4)	5 (1.2)
3	0	0	0
4	0	0	0
5	0	0	0
>=3	0	0	0
リンパ球減少	40 (78.4)	6 (1.7)	46 (11.4)
1	1 (2.0)	2 (0.6)	3 (0.7)
2	22 (43.1)	1 (0.3)	23 (5.7)
3	15 (29.4)	2 (0.6)	17 (4.2)
4	2 (3.9)	1 (0.3)	3 (0.7)
5	0	0	0
>=3	17 (33.3)	3 (0.8)	20 (5.0)

CTCAE = Common Terminology Criteria for Adverse Events. Adverse events of interest are presented in pre-defined event classes; each class is based on pre-specified preferred terms.
A subject with two or more adverse events in the same event class (or with same package insert term/preferred term) is counted only once for that event class (or package insert term/preferred term).
A subject is counted once by the highest non-missing CTCAE grade as applicable for preferred term and event class respectively.
Adverse event terms are coded using Medical Dictionary for Regulatory Activities (MedDRA) version 17.1.
This table is based on adverse events data as available. Study 207 did not record laboratory abnormalities into adverse events data.

Program: V:¥projects¥e7389¥iss309¥csr¥dev¥pg¥tables¥T_2_7_4_19.sas 18JUN201513:38

付録 2.7.4-19
Japanese and Non-Japanese
Treatment-Emergent Adverse Events of Interest Specified in Japan by CTCAE Grade
Eribulin Treated Safety Population

Event class Package insert term or preferred term Preferred term CTCAE grade	日本人 Study 217 (N=51) n(%)	外国人 Studies 207+309 (N=353) n(%)	全体 Studies 217+207+309 (N=404) n(%)
骨髄抑制			
リンパ球数減少	0	3 (0.8)	3 (0.7)
1	0	2 (0.6)	2 (0.5)
2	0	1 (0.3)	1 (0.2)
3	0	0	0
4	0	0	0
5	0	0	0
>=3	0	0	0
リンパ球減少症	40 (78.4)	3 (0.8)	43 (10.6)
1	1 (2.0)	0	1 (0.2)
2	22 (43.1)	0	22 (5.4)
3	15 (29.4)	2 (0.6)	17 (4.2)
4	2 (3.9)	1 (0.3)	3 (0.7)
5	0	0	0
>=3	17 (33.3)	3 (0.8)	20 (5.0)

CTCAE = Common Terminology Criteria for Adverse Events. Adverse events of interest are presented in pre-defined event classes; each class is based on pre-specified preferred terms.
A subject with two or more adverse events in the same event class (or with same package insert term/preferred term) is counted only once for that event class (or package insert term/preferred term).
A subject is counted once by the highest non-missing CTCAE grade as applicable for preferred term and event class respectively.
Adverse event terms are coded using Medical Dictionary for Regulatory Activities (MedDRA) version 17.1.
This table is based on adverse events data as available. Study 207 did not record laboratory abnormalities into adverse events data.

Program: V:¥projects¥e7389¥iss309¥csr¥dev¥pg¥tables¥T_2_7_4_19.sas 18JUN201513:38

付録 2.7.4-19
Japanese and Non-Japanese
Treatment-Emergent Adverse Events of Interest Specified in Japan by CTCAE Grade
Eribulin Treated Safety Population

Event class Package insert term or preferred term Preferred term CTCAE grade	日本人 Study 217 (N=51) n(%)	外国人 Studies 207+309 (N=353) n(%)	全体 Studies 217+207+309 (N=404) n(%)
骨髄抑制			
血小板減少	3 (5.9)	15 (4.2)	18 (4.5)
1	2 (3.9)	7 (2.0)	9 (2.2)
2	1 (2.0)	5 (1.4)	6 (1.5)
3	0	2 (0.6)	2 (0.5)
4	0	1 (0.3)	1 (0.2)
5	0	0	0
>=3	0	3 (0.8)	3 (0.7)
血小板数減少	0	2 (0.6)	2 (0.5)
1	0	0	0
2	0	0	0
3	0	1 (0.3)	1 (0.2)
4	0	1 (0.3)	1 (0.2)
5	0	0	0
>=3	0	2 (0.6)	2 (0.5)

CTCAE = Common Terminology Criteria for Adverse Events. Adverse events of interest are presented in pre-defined event classes; each class is based on pre-specified preferred terms.
A subject with two or more adverse events in the same event class (or with same package insert term/preferred term) is counted only once for that event class (or package insert term/preferred term).
A subject is counted once by the highest non-missing CTCAE grade as applicable for preferred term and event class respectively.
Adverse event terms are coded using Medical Dictionary for Regulatory Activities (MedDRA) version 17.1.
This table is based on adverse events data as available. Study 207 did not record laboratory abnormalities into adverse events data.

Program: V:¥projects¥e7389¥iss309¥csr¥dev¥pg¥tables¥T_2_7_4_19.sas 18JUN201513:38

付録 2.7.4-19
Japanese and Non-Japanese
Treatment-Emergent Adverse Events of Interest Specified in Japan by CTCAE Grade
Eribulin Treated Safety Population

Event class Package insert term or preferred term Preferred term CTCAE grade	日本人 Study 217 (N=51) n(%)	外国人 Studies 207+309 (N=353) n(%)	全体 Studies 217+207+309 (N=404) n(%)
骨髄抑制			
血小板減少症	3 (5.9)	13 (3.7)	16 (4.0)
1	2 (3.9)	7 (2.0)	9 (2.2)
2	1 (2.0)	5 (1.4)	6 (1.5)
3	0	1 (0.3)	1 (0.2)
4	0	0	0
5	0	0	0
>=3	0	1 (0.3)	1 (0.2)
好中球減少	50 (98.0)	119 (33.7)	169 (41.8)
1	1 (2.0)	2 (0.6)	3 (0.7)
2	5 (9.8)	20 (5.7)	25 (6.2)
3	5 (9.8)	53 (15.0)	58 (14.4)
4	39 (76.5)	44 (12.5)	83 (20.5)
5	0	0	0
>=3	44 (86.3)	97 (27.5)	141 (34.9)

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付録 2.7.4-19
Japanese and Non-Japanese
Treatment-Emergent Adverse Events of Interest Specified in Japan by CTCAE Grade
Eribulin Treated Safety Population

Event class Package insert term or preferred term Preferred term CTCAE grade	日本人 Study 217 (N=51) n(%)	外国人 Studies 207+309 (N=353) n(%)	全体 Studies 217+207+309 (N=404) n(%)
骨髄抑制			
好中球減少症	50 (98.0)	101 (28.6)	151 (37.4)
1	1 (2.0)	2 (0.6)	3 (0.7)
2	5 (9.8)	17 (4.8)	22 (5.4)
3	5 (9.8)	46 (13.0)	51 (12.6)
4	39 (76.5)	36 (10.2)	75 (18.6)
5	0	0	0
>=3	44 (86.3)	82 (23.2)	126 (31.2)
好中球数減少	0	19 (5.4)	19 (4.7)
1	0	0	0
2	0	3 (0.8)	3 (0.7)
3	0	7 (2.0)	7 (1.7)
4	0	9 (2.5)	9 (2.2)
5	0	0	0
>=3	0	16 (4.5)	16 (4.0)

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Adverse event terms are coded using Medical Dictionary for Regulatory Activities (MedDRA) version 17.1.
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付録 2.7.4-19
Japanese and Non-Japanese
Treatment-Emergent Adverse Events of Interest Specified in Japan by CTCAE Grade
Eribulin Treated Safety Population

Event class Package insert term or preferred term Preferred term CTCAE grade	日本人 Study 217 (N=51) n(%)	外国人 Studies 207+309 (N=353) n(%)	全体 Studies 217+207+309 (N=404) n(%)
骨髄抑制			
赤血球減少	0	2 (0.6)	2 (0.5)
1	0	2 (0.6)	2 (0.5)
2	0	0	0
3	0	0	0
4	0	0	0
5	0	0	0
>=3	0	0	0
赤血球数減少	0	2 (0.6)	2 (0.5)
1	0	2 (0.6)	2 (0.5)
2	0	0	0
3	0	0	0
4	0	0	0
5	0	0	0
>=3	0	0	0

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Adverse event terms are coded using Medical Dictionary for Regulatory Activities (MedDRA) version 17.1.
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付録 2.7.4-19
Japanese and Non-Japanese
Treatment-Emergent Adverse Events of Interest Specified in Japan by CTCAE Grade
Eribulin Treated Safety Population

Event class Package insert term or preferred term Preferred term CTCAE grade	日本人 Study 217 (N=51) n(%)	外国人 Studies 207+309 (N=353) n(%)	全体 Studies 217+207+309 (N=404) n(%)
骨髄抑制			
白血球減少	51 (100.0)	52 (14.7)	103 (25.5)
1	0	5 (1.4)	5 (1.2)
2	13 (25.5)	16 (4.5)	29 (7.2)
3	28 (54.9)	25 (7.1)	53 (13.1)
4	10 (19.6)	6 (1.7)	16 (4.0)
5	0	0	0
>=3	38 (74.5)	31 (8.8)	69 (17.1)
白血球減少症	51 (100.0)	36 (10.2)	87 (21.5)
1	0	3 (0.8)	3 (0.7)
2	13 (25.5)	10 (2.8)	23 (5.7)
3	28 (54.9)	18 (5.1)	46 (11.4)
4	10 (19.6)	5 (1.4)	15 (3.7)
5	0	0	0
>=3	38 (74.5)	23 (6.5)	61 (15.1)

CTCAE = Common Terminology Criteria for Adverse Events. Adverse events of interest are presented in pre-defined event classes; each class is based on pre-specified preferred terms.
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Adverse event terms are coded using Medical Dictionary for Regulatory Activities (MedDRA) version 17.1.
This table is based on adverse events data as available. Study 207 did not record laboratory abnormalities into adverse events data.

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付録 2.7.4-19
Japanese and Non-Japanese
Treatment-Emergent Adverse Events of Interest Specified in Japan by CTCAE Grade
Eribulin Treated Safety Population

Event class Package insert term or preferred term Preferred term CTCAE grade	日本人 Study 217 (N=51) n(%)	外国人 Studies 207+309 (N=353) n(%)	全体 Studies 217+207+309 (N=404) n(%)
骨髄抑制			
白血球数減少	0	16 (4.5)	16 (4.0)
1	0	2 (0.6)	2 (0.5)
2	0	6 (1.7)	6 (1.5)
3	0	7 (2.0)	7 (1.7)
4	0	1 (0.3)	1 (0.2)
5	0	0	0
>=3	0	8 (2.3)	8 (2.0)
発熱性好中球減少	4 (7.8)	10 (2.8)	14 (3.5)
1	0	0	0
2	0	0	0
3	4 (7.8)	10 (2.8)	14 (3.5)
4	0	0	0
5	0	0	0
>=3	4 (7.8)	10 (2.8)	14 (3.5)

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付録 2.7.4-19
Japanese and Non-Japanese
Treatment-Emergent Adverse Events of Interest Specified in Japan by CTCAE Grade
Eribulin Treated Safety Population

Event class Package insert term or preferred term Preferred term CTCAE grade	日本人 Study 217 (N=51) n(%)	外国人 Studies 207+309 (N=353) n(%)	全体 Studies 217+207+309 (N=404) n(%)
骨髄抑制			
発熱性好中球減少症	4 (7.8)	10 (2.8)	14 (3.5)
1	0	0	0
2	0	0	0
3	4 (7.8)	10 (2.8)	14 (3.5)
4	0	0	0
5	0	0	0
>=3	4 (7.8)	10 (2.8)	14 (3.5)
貧血	24 (47.1)	68 (19.3)	92 (22.8)
1	3 (5.9)	14 (4.0)	17 (4.2)
2	14 (27.5)	37 (10.5)	51 (12.6)
3	7 (13.7)	14 (4.0)	21 (5.2)
4	0	3 (0.8)	3 (0.7)
5	0	0	0
>=3	7 (13.7)	17 (4.8)	24 (5.9)

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付録 2.7.4-19
Japanese and Non-Japanese
Treatment-Emergent Adverse Events of Interest Specified in Japan by CTCAE Grade
Eribulin Treated Safety Population

Event class Package insert term or preferred term Preferred term CTCAE grade	日本人 Study 217 (N=51) n(%)	外国人 Studies 207+309 (N=353) n(%)	全体 Studies 217+207+309 (N=404) n(%)
骨髄抑制			
貧血	24 (47.1)	68 (19.3)	92 (22.8)
1	3 (5.9)	14 (4.0)	17 (4.2)
2	14 (27.5)	37 (10.5)	51 (12.6)
3	7 (13.7)	14 (4.0)	21 (5.2)
4	0	3 (0.8)	3 (0.7)
5	0	0	0
>=3	7 (13.7)	17 (4.8)	24 (5.9)
感染症			
Any preferred term	22 (43.1)	121 (34.3)	143 (35.4)
1	5 (9.8)	47 (13.3)	52 (12.9)
2	14 (27.5)	45 (12.7)	59 (14.6)
3	3 (5.9)	24 (6.8)	27 (6.7)
4	0	3 (0.8)	3 (0.7)
5	0	2 (0.6)	2 (0.5)
>=3	3 (5.9)	29 (8.2)	32 (7.9)

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付録 2.7.4-19
Japanese and Non-Japanese
Treatment-Emergent Adverse Events of Interest Specified in Japan by CTCAE Grade
Eribulin Treated Safety Population

Event class Package insert term or preferred term Preferred term CTCAE grade	日本人 Study 217 (N=51) n(%)	外国人 Studies 207+309 (N=353) n(%)	全体 Studies 217+207+309 (N=404) n(%)
感染症			
せつ	0	1 (0.3)	1 (0.2)
1	0	1 (0.3)	1 (0.2)
2	0	0	0
3	0	0	0
4	0	0	0
5	0	0	0
>=3	0	0	0
せつ	0	1 (0.3)	1 (0.2)
1	0	1 (0.3)	1 (0.2)
2	0	0	0
3	0	0	0
4	0	0	0
5	0	0	0
>=3	0	0	0

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付録 2.7.4-19
Japanese and Non-Japanese
Treatment-Emergent Adverse Events of Interest Specified in Japan by CTCAE Grade
Eribulin Treated Safety Population

Event class Package insert term or preferred term Preferred term CTCAE grade	日本人 Study 217 (N=51) n(%)	外国人 Studies 207+309 (N=353) n(%)	全体 Studies 217+207+309 (N=404) n(%)
感染症			
リンパ節感染	0	1 (0.3)	1 (0.2)
1	0	0	0
2	0	0	0
3	0	1 (0.3)	1 (0.2)
4	0	0	0
5	0	0	0
>=3	0	1 (0.3)	1 (0.2)
リンパ節感染	0	1 (0.3)	1 (0.2)
1	0	0	0
2	0	0	0
3	0	1 (0.3)	1 (0.2)
4	0	0	0
5	0	0	0
>=3	0	1 (0.3)	1 (0.2)

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付録 2.7.4-19
Japanese and Non-Japanese
Treatment-Emergent Adverse Events of Interest Specified in Japan by CTCAE Grade
Eribulin Treated Safety Population

Event class Package insert term or preferred term Preferred term CTCAE grade	日本人 Study 217 (N=51) n(%)	外国人 Studies 207+309 (N=353) n(%)	全体 Studies 217+207+309 (N=404) n(%)
感染症			
胃腸炎	2 (3.9)	3 (0.8)	5 (1.2)
1	0	2 (0.6)	2 (0.5)
2	2 (3.9)	1 (0.3)	3 (0.7)
3	0	0	0
4	0	0	0
5	0	0	0
>=3	0	0	0
感染性腸炎	1 (2.0)	0	1 (0.2)
1	0	0	0
2	1 (2.0)	0	1 (0.2)
3	0	0	0
4	0	0	0
5	0	0	0
>=3	0	0	0

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付録 2.7.4-19
Japanese and Non-Japanese
Treatment-Emergent Adverse Events of Interest Specified in Japan by CTCAE Grade
Eribulin Treated Safety Population

Event class Package insert term or preferred term Preferred term CTCAE grade	日本人 Study 217 (N=51) n(%)	外国人 Studies 207+309 (N=353) n(%)	全体 Studies 217+207+309 (N=404) n(%)
感染症			
胃腸炎	1 (2.0)	3 (0.8)	4 (1.0)
1	0	2 (0.6)	2 (0.5)
2	1 (2.0)	1 (0.3)	2 (0.5)
3	0	0	0
4	0	0	0
5	0	0	0
>=3	0	0	0
医療機器関連感染	0	9 (2.5)	9 (2.2)
1	0	1 (0.3)	1 (0.2)
2	0	2 (0.6)	2 (0.5)
3	0	6 (1.7)	6 (1.5)
4	0	0	0
5	0	0	0
>=3	0	6 (1.7)	6 (1.5)

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付録 2.7.4-19
Japanese and Non-Japanese
Treatment-Emergent Adverse Events of Interest Specified in Japan by CTCAE Grade
Eribulin Treated Safety Population

Event class Package insert term or preferred term Preferred term CTCAE grade	日本人 Study 217 (N=51) n(%)	外国人 Studies 207+309 (N=353) n(%)	全体 Studies 217+207+309 (N=404) n(%)
感染症			
カテーテル留置部位蜂巣炎	0	1 (0.3)	1 (0.2)
1	0	1 (0.3)	1 (0.2)
2	0	0	0
3	0	0	0
4	0	0	0
5	0	0	0
>=3	0	0	0
カテーテル留置部位感染	0	1 (0.3)	1 (0.2)
1	0	0	0
2	0	0	0
3	0	1 (0.3)	1 (0.2)
4	0	0	0
5	0	0	0
>=3	0	1 (0.3)	1 (0.2)

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A subject is counted once by the highest non-missing CTCAE grade as applicable for preferred term and event class respectively.
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付録 2.7.4-19
Japanese and Non-Japanese
Treatment-Emergent Adverse Events of Interest Specified in Japan by CTCAE Grade
Eribulin Treated Safety Population

Event class Package insert term or preferred term Preferred term CTCAE grade	日本人 Study 217 (N=51) n(%)	外国人 Studies 207+309 (N=353) n(%)	全体 Studies 217+207+309 (N=404) n(%)
感染症			
医療機器関連感染	0	7 (2.0)	7 (1.7)
1	0	0	0
2	0	2 (0.6)	2 (0.5)
3	0	5 (1.4)	5 (1.2)
4	0	0	0
5	0	0	0
>=3	0	5 (1.4)	5 (1.2)
下気道感染	0	2 (0.6)	2 (0.5)
1	0	0	0
2	0	1 (0.3)	1 (0.2)
3	0	1 (0.3)	1 (0.2)
4	0	0	0
5	0	0	0
>=3	0	1 (0.3)	1 (0.2)

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A subject is counted once by the highest non-missing CTCAE grade as applicable for preferred term and event class respectively.
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付録 2.7.4-19
Japanese and Non-Japanese
Treatment-Emergent Adverse Events of Interest Specified in Japan by CTCAE Grade
Eribulin Treated Safety Population

Event class Package insert term or preferred term Preferred term CTCAE grade	日本人 Study 217 (N=51) n(%)	外国人 Studies 207+309 (N=353) n(%)	全体 Studies 217+207+309 (N=404) n(%)
感染症			
下気道感染	0	1 (0.3)	1 (0.2)
1	0	0	0
2	0	1 (0.3)	1 (0.2)
3	0	0	0
4	0	0	0
5	0	0	0
>=3	0	0	0
真菌性下気道感染	0	1 (0.3)	1 (0.2)
1	0	0	0
2	0	0	0
3	0	1 (0.3)	1 (0.2)
4	0	0	0
5	0	0	0
>=3	0	1 (0.3)	1 (0.2)

CTCAE = Common Terminology Criteria for Adverse Events. Adverse events of interest are presented in pre-defined event classes; each class is based on pre-specified preferred terms.
A subject with two or more adverse events in the same event class (or with same package insert term/preferred term) is counted only once for that event class (or package insert term/preferred term).
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Program: V:¥projects¥e7389¥iss309¥csr¥dev¥pg¥tables¥T_2_7_4_19.sas 18JUN201513:38

付録 2.7.4-19
Japanese and Non-Japanese
Treatment-Emergent Adverse Events of Interest Specified in Japan by CTCAE Grade
Eribulin Treated Safety Population

Event class Package insert term or preferred term Preferred term CTCAE grade	日本人 Study 217 (N=51) n(%)	外国人 Studies 207+309 (N=353) n(%)	全体 Studies 217+207+309 (N=404) n(%)
感染症			
感染	1 (2.0)	11 (3.1)	12 (3.0)
1	0	6 (1.7)	6 (1.5)
2	0	4 (1.1)	4 (1.0)
3	1 (2.0)	1 (0.3)	2 (0.5)
4	0	0	0
5	0	0	0
>=3	1 (2.0)	1 (0.3)	2 (0.5)
アメーバ症	0	1 (0.3)	1 (0.2)
1	0	1 (0.3)	1 (0.2)
2	0	0	0
3	0	0	0
4	0	0	0
5	0	0	0
>=3	0	0	0

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付録 2.7.4-19
Japanese and Non-Japanese
Treatment-Emergent Adverse Events of Interest Specified in Japan by CTCAE Grade
Eribulin Treated Safety Population

Event class Package insert term or preferred term Preferred term CTCAE grade	日本人 Study 217 (N=51) n(%)	外国人 Studies 207+309 (N=353) n(%)	全体 Studies 217+207+309 (N=404) n(%)
感染症			
感染	0	2 (0.6)	2 (0.5)
1	0	0	0
2	0	2 (0.6)	2 (0.5)
3	0	0	0
4	0	0	0
5	0	0	0
>=3	0	0	0
インフルエンザ	1 (2.0)	6 (1.7)	7 (1.7)
1	1 (2.0)	5 (1.4)	6 (1.5)
2	0	1 (0.3)	1 (0.2)
3	0	0	0
4	0	0	0
5	0	0	0
>=3	0	0	0

CTCAE = Common Terminology Criteria for Adverse Events. Adverse events of interest are presented in pre-defined event classes; each class is based on pre-specified preferred terms.
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付録 2.7.4-19
Japanese and Non-Japanese
Treatment-Emergent Adverse Events of Interest Specified in Japan by CTCAE Grade
Eribulin Treated Safety Population

Event class Package insert term or preferred term Preferred term CTCAE grade	日本人 Study 217 (N=51) n(%)	外国人 Studies 207+309 (N=353) n(%)	全体 Studies 217+207+309 (N=404) n(%)
感染症			
限局性感染	0	1 (0.3)	1 (0.2)
1	0	0	0
2	0	1 (0.3)	1 (0.2)
3	0	0	0
4	0	0	0
5	0	0	0
>=3	0	0	0
ブドウ球菌感染	0	1 (0.3)	1 (0.2)
1	0	0	0
2	0	0	0
3	0	1 (0.3)	1 (0.2)
4	0	0	0
5	0	0	0
>=3	0	1 (0.3)	1 (0.2)

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付録 2.7.4-19
Japanese and Non-Japanese
Treatment-Emergent Adverse Events of Interest Specified in Japan by CTCAE Grade
Eribulin Treated Safety Population

Event class Package insert term or preferred term Preferred term CTCAE grade	日本人 Study 217 (N=51) n(%)	外国人 Studies 207+309 (N=353) n(%)	全体 Studies 217+207+309 (N=404) n(%)
感染症			
レンサ球菌感染	1 (2.0)	0	1 (0.2)
1	0	0	0
2	0	0	0
3	1 (2.0)	0	1 (0.2)
4	0	0	0
5	0	0	0
>=3	1 (2.0)	0	1 (0.2)
白癬感染	0	1 (0.3)	1 (0.2)
1	0	1 (0.3)	1 (0.2)
2	0	0	0
3	0	0	0
4	0	0	0
5	0	0	0
>=3	0	0	0

CTCAE = Common Terminology Criteria for Adverse Events. Adverse events of interest are presented in pre-defined event classes; each class is based on pre-specified preferred terms.
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付録 2.7.4-19
Japanese and Non-Japanese
Treatment-Emergent Adverse Events of Interest Specified in Japan by CTCAE Grade
Eribulin Treated Safety Population

Event class Package insert term or preferred term Preferred term CTCAE grade	日本人 Study 217 (N=51) n(%)	外国人 Studies 207+309 (N=353) n(%)	全体 Studies 217+207+309 (N=404) n(%)
感染症			
感染性関節炎	0	1 (0.3)	1 (0.2)
1	0	0	0
2	0	0	0
3	0	1 (0.3)	1 (0.2)
4	0	0	0
5	0	0	0
>=3	0	1 (0.3)	1 (0.2)
細菌性関節炎	0	1 (0.3)	1 (0.2)
1	0	0	0
2	0	0	0
3	0	1 (0.3)	1 (0.2)
4	0	0	0
5	0	0	0
>=3	0	1 (0.3)	1 (0.2)

CTCAE = Common Terminology Criteria for Adverse Events. Adverse events of interest are presented in pre-defined event classes; each class is based on pre-specified preferred terms.
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付録 2.7.4-19
Japanese and Non-Japanese
Treatment-Emergent Adverse Events of Interest Specified in Japan by CTCAE Grade
Eribulin Treated Safety Population

Event class Package insert term or preferred term Preferred term CTCAE grade	日本人 Study 217 (N=51) n(%)	外国人 Studies 207+309 (N=353) n(%)	全体 Studies 217+207+309 (N=404) n(%)
感染症			
感染性胸水	1 (2.0)	0	1 (0.2)
1	0	0	0
2	0	0	0
3	1 (2.0)	0	1 (0.2)
4	0	0	0
5	0	0	0
>=3	1 (2.0)	0	1 (0.2)
蓄膿	1 (2.0)	0	1 (0.2)
1	0	0	0
2	0	0	0
3	1 (2.0)	0	1 (0.2)
4	0	0	0
5	0	0	0
>=3	1 (2.0)	0	1 (0.2)

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付録 2.7.4-19
Japanese and Non-Japanese
Treatment-Emergent Adverse Events of Interest Specified in Japan by CTCAE Grade
Eribulin Treated Safety Population

Event class Package insert term or preferred term Preferred term CTCAE grade	日本人 Study 217 (N=51) n(%)	外国人 Studies 207+309 (N=353) n(%)	全体 Studies 217+207+309 (N=404) n(%)
感染症			
眼窩感染	0	1 (0.3)	1 (0.2)
1	0	0	0
2	0	1 (0.3)	1 (0.2)
3	0	0	0
4	0	0	0
5	0	0	0
>=3	0	0	0
眼窩感染	0	1 (0.3)	1 (0.2)
1	0	0	0
2	0	1 (0.3)	1 (0.2)
3	0	0	0
4	0	0	0
5	0	0	0
>=3	0	0	0

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付録 2.7.4-19
Japanese and Non-Japanese
Treatment-Emergent Adverse Events of Interest Specified in Japan by CTCAE Grade
Eribulin Treated Safety Population

Event class Package insert term or preferred term Preferred term CTCAE grade	日本人 Study 217 (N=51) n(%)	外国人 Studies 207+309 (N=353) n(%)	全体 Studies 217+207+309 (N=404) n(%)
感染症			
気管気管支炎	0	4 (1.1)	4 (1.0)
1	0	2 (0.6)	2 (0.5)
2	0	2 (0.6)	2 (0.5)
3	0	0	0
4	0	0	0
5	0	0	0
>=3	0	0	0
気管支炎	0	4 (1.1)	4 (1.0)
1	0	2 (0.6)	2 (0.5)
2	0	2 (0.6)	2 (0.5)
3	0	0	0
4	0	0	0
5	0	0	0
>=3	0	0	0

CTCAE = Common Terminology Criteria for Adverse Events. Adverse events of interest are presented in pre-defined event classes; each class is based on pre-specified preferred terms.
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付録 2.7.4-19
Japanese and Non-Japanese
Treatment-Emergent Adverse Events of Interest Specified in Japan by CTCAE Grade
Eribulin Treated Safety Population

Event class Package insert term or preferred term Preferred term CTCAE grade	日本人 Study 217 (N=51) n(%)	外国人 Studies 207+309 (N=353) n(%)	全体 Studies 217+207+309 (N=404) n(%)
感染症			
気道感染	0	1 (0.3)	1 (0.2)
1	0	0	0
2	0	1 (0.3)	1 (0.2)
3	0	0	0
4	0	0	0
5	0	0	0
>=3	0	0	0
気道感染	0	1 (0.3)	1 (0.2)
1	0	0	0
2	0	1 (0.3)	1 (0.2)
3	0	0	0
4	0	0	0
5	0	0	0
>=3	0	0	0

CTCAE = Common Terminology Criteria for Adverse Events. Adverse events of interest are presented in pre-defined event classes; each class is based on pre-specified preferred terms.
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付録 2.7.4-19
Japanese and Non-Japanese
Treatment-Emergent Adverse Events of Interest Specified in Japan by CTCAE Grade
Eribulin Treated Safety Population

Event class Package insert term or preferred term Preferred term CTCAE grade	日本人 Study 217 (N=51) n(%)	外国人 Studies 207+309 (N=353) n(%)	全体 Studies 217+207+309 (N=404) n(%)
感染症			
菌血症	0	3 (0.8)	3 (0.7)
1	0	0	0
2	0	0	0
3	0	2 (0.6)	2 (0.5)
4	0	1 (0.3)	1 (0.2)
5	0	0	0
>=3	0	3 (0.8)	3 (0.7)
シュードモナス性菌血症	0	1 (0.3)	1 (0.2)
1	0	0	0
2	0	0	0
3	0	1 (0.3)	1 (0.2)
4	0	0	0
5	0	0	0
>=3	0	1 (0.3)	1 (0.2)

CTCAE = Common Terminology Criteria for Adverse Events. Adverse events of interest are presented in pre-defined event classes; each class is based on pre-specified preferred terms.
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付録 2.7.4-19
Japanese and Non-Japanese
Treatment-Emergent Adverse Events of Interest Specified in Japan by CTCAE Grade
Eribulin Treated Safety Population

Event class Package insert term or preferred term Preferred term CTCAE grade	日本人 Study 217 (N=51) n(%)	外国人 Studies 207+309 (N=353) n(%)	全体 Studies 217+207+309 (N=404) n(%)
感染症			
セラチア性菌血症	0	1 (0.3)	1 (0.2)
1	0	0	0
2	0	0	0
3	0	1 (0.3)	1 (0.2)
4	0	0	0
5	0	0	0
>=3	0	1 (0.3)	1 (0.2)
ブドウ球菌性菌血症	0	1 (0.3)	1 (0.2)
1	0	0	0
2	0	0	0
3	0	0	0
4	0	1 (0.3)	1 (0.2)
5	0	0	0
>=3	0	1 (0.3)	1 (0.2)

CTCAE = Common Terminology Criteria for Adverse Events. Adverse events of interest are presented in pre-defined event classes; each class is based on pre-specified preferred terms.
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付録 2.7.4-19
Japanese and Non-Japanese
Treatment-Emergent Adverse Events of Interest Specified in Japan by CTCAE Grade
Eribulin Treated Safety Population

Event class Package insert term or preferred term Preferred term CTCAE grade	日本人 Study 217 (N=51) n(%)	外国人 Studies 207+309 (N=353) n(%)	全体 Studies 217+207+309 (N=404) n(%)
感染症			
口腔感染	0	8 (2.3)	8 (2.0)
1	0	3 (0.8)	3 (0.7)
2	0	5 (1.4)	5 (1.2)
3	0	0	0
4	0	0	0
5	0	0	0
>=3	0	0	0
口腔細菌感染	0	1 (0.3)	1 (0.2)
1	0	1 (0.3)	1 (0.2)
2	0	0	0
3	0	0	0
4	0	0	0
5	0	0	0
>=3	0	0	0

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付録 2.7.4-19
Japanese and Non-Japanese
Treatment-Emergent Adverse Events of Interest Specified in Japan by CTCAE Grade
Eribulin Treated Safety Population

Event class Package insert term or preferred term Preferred term CTCAE grade	日本人 Study 217 (N=51) n(%)	外国人 Studies 207+309 (N=353) n(%)	全体 Studies 217+207+309 (N=404) n(%)
感染症			
口腔カンジダ症	0	5 (1.4)	5 (1.2)
1	0	2 (0.6)	2 (0.5)
2	0	3 (0.8)	3 (0.7)
3	0	0	0
4	0	0	0
5	0	0	0
>=3	0	0	0
口腔ヘルペス	0	1 (0.3)	1 (0.2)
1	0	0	0
2	0	1 (0.3)	1 (0.2)
3	0	0	0
4	0	0	0
5	0	0	0
>=3	0	0	0

CTCAE = Common Terminology Criteria for Adverse Events. Adverse events of interest are presented in pre-defined event classes; each class is based on pre-specified preferred terms.
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A subject is counted once by the highest non-missing CTCAE grade as applicable for preferred term and event class respectively.
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付録 2.7.4-19
Japanese and Non-Japanese
Treatment-Emergent Adverse Events of Interest Specified in Japan by CTCAE Grade
Eribulin Treated Safety Population

Event class Package insert term or preferred term Preferred term CTCAE grade	日本人 Study 217 (N=51) n(%)	外国人 Studies 207+309 (N=353) n(%)	全体 Studies 217+207+309 (N=404) n(%)
感染症			
口腔感染	0	1 (0.3)	1 (0.2)
1	0	0	0
2	0	1 (0.3)	1 (0.2)
3	0	0	0
4	0	0	0
5	0	0	0
>=3	0	0	0
喉頭炎	0	1 (0.3)	1 (0.2)
1	0	0	0
2	0	1 (0.3)	1 (0.2)
3	0	0	0
4	0	0	0
5	0	0	0
>=3	0	0	0

CTCAE = Common Terminology Criteria for Adverse Events. Adverse events of interest are presented in pre-defined event classes; each class is based on pre-specified preferred terms.
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付録 2.7.4-19
Japanese and Non-Japanese
Treatment-Emergent Adverse Events of Interest Specified in Japan by CTCAE Grade
Eribulin Treated Safety Population

Event class Package insert term or preferred term Preferred term CTCAE grade	日本人 Study 217 (N=51) n(%)	外国人 Studies 207+309 (N=353) n(%)	全体 Studies 217+207+309 (N=404) n(%)
感染症			
喉頭炎	0	1 (0.3)	1 (0.2)
1	0	0	0
2	0	1 (0.3)	1 (0.2)
3	0	0	0
4	0	0	0
5	0	0	0
>=3	0	0	0
歯感染	0	1 (0.3)	1 (0.2)
1	0	0	0
2	0	0	0
3	0	1 (0.3)	1 (0.2)
4	0	0	0
5	0	0	0
>=3	0	1 (0.3)	1 (0.2)

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A subject with two or more adverse events in the same event class (or with same package insert term/preferred term) is counted only once for that event class (or package insert term/preferred term).
A subject is counted once by the highest non-missing CTCAE grade as applicable for preferred term and event class respectively.
Adverse event terms are coded using Medical Dictionary for Regulatory Activities (MedDRA) version 17.1.
This table is based on adverse events data as available. Study 207 did not record laboratory abnormalities into adverse events data.

Program: V:¥projects¥e7389¥iss309¥csr¥dev¥pg¥tables¥T_2_7_4_19.sas 18JUN201513:38

付録 2.7.4-19
Japanese and Non-Japanese
Treatment-Emergent Adverse Events of Interest Specified in Japan by CTCAE Grade
Eribulin Treated Safety Population

Event class Package insert term or preferred term Preferred term CTCAE grade	日本人 Study 217 (N=51) n(%)	外国人 Studies 207+309 (N=353) n(%)	全体 Studies 217+207+309 (N=404) n(%)
感染症			
歯感染	0	1 (0.3)	1 (0.2)
1	0	0	0
2	0	0	0
3	0	1 (0.3)	1 (0.2)
4	0	0	0
5	0	0	0
>=3	0	1 (0.3)	1 (0.2)
耳感染	0	3 (0.8)	3 (0.7)
1	0	2 (0.6)	2 (0.5)
2	0	1 (0.3)	1 (0.2)
3	0	0	0
4	0	0	0
5	0	0	0
>=3	0	0	0

CTCAE = Common Terminology Criteria for Adverse Events. Adverse events of interest are presented in pre-defined event classes; each class is based on pre-specified preferred terms.
A subject with two or more adverse events in the same event class (or with same package insert term/preferred term) is counted only once for that event class (or package insert term/preferred term).
A subject is counted once by the highest non-missing CTCAE grade as applicable for preferred term and event class respectively.
Adverse event terms are coded using Medical Dictionary for Regulatory Activities (MedDRA) version 17.1.
This table is based on adverse events data as available. Study 207 did not record laboratory abnormalities into adverse events data.

Program: V:¥projects¥e7389¥iss309¥csr¥dev¥pg¥tables¥T_2_7_4_19.sas 18JUN201513:38

付録 2.7.4-19
Japanese and Non-Japanese
Treatment-Emergent Adverse Events of Interest Specified in Japan by CTCAE Grade
Eribulin Treated Safety Population

Event class Package insert term or preferred term Preferred term CTCAE grade	日本人 Study 217 (N=51) n(%)	外国人 Studies 207+309 (N=353) n(%)	全体 Studies 217+207+309 (N=404) n(%)
感染症			
耳感染	0	3 (0.8)	3 (0.7)
1	0	2 (0.6)	2 (0.5)
2	0	1 (0.3)	1 (0.2)
3	0	0	0
4	0	0	0
5	0	0	0
>=3	0	0	0
上気道感染	11 (21.6)	22 (6.2)	33 (8.2)
1	5 (9.8)	9 (2.5)	14 (3.5)
2	6 (11.8)	12 (3.4)	18 (4.5)
3	0	1 (0.3)	1 (0.2)
4	0	0	0
5	0	0	0
>=3	0	1 (0.3)	1 (0.2)

CTCAE = Common Terminology Criteria for Adverse Events. Adverse events of interest are presented in pre-defined event classes; each class is based on pre-specified preferred terms.
A subject with two or more adverse events in the same event class (or with same package insert term/preferred term) is counted only once for that event class (or package insert term/preferred term).
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Adverse event terms are coded using Medical Dictionary for Regulatory Activities (MedDRA) version 17.1.
This table is based on adverse events data as available. Study 207 did not record laboratory abnormalities into adverse events data.

Program: V:¥projects¥e7389¥iss309¥csr¥dev¥pg¥tables¥T_2_7_4_19.sas 18JUN201513:38

付録 2.7.4-19
Japanese and Non-Japanese
Treatment-Emergent Adverse Events of Interest Specified in Japan by CTCAE Grade
Eribulin Treated Safety Population

Event class Package insert term or preferred term Preferred term CTCAE grade	日本人 Study 217 (N=51) n(%)	外国人 Studies 207+309 (N=353) n(%)	全体 Studies 217+207+309 (N=404) n(%)
感染症			
上気道感染	11 (21.6)	21 (5.9)	32 (7.9)
1	5 (9.8)	9 (2.5)	14 (3.5)
2	6 (11.8)	11 (3.1)	17 (4.2)
3	0	1 (0.3)	1 (0.2)
4	0	0	0
5	0	0	0
>=3	0	1 (0.3)	1 (0.2)
ウイルス性上気道感染	0	1 (0.3)	1 (0.2)
1	0	0	0
2	0	1 (0.3)	1 (0.2)
3	0	0	0
4	0	0	0
5	0	0	0
>=3	0	0	0

CTCAE = Common Terminology Criteria for Adverse Events. Adverse events of interest are presented in pre-defined event classes; each class is based on pre-specified preferred terms.
A subject with two or more adverse events in the same event class (or with same package insert term/preferred term) is counted only once for that event class (or package insert term/preferred term).
A subject is counted once by the highest non-missing CTCAE grade as applicable for preferred term and event class respectively.
Adverse event terms are coded using Medical Dictionary for Regulatory Activities (MedDRA) version 17.1.
This table is based on adverse events data as available. Study 207 did not record laboratory abnormalities into adverse events data.

Program: V:¥projects¥e7389¥iss309¥csr¥dev¥pg¥tables¥T_2_7_4_19.sas 18JUN201513:38

付録 2.7.4-19
Japanese and Non-Japanese
Treatment-Emergent Adverse Events of Interest Specified in Japan by CTCAE Grade
Eribulin Treated Safety Population

Event class Package insert term or preferred term Preferred term CTCAE grade	日本人 Study 217 (N=51) n(%)	外国人 Studies 207+309 (N=353) n(%)	全体 Studies 217+207+309 (N=404) n(%)
感染症			
腎盂腎炎	0	1 (0.3)	1 (0.2)
1	0	0	0
2	0	0	0
3	0	1 (0.3)	1 (0.2)
4	0	0	0
5	0	0	0
>=3	0	1 (0.3)	1 (0.2)
腎盂腎炎	0	1 (0.3)	1 (0.2)
1	0	0	0
2	0	0	0
3	0	1 (0.3)	1 (0.2)
4	0	0	0
5	0	0	0
>=3	0	1 (0.3)	1 (0.2)

CTCAE = Common Terminology Criteria for Adverse Events. Adverse events of interest are presented in pre-defined event classes; each class is based on pre-specified preferred terms.
A subject with two or more adverse events in the same event class (or with same package insert term/preferred term) is counted only once for that event class (or package insert term/preferred term).
A subject is counted once by the highest non-missing CTCAE grade as applicable for preferred term and event class respectively.
Adverse event terms are coded using Medical Dictionary for Regulatory Activities (MedDRA) version 17.1.
This table is based on adverse events data as available. Study 207 did not record laboratory abnormalities into adverse events data.

Program: V:¥projects¥e7389¥iss309¥csr¥dev¥pg¥tables¥T_2_7_4_19.sas 18JUN201513:38

付録 2.7.4-19
Japanese and Non-Japanese
Treatment-Emergent Adverse Events of Interest Specified in Japan by CTCAE Grade
Eribulin Treated Safety Population

Event class Package insert term or preferred term Preferred term CTCAE grade	日本人 Study 217 (N=51) n(%)	外国人 Studies 207+309 (N=353) n(%)	全体 Studies 217+207+309 (N=404) n(%)
感染症			
生殖器感染	0	1 (0.3)	1 (0.2)
1	0	1 (0.3)	1 (0.2)
2	0	0	0
3	0	0	0
4	0	0	0
5	0	0	0
>=3	0	0	0
外陰膣真菌感染	0	1 (0.3)	1 (0.2)
1	0	1 (0.3)	1 (0.2)
2	0	0	0
3	0	0	0
4	0	0	0
5	0	0	0
>=3	0	0	0

CTCAE = Common Terminology Criteria for Adverse Events. Adverse events of interest are presented in pre-defined event classes; each class is based on pre-specified preferred terms.
A subject with two or more adverse events in the same event class (or with same package insert term/preferred term) is counted only once for that event class (or package insert term/preferred term).
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Adverse event terms are coded using Medical Dictionary for Regulatory Activities (MedDRA) version 17.1.
This table is based on adverse events data as available. Study 207 did not record laboratory abnormalities into adverse events data.

Program: V:¥projects¥e7389¥iss309¥csr¥dev¥pg¥tables¥T_2_7_4_19.sas 18JUN201513:38

付録 2.7.4-19
Japanese and Non-Japanese
Treatment-Emergent Adverse Events of Interest Specified in Japan by CTCAE Grade
Eribulin Treated Safety Population

Event class Package insert term or preferred term Preferred term CTCAE grade	日本人 Study 217 (N=51) n(%)	外国人 Studies 207+309 (N=353) n(%)	全体 Studies 217+207+309 (N=404) n(%)
感染症			
腎髄炎	0	1 (0.3)	1 (0.2)
1	0	0	0
2	0	1 (0.3)	1 (0.2)
3	0	0	0
4	0	0	0
5	0	0	0
>=3	0	0	0
腎髄炎	0	1 (0.3)	1 (0.2)
1	0	0	0
2	0	1 (0.3)	1 (0.2)
3	0	0	0
4	0	0	0
5	0	0	0
>=3	0	0	0

CTCAE = Common Terminology Criteria for Adverse Events. Adverse events of interest are presented in pre-defined event classes; each class is based on pre-specified preferred terms.
A subject with two or more adverse events in the same event class (or with same package insert term/preferred term) is counted only once for that event class (or package insert term/preferred term).
A subject is counted once by the highest non-missing CTCAE grade as applicable for preferred term and event class respectively.
Adverse event terms are coded using Medical Dictionary for Regulatory Activities (MedDRA) version 17.1.
This table is based on adverse events data as available. Study 207 did not record laboratory abnormalities into adverse events data.

Program: V:¥projects¥e7389¥iss309¥csr¥dev¥pg¥tables¥T_2_7_4_19.sas 18JUN201513:38

付録 2.7.4-19
Japanese and Non-Japanese
Treatment-Emergent Adverse Events of Interest Specified in Japan by CTCAE Grade
Eribulin Treated Safety Population

Event class Package insert term or preferred term Preferred term CTCAE grade	日本人 Study 217 (N=51) n(%)	外国人 Studies 207+309 (N=353) n(%)	全体 Studies 217+207+309 (N=404) n(%)
感染症			
創傷感染	1 (2.0)	0	1 (0.2)
1	0	0	0
2	1 (2.0)	0	1 (0.2)
3	0	0	0
4	0	0	0
5	0	0	0
>=3	0	0	0
創傷感染	1 (2.0)	0	1 (0.2)
1	0	0	0
2	1 (2.0)	0	1 (0.2)
3	0	0	0
4	0	0	0
5	0	0	0
>=3	0	0	0

CTCAE = Common Terminology Criteria for Adverse Events. Adverse events of interest are presented in pre-defined event classes; each class is based on pre-specified preferred terms.
A subject with two or more adverse events in the same event class (or with same package insert term/preferred term) is counted only once for that event class (or package insert term/preferred term).
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Adverse event terms are coded using Medical Dictionary for Regulatory Activities (MedDRA) version 17.1.
This table is based on adverse events data as available. Study 207 did not record laboratory abnormalities into adverse events data.

Program: V:¥projects¥e7389¥iss309¥csr¥dev¥pg¥tables¥T_2_7_4_19.sas 18JUN201513:38

付録 2.7.4-19
Japanese and Non-Japanese
Treatment-Emergent Adverse Events of Interest Specified in Japan by CTCAE Grade
Eribulin Treated Safety Population

Event class Package insert term or preferred term Preferred term CTCAE grade	日本人 Study 217 (N=51) n(%)	外国人 Studies 207+309 (N=353) n(%)	全体 Studies 217+207+309 (N=404) n(%)
感染症			
帯状疱疹	1 (2.0)	5 (1.4)	6 (1.5)
1	0	2 (0.6)	2 (0.5)
2	1 (2.0)	3 (0.8)	4 (1.0)
3	0	0	0
4	0	0	0
5	0	0	0
>=3	0	0	0
帯状疱疹	1 (2.0)	5 (1.4)	6 (1.5)
1	0	2 (0.6)	2 (0.5)
2	1 (2.0)	3 (0.8)	4 (1.0)
3	0	0	0
4	0	0	0
5	0	0	0
>=3	0	0	0

CTCAE = Common Terminology Criteria for Adverse Events. Adverse events of interest are presented in pre-defined event classes; each class is based on pre-specified preferred terms.
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Adverse event terms are coded using Medical Dictionary for Regulatory Activities (MedDRA) version 17.1.
This table is based on adverse events data as available. Study 207 did not record laboratory abnormalities into adverse events data.

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付録 2.7.4-19
Japanese and Non-Japanese
Treatment-Emergent Adverse Events of Interest Specified in Japan by CTCAE Grade
Eribulin Treated Safety Population

Event class Package insert term or preferred term Preferred term CTCAE grade	日本人 Study 217 (N=51) n(%)	外国人 Studies 207+309 (N=353) n(%)	全体 Studies 217+207+309 (N=404) n(%)
感染症			
丹毒	0	1 (0.3)	1 (0.2)
1	0	1 (0.3)	1 (0.2)
2	0	0	0
3	0	0	0
4	0	0	0
5	0	0	0
>=3	0	0	0
丹毒	0	1 (0.3)	1 (0.2)
1	0	1 (0.3)	1 (0.2)
2	0	0	0
3	0	0	0
4	0	0	0
5	0	0	0
>=3	0	0	0

CTCAE = Common Terminology Criteria for Adverse Events. Adverse events of interest are presented in pre-defined event classes; each class is based on pre-specified preferred terms.
A subject with two or more adverse events in the same event class (or with same package insert term/preferred term) is counted only once for that event class (or package insert term/preferred term).
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付録 2.7.4-19
Japanese and Non-Japanese
Treatment-Emergent Adverse Events of Interest Specified in Japan by CTCAE Grade
Eribulin Treated Safety Population

Event class Package insert term or preferred term Preferred term CTCAE grade	日本人 Study 217 (N=51) n(%)	外国人 Studies 207+309 (N=353) n(%)	全体 Studies 217+207+309 (N=404) n(%)
感染症			
中耳炎	2 (3.9)	0	2 (0.5)
1	0	0	0
2	2 (3.9)	0	2 (0.5)
3	0	0	0
4	0	0	0
5	0	0	0
>=3	0	0	0
中耳炎	1 (2.0)	0	1 (0.2)
1	0	0	0
2	1 (2.0)	0	1 (0.2)
3	0	0	0
4	0	0	0
5	0	0	0
>=3	0	0	0

CTCAE = Common Terminology Criteria for Adverse Events. Adverse events of interest are presented in pre-defined event classes; each class is based on pre-specified preferred terms.
A subject with two or more adverse events in the same event class (or with same package insert term/preferred term) is counted only once for that event class (or package insert term/preferred term).
A subject is counted once by the highest non-missing CTCAE grade as applicable for preferred term and event class respectively.
Adverse event terms are coded using Medical Dictionary for Regulatory Activities (MedDRA) version 17.1.
This table is based on adverse events data as available. Study 207 did not record laboratory abnormalities into adverse events data.

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付録 2.7.4-19
Japanese and Non-Japanese
Treatment-Emergent Adverse Events of Interest Specified in Japan by CTCAE Grade
Eribulin Treated Safety Population

Event class Package insert term or preferred term Preferred term CTCAE grade	日本人 Study 217 (N=51) n(%)	外国人 Studies 207+309 (N=353) n(%)	全体 Studies 217+207+309 (N=404) n(%)
感染症			
急性中耳炎	1 (2.0)	0	1 (0.2)
1	0	0	0
2	1 (2.0)	0	1 (0.2)
3	0	0	0
4	0	0	0
5	0	0	0
>=3	0	0	0
軟部組織感染	0	1 (0.3)	1 (0.2)
1	0	0	0
2	0	1 (0.3)	1 (0.2)
3	0	0	0
4	0	0	0
5	0	0	0
>=3	0	0	0

CTCAE = Common Terminology Criteria for Adverse Events. Adverse events of interest are presented in pre-defined event classes; each class is based on pre-specified preferred terms.
A subject with two or more adverse events in the same event class (or with same package insert term/preferred term) is counted only once for that event class (or package insert term/preferred term).
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付録 2.7.4-19
Japanese and Non-Japanese
Treatment-Emergent Adverse Events of Interest Specified in Japan by CTCAE Grade
Eribulin Treated Safety Population

Event class Package insert term or preferred term Preferred term CTCAE grade	日本人 Study 217 (N=51) n(%)	外国人 Studies 207+309 (N=353) n(%)	全体 Studies 217+207+309 (N=404) n(%)
感染症			
軟部組織感染	0	1 (0.3)	1 (0.2)
1	0	0	0
2	0	1 (0.3)	1 (0.2)
3	0	0	0
4	0	0	0
5	0	0	0
>=3	0	0	0
膿尿	0	1 (0.3)	1 (0.2)
1	0	1 (0.3)	1 (0.2)
2	0	0	0
3	0	0	0
4	0	0	0
5	0	0	0
>=3	0	0	0

CTCAE = Common Terminology Criteria for Adverse Events. Adverse events of interest are presented in pre-defined event classes; each class is based on pre-specified preferred terms.
A subject with two or more adverse events in the same event class (or with same package insert term/preferred term) is counted only once for that event class (or package insert term/preferred term).
A subject is counted once by the highest non-missing CTCAE grade as applicable for preferred term and event class respectively.
Adverse event terms are coded using Medical Dictionary for Regulatory Activities (MedDRA) version 17.1.
This table is based on adverse events data as available. Study 207 did not record laboratory abnormalities into adverse events data.

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付録 2.7.4-19
Japanese and Non-Japanese
Treatment-Emergent Adverse Events of Interest Specified in Japan by CTCAE Grade
Eribulin Treated Safety Population

Event class Package insert term or preferred term Preferred term CTCAE grade	日本人 Study 217 (N=51) n(%)	外国人 Studies 207+309 (N=353) n(%)	全体 Studies 217+207+309 (N=404) n(%)
感染症			
膿尿	0	1 (0.3)	1 (0.2)
1	0	1 (0.3)	1 (0.2)
2	0	0	0
3	0	0	0
4	0	0	0
5	0	0	0
>=3	0	0	0
膿瘍	0	2 (0.6)	2 (0.5)
1	0	0	0
2	0	2 (0.6)	2 (0.5)
3	0	0	0
4	0	0	0
5	0	0	0
>=3	0	0	0

CTCAE = Common Terminology Criteria for Adverse Events. Adverse events of interest are presented in pre-defined event classes; each class is based on pre-specified preferred terms.
A subject with two or more adverse events in the same event class (or with same package insert term/preferred term) is counted only once for that event class (or package insert term/preferred term).
A subject is counted once by the highest non-missing CTCAE grade as applicable for preferred term and event class respectively.
Adverse event terms are coded using Medical Dictionary for Regulatory Activities (MedDRA) version 17.1.
This table is based on adverse events data as available. Study 207 did not record laboratory abnormalities into adverse events data.

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付録 2.7.4-19
Japanese and Non-Japanese
Treatment-Emergent Adverse Events of Interest Specified in Japan by CTCAE Grade
Eribulin Treated Safety Population

Event class Package insert term or preferred term Preferred term CTCAE grade	日本人 Study 217 (N=51) n(%)	外国人 Studies 207+309 (N=353) n(%)	全体 Studies 217+207+309 (N=404) n(%)
感染症			
肝膿瘍	0	1 (0.3)	1 (0.2)
1	0	0	0
2	0	1 (0.3)	1 (0.2)
3	0	0	0
4	0	0	0
5	0	0	0
>=3	0	0	0
皮下組織膿瘍	0	1 (0.3)	1 (0.2)
1	0	0	0
2	0	1 (0.3)	1 (0.2)
3	0	0	0
4	0	0	0
5	0	0	0
>=3	0	0	0

CTCAE = Common Terminology Criteria for Adverse Events. Adverse events of interest are presented in pre-defined event classes; each class is based on pre-specified preferred terms.
A subject with two or more adverse events in the same event class (or with same package insert term/preferred term) is counted only once for that event class (or package insert term/preferred term).
A subject is counted once by the highest non-missing CTCAE grade as applicable for preferred term and event class respectively.
Adverse event terms are coded using Medical Dictionary for Regulatory Activities (MedDRA) version 17.1.
This table is based on adverse events data as available. Study 207 did not record laboratory abnormalities into adverse events data.

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付録 2.7.4-19
Japanese and Non-Japanese
Treatment-Emergent Adverse Events of Interest Specified in Japan by CTCAE Grade
Eribulin Treated Safety Population

Event class Package insert term or preferred term Preferred term CTCAE grade	日本人 Study 217 (N=51) n(%)	外国人 Studies 207+309 (N=353) n(%)	全体 Studies 217+207+309 (N=404) n(%)
感染症			
敗血症	0	6 (1.7)	6 (1.5)
1	0	1 (0.3)	1 (0.2)
2	0	2 (0.6)	2 (0.5)
3	0	0	0
4	0	1 (0.3)	1 (0.2)
5	0	2 (0.6)	2 (0.5)
>=3	0	3 (0.8)	3 (0.7)
腹部敗血症	0	1 (0.3)	1 (0.2)
1	0	1 (0.3)	1 (0.2)
2	0	0	0
3	0	0	0
4	0	0	0
5	0	0	0
>=3	0	0	0

CTCAE = Common Terminology Criteria for Adverse Events. Adverse events of interest are presented in pre-defined event classes; each class is based on pre-specified preferred terms.
A subject with two or more adverse events in the same event class (or with same package insert term/preferred term) is counted only once for that event class (or package insert term/preferred term).
A subject is counted once by the highest non-missing CTCAE grade as applicable for preferred term and event class respectively.
Adverse event terms are coded using Medical Dictionary for Regulatory Activities (MedDRA) version 17.1.
This table is based on adverse events data as available. Study 207 did not record laboratory abnormalities into adverse events data.

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付録 2.7.4-19
Japanese and Non-Japanese
Treatment-Emergent Adverse Events of Interest Specified in Japan by CTCAE Grade
Eribulin Treated Safety Population

Event class Package insert term or preferred term Preferred term CTCAE grade	日本人 Study 217 (N=51) n(%)	外国人 Studies 207+309 (N=353) n(%)	全体 Studies 217+207+309 (N=404) n(%)
感染症			
好中球減少性敗血症	0	1 (0.3)	1 (0.2)
1	0	0	0
2	0	0	0
3	0	0	0
4	0	0	0
5	0	1 (0.3)	1 (0.2)
>=3	0	1 (0.3)	1 (0.2)
敗血症	0	2 (0.6)	2 (0.5)
1	0	0	0
2	0	1 (0.3)	1 (0.2)
3	0	0	0
4	0	1 (0.3)	1 (0.2)
5	0	0	0
>=3	0	1 (0.3)	1 (0.2)

CTCAE = Common Terminology Criteria for Adverse Events. Adverse events of interest are presented in pre-defined event classes; each class is based on pre-specified preferred terms.
A subject with two or more adverse events in the same event class (or with same package insert term/preferred term) is counted only once for that event class (or package insert term/preferred term).
A subject is counted once by the highest non-missing CTCAE grade as applicable for preferred term and event class respectively.
Adverse event terms are coded using Medical Dictionary for Regulatory Activities (MedDRA) version 17.1.
This table is based on adverse events data as available. Study 207 did not record laboratory abnormalities into adverse events data.

Program: V:¥projects¥e7389¥iss309¥csr¥dev¥pg¥tables¥T_2_7_4_19.sas 18JUN201513:38

付録 2.7.4-19
Japanese and Non-Japanese
Treatment-Emergent Adverse Events of Interest Specified in Japan by CTCAE Grade
Eribulin Treated Safety Population

Event class Package insert term or preferred term Preferred term CTCAE grade	日本人 Study 217 (N=51) n(%)	外国人 Studies 207+309 (N=353) n(%)	全体 Studies 217+207+309 (N=404) n(%)
感染症			
敗血症性ショック	0	1 (0.3)	1 (0.2)
1	0	0	0
2	0	0	0
3	0	0	0
4	0	0	0
5	0	1 (0.3)	1 (0.2)
>=3	0	1 (0.3)	1 (0.2)
尿路性敗血症	0	1 (0.3)	1 (0.2)
1	0	0	0
2	0	1 (0.3)	1 (0.2)
3	0	0	0
4	0	0	0
5	0	0	0
>=3	0	0	0

CTCAE = Common Terminology Criteria for Adverse Events. Adverse events of interest are presented in pre-defined event classes; each class is based on pre-specified preferred terms.
A subject with two or more adverse events in the same event class (or with same package insert term/preferred term) is counted only once for that event class (or package insert term/preferred term).
A subject is counted once by the highest non-missing CTCAE grade as applicable for preferred term and event class respectively.
Adverse event terms are coded using Medical Dictionary for Regulatory Activities (MedDRA) version 17.1.
This table is based on adverse events data as available. Study 207 did not record laboratory abnormalities into adverse events data.

Program: V:¥projects¥e7389¥iss309¥csr¥dev¥pg¥tables¥T_2_7_4_19.sas 18JUN201513:38

付録 2.7.4-19
Japanese and Non-Japanese
Treatment-Emergent Adverse Events of Interest Specified in Japan by CTCAE Grade
Eribulin Treated Safety Population

Event class Package insert term or preferred term Preferred term CTCAE grade	日本人 Study 217 (N=51) n(%)	外国人 Studies 207+309 (N=353) n(%)	全体 Studies 217+207+309 (N=404) n(%)
感染症			
肺炎	1 (2.0)	14 (4.0)	15 (3.7)
1	0	1 (0.3)	1 (0.2)
2	0	5 (1.4)	5 (1.2)
3	1 (2.0)	7 (2.0)	8 (2.0)
4	0	1 (0.3)	1 (0.2)
5	0	0	0
>=3	1 (2.0)	8 (2.3)	9 (2.2)
気管支肺炎	0	1 (0.3)	1 (0.2)
1	0	0	0
2	0	0	0
3	0	1 (0.3)	1 (0.2)
4	0	0	0
5	0	0	0
>=3	0	1 (0.3)	1 (0.2)

CTCAE = Common Terminology Criteria for Adverse Events. Adverse events of interest are presented in pre-defined event classes; each class is based on pre-specified preferred terms.
A subject with two or more adverse events in the same event class (or with same package insert term/preferred term) is counted only once for that event class (or package insert term/preferred term).
A subject is counted once by the highest non-missing CTCAE grade as applicable for preferred term and event class respectively.
Adverse event terms are coded using Medical Dictionary for Regulatory Activities (MedDRA) version 17.1.
This table is based on adverse events data as available. Study 207 did not record laboratory abnormalities into adverse events data.

Program: V:¥projects¥e7389¥iss309¥csr¥dev¥pg¥tables¥T_2_7_4_19.sas 18JUN201513:38

付録 2.7.4-19
Japanese and Non-Japanese
Treatment-Emergent Adverse Events of Interest Specified in Japan by CTCAE Grade
Eribulin Treated Safety Population

Event class Package insert term or preferred term Preferred term CTCAE grade	日本人 Study 217 (N=51) n(%)	外国人 Studies 207+309 (N=353) n(%)	全体 Studies 217+207+309 (N=404) n(%)
感染症			
肺感染	0	2 (0.6)	2 (0.5)
1	0	0	0
2	0	1 (0.3)	1 (0.2)
3	0	1 (0.3)	1 (0.2)
4	0	0	0
5	0	0	0
>=3	0	1 (0.3)	1 (0.2)
肺炎	1 (2.0)	11 (3.1)	12 (3.0)
1	0	1 (0.3)	1 (0.2)
2	0	4 (1.1)	4 (1.0)
3	1 (2.0)	5 (1.4)	6 (1.5)
4	0	1 (0.3)	1 (0.2)
5	0	0	0
>=3	1 (2.0)	6 (1.7)	7 (1.7)

CTCAE = Common Terminology Criteria for Adverse Events. Adverse events of interest are presented in pre-defined event classes; each class is based on pre-specified preferred terms.
A subject with two or more adverse events in the same event class (or with same package insert term/preferred term) is counted only once for that event class (or package insert term/preferred term).
A subject is counted once by the highest non-missing CTCAE grade as applicable for preferred term and event class respectively.
Adverse event terms are coded using Medical Dictionary for Regulatory Activities (MedDRA) version 17.1.
This table is based on adverse events data as available. Study 207 did not record laboratory abnormalities into adverse events data.

Program: V:¥projects¥e7389¥iss309¥csr¥dev¥pg¥tables¥T_2_7_4_19.sas 18JUN201513:38

付録 2.7.4-19
Japanese and Non-Japanese
Treatment-Emergent Adverse Events of Interest Specified in Japan by CTCAE Grade
Eribulin Treated Safety Population

Event class Package insert term or preferred term Preferred term CTCAE grade	日本人 Study 217 (N=51) n(%)	外国人 Studies 207+309 (N=353) n(%)	全体 Studies 217+207+309 (N=404) n(%)
感染症			
皮膚感染	0	1 (0.3)	1 (0.2)
1	0	1 (0.3)	1 (0.2)
2	0	0	0
3	0	0	0
4	0	0	0
5	0	0	0
>=3	0	0	0
皮膚カンジダ	0	1 (0.3)	1 (0.2)
1	0	1 (0.3)	1 (0.2)
2	0	0	0
3	0	0	0
4	0	0	0
5	0	0	0
>=3	0	0	0

CTCAE = Common Terminology Criteria for Adverse Events. Adverse events of interest are presented in pre-defined event classes; each class is based on pre-specified preferred terms.
A subject with two or more adverse events in the same event class (or with same package insert term/preferred term) is counted only once for that event class (or package insert term/preferred term).
A subject is counted once by the highest non-missing CTCAE grade as applicable for preferred term and event class respectively.
Adverse event terms are coded using Medical Dictionary for Regulatory Activities (MedDRA) version 17.1.
This table is based on adverse events data as available. Study 207 did not record laboratory abnormalities into adverse events data.

Program: V:¥projects¥e7389¥iss309¥csr¥dev¥pg¥tables¥T_2_7_4_19.sas 18JUN201513:38

付録 2.7.4-19
Japanese and Non-Japanese
Treatment-Emergent Adverse Events of Interest Specified in Japan by CTCAE Grade
Eribulin Treated Safety Population

Event class Package insert term or preferred term Preferred term CTCAE grade	日本人 Study 217 (N=51) n(%)	外国人 Studies 207+309 (N=353) n(%)	全体 Studies 217+207+309 (N=404) n(%)
感染症			
皮膚嚢腫	0	1 (0.3)	1 (0.2)
1	0	0	0
2	0	1 (0.3)	1 (0.2)
3	0	0	0
4	0	0	0
5	0	0	0
>=3	0	0	0
感染性皮膚嚢腫	0	1 (0.3)	1 (0.2)
1	0	0	0
2	0	1 (0.3)	1 (0.2)
3	0	0	0
4	0	0	0
5	0	0	0
>=3	0	0	0

CTCAE = Common Terminology Criteria for Adverse Events. Adverse events of interest are presented in pre-defined event classes; each class is based on pre-specified preferred terms.
A subject with two or more adverse events in the same event class (or with same package insert term/preferred term) is counted only once for that event class (or package insert term/preferred term).
A subject is counted once by the highest non-missing CTCAE grade as applicable for preferred term and event class respectively.
Adverse event terms are coded using Medical Dictionary for Regulatory Activities (MedDRA) version 17.1.
This table is based on adverse events data as available. Study 207 did not record laboratory abnormalities into adverse events data.

Program: V:¥projects¥e7389¥iss309¥csr¥dev¥pg¥tables¥T_2_7_4_19.sas 18JUN201513:38

付録 2.7.4-19
Japanese and Non-Japanese
Treatment-Emergent Adverse Events of Interest Specified in Japan by CTCAE Grade
Eribulin Treated Safety Population

Event class Package insert term or preferred term Preferred term CTCAE grade	日本人 Study 217 (N=51) n(%)	外国人 Studies 207+309 (N=353) n(%)	全体 Studies 217+207+309 (N=404) n(%)
感染症			
鼻咽頭炎	13 (25.5)	30 (8.5)	43 (10.6)
1	8 (15.7)	22 (6.2)	30 (7.4)
2	5 (9.8)	5 (1.4)	10 (2.5)
3	0	3 (0.8)	3 (0.7)
4	0	0	0
5	0	0	0
>=3	0	3 (0.8)	3 (0.7)
鼻咽頭炎	11 (21.6)	20 (5.7)	31 (7.7)
1	8 (15.7)	19 (5.4)	27 (6.7)
2	3 (5.9)	1 (0.3)	4 (1.0)
3	0	0	0
4	0	0	0
5	0	0	0
>=3	0	0	0

CTCAE = Common Terminology Criteria for Adverse Events. Adverse events of interest are presented in pre-defined event classes; each class is based on pre-specified preferred terms.
A subject with two or more adverse events in the same event class (or with same package insert term/preferred term) is counted only once for that event class (or package insert term/preferred term).
A subject is counted once by the highest non-missing CTCAE grade as applicable for preferred term and event class respectively.
Adverse event terms are coded using Medical Dictionary for Regulatory Activities (MedDRA) version 17.1.
This table is based on adverse events data as available. Study 207 did not record laboratory abnormalities into adverse events data.

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付録 2.7.4-19
Japanese and Non-Japanese
Treatment-Emergent Adverse Events of Interest Specified in Japan by CTCAE Grade
Eribulin Treated Safety Population

Event class Package insert term or preferred term Preferred term CTCAE grade	日本人 Study 217 (N=51) n(%)	外国人 Studies 207+309 (N=353) n(%)	全体 Studies 217+207+309 (N=404) n(%)
感染症			
真菌性口腔咽頭炎	0	1 (0.3)	1 (0.2)
1	0	1 (0.3)	1 (0.2)
2	0	0	0
3	0	0	0
4	0	0	0
5	0	0	0
>=3	0	0	0
咽頭炎	2 (3.9)	9 (2.5)	11 (2.7)
1	0	2 (0.6)	2 (0.5)
2	2 (3.9)	4 (1.1)	6 (1.5)
3	0	3 (0.8)	3 (0.7)
4	0	0	0
5	0	0	0
>=3	0	3 (0.8)	3 (0.7)

CTCAE = Common Terminology Criteria for Adverse Events. Adverse events of interest are presented in pre-defined event classes; each class is based on pre-specified preferred terms.
A subject with two or more adverse events in the same event class (or with same package insert term/preferred term) is counted only once for that event class (or package insert term/preferred term).
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Adverse event terms are coded using Medical Dictionary for Regulatory Activities (MedDRA) version 17.1.
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付録 2.7.4-19
Japanese and Non-Japanese
Treatment-Emergent Adverse Events of Interest Specified in Japan by CTCAE Grade
Eribulin Treated Safety Population

Event class Package insert term or preferred term Preferred term CTCAE grade	日本人 Study 217 (N=51) n(%)	外国人 Studies 207+309 (N=353) n(%)	全体 Studies 217+207+309 (N=404) n(%)
感染症			
鼻炎	1 (2.0)	6 (1.7)	7 (1.7)
1	0	4 (1.1)	4 (1.0)
2	1 (2.0)	1 (0.3)	2 (0.5)
3	0	1 (0.3)	1 (0.2)
4	0	0	0
5	0	0	0
>=3	0	1 (0.3)	1 (0.2)
鼻炎	1 (2.0)	6 (1.7)	7 (1.7)
1	0	4 (1.1)	4 (1.0)
2	1 (2.0)	1 (0.3)	2 (0.5)
3	0	1 (0.3)	1 (0.2)
4	0	0	0
5	0	0	0
>=3	0	1 (0.3)	1 (0.2)

CTCAE = Common Terminology Criteria for Adverse Events. Adverse events of interest are presented in pre-defined event classes; each class is based on pre-specified preferred terms.
A subject with two or more adverse events in the same event class (or with same package insert term/preferred term) is counted only once for that event class (or package insert term/preferred term).
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付録 2.7.4-19
Japanese and Non-Japanese
Treatment-Emergent Adverse Events of Interest Specified in Japan by CTCAE Grade
Eribulin Treated Safety Population

Event class Package insert term or preferred term Preferred term CTCAE grade	日本人 Study 217 (N=51) n(%)	外国人 Studies 207+309 (N=353) n(%)	全体 Studies 217+207+309 (N=404) n(%)
感染症			
副鼻腔炎	0	3 (0.8)	3 (0.7)
1	0	2 (0.6)	2 (0.5)
2	0	1 (0.3)	1 (0.2)
3	0	0	0
4	0	0	0
5	0	0	0
>=3	0	0	0
副鼻腔炎	0	3 (0.8)	3 (0.7)
1	0	2 (0.6)	2 (0.5)
2	0	1 (0.3)	1 (0.2)
3	0	0	0
4	0	0	0
5	0	0	0
>=3	0	0	0

CTCAE = Common Terminology Criteria for Adverse Events. Adverse events of interest are presented in pre-defined event classes; each class is based on pre-specified preferred terms.
A subject with two or more adverse events in the same event class (or with same package insert term/preferred term) is counted only once for that event class (or package insert term/preferred term).
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Adverse event terms are coded using Medical Dictionary for Regulatory Activities (MedDRA) version 17.1.
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付録 2.7.4-19
Japanese and Non-Japanese
Treatment-Emergent Adverse Events of Interest Specified in Japan by CTCAE Grade
Eribulin Treated Safety Population

Event class Package insert term or preferred term Preferred term CTCAE grade	日本人 Study 217 (N=51) n(%)	外国人 Studies 207+309 (N=353) n(%)	全体 Studies 217+207+309 (N=404) n(%)
感染症			
腹部感染	0	1 (0.3)	1 (0.2)
1	0	1 (0.3)	1 (0.2)
2	0	0	0
3	0	0	0
4	0	0	0
5	0	0	0
>=3	0	0	0
腹部感染	0	1 (0.3)	1 (0.2)
1	0	1 (0.3)	1 (0.2)
2	0	0	0
3	0	0	0
4	0	0	0
5	0	0	0
>=3	0	0	0

CTCAE = Common Terminology Criteria for Adverse Events. Adverse events of interest are presented in pre-defined event classes; each class is based on pre-specified preferred terms.
A subject with two or more adverse events in the same event class (or with same package insert term/preferred term) is counted only once for that event class (or package insert term/preferred term).
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Adverse event terms are coded using Medical Dictionary for Regulatory Activities (MedDRA) version 17.1.
This table is based on adverse events data as available. Study 207 did not record laboratory abnormalities into adverse events data.

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付録 2.7.4-19
Japanese and Non-Japanese
Treatment-Emergent Adverse Events of Interest Specified in Japan by CTCAE Grade
Eribulin Treated Safety Population

Event class Package insert term or preferred term Preferred term CTCAE grade	日本人 Study 217 (N=51) n(%)	外国人 Studies 207+309 (N=353) n(%)	全体 Studies 217+207+309 (N=404) n(%)
感染症			
腹膜炎	0	4 (1.1)	4 (1.0)
1	0	0	0
2	0	1 (0.3)	1 (0.2)
3	0	3 (0.8)	3 (0.7)
4	0	0	0
5	0	0	0
>=3	0	3 (0.8)	3 (0.7)
腹膜炎	0	2 (0.6)	2 (0.5)
1	0	0	0
2	0	1 (0.3)	1 (0.2)
3	0	1 (0.3)	1 (0.2)
4	0	0	0
5	0	0	0
>=3	0	1 (0.3)	1 (0.2)

CTCAE = Common Terminology Criteria for Adverse Events. Adverse events of interest are presented in pre-defined event classes; each class is based on pre-specified preferred terms.
A subject with two or more adverse events in the same event class (or with same package insert term/preferred term) is counted only once for that event class (or package insert term/preferred term).
A subject is counted once by the highest non-missing CTCAE grade as applicable for preferred term and event class respectively.
Adverse event terms are coded using Medical Dictionary for Regulatory Activities (MedDRA) version 17.1.
This table is based on adverse events data as available. Study 207 did not record laboratory abnormalities into adverse events data.

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付録 2.7.4-19
Japanese and Non-Japanese
Treatment-Emergent Adverse Events of Interest Specified in Japan by CTCAE Grade
Eribulin Treated Safety Population

Event class Package insert term or preferred term Preferred term CTCAE grade	日本人 Study 217 (N=51) n(%)	外国人 Studies 207+309 (N=353) n(%)	全体 Studies 217+207+309 (N=404) n(%)
感染症			
細菌性腹膜炎	0	2 (0.6)	2 (0.5)
1	0	0	0
2	0	0	0
3	0	2 (0.6)	2 (0.5)
4	0	0	0
5	0	0	0
>=3	0	2 (0.6)	2 (0.5)
蜂巣炎	0	4 (1.1)	4 (1.0)
1	0	2 (0.6)	2 (0.5)
2	0	2 (0.6)	2 (0.5)
3	0	0	0
4	0	0	0
5	0	0	0
>=3	0	0	0

CTCAE = Common Terminology Criteria for Adverse Events. Adverse events of interest are presented in pre-defined event classes; each class is based on pre-specified preferred terms.
A subject with two or more adverse events in the same event class (or with same package insert term/preferred term) is counted only once for that event class (or package insert term/preferred term).
A subject is counted once by the highest non-missing CTCAE grade as applicable for preferred term and event class respectively.
Adverse event terms are coded using Medical Dictionary for Regulatory Activities (MedDRA) version 17.1.
This table is based on adverse events data as available. Study 207 did not record laboratory abnormalities into adverse events data.

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付録 2.7.4-19
Japanese and Non-Japanese
Treatment-Emergent Adverse Events of Interest Specified in Japan by CTCAE Grade
Eribulin Treated Safety Population

Event class Package insert term or preferred term Preferred term CTCAE grade	日本人 Study 217 (N=51) n(%)	外国人 Studies 207+309 (N=353) n(%)	全体 Studies 217+207+309 (N=404) n(%)
感染症			
蜂巣炎	0	4 (1.1)	4 (1.0)
1	0	2 (0.6)	2 (0.5)
2	0	2 (0.6)	2 (0.5)
3	0	0	0
4	0	0	0
5	0	0	0
>=3	0	0	0
毛包炎	1 (2.0)	3 (0.8)	4 (1.0)
1	1 (2.0)	2 (0.6)	3 (0.7)
2	0	1 (0.3)	1 (0.2)
3	0	0	0
4	0	0	0
5	0	0	0
>=3	0	0	0

CTCAE = Common Terminology Criteria for Adverse Events. Adverse events of interest are presented in pre-defined event classes; each class is based on pre-specified preferred terms.
A subject with two or more adverse events in the same event class (or with same package insert term/preferred term) is counted only once for that event class (or package insert term/preferred term).
A subject is counted once by the highest non-missing CTCAE grade as applicable for preferred term and event class respectively.
Adverse event terms are coded using Medical Dictionary for Regulatory Activities (MedDRA) version 17.1.
This table is based on adverse events data as available. Study 207 did not record laboratory abnormalities into adverse events data.

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付録 2.7.4-19
Japanese and Non-Japanese
Treatment-Emergent Adverse Events of Interest Specified in Japan by CTCAE Grade
Eribulin Treated Safety Population

Event class Package insert term or preferred term Preferred term CTCAE grade	日本人 Study 217 (N=51) n(%)	外国人 Studies 207+309 (N=353) n(%)	全体 Studies 217+207+309 (N=404) n(%)
感染症			
毛包炎	1 (2.0)	3 (0.8)	4 (1.0)
1	1 (2.0)	2 (0.6)	3 (0.7)
2	0	1 (0.3)	1 (0.2)
3	0	0	0
4	0	0	0
5	0	0	0
>=3	0	0	0
膀胱炎	2 (3.9)	7 (2.0)	9 (2.2)
1	0	0	0
2	2 (3.9)	4 (1.1)	6 (1.5)
3	0	3 (0.8)	3 (0.7)
4	0	0	0
5	0	0	0
>=3	0	3 (0.8)	3 (0.7)

CTCAE = Common Terminology Criteria for Adverse Events. Adverse events of interest are presented in pre-defined event classes; each class is based on pre-specified preferred terms.
A subject with two or more adverse events in the same event class (or with same package insert term/preferred term) is counted only once for that event class (or package insert term/preferred term).
A subject is counted once by the highest non-missing CTCAE grade as applicable for preferred term and event class respectively.
Adverse event terms are coded using Medical Dictionary for Regulatory Activities (MedDRA) version 17.1.
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付録 2.7.4-19
Japanese and Non-Japanese
Treatment-Emergent Adverse Events of Interest Specified in Japan by CTCAE Grade
Eribulin Treated Safety Population

Event class Package insert term or preferred term Preferred term CTCAE grade	日本人 Study 217 (N=51) n(%)	外国人 Studies 207+309 (N=353) n(%)	全体 Studies 217+207+309 (N=404) n(%)
感染症			
膀胱炎	2 (3.9)	7 (2.0)	9 (2.2)
1	0	0	0
2	2 (3.9)	4 (1.1)	6 (1.5)
3	0	3 (0.8)	3 (0.7)
4	0	0	0
5	0	0	0
>=3	0	3 (0.8)	3 (0.7)
単径部感染	0	1 (0.3)	1 (0.2)
1	0	1 (0.3)	1 (0.2)
2	0	0	0
3	0	0	0
4	0	0	0
5	0	0	0
>=3	0	0	0

CTCAE = Common Terminology Criteria for Adverse Events. Adverse events of interest are presented in pre-defined event classes; each class is based on pre-specified preferred terms.
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Adverse event terms are coded using Medical Dictionary for Regulatory Activities (MedDRA) version 17.1.
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Program: V:¥projects¥e7389¥iss309¥csr¥dev¥pg¥tables¥T_2_7_4_19.sas 18JUN201513:38

付録 2.7.4-19
Japanese and Non-Japanese
Treatment-Emergent Adverse Events of Interest Specified in Japan by CTCAE Grade
Eribulin Treated Safety Population

Event class Package insert term or preferred term Preferred term CTCAE grade	日本人 Study 217 (N=51) n(%)	外国人 Studies 207+309 (N=353) n(%)	全体 Studies 217+207+309 (N=404) n(%)
感染症			
単径部感染	0	1 (0.3)	1 (0.2)
1	0	1 (0.3)	1 (0.2)
2	0	0	0
3	0	0	0
4	0	0	0
5	0	0	0
>=3	0	0	0
末梢神経障害			
Any preferred term	19 (37.3)	116 (32.9)	135 (33.4)
1	12 (23.5)	69 (19.5)	81 (20.0)
2	7 (13.7)	32 (9.1)	39 (9.7)
3	0	15 (4.2)	15 (3.7)
4	0	0	0
5	0	0	0
>=3	0	15 (4.2)	15 (3.7)

CTCAE = Common Terminology Criteria for Adverse Events. Adverse events of interest are presented in pre-defined event classes; each class is based on pre-specified preferred terms.
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付録 2.7.4-19
Japanese and Non-Japanese
Treatment-Emergent Adverse Events of Interest Specified in Japan by CTCAE Grade
Eribulin Treated Safety Population

Event class Package insert term or preferred term Preferred term CTCAE grade	日本人 Study 217 (N=51) n(%)	外国人 Studies 207+309 (N=353) n(%)	全体 Studies 217+207+309 (N=404) n(%)
末梢神経障害			
錯感覚	0	20 (5.7)	20 (5.0)
1	0	17 (4.8)	17 (4.2)
2	0	2 (0.6)	2 (0.5)
3	0	1 (0.3)	1 (0.2)
4	0	0	0
5	0	0	0
>=3	0	1 (0.3)	1 (0.2)
錯感覚	0	20 (5.7)	20 (5.0)
1	0	17 (4.8)	17 (4.2)
2	0	2 (0.6)	2 (0.5)
3	0	1 (0.3)	1 (0.2)
4	0	0	0
5	0	0	0
>=3	0	1 (0.3)	1 (0.2)

CTCAE = Common Terminology Criteria for Adverse Events. Adverse events of interest are presented in pre-defined event classes; each class is based on pre-specified preferred terms.
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付録 2.7.4-19
Japanese and Non-Japanese
Treatment-Emergent Adverse Events of Interest Specified in Japan by CTCAE Grade
Eribulin Treated Safety Population

Event class Package insert term or preferred term Preferred term CTCAE grade	日本人 Study 217 (N=51) n(%)	外国人 Studies 207+309 (N=353) n(%)	全体 Studies 217+207+309 (N=404) n(%)
末梢神経障害			
神経痛	2 (3.9)	6 (1.7)	8 (2.0)
1	1 (2.0)	3 (0.8)	4 (1.0)
2	1 (2.0)	3 (0.8)	4 (1.0)
3	0	0	0
4	0	0	0
5	0	0	0
>=3	0	0	0
神経痛	0	4 (1.1)	4 (1.0)
1	0	3 (0.8)	3 (0.7)
2	0	1 (0.3)	1 (0.2)
3	0	0	0
4	0	0	0
5	0	0	0
>=3	0	0	0

CTCAE = Common Terminology Criteria for Adverse Events. Adverse events of interest are presented in pre-defined event classes; each class is based on pre-specified preferred terms.
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付録 2.7.4-19
Japanese and Non-Japanese
Treatment-Emergent Adverse Events of Interest Specified in Japan by CTCAE Grade
Eribulin Treated Safety Population

Event class Package insert term or preferred term Preferred term CTCAE grade	日本人 Study 217 (N=51) n(%)	外国人 Studies 207+309 (N=353) n(%)	全体 Studies 217+207+309 (N=404) n(%)
末梢神経障害			
ヘルペス後神経痛	1 (2.0)	0	1 (0.2)
1	1 (2.0)	0	1 (0.2)
2	0	0	0
3	0	0	0
4	0	0	0
5	0	0	0
>=3	0	0	0
坐骨神経痛	1 (2.0)	2 (0.6)	3 (0.7)
1	0	0	0
2	1 (2.0)	2 (0.6)	3 (0.7)
3	0	0	0
4	0	0	0
5	0	0	0
>=3	0	0	0

CTCAE = Common Terminology Criteria for Adverse Events. Adverse events of interest are presented in pre-defined event classes; each class is based on pre-specified preferred terms.
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付録 2.7.4-19
Japanese and Non-Japanese
Treatment-Emergent Adverse Events of Interest Specified in Japan by CTCAE Grade
Eribulin Treated Safety Population

Event class Package insert term or preferred term Preferred term CTCAE grade	日本人 Study 217 (N=51) n(%)	外国人 Studies 207+309 (N=353) n(%)	全体 Studies 217+207+309 (N=404) n(%)
末梢神経障害			
多発ニューロパチー	0	1 (0.3)	1 (0.2)
1	0	0	0
2	0	0	0
3	0	1 (0.3)	1 (0.2)
4	0	0	0
5	0	0	0
>=3	0	1 (0.3)	1 (0.2)
多発ニューロパチー	0	1 (0.3)	1 (0.2)
1	0	0	0
2	0	0	0
3	0	1 (0.3)	1 (0.2)
4	0	0	0
5	0	0	0
>=3	0	1 (0.3)	1 (0.2)

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付録 2.7.4-19
Japanese and Non-Japanese
Treatment-Emergent Adverse Events of Interest Specified in Japan by CTCAE Grade
Eribulin Treated Safety Population

Event class Package insert term or preferred term Preferred term CTCAE grade	日本人 Study 217 (N=51) n(%)	外国人 Studies 207+309 (N=353) n(%)	全体 Studies 217+207+309 (N=404) n(%)
末梢神経障害			
末梢性ニューロパチー	16 (31.4)	1 (0.3)	17 (4.2)
1	11 (21.6)	1 (0.3)	12 (3.0)
2	5 (9.8)	0	5 (1.2)
3	0	0	0
4	0	0	0
5	0	0	0
>=3	0	0	0
末梢性ニューロパチー	16 (31.4)	1 (0.3)	17 (4.2)
1	11 (21.6)	1 (0.3)	12 (3.0)
2	5 (9.8)	0	5 (1.2)
3	0	0	0
4	0	0	0
5	0	0	0
>=3	0	0	0

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付録 2.7.4-19
Japanese and Non-Japanese
Treatment-Emergent Adverse Events of Interest Specified in Japan by CTCAE Grade
Eribulin Treated Safety Population

Event class Package insert term or preferred term Preferred term CTCAE grade	日本人 Study 217 (N=51) n(%)	外国人 Studies 207+309 (N=353) n(%)	全体 Studies 217+207+309 (N=404) n(%)
末梢神経障害			
末梢性運動ニューロパチー	0	16 (4.5)	16 (4.0)
1	0	6 (1.7)	6 (1.5)
2	0	3 (0.8)	3 (0.7)
3	0	7 (2.0)	7 (1.7)
4	0	0	0
5	0	0	0
>=3	0	7 (2.0)	7 (1.7)
末梢性運動ニューロパチー	0	16 (4.5)	16 (4.0)
1	0	6 (1.7)	6 (1.5)
2	0	3 (0.8)	3 (0.7)
3	0	7 (2.0)	7 (1.7)
4	0	0	0
5	0	0	0
>=3	0	7 (2.0)	7 (1.7)

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付録 2.7.4-19
Japanese and Non-Japanese
Treatment-Emergent Adverse Events of Interest Specified in Japan by CTCAE Grade
Eribulin Treated Safety Population

Event class Package insert term or preferred term Preferred term CTCAE grade	日本人 Study 217 (N=51) n(%)	外国人 Studies 207+309 (N=353) n(%)	全体 Studies 217+207+309 (N=404) n(%)
末梢神経障害			
末梢性感覚ニューロパチー	3 (5.9)	92 (26.1)	95 (23.5)
1	2 (3.9)	51 (14.4)	53 (13.1)
2	1 (2.0)	33 (9.3)	34 (8.4)
3	0	8 (2.3)	8 (2.0)
4	0	0	0
5	0	0	0
>=3	0	8 (2.3)	8 (2.0)
末梢性感覚ニューロパチー	3 (5.9)	92 (26.1)	95 (23.5)
1	2 (3.9)	51 (14.4)	53 (13.1)
2	1 (2.0)	33 (9.3)	34 (8.4)
3	0	8 (2.3)	8 (2.0)
4	0	0	0
5	0	0	0
>=3	0	8 (2.3)	8 (2.0)

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付録 2.7.4-19
Japanese and Non-Japanese
Treatment-Emergent Adverse Events of Interest Specified in Japan by CTCAE Grade
Eribulin Treated Safety Population

Event class Package insert term or preferred term Preferred term CTCAE grade	日本人 Study 217 (N=51) n(%)	外国人 Studies 207+309 (N=353) n(%)	全体 Studies 217+207+309 (N=404) n(%)
末梢神経障害			
末梢性感覚運動ニューロパチー	0	2 (0.6)	2 (0.5)
1	0	2 (0.6)	2 (0.5)
2	0	0	0
3	0	0	0
4	0	0	0
5	0	0	0
>=3	0	0	0
末梢性感覚運動ニューロパチー	0	2 (0.6)	2 (0.5)
1	0	2 (0.6)	2 (0.5)
2	0	0	0
3	0	0	0
4	0	0	0
5	0	0	0
>=3	0	0	0

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付録 2.7.4-19
Japanese and Non-Japanese
Treatment-Emergent Adverse Events of Interest Specified in Japan by CTCAE Grade
Eribulin Treated Safety Population

Event class Package insert term or preferred term Preferred term CTCAE grade	日本人 Study 217 (N=51) n(%)	外国人 Studies 207+309 (N=353) n(%)	全体 Studies 217+207+309 (N=404) n(%)
肝機能障害			
Any preferred term	6 (11.8)	4 (1.1)	10 (2.5)
1	5 (9.8)	1 (0.3)	6 (1.5)
2	1 (2.0)	2 (0.6)	3 (0.7)
3	0	0	0
4	0	1 (0.3)	1 (0.2)
5	0	0	0
>=3	0	1 (0.3)	1 (0.2)
トランスアミナーゼ上昇	0	1 (0.3)	1 (0.2)
1	0	0	0
2	0	1 (0.3)	1 (0.2)
3	0	0	0
4	0	0	0
5	0	0	0
>=3	0	0	0

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付録 2.7.4-19
Japanese and Non-Japanese
Treatment-Emergent Adverse Events of Interest Specified in Japan by CTCAE Grade
Eribulin Treated Safety Population

Event class Package insert term or preferred term Preferred term CTCAE grade	日本人 Study 217 (N=51) n(%)	外国人 Studies 207+309 (N=353) n(%)	全体 Studies 217+207+309 (N=404) n(%)
肝機能障害			
トランスアミナーゼ上昇	0	1 (0.3)	1 (0.2)
1	0	0	0
2	0	1 (0.3)	1 (0.2)
3	0	0	0
4	0	0	0
5	0	0	0
>=3	0	0	0
黄疸	0	2 (0.6)	2 (0.5)
1	0	1 (0.3)	1 (0.2)
2	0	1 (0.3)	1 (0.2)
3	0	0	0
4	0	0	0
5	0	0	0
>=3	0	0	0

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付録 2.7.4-19
Japanese and Non-Japanese
Treatment-Emergent Adverse Events of Interest Specified in Japan by CTCAE Grade
Eribulin Treated Safety Population

Event class Package insert term or preferred term Preferred term CTCAE grade	日本人 Study 217 (N=51) n(%)	外国人 Studies 207+309 (N=353) n(%)	全体 Studies 217+207+309 (N=404) n(%)
肝機能障害			
黄疸	0	1 (0.3)	1 (0.2)
1	0	0	0
2	0	1 (0.3)	1 (0.2)
3	0	0	0
4	0	0	0
5	0	0	0
>=3	0	0	0
黄疸眼	0	1 (0.3)	1 (0.2)
1	0	1 (0.3)	1 (0.2)
2	0	0	0
3	0	0	0
4	0	0	0
5	0	0	0
>=3	0	0	0

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付録 2.7.4-19
Japanese and Non-Japanese
Treatment-Emergent Adverse Events of Interest Specified in Japan by CTCAE Grade
Eribulin Treated Safety Population

Event class Package insert term or preferred term Preferred term CTCAE grade	日本人 Study 217 (N=51) n(%)	外国人 Studies 207+309 (N=353) n(%)	全体 Studies 217+207+309 (N=404) n(%)
肝機能障害			
肝機能異常	5 (9.8)	0	5 (1.2)
1	4 (7.8)	0	4 (1.0)
2	1 (2.0)	0	1 (0.2)
3	0	0	0
4	0	0	0
5	0	0	0
>=3	0	0	0
肝機能異常	5 (9.8)	0	5 (1.2)
1	4 (7.8)	0	4 (1.0)
2	1 (2.0)	0	1 (0.2)
3	0	0	0
4	0	0	0
5	0	0	0
>=3	0	0	0

CTCAE = Common Terminology Criteria for Adverse Events. Adverse events of interest are presented in pre-defined event classes; each class is based on pre-specified preferred terms.
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付録 2.7.4-19
Japanese and Non-Japanese
Treatment-Emergent Adverse Events of Interest Specified in Japan by CTCAE Grade
Eribulin Treated Safety Population

Event class Package insert term or preferred term Preferred term CTCAE grade	日本人 Study 217 (N=51) n(%)	外国人 Studies 207+309 (N=353) n(%)	全体 Studies 217+207+309 (N=404) n(%)
肝機能障害			
肝機能検査異常	1 (2.0)	0	1 (0.2)
1	1 (2.0)	0	1 (0.2)
2	0	0	0
3	0	0	0
4	0	0	0
5	0	0	0
>=3	0	0	0
肝機能検査異常	1 (2.0)	0	1 (0.2)
1	1 (2.0)	0	1 (0.2)
2	0	0	0
3	0	0	0
4	0	0	0
5	0	0	0
>=3	0	0	0

CTCAE = Common Terminology Criteria for Adverse Events. Adverse events of interest are presented in pre-defined event classes; each class is based on pre-specified preferred terms.
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A subject is counted once by the highest non-missing CTCAE grade as applicable for preferred term and event class respectively.
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付録 2.7.4-19
Japanese and Non-Japanese
Treatment-Emergent Adverse Events of Interest Specified in Japan by CTCAE Grade
Eribulin Treated Safety Population

Event class Package insert term or preferred term Preferred term CTCAE grade	日本人 Study 217 (N=51) n(%)	外国人 Studies 207+309 (N=353) n(%)	全体 Studies 217+207+309 (N=404) n(%)
肝機能障害			
肝細胞損傷	0	1 (0.3)	1 (0.2)
1	0	0	0
2	0	1 (0.3)	1 (0.2)
3	0	0	0
4	0	0	0
5	0	0	0
>=3	0	0	0
肝細胞損傷	0	1 (0.3)	1 (0.2)
1	0	0	0
2	0	1 (0.3)	1 (0.2)
3	0	0	0
4	0	0	0
5	0	0	0
>=3	0	0	0

CTCAE = Common Terminology Criteria for Adverse Events. Adverse events of interest are presented in pre-defined event classes; each class is based on pre-specified preferred terms.
A subject with two or more adverse events in the same event class (or with same package insert term/preferred term) is counted only once for that event class (or package insert term/preferred term).
A subject is counted once by the highest non-missing CTCAE grade as applicable for preferred term and event class respectively.
Adverse event terms are coded using Medical Dictionary for Regulatory Activities (MedDRA) version 17.1.
This table is based on adverse events data as available. Study 207 did not record laboratory abnormalities into adverse events data.

Program: V:¥projects¥e7389¥iss309¥csr¥dev¥pg¥tables¥T_2_7_4_19.sas 18JUN201513:38

付録 2.7.4-19
Japanese and Non-Japanese
Treatment-Emergent Adverse Events of Interest Specified in Japan by CTCAE Grade
Eribulin Treated Safety Population

Event class Package insert term or preferred term Preferred term CTCAE grade	日本人 Study 217 (N=51) n(%)	外国人 Studies 207+309 (N=353) n(%)	全体 Studies 217+207+309 (N=404) n(%)
肝機能障害			
肝毒性	0	1 (0.3)	1 (0.2)
1	0	0	0
2	0	0	0
3	0	0	0
4	0	1 (0.3)	1 (0.2)
5	0	0	0
>=3	0	1 (0.3)	1 (0.2)
肝毒性	0	1 (0.3)	1 (0.2)
1	0	0	0
2	0	0	0
3	0	0	0
4	0	1 (0.3)	1 (0.2)
5	0	0	0
>=3	0	1 (0.3)	1 (0.2)

CTCAE = Common Terminology Criteria for Adverse Events. Adverse events of interest are presented in pre-defined event classes; each class is based on pre-specified preferred terms.
A subject with two or more adverse events in the same event class (or with same package insert term/preferred term) is counted only once for that event class (or package insert term/preferred term).
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Adverse event terms are coded using Medical Dictionary for Regulatory Activities (MedDRA) version 17.1.
This table is based on adverse events data as available. Study 207 did not record laboratory abnormalities into adverse events data.

Program: V:¥projects¥e7389¥iss309¥csr¥dev¥pg¥tables¥T_2_7_4_19.sas 18JUN201513:38

付録 2.7.4-19
Japanese and Non-Japanese
Treatment-Emergent Adverse Events of Interest Specified in Japan by CTCAE Grade
Eribulin Treated Safety Population

Event class Package insert term or preferred term Preferred term CTCAE grade	日本人 Study 217 (N=51) n(%)	外国人 Studies 207+309 (N=353) n(%)	全体 Studies 217+207+309 (N=404) n(%)
間質性肺炎			
Any preferred term	1 (2.0)	0	1 (0.2)
1	1 (2.0)	0	1 (0.2)
2	0	0	0
3	0	0	0
4	0	0	0
5	0	0	0
>=3	0	0	0
間質性肺炎	1 (2.0)	0	1 (0.2)
1	1 (2.0)	0	1 (0.2)
2	0	0	0
3	0	0	0
4	0	0	0
5	0	0	0
>=3	0	0	0

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A subject with two or more adverse events in the same event class (or with same package insert term/preferred term) is counted only once for that event class (or package insert term/preferred term).
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付録 2.7.4-19
Japanese and Non-Japanese
Treatment-Emergent Adverse Events of Interest Specified in Japan by CTCAE Grade
Eribulin Treated Safety Population

Event class Package insert term or preferred term Preferred term CTCAE grade	日本人 Study 217 (N=51) n(%)	外国人 Studies 207+309 (N=353) n(%)	全体 Studies 217+207+309 (N=404) n(%)
間質性肺炎			
間質性肺疾患	1 (2.0)	0	1 (0.2)
1	1 (2.0)	0	1 (0.2)
2	0	0	0
3	0	0	0
4	0	0	0
5	0	0	0
>=3	0	0	0
無力症・疲労・倦怠感			
Any preferred term	27 (52.9)	228 (64.6)	255 (63.1)
1	26 (51.0)	101 (28.6)	127 (31.4)
2	1 (2.0)	102 (28.9)	103 (25.5)
3	0	24 (6.8)	24 (5.9)
4	0	1 (0.3)	1 (0.2)
5	0	0	0
>=3	0	25 (7.1)	25 (6.2)

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Adverse event terms are coded using Medical Dictionary for Regulatory Activities (MedDRA) version 17.1.
This table is based on adverse events data as available. Study 207 did not record laboratory abnormalities into adverse events data.

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付録 2.7.4-19
Japanese and Non-Japanese
Treatment-Emergent Adverse Events of Interest Specified in Japan by CTCAE Grade
Eribulin Treated Safety Population

Event class Package insert term or preferred term Preferred term CTCAE grade	日本人 Study 217 (N=51) n(%)	外国人 Studies 207+309 (N=353) n(%)	全体 Studies 217+207+309 (N=404) n(%)
無力症・疲労・倦怠感			
倦怠感	20 (39.2)	2 (0.6)	22 (5.4)
1	19 (37.3)	0	19 (4.7)
2	1 (2.0)	2 (0.6)	3 (0.7)
3	0	0	0
4	0	0	0
5	0	0	0
>=3	0	0	0
倦怠感	20 (39.2)	2 (0.6)	22 (5.4)
1	19 (37.3)	0	19 (4.7)
2	1 (2.0)	2 (0.6)	3 (0.7)
3	0	0	0
4	0	0	0
5	0	0	0
>=3	0	0	0

CTCAE = Common Terminology Criteria for Adverse Events. Adverse events of interest are presented in pre-defined event classes; each class is based on pre-specified preferred terms.
A subject with two or more adverse events in the same event class (or with same package insert term/preferred term) is counted only once for that event class (or package insert term/preferred term).
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Adverse event terms are coded using Medical Dictionary for Regulatory Activities (MedDRA) version 17.1.
This table is based on adverse events data as available. Study 207 did not record laboratory abnormalities into adverse events data.

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付録 2.7.4-19
Japanese and Non-Japanese
Treatment-Emergent Adverse Events of Interest Specified in Japan by CTCAE Grade
Eribulin Treated Safety Population

Event class Package insert term or preferred term Preferred term CTCAE grade	日本人 Study 217 (N=51) n(%)	外国人 Studies 207+309 (N=353) n(%)	全体 Studies 217+207+309 (N=404) n(%)
無力症・疲労・倦怠感			
疲労	9 (17.6)	188 (53.3)	197 (48.8)
1	9 (17.6)	92 (26.1)	101 (25.0)
2	0	75 (21.2)	75 (18.6)
3	0	21 (5.9)	21 (5.2)
4	0	0	0
5	0	0	0
>=3	0	21 (5.9)	21 (5.2)
疲労	9 (17.6)	188 (53.3)	197 (48.8)
1	9 (17.6)	92 (26.1)	101 (25.0)
2	0	75 (21.2)	75 (18.6)
3	0	21 (5.9)	21 (5.2)
4	0	0	0
5	0	0	0
>=3	0	21 (5.9)	21 (5.2)

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Adverse event terms are coded using Medical Dictionary for Regulatory Activities (MedDRA) version 17.1.
This table is based on adverse events data as available. Study 207 did not record laboratory abnormalities into adverse events data.

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付録 2.7.4-19
Japanese and Non-Japanese
Treatment-Emergent Adverse Events of Interest Specified in Japan by CTCAE Grade
Eribulin Treated Safety Population

Event class Package insert term or preferred term Preferred term CTCAE grade	日本人 Study 217 (N=51) n(%)	外国人 Studies 207+309 (N=353) n(%)	全体 Studies 217+207+309 (N=404) n(%)
無力症・疲労・倦怠感			
無力症	0	47 (13.3)	47 (11.6)
1	0	15 (4.2)	15 (3.7)
2	0	28 (7.9)	28 (6.9)
3	0	3 (0.8)	3 (0.7)
4	0	1 (0.3)	1 (0.2)
5	0	0	0
>=3	0	4 (1.1)	4 (1.0)
無力症	0	47 (13.3)	47 (11.6)
1	0	15 (4.2)	15 (3.7)
2	0	28 (7.9)	28 (6.9)
3	0	3 (0.8)	3 (0.7)
4	0	1 (0.3)	1 (0.2)
5	0	0	0
>=3	0	4 (1.1)	4 (1.0)

CTCAE = Common Terminology Criteria for Adverse Events. Adverse events of interest are presented in pre-defined event classes; each class is based on pre-specified preferred terms.
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Adverse event terms are coded using Medical Dictionary for Regulatory Activities (MedDRA) version 17.1.
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付録 2.7.4-19
Japanese and Non-Japanese
Treatment-Emergent Adverse Events of Interest Specified in Japan by CTCAE Grade
Eribulin Treated Safety Population

Event class Package insert term or preferred term Preferred term CTCAE grade	日本人 Study 217 (N=51) n(%)	外国人 Studies 207+309 (N=353) n(%)	全体 Studies 217+207+309 (N=404) n(%)
味覚異常			
Any preferred term	12 (23.5)	37 (10.5)	49 (12.1)
1	11 (21.6)	33 (9.3)	44 (10.9)
2	1 (2.0)	4 (1.1)	5 (1.2)
味覚異常	12 (23.5)	37 (10.5)	49 (12.1)
1	11 (21.6)	33 (9.3)	44 (10.9)
2	1 (2.0)	4 (1.1)	5 (1.2)

CTCAE = Common Terminology Criteria for Adverse Events. Adverse events of interest are presented in pre-defined event classes; each class is based on pre-specified preferred terms.
A subject with two or more adverse events in the same event class (or with same package insert term/preferred term) is counted only once for that event class (or package insert term/preferred term).
A subject is counted once by the highest non-missing CTCAE grade as applicable for preferred term and event class respectively.
Adverse event terms are coded using Medical Dictionary for Regulatory Activities (MedDRA) version 17.1.
This table is based on adverse events data as available. Study 207 did not record laboratory abnormalities into adverse events data.

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付録 2.7.4-19
Japanese and Non-Japanese
Treatment-Emergent Adverse Events of Interest Specified in Japan by CTCAE Grade
Eribulin Treated Safety Population

Event class Package insert term or preferred term Preferred term CTCAE grade	日本人 Study 217 (N=51) n(%)	外国人 Studies 207+309 (N=353) n(%)	全体 Studies 217+207+309 (N=404) n(%)
味覚異常			
味覚異常	12 (23.5)	37 (10.5)	49 (12.1)
1	11 (21.6)	33 (9.3)	44 (10.9)
2	1 (2.0)	4 (1.1)	5 (1.2)

CTCAE = Common Terminology Criteria for Adverse Events. Adverse events of interest are presented in pre-defined event classes; each class is based on pre-specified preferred terms.
A subject with two or more adverse events in the same event class (or with same package insert term/preferred term) is counted only once for that event class (or package insert term/preferred term).
A subject is counted once by the highest non-missing CTCAE grade as applicable for preferred term and event class respectively.
Adverse event terms are coded using Medical Dictionary for Regulatory Activities (MedDRA) version 17.1.
This table is based on adverse events data as available. Study 207 did not record laboratory abnormalities into adverse events data.

Program: V:¥projects¥e7389¥iss309¥csr¥dev¥pg¥tables¥T_2_7_4_19.sas 18JUN201513:38

付録 2.7.4-20
Japanese and Non-Japanese (Excluding Study 207)/骨髄抑制, 肝機能障害
Treatment-Emergent Adverse Events of Interest Specified in Japan by CTCAE Grade
Eribulin Treated Safety Population

Event class Package insert term or preferred term Preferred term CTCAE grade	日本人 Study 217 (N=51) n(%)	外国人 Study 309 (N=226) n(%)	全体 Studies 217+309 (N=277) n(%)
骨髄抑制			
Any preferred term	51 (100.0)	148 (65.5)	199 (71.8)
1	0	5 (2.2)	5 (1.8)
2	3 (5.9)	37 (16.4)	40 (14.4)
3	9 (17.6)	59 (26.1)	68 (24.5)
4	39 (76.5)	47 (20.8)	86 (31.0)
5	0	0	0
>=3	48 (94.1)	106 (46.9)	154 (55.6)
ヘマトクリット減少	0	1 (0.4)	1 (0.4)
1	0	1 (0.4)	1 (0.4)
2	0	0	0
3	0	0	0
4	0	0	0
5	0	0	0
>=3	0	0	0

CTCAE = Common Terminology Criteria for Adverse Events. Adverse events of interest are presented in pre-defined event classes; each class is based on pre-specified preferred terms.
A subject with two or more adverse events in the same event class (or with same package insert term/preferred term) is counted only once for that event class (or package insert term/preferred term).
A subject is counted once by the highest non-missing CTCAE grade as applicable for preferred term and event class respectively.
Adverse event terms are coded using Medical Dictionary for Regulatory Activities (MedDRA) version 17.1.

Program: V:¥projects¥e7389¥iss309¥csr¥dev¥pg¥tables¥T_2_7_4_20.sas 18JUN201513:38

付録 2.7.4-20
Japanese and Non-Japanese (Excluding Study 207)/骨髄抑制, 肝機能障害
Treatment-Emergent Adverse Events of Interest Specified in Japan by CTCAE Grade
Eribulin Treated Safety Population

Event class Package insert term or preferred term Preferred term CTCAE grade	日本人 Study 217 (N=51) n(%)	外国人 Study 309 (N=226) n(%)	全体 Studies 217+309 (N=277) n(%)
骨髄抑制			
ヘマトクリット減少	0	1 (0.4)	1 (0.4)
1	0	1 (0.4)	1 (0.4)
2	0	0	0
3	0	0	0
4	0	0	0
5	0	0	0
>=3	0	0	0
ヘモグロビン減少	2 (3.9)	7 (3.1)	9 (3.2)
1	2 (3.9)	2 (0.9)	4 (1.4)
2	0	5 (2.2)	5 (1.8)
3	0	0	0
4	0	0	0
5	0	0	0
>=3	0	0	0

CTCAE = Common Terminology Criteria for Adverse Events. Adverse events of interest are presented in pre-defined event classes; each class is based on pre-specified preferred terms.
A subject with two or more adverse events in the same event class (or with same package insert term/preferred term) is counted only once for that event class (or package insert term/preferred term).
A subject is counted once by the highest non-missing CTCAE grade as applicable for preferred term and event class respectively.
Adverse event terms are coded using Medical Dictionary for Regulatory Activities (MedDRA) version 17.1.

Program: V:¥projects¥e7389¥iss309¥csr¥dev¥pg¥tables¥T_2_7_4_20.sas 18JUN201513:38

付録 2.7.4-20

Japanese and Non-Japanese (Excluding Study 207)/骨髄抑制, 肝機能障害

Treatment-Emergent Adverse Events of Interest Specified in Japan by CTCAE Grade

Eribulin Treated Safety Population

Event class Package insert term or preferred term Preferred term CTCAE grade	日本人 Study 217 (N=51) n(%)	外国人 Study 309 (N=226) n(%)	全体 Studies 217+309 (N=277) n(%)
骨髄抑制			
ヘモグロビン減少	2 (3.9)	7 (3.1)	9 (3.2)
1	2 (3.9)	2 (0.9)	4 (1.4)
2	0	5 (2.2)	5 (1.8)
3	0	0	0
4	0	0	0
5	0	0	0
>=3	0	0	0
リンパ球減少	40 (78.4)	6 (2.7)	46 (16.6)
1	1 (2.0)	2 (0.9)	3 (1.1)
2	22 (43.1)	1 (0.4)	23 (8.3)
3	15 (29.4)	2 (0.9)	17 (6.1)
4	2 (3.9)	1 (0.4)	3 (1.1)
5	0	0	0
>=3	17 (33.3)	3 (1.3)	20 (7.2)

CTCAE = Common Terminology Criteria for Adverse Events. Adverse events of interest are presented in pre-defined event classes; each class is based on pre-specified preferred terms.

A subject with two or more adverse events in the same event class (or with same package insert term/preferred term) is counted only once for that event class (or package insert term/preferred term).

A subject is counted once by the highest non-missing CTCAE grade as applicable for preferred term and event class respectively.

Adverse event terms are coded using Medical Dictionary for Regulatory Activities (MedDRA) version 17.1.

Program: V:¥projects¥e7389¥iss309¥csr¥dev¥pg¥tables¥T_2_7_4_20.sas 18JUN201513:38

付録 2.7.4-20
Japanese and Non-Japanese (Excluding Study 207)/骨髄抑制, 肝機能障害
Treatment-Emergent Adverse Events of Interest Specified in Japan by CTCAE Grade
Eribulin Treated Safety Population

Event class Package insert term or preferred term Preferred term CTCAE grade	日本人 Study 217 (N=51) n(%)	外国人 Study 309 (N=226) n(%)	全体 Studies 217+309 (N=277) n(%)
骨髄抑制			
リンパ球数減少	0	3 (1.3)	3 (1.1)
1	0	2 (0.9)	2 (0.7)
2	0	1 (0.4)	1 (0.4)
3	0	0	0
4	0	0	0
5	0	0	0
>=3	0	0	0
リンパ球減少症	40 (78.4)	3 (1.3)	43 (15.5)
1	1 (2.0)	0	1 (0.4)
2	22 (43.1)	0	22 (7.9)
3	15 (29.4)	2 (0.9)	17 (6.1)
4	2 (3.9)	1 (0.4)	3 (1.1)
5	0	0	0
>=3	17 (33.3)	3 (1.3)	20 (7.2)

CTCAE = Common Terminology Criteria for Adverse Events. Adverse events of interest are presented in pre-defined event classes; each class is based on pre-specified preferred terms.
A subject with two or more adverse events in the same event class (or with same package insert term/preferred term) is counted only once for that event class (or package insert term/preferred term).
A subject is counted once by the highest non-missing CTCAE grade as applicable for preferred term and event class respectively.
Adverse event terms are coded using Medical Dictionary for Regulatory Activities (MedDRA) version 17.1.

Program: V:¥projects¥e7389¥iss309¥csr¥dev¥pg¥tables¥T_2_7_4_20.sas 18JUN201513:38

付録 2.7.4-20
Japanese and Non-Japanese (Excluding Study 207)/骨髄抑制, 肝機能障害
Treatment-Emergent Adverse Events of Interest Specified in Japan by CTCAE Grade
Eribulin Treated Safety Population

Event class Package insert term or preferred term Preferred term CTCAE grade	日本人 Study 217 (N=51) n(%)	外国人 Study 309 (N=226) n(%)	全体 Studies 217+309 (N=277) n(%)
骨髄抑制			
血小板減少	3 (5.9)	15 (6.6)	18 (6.5)
1	2 (3.9)	7 (3.1)	9 (3.2)
2	1 (2.0)	5 (2.2)	6 (2.2)
3	0	2 (0.9)	2 (0.7)
4	0	1 (0.4)	1 (0.4)
5	0	0	0
>=3	0	3 (1.3)	3 (1.1)
血小板数減少	0	2 (0.9)	2 (0.7)
1	0	0	0
2	0	0	0
3	0	1 (0.4)	1 (0.4)
4	0	1 (0.4)	1 (0.4)
5	0	0	0
>=3	0	2 (0.9)	2 (0.7)

CTCAE = Common Terminology Criteria for Adverse Events. Adverse events of interest are presented in pre-defined event classes; each class is based on pre-specified preferred terms.
A subject with two or more adverse events in the same event class (or with same package insert term/preferred term) is counted only once for that event class (or package insert term/preferred term).
A subject is counted once by the highest non-missing CTCAE grade as applicable for preferred term and event class respectively.
Adverse event terms are coded using Medical Dictionary for Regulatory Activities (MedDRA) version 17.1.

Program: V:¥projects¥e7389¥iss309¥csr¥dev¥pg¥tables¥T_2_7_4_20.sas 18JUN201513:38

付録 2.7.4-20

Japanese and Non-Japanese (Excluding Study 207)/骨髄抑制, 肝機能障害

Treatment-Emergent Adverse Events of Interest Specified in Japan by CTCAE Grade

Eribulin Treated Safety Population

Event class Package insert term or preferred term Preferred term CTCAE grade	日本人 Study 217 (N=51) n(%)	外国人 Study 309 (N=226) n(%)	全体 Studies 217+309 (N=277) n(%)
骨髄抑制			
血小板減少症	3 (5.9)	13 (5.8)	16 (5.8)
1	2 (3.9)	7 (3.1)	9 (3.2)
2	1 (2.0)	5 (2.2)	6 (2.2)
3	0	1 (0.4)	1 (0.4)
4	0	0	0
5	0	0	0
>=3	0	1 (0.4)	1 (0.4)
好中球減少	50 (98.0)	117 (51.8)	167 (60.3)
1	1 (2.0)	2 (0.9)	3 (1.1)
2	5 (9.8)	20 (8.8)	25 (9.0)
3	5 (9.8)	52 (23.0)	57 (20.6)
4	39 (76.5)	43 (19.0)	82 (29.6)
5	0	0	0
>=3	44 (86.3)	95 (42.0)	139 (50.2)

CTCAE = Common Terminology Criteria for Adverse Events. Adverse events of interest are presented in pre-defined event classes; each class is based on pre-specified preferred terms.

A subject with two or more adverse events in the same event class (or with same package insert term/preferred term) is counted only once for that event class (or package insert term/preferred term).

A subject is counted once by the highest non-missing CTCAE grade as applicable for preferred term and event class respectively.

Adverse event terms are coded using Medical Dictionary for Regulatory Activities (MedDRA) version 17.1.

Program: V:¥projects¥e7389¥iss309¥csr¥dev¥pg¥tables¥T_2_7_4_20.sas 18JUN201513:38

付録 2.7.4-20
Japanese and Non-Japanese (Excluding Study 207)/骨髄抑制, 肝機能障害
Treatment-Emergent Adverse Events of Interest Specified in Japan by CTCAE Grade
Eribulin Treated Safety Population

Event class Package insert term or preferred term Preferred term CTCAE grade	日本人 Study 217 (N=51) n(%)	外国人 Study 309 (N=226) n(%)	全体 Studies 217+309 (N=277) n(%)
骨髄抑制			
好中球減少症	50 (98.0)	99 (43.8)	149 (53.8)
1	1 (2.0)	2 (0.9)	3 (1.1)
2	5 (9.8)	17 (7.5)	22 (7.9)
3	5 (9.8)	45 (19.9)	50 (18.1)
4	39 (76.5)	35 (15.5)	74 (26.7)
5	0	0	0
>=3	44 (86.3)	80 (35.4)	124 (44.8)
好中球数減少	0	19 (8.4)	19 (6.9)
1	0	0	0
2	0	3 (1.3)	3 (1.1)
3	0	7 (3.1)	7 (2.5)
4	0	9 (4.0)	9 (3.2)
5	0	0	0
>=3	0	16 (7.1)	16 (5.8)

CTCAE = Common Terminology Criteria for Adverse Events. Adverse events of interest are presented in pre-defined event classes; each class is based on pre-specified preferred terms.
A subject with two or more adverse events in the same event class (or with same package insert term/preferred term) is counted only once for that event class (or package insert term/preferred term).
A subject is counted once by the highest non-missing CTCAE grade as applicable for preferred term and event class respectively.
Adverse event terms are coded using Medical Dictionary for Regulatory Activities (MedDRA) version 17.1.

Program: V:¥projects¥e7389¥iss309¥csr¥dev¥pg¥tables¥T_2_7_4_20.sas 18JUN201513:38

付録 2.7.4-20
Japanese and Non-Japanese (Excluding Study 207)/骨髄抑制, 肝機能障害
Treatment-Emergent Adverse Events of Interest Specified in Japan by CTCAE Grade
Eribulin Treated Safety Population

Event class Package insert term or preferred term Preferred term CTCAE grade	日本人 Study 217 (N=51) n(%)	外国人 Study 309 (N=226) n(%)	全体 Studies 217+309 (N=277) n(%)
骨髄抑制			
赤血球減少	0	2 (0.9)	2 (0.7)
1	0	2 (0.9)	2 (0.7)
2	0	0	0
3	0	0	0
4	0	0	0
5	0	0	0
>=3	0	0	0
赤血球数減少	0	2 (0.9)	2 (0.7)
1	0	2 (0.9)	2 (0.7)
2	0	0	0
3	0	0	0
4	0	0	0
5	0	0	0
>=3	0	0	0

CTCAE = Common Terminology Criteria for Adverse Events. Adverse events of interest are presented in pre-defined event classes; each class is based on pre-specified preferred terms.
A subject with two or more adverse events in the same event class (or with same package insert term/preferred term) is counted only once for that event class (or package insert term/preferred term).
A subject is counted once by the highest non-missing CTCAE grade as applicable for preferred term and event class respectively.
Adverse event terms are coded using Medical Dictionary for Regulatory Activities (MedDRA) version 17.1.

Program: V:¥projects¥e7389¥iss309¥csr¥dev¥pg¥tables¥T_2_7_4_20.sas 18JUN201513:38

付録 2.7.4-20

Japanese and Non-Japanese (Excluding Study 207)/骨髄抑制, 肝機能障害

Treatment-Emergent Adverse Events of Interest Specified in Japan by CTCAE Grade

Eribulin Treated Safety Population

Event class Package insert term or preferred term Preferred term CTCAE grade	日本人 Study 217 (N=51) n(%)	外国人 Study 309 (N=226) n(%)	全体 Studies 217+309 (N=277) n(%)
骨髄抑制			
白血球減少	51 (100.0)	52 (23.0)	103 (37.2)
1	0	5 (2.2)	5 (1.8)
2	13 (25.5)	16 (7.1)	29 (10.5)
3	28 (54.9)	25 (11.1)	53 (19.1)
4	10 (19.6)	6 (2.7)	16 (5.8)
5	0	0	0
>=3	38 (74.5)	31 (13.7)	69 (24.9)
白血球減少症	51 (100.0)	36 (15.9)	87 (31.4)
1	0	3 (1.3)	3 (1.1)
2	13 (25.5)	10 (4.4)	23 (8.3)
3	28 (54.9)	18 (8.0)	46 (16.6)
4	10 (19.6)	5 (2.2)	15 (5.4)
5	0	0	0
>=3	38 (74.5)	23 (10.2)	61 (22.0)

CTCAE = Common Terminology Criteria for Adverse Events. Adverse events of interest are presented in pre-defined event classes; each class is based on pre-specified preferred terms.

A subject with two or more adverse events in the same event class (or with same package insert term/preferred term) is counted only once for that event class (or package insert term/preferred term).

A subject is counted once by the highest non-missing CTCAE grade as applicable for preferred term and event class respectively.

Adverse event terms are coded using Medical Dictionary for Regulatory Activities (MedDRA) version 17.1.

Program: V:¥projects¥e7389¥iss309¥csr¥dev¥pg¥tables¥T_2_7_4_20.sas 18JUN201513:38

付録 2.7.4-20
Japanese and Non-Japanese (Excluding Study 207)/骨髄抑制, 肝機能障害
Treatment-Emergent Adverse Events of Interest Specified in Japan by CTCAE Grade
Eribulin Treated Safety Population

Event class Package insert term or preferred term Preferred term CTCAE grade	日本人 Study 217 (N=51) n(%)	外国人 Study 309 (N=226) n(%)	全体 Studies 217+309 (N=277) n(%)
骨髄抑制			
白血球数減少	0	16 (7.1)	16 (5.8)
1	0	2 (0.9)	2 (0.7)
2	0	6 (2.7)	6 (2.2)
3	0	7 (3.1)	7 (2.5)
4	0	1 (0.4)	1 (0.4)
5	0	0	0
>=3	0	8 (3.5)	8 (2.9)
発熱性好中球減少	4 (7.8)	2 (0.9)	6 (2.2)
1	0	0	0
2	0	0	0
3	4 (7.8)	2 (0.9)	6 (2.2)
4	0	0	0
5	0	0	0
>=3	4 (7.8)	2 (0.9)	6 (2.2)

CTCAE = Common Terminology Criteria for Adverse Events. Adverse events of interest are presented in pre-defined event classes; each class is based on pre-specified preferred terms.
A subject with two or more adverse events in the same event class (or with same package insert term/preferred term) is counted only once for that event class (or package insert term/preferred term).
A subject is counted once by the highest non-missing CTCAE grade as applicable for preferred term and event class respectively.
Adverse event terms are coded using Medical Dictionary for Regulatory Activities (MedDRA) version 17.1.

Program: V:¥projects¥e7389¥iss309¥csr¥dev¥pg¥tables¥T_2_7_4_20.sas 18JUN201513:38

付録 2.7.4-20

Japanese and Non-Japanese (Excluding Study 207)/骨髄抑制, 肝機能障害

Treatment-Emergent Adverse Events of Interest Specified in Japan by CTCAE Grade

Eribulin Treated Safety Population

Event class Package insert term or preferred term Preferred term CTCAE grade	日本人 Study 217 (N=51) n(%)	外国人 Study 309 (N=226) n(%)	全体 Studies 217+309 (N=277) n(%)
骨髄抑制			
発熱性好中球減少症	4 (7.8)	2 (0.9)	6 (2.2)
1	0	0	0
2	0	0	0
3	4 (7.8)	2 (0.9)	6 (2.2)
4	0	0	0
5	0	0	0
>=3	4 (7.8)	2 (0.9)	6 (2.2)
貧血	24 (47.1)	67 (29.6)	91 (32.9)
1	3 (5.9)	14 (6.2)	17 (6.1)
2	14 (27.5)	37 (16.4)	51 (18.4)
3	7 (13.7)	14 (6.2)	21 (7.6)
4	0	2 (0.9)	2 (0.7)
5	0	0	0
>=3	7 (13.7)	16 (7.1)	23 (8.3)

CTCAE = Common Terminology Criteria for Adverse Events. Adverse events of interest are presented in pre-defined event classes; each class is based on pre-specified preferred terms.

A subject with two or more adverse events in the same event class (or with same package insert term/preferred term) is counted only once for that event class (or package insert term/preferred term).

A subject is counted once by the highest non-missing CTCAE grade as applicable for preferred term and event class respectively.

Adverse event terms are coded using Medical Dictionary for Regulatory Activities (MedDRA) version 17.1.

Program: V:¥projects¥e7389¥iss309¥csr¥dev¥pg¥tables¥T_2_7_4_20.sas 18JUN201513:38

付録 2.7.4-20

Japanese and Non-Japanese (Excluding Study 207)/骨髄抑制, 肝機能障害

Treatment-Emergent Adverse Events of Interest Specified in Japan by CTCAE Grade

Eribulin Treated Safety Population

Event class Package insert term or preferred term Preferred term CTCAE grade	日本人 Study 217 (N=51) n(%)	外国人 Study 309 (N=226) n(%)	全体 Studies 217+309 (N=277) n(%)
骨髄抑制			
貧血	24 (47.1)	67 (29.6)	91 (32.9)
1	3 (5.9)	14 (6.2)	17 (6.1)
2	14 (27.5)	37 (16.4)	51 (18.4)
3	7 (13.7)	14 (6.2)	21 (7.6)
4	0	2 (0.9)	2 (0.7)
5	0	0	0
>=3	7 (13.7)	16 (7.1)	23 (8.3)
肝機能障害			
Any preferred term	6 (11.8)	4 (1.8)	10 (3.6)
1	5 (9.8)	1 (0.4)	6 (2.2)
2	1 (2.0)	2 (0.9)	3 (1.1)
3	0	0	0
4	0	1 (0.4)	1 (0.4)
5	0	0	0
>=3	0	1 (0.4)	1 (0.4)

CTCAE = Common Terminology Criteria for Adverse Events. Adverse events of interest are presented in pre-defined event classes; each class is based on pre-specified preferred terms.

A subject with two or more adverse events in the same event class (or with same package insert term/preferred term) is counted only once for that event class (or package insert term/preferred term).

A subject is counted once by the highest non-missing CTCAE grade as applicable for preferred term and event class respectively.

Adverse event terms are coded using Medical Dictionary for Regulatory Activities (MedDRA) version 17.1.

Program: V:¥projects¥e7389¥iss309¥csr¥dev¥pg¥tables¥T_2_7_4_20.sas 18JUN201513:38

付録 2.7.4-20
Japanese and Non-Japanese (Excluding Study 207)/骨髄抑制，肝機能障害
Treatment-Emergent Adverse Events of Interest Specified in Japan by CTCAE Grade
Eribulin Treated Safety Population

Event class Package insert term or preferred term Preferred term CTCAE grade	日本人 Study 217 (N=51) n(%)	外国人 Study 309 (N=226) n(%)	全体 Studies 217+309 (N=277) n(%)
肝機能障害			
トランスアミナーゼ上昇	0	1 (0.4)	1 (0.4)
1	0	0	0
2	0	1 (0.4)	1 (0.4)
3	0	0	0
4	0	0	0
5	0	0	0
>=3	0	0	0
トランスアミナーゼ上昇	0	1 (0.4)	1 (0.4)
1	0	0	0
2	0	1 (0.4)	1 (0.4)
3	0	0	0
4	0	0	0
5	0	0	0
>=3	0	0	0

CTCAE = Common Terminology Criteria for Adverse Events. Adverse events of interest are presented in pre-defined event classes; each class is based on pre-specified preferred terms.
A subject with two or more adverse events in the same event class (or with same package insert term/preferred term) is counted only once for that event class (or package insert term/preferred term).
A subject is counted once by the highest non-missing CTCAE grade as applicable for preferred term and event class respectively.
Adverse event terms are coded using Medical Dictionary for Regulatory Activities (MedDRA) version 17.1.

Program: V:¥projects¥e7389¥iss309¥csr¥dev¥pg¥tables¥T_2_7_4_20.sas 18JUN201513:38

付録 2.7.4-20
Japanese and Non-Japanese (Excluding Study 207)/骨髄抑制，肝機能障害
Treatment-Emergent Adverse Events of Interest Specified in Japan by CTCAE Grade
Eribulin Treated Safety Population

Event class Package insert term or preferred term Preferred term CTCAE grade	日本人 Study 217 (N=51) n(%)	外国人 Study 309 (N=226) n(%)	全体 Studies 217+309 (N=277) n(%)
肝機能障害			
黄疸	0	2 (0.9)	2 (0.7)
1	0	1 (0.4)	1 (0.4)
2	0	1 (0.4)	1 (0.4)
3	0	0	0
4	0	0	0
5	0	0	0
>=3	0	0	0
黄疸	0	1 (0.4)	1 (0.4)
1	0	0	0
2	0	1 (0.4)	1 (0.4)
3	0	0	0
4	0	0	0
5	0	0	0
>=3	0	0	0

CTCAE = Common Terminology Criteria for Adverse Events. Adverse events of interest are presented in pre-defined event classes; each class is based on pre-specified preferred terms.
A subject with two or more adverse events in the same event class (or with same package insert term/preferred term) is counted only once for that event class (or package insert term/preferred term).
A subject is counted once by the highest non-missing CTCAE grade as applicable for preferred term and event class respectively.
Adverse event terms are coded using Medical Dictionary for Regulatory Activities (MedDRA) version 17.1.

Program: V:¥projects¥e7389¥iss309¥csr¥dev¥pg¥tables¥T_2_7_4_20.sas 18JUN201513:38

付録 2.7.4-20
Japanese and Non-Japanese (Excluding Study 207)/骨髄抑制，肝機能障害
Treatment-Emergent Adverse Events of Interest Specified in Japan by CTCAE Grade
Eribulin Treated Safety Population

Event class Package insert term or preferred term Preferred term CTCAE grade	日本人 Study 217 (N=51) n(%)	外国人 Study 309 (N=226) n(%)	全体 Studies 217+309 (N=277) n(%)
肝機能障害			
黄疸眼	0	1 (0.4)	1 (0.4)
1	0	1 (0.4)	1 (0.4)
2	0	0	0
3	0	0	0
4	0	0	0
5	0	0	0
>=3	0	0	0
肝機能異常	5 (9.8)	0	5 (1.8)
1	4 (7.8)	0	4 (1.4)
2	1 (2.0)	0	1 (0.4)
3	0	0	0
4	0	0	0
5	0	0	0
>=3	0	0	0

CTCAE = Common Terminology Criteria for Adverse Events. Adverse events of interest are presented in pre-defined event classes; each class is based on pre-specified preferred terms.
A subject with two or more adverse events in the same event class (or with same package insert term/preferred term) is counted only once for that event class (or package insert term/preferred term).
A subject is counted once by the highest non-missing CTCAE grade as applicable for preferred term and event class respectively.
Adverse event terms are coded using Medical Dictionary for Regulatory Activities (MedDRA) version 17.1.

Program: V:¥projects¥e7389¥iss309¥csr¥dev¥pg¥tables¥T_2_7_4_20.sas 18JUN201513:38

付録 2.7.4-20
Japanese and Non-Japanese (Excluding Study 207)/骨髄抑制, 肝機能障害
Treatment-Emergent Adverse Events of Interest Specified in Japan by CTCAE Grade
Eribulin Treated Safety Population

Event class Package insert term or preferred term Preferred term CTCAE grade	日本人 Study 217 (N=51) n(%)	外国人 Study 309 (N=226) n(%)	全体 Studies 217+309 (N=277) n(%)
肝機能障害			
肝機能異常	5 (9.8)	0	5 (1.8)
1	4 (7.8)	0	4 (1.4)
2	1 (2.0)	0	1 (0.4)
3	0	0	0
4	0	0	0
5	0	0	0
>=3	0	0	0
肝機能検査異常	1 (2.0)	0	1 (0.4)
1	1 (2.0)	0	1 (0.4)
2	0	0	0
3	0	0	0
4	0	0	0
5	0	0	0
>=3	0	0	0

CTCAE = Common Terminology Criteria for Adverse Events. Adverse events of interest are presented in pre-defined event classes; each class is based on pre-specified preferred terms.
A subject with two or more adverse events in the same event class (or with same package insert term/preferred term) is counted only once for that event class (or package insert term/preferred term).
A subject is counted once by the highest non-missing CTCAE grade as applicable for preferred term and event class respectively.
Adverse event terms are coded using Medical Dictionary for Regulatory Activities (MedDRA) version 17.1.

Program: V:¥projects¥e7389¥iss309¥csr¥dev¥pg¥tables¥T_2_7_4_20.sas 18JUN201513:38

付録 2.7.4-20
Japanese and Non-Japanese (Excluding Study 207)/骨髄抑制, 肝機能障害
Treatment-Emergent Adverse Events of Interest Specified in Japan by CTCAE Grade
Eribulin Treated Safety Population

Event class Package insert term or preferred term Preferred term CTCAE grade	日本人 Study 217 (N=51) n(%)	外国人 Study 309 (N=226) n(%)	全体 Studies 217+309 (N=277) n(%)
肝機能障害			
肝機能検査異常	1 (2.0)	0	1 (0.4)
1	1 (2.0)	0	1 (0.4)
2	0	0	0
3	0	0	0
4	0	0	0
5	0	0	0
>=3	0	0	0
肝細胞損傷	0	1 (0.4)	1 (0.4)
1	0	0	0
2	0	1 (0.4)	1 (0.4)
3	0	0	0
4	0	0	0
5	0	0	0
>=3	0	0	0

CTCAE = Common Terminology Criteria for Adverse Events. Adverse events of interest are presented in pre-defined event classes; each class is based on pre-specified preferred terms.
A subject with two or more adverse events in the same event class (or with same package insert term/preferred term) is counted only once for that event class (or package insert term/preferred term).
A subject is counted once by the highest non-missing CTCAE grade as applicable for preferred term and event class respectively.
Adverse event terms are coded using Medical Dictionary for Regulatory Activities (MedDRA) version 17.1.

Program: V:¥projects¥e7389¥iss309¥csr¥dev¥pg¥tables¥T_2_7_4_20.sas 18JUN201513:38

付録 2.7.4-20
Japanese and Non-Japanese (Excluding Study 207)/骨髄抑制, 肝機能障害
Treatment-Emergent Adverse Events of Interest Specified in Japan by CTCAE Grade
Eribulin Treated Safety Population

Event class Package insert term or preferred term Preferred term CTCAE grade	日本人 Study 217 (N=51) n(%)	外国人 Study 309 (N=226) n(%)	全体 Studies 217+309 (N=277) n(%)
肝機能障害			
肝細胞損傷	0	1 (0.4)	1 (0.4)
1	0	0	0
2	0	1 (0.4)	1 (0.4)
3	0	0	0
4	0	0	0
5	0	0	0
>=3	0	0	0
肝毒性	0	1 (0.4)	1 (0.4)
1	0	0	0
2	0	0	0
3	0	0	0
4	0	1 (0.4)	1 (0.4)
5	0	0	0
>=3	0	1 (0.4)	1 (0.4)

CTCAE = Common Terminology Criteria for Adverse Events. Adverse events of interest are presented in pre-defined event classes; each class is based on pre-specified preferred terms.
A subject with two or more adverse events in the same event class (or with same package insert term/preferred term) is counted only once for that event class (or package insert term/preferred term).
A subject is counted once by the highest non-missing CTCAE grade as applicable for preferred term and event class respectively.
Adverse event terms are coded using Medical Dictionary for Regulatory Activities (MedDRA) version 17.1.

Program: V:¥projects¥e7389¥iss309¥csr¥dev¥pg¥tables¥T_2_7_4_20.sas 18JUN201513:38

付録 2.7.4-20

Japanese and Non-Japanese (Excluding Study 207)/骨髄抑制，肝機能障害

Treatment-Emergent Adverse Events of Interest Specified in Japan by CTCAE Grade

Eribulin Treated Safety Population

Event class Package insert term or preferred term Preferred term CTCAE grade	日本人 Study 217 (N=51) n(%)	外国人 Study 309 (N=226) n(%)	全体 Studies 217+309 (N=277) n(%)
肝機能障害			
肝毒性	0	1 (0.4)	1 (0.4)
1	0	0	0
2	0	0	0
3	0	0	0
4	0	1 (0.4)	1 (0.4)
5	0	0	0
>=3	0	1 (0.4)	1 (0.4)

CTCAE = Common Terminology Criteria for Adverse Events. Adverse events of interest are presented in pre-defined event classes; each class is based on pre-specified preferred terms.

A subject with two or more adverse events in the same event class (or with same package insert term/preferred term) is counted only once for that event class (or package insert term/preferred term).

A subject is counted once by the highest non-missing CTCAE grade as applicable for preferred term and event class respectively.

Adverse event terms are coded using Medical Dictionary for Regulatory Activities (MedDRA) version 17.1.

Program: V:¥projects¥e7389¥iss309¥csr¥dev¥pg¥tables¥T_2_7_4_20.sas 18JUN201513:38

付録 2.7.4-21
Japanese and Non-Japanese
Treatment-Related Treatment-Emergent Adverse Events of Interest Specified in Japan by CTCAE Grade
Eribulin Treated Safety Population

Event class Package insert term or preferred term Preferred term CTCAE grade	日本人 Study 217 (N=51) n(%)	外国人 Studies 207+309 (N=353) n(%)	全体 Studies 217+207+309 (N=404) n(%)
骨髄抑制			
Any preferred term	51 (100.0)	148 (41.9)	199 (49.3)
1	0	6 (1.7)	6 (1.5)
2	3 (5.9)	32 (9.1)	35 (8.7)
3	9 (17.6)	65 (18.4)	74 (18.3)
4	39 (76.5)	45 (12.7)	84 (20.8)
5	0	0	0
>=3	48 (94.1)	110 (31.2)	158 (39.1)
ヘマトクリット減少	0	1 (0.3)	1 (0.2)
1	0	1 (0.3)	1 (0.2)
2	0	0	0
3	0	0	0
4	0	0	0
5	0	0	0
>=3	0	0	0

CTCAE = Common Terminology Criteria for Adverse Events. Adverse events of interest are presented in pre-defined event classes; each class is based on pre-specified preferred terms.
Treatment-related adverse events include adverse events that were considered by the investigator to be possibly or probably related to study drug and adverse events with missing relationship to study drug.
A subject with two or more adverse events in the same event class (or with same package insert term/preferred term) is counted only once for that event class (or package insert term/preferred term).
A subject is counted once by the highest non-missing CTCAE grade as applicable for preferred term and event class respectively.
Adverse event terms are coded using Medical Dictionary for Regulatory Activities (MedDRA) version 17.1.
This table is based on adverse events data as available. Study 207 did not record laboratory abnormalities into adverse events data.

Program: V:¥projects¥e7389¥iss309¥csr¥dev¥pg¥tables¥T_2_7_4_21.sas 18JUN201513:39

付録 2.7.4-21
Japanese and Non-Japanese
Treatment-Related Treatment-Emergent Adverse Events of Interest Specified in Japan by CTCAE Grade
Eribulin Treated Safety Population

Event class Package insert term or preferred term Preferred term CTCAE grade	日本人 Study 217 (N=51) n(%)	外国人 Studies 207+309 (N=353) n(%)	全体 Studies 217+207+309 (N=404) n(%)
骨髄抑制			
ヘマトクリット減少	0	1 (0.3)	1 (0.2)
1	0	1 (0.3)	1 (0.2)
2	0	0	0
3	0	0	0
4	0	0	0
5	0	0	0
>=3	0	0	0
ヘモグロビン減少	2 (3.9)	6 (1.7)	8 (2.0)
1	2 (3.9)	2 (0.6)	4 (1.0)
2	0	4 (1.1)	4 (1.0)
3	0	0	0
4	0	0	0
5	0	0	0
>=3	0	0	0

CTCAE = Common Terminology Criteria for Adverse Events. Adverse events of interest are presented in pre-defined event classes; each class is based on pre-specified preferred terms.
Treatment-related adverse events include adverse events that were considered by the investigator to be possibly or probably related to study drug and adverse events with missing relationship to study drug.
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Adverse event terms are coded using Medical Dictionary for Regulatory Activities (MedDRA) version 17.1.
This table is based on adverse events data as available. Study 207 did not record laboratory abnormalities into adverse events data.

Program: V:¥projects¥e7389¥iss309¥csr¥dev¥pg¥tables¥T_2_7_4_21.sas 18JUN201513:39

付録 2.7.4-21
Japanese and Non-Japanese
Treatment-Related Treatment-Emergent Adverse Events of Interest Specified in Japan by CTCAE Grade
Eribulin Treated Safety Population

Event class Package insert term or preferred term Preferred term CTCAE grade	日本人 Study 217 (N=51) n(%)	外国人 Studies 207+309 (N=353) n(%)	全体 Studies 217+207+309 (N=404) n(%)
骨髄抑制			
ヘモグロビン減少	2 (3.9)	6 (1.7)	8 (2.0)
1	2 (3.9)	2 (0.6)	4 (1.0)
2	0	4 (1.1)	4 (1.0)
3	0	0	0
4	0	0	0
5	0	0	0
>=3	0	0	0
リンパ球減少	40 (78.4)	3 (0.8)	43 (10.6)
1	1 (2.0)	1 (0.3)	2 (0.5)
2	23 (45.1)	1 (0.3)	24 (5.9)
3	14 (27.5)	0	14 (3.5)
4	2 (3.9)	1 (0.3)	3 (0.7)
5	0	0	0
>=3	16 (31.4)	1 (0.3)	17 (4.2)

CTCAE = Common Terminology Criteria for Adverse Events. Adverse events of interest are presented in pre-defined event classes; each class is based on pre-specified preferred terms.
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付録 2.7.4-21
Japanese and Non-Japanese
Treatment-Related Treatment-Emergent Adverse Events of Interest Specified in Japan by CTCAE Grade
Eribulin Treated Safety Population

Event class Package insert term or preferred term Preferred term CTCAE grade	日本人 Study 217 (N=51) n(%)	外国人 Studies 207+309 (N=353) n(%)	全体 Studies 217+207+309 (N=404) n(%)
骨髄抑制			
リンパ球数減少	0	2 (0.6)	2 (0.5)
1	0	1 (0.3)	1 (0.2)
2	0	1 (0.3)	1 (0.2)
3	0	0	0
4	0	0	0
5	0	0	0
>=3	0	0	0
リンパ球減少症	40 (78.4)	1 (0.3)	41 (10.1)
1	1 (2.0)	0	1 (0.2)
2	23 (45.1)	0	23 (5.7)
3	14 (27.5)	0	14 (3.5)
4	2 (3.9)	1 (0.3)	3 (0.7)
5	0	0	0
>=3	16 (31.4)	1 (0.3)	17 (4.2)

CTCAE = Common Terminology Criteria for Adverse Events. Adverse events of interest are presented in pre-defined event classes; each class is based on pre-specified preferred terms.
Treatment-related adverse events include adverse events that were considered by the investigator to be possibly or probably related to study drug and adverse events with missing relationship to study drug.
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付録 2.7.4-21
Japanese and Non-Japanese
Treatment-Related Treatment-Emergent Adverse Events of Interest Specified in Japan by CTCAE Grade
Eribulin Treated Safety Population

Event class Package insert term or preferred term Preferred term CTCAE grade	日本人 Study 217 (N=51) n(%)	外国人 Studies 207+309 (N=353) n(%)	全体 Studies 217+207+309 (N=404) n(%)
骨髄抑制			
血小板減少	3 (5.9)	14 (4.0)	17 (4.2)
1	2 (3.9)	7 (2.0)	9 (2.2)
2	1 (2.0)	5 (1.4)	6 (1.5)
3	0	1 (0.3)	1 (0.2)
4	0	1 (0.3)	1 (0.2)
5	0	0	0
>=3	0	2 (0.6)	2 (0.5)
血小板数減少	0	1 (0.3)	1 (0.2)
1	0	0	0
2	0	0	0
3	0	0	0
4	0	1 (0.3)	1 (0.2)
5	0	0	0
>=3	0	1 (0.3)	1 (0.2)

CTCAE = Common Terminology Criteria for Adverse Events. Adverse events of interest are presented in pre-defined event classes; each class is based on pre-specified preferred terms.
Treatment-related adverse events include adverse events that were considered by the investigator to be possibly or probably related to study drug and adverse events with missing relationship to study drug.
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付録 2.7.4-21
Japanese and Non-Japanese
Treatment-Related Treatment-Emergent Adverse Events of Interest Specified in Japan by CTCAE Grade
Eribulin Treated Safety Population

Event class Package insert term or preferred term Preferred term CTCAE grade	日本人 Study 217 (N=51) n(%)	外国人 Studies 207+309 (N=353) n(%)	全体 Studies 217+207+309 (N=404) n(%)
骨髄抑制			
血小板減少症	3 (5.9)	13 (3.7)	16 (4.0)
1	2 (3.9)	7 (2.0)	9 (2.2)
2	1 (2.0)	5 (1.4)	6 (1.5)
3	0	1 (0.3)	1 (0.2)
4	0	0	0
5	0	0	0
>=3	0	1 (0.3)	1 (0.2)
好中球減少	50 (98.0)	115 (32.6)	165 (40.8)
1	1 (2.0)	2 (0.6)	3 (0.7)
2	5 (9.8)	21 (5.9)	26 (6.4)
3	5 (9.8)	50 (14.2)	55 (13.6)
4	39 (76.5)	42 (11.9)	81 (20.0)
5	0	0	0
>=3	44 (86.3)	92 (26.1)	136 (33.7)

CTCAE = Common Terminology Criteria for Adverse Events. Adverse events of interest are presented in pre-defined event classes; each class is based on pre-specified preferred terms.
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付録 2.7.4-21
Japanese and Non-Japanese
Treatment-Related Treatment-Emergent Adverse Events of Interest Specified in Japan by CTCAE Grade
Eribulin Treated Safety Population

Event class Package insert term or preferred term Preferred term CTCAE grade	日本人 Study 217 (N=51) n(%)	外国人 Studies 207+309 (N=353) n(%)	全体 Studies 217+207+309 (N=404) n(%)
骨髄抑制			
好中球減少症	50 (98.0)	98 (27.8)	148 (36.6)
1	1 (2.0)	2 (0.6)	3 (0.7)
2	5 (9.8)	18 (5.1)	23 (5.7)
3	5 (9.8)	43 (12.2)	48 (11.9)
4	39 (76.5)	35 (9.9)	74 (18.3)
5	0	0	0
>=3	44 (86.3)	78 (22.1)	122 (30.2)
好中球数減少	0	18 (5.1)	18 (4.5)
1	0	0	0
2	0	3 (0.8)	3 (0.7)
3	0	7 (2.0)	7 (1.7)
4	0	8 (2.3)	8 (2.0)
5	0	0	0
>=3	0	15 (4.2)	15 (3.7)

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Treatment-related adverse events include adverse events that were considered by the investigator to be possibly or probably related to study drug and adverse events with missing relationship to study drug.
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付録 2.7.4-21
Japanese and Non-Japanese
Treatment-Related Treatment-Emergent Adverse Events of Interest Specified in Japan by CTCAE Grade
Eribulin Treated Safety Population

Event class Package insert term or preferred term Preferred term CTCAE grade	日本人 Study 217 (N=51) n(%)	外国人 Studies 207+309 (N=353) n(%)	全体 Studies 217+207+309 (N=404) n(%)
骨髄抑制			
赤血球減少	0	2 (0.6)	2 (0.5)
1	0	2 (0.6)	2 (0.5)
2	0	0	0
3	0	0	0
4	0	0	0
5	0	0	0
>=3	0	0	0
赤血球数減少	0	2 (0.6)	2 (0.5)
1	0	2 (0.6)	2 (0.5)
2	0	0	0
3	0	0	0
4	0	0	0
5	0	0	0
>=3	0	0	0

CTCAE = Common Terminology Criteria for Adverse Events. Adverse events of interest are presented in pre-defined event classes; each class is based on pre-specified preferred terms.
Treatment-related adverse events include adverse events that were considered by the investigator to be possibly or probably related to study drug and adverse events with missing relationship to study drug.
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付録 2.7.4-21
Japanese and Non-Japanese
Treatment-Related Treatment-Emergent Adverse Events of Interest Specified in Japan by CTCAE Grade
Eribulin Treated Safety Population

Event class Package insert term or preferred term Preferred term CTCAE grade	日本人 Study 217 (N=51) n(%)	外国人 Studies 207+309 (N=353) n(%)	全体 Studies 217+207+309 (N=404) n(%)
骨髄抑制			
白血球減少	51 (100.0)	51 (14.4)	102 (25.2)
1	0	5 (1.4)	5 (1.2)
2	13 (25.5)	17 (4.8)	30 (7.4)
3	28 (54.9)	25 (7.1)	53 (13.1)
4	10 (19.6)	4 (1.1)	14 (3.5)
5	0	0	0
>=3	38 (74.5)	29 (8.2)	67 (16.6)
白血球減少症	51 (100.0)	35 (9.9)	86 (21.3)
1	0	3 (0.8)	3 (0.7)
2	13 (25.5)	10 (2.8)	23 (5.7)
3	28 (54.9)	18 (5.1)	46 (11.4)
4	10 (19.6)	4 (1.1)	14 (3.5)
5	0	0	0
>=3	38 (74.5)	22 (6.2)	60 (14.9)

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付録 2.7.4-21
Japanese and Non-Japanese
Treatment-Related Treatment-Emergent Adverse Events of Interest Specified in Japan by CTCAE Grade
Eribulin Treated Safety Population

Event class Package insert term or preferred term Preferred term CTCAE grade	日本人 Study 217 (N=51) n(%)	外国人 Studies 207+309 (N=353) n(%)	全体 Studies 217+207+309 (N=404) n(%)
骨髄抑制			
白血球数減少	0	16 (4.5)	16 (4.0)
1	0	2 (0.6)	2 (0.5)
2	0	7 (2.0)	7 (1.7)
3	0	7 (2.0)	7 (1.7)
4	0	0	0
5	0	0	0
>=3	0	7 (2.0)	7 (1.7)
発熱性好中球減少	4 (7.8)	9 (2.5)	13 (3.2)
1	0	0	0
2	0	0	0
3	4 (7.8)	9 (2.5)	13 (3.2)
4	0	0	0
5	0	0	0
>=3	4 (7.8)	9 (2.5)	13 (3.2)

CTCAE = Common Terminology Criteria for Adverse Events. Adverse events of interest are presented in pre-defined event classes; each class is based on pre-specified preferred terms.
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付録 2.7.4-21
Japanese and Non-Japanese
Treatment-Related Treatment-Emergent Adverse Events of Interest Specified in Japan by CTCAE Grade
Eribulin Treated Safety Population

Event class Package insert term or preferred term Preferred term CTCAE grade	日本人 Study 217 (N=51) n(%)	外国人 Studies 207+309 (N=353) n(%)	全体 Studies 217+207+309 (N=404) n(%)
骨髄抑制			
発熱性好中球減少症	4 (7.8)	9 (2.5)	13 (3.2)
1	0	0	0
2	0	0	0
3	4 (7.8)	9 (2.5)	13 (3.2)
4	0	0	0
5	0	0	0
>=3	4 (7.8)	9 (2.5)	13 (3.2)
貧血	24 (47.1)	55 (15.6)	79 (19.6)
1	3 (5.9)	11 (3.1)	14 (3.5)
2	15 (29.4)	34 (9.6)	49 (12.1)
3	6 (11.8)	9 (2.5)	15 (3.7)
4	0	1 (0.3)	1 (0.2)
5	0	0	0
>=3	6 (11.8)	10 (2.8)	16 (4.0)

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付録 2.7.4-21
Japanese and Non-Japanese
Treatment-Related Treatment-Emergent Adverse Events of Interest Specified in Japan by CTCAE Grade
Eribulin Treated Safety Population

Event class Package insert term or preferred term Preferred term CTCAE grade	日本人 Study 217 (N=51) n(%)	外国人 Studies 207+309 (N=353) n(%)	全体 Studies 217+207+309 (N=404) n(%)
骨髄抑制			
貧血	24 (47.1)	55 (15.6)	79 (19.6)
1	3 (5.9)	11 (3.1)	14 (3.5)
2	15 (29.4)	34 (9.6)	49 (12.1)
3	6 (11.8)	9 (2.5)	15 (3.7)
4	0	1 (0.3)	1 (0.2)
5	0	0	0
>=3	6 (11.8)	10 (2.8)	16 (4.0)
感染症			
Any preferred term	15 (29.4)	35 (9.9)	50 (12.4)
1	5 (9.8)	14 (4.0)	19 (4.7)
2	8 (15.7)	11 (3.1)	19 (4.7)
3	2 (3.9)	9 (2.5)	11 (2.7)
4	0	0	0
5	0	1 (0.3)	1 (0.2)
>=3	2 (3.9)	10 (2.8)	12 (3.0)

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付録 2.7.4-21
Japanese and Non-Japanese
Treatment-Related Treatment-Emergent Adverse Events of Interest Specified in Japan by CTCAE Grade
Eribulin Treated Safety Population

Event class Package insert term or preferred term Preferred term CTCAE grade	日本人 Study 217 (N=51) n(%)	外国人 Studies 207+309 (N=353) n(%)	全体 Studies 217+207+309 (N=404) n(%)
感染症			
胃腸炎	2 (3.9)	0	2 (0.5)
1	0	0	0
2	2 (3.9)	0	2 (0.5)
3	0	0	0
4	0	0	0
5	0	0	0
>=3	0	0	0
感染性腸炎	1 (2.0)	0	1 (0.2)
1	0	0	0
2	1 (2.0)	0	1 (0.2)
3	0	0	0
4	0	0	0
5	0	0	0
>=3	0	0	0

CTCAE = Common Terminology Criteria for Adverse Events. Adverse events of interest are presented in pre-defined event classes; each class is based on pre-specified preferred terms.
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Adverse event terms are coded using Medical Dictionary for Regulatory Activities (MedDRA) version 17.1.
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付録 2.7.4-21
Japanese and Non-Japanese
Treatment-Related Treatment-Emergent Adverse Events of Interest Specified in Japan by CTCAE Grade
Eribulin Treated Safety Population

Event class Package insert term or preferred term Preferred term CTCAE grade	日本人 Study 217 (N=51) n(%)	外国人 Studies 207+309 (N=353) n(%)	全体 Studies 217+207+309 (N=404) n(%)
感染症			
胃腸炎	1 (2.0)	0	1 (0.2)
1	0	0	0
2	1 (2.0)	0	1 (0.2)
3	0	0	0
4	0	0	0
5	0	0	0
>=3	0	0	0
医療機器関連感染	0	1 (0.3)	1 (0.2)
1	0	1 (0.3)	1 (0.2)
2	0	0	0
3	0	0	0
4	0	0	0
5	0	0	0
>=3	0	0	0

CTCAE = Common Terminology Criteria for Adverse Events. Adverse events of interest are presented in pre-defined event classes; each class is based on pre-specified preferred terms.
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A subject is counted once by the highest non-missing CTCAE grade as applicable for preferred term and event class respectively.
Adverse event terms are coded using Medical Dictionary for Regulatory Activities (MedDRA) version 17.1.
This table is based on adverse events data as available. Study 207 did not record laboratory abnormalities into adverse events data.

Program: V:¥projects¥e7389¥iss309¥csr¥dev¥pg¥tables¥T_2_7_4_21.sas 18JUN201513:39

付録 2.7.4-21
Japanese and Non-Japanese
Treatment-Related Treatment-Emergent Adverse Events of Interest Specified in Japan by CTCAE Grade
Eribulin Treated Safety Population

Event class Package insert term or preferred term Preferred term CTCAE grade	日本人 Study 217 (N=51) n(%)	外国人 Studies 207+309 (N=353) n(%)	全体 Studies 217+207+309 (N=404) n(%)
感染症			
カテーテル留置部位蜂巣炎	0	1 (0.3)	1 (0.2)
1	0	1 (0.3)	1 (0.2)
2	0	0	0
3	0	0	0
4	0	0	0
5	0	0	0
>=3	0	0	0
下気道感染	0	1 (0.3)	1 (0.2)
1	0	0	0
2	0	0	0
3	0	1 (0.3)	1 (0.2)
4	0	0	0
5	0	0	0
>=3	0	1 (0.3)	1 (0.2)

CTCAE = Common Terminology Criteria for Adverse Events. Adverse events of interest are presented in pre-defined event classes; each class is based on pre-specified preferred terms.
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A subject with two or more adverse events in the same event class (or with same package insert term/preferred term) is counted only once for that event class (or package insert term/preferred term).
A subject is counted once by the highest non-missing CTCAE grade as applicable for preferred term and event class respectively.
Adverse event terms are coded using Medical Dictionary for Regulatory Activities (MedDRA) version 17.1.
This table is based on adverse events data as available. Study 207 did not record laboratory abnormalities into adverse events data.

Program: V:¥projects¥e7389¥iss309¥csr¥dev¥pg¥tables¥T_2_7_4_21.sas 18JUN201513:39

付録 2.7.4-21
Japanese and Non-Japanese
Treatment-Related Treatment-Emergent Adverse Events of Interest Specified in Japan by CTCAE Grade
Eribulin Treated Safety Population

Event class Package insert term or preferred term Preferred term CTCAE grade	日本人 Study 217 (N=51) n(%)	外国人 Studies 207+309 (N=353) n(%)	全体 Studies 217+207+309 (N=404) n(%)
感染症			
真菌性下気道感染	0	1 (0.3)	1 (0.2)
1	0	0	0
2	0	0	0
3	0	1 (0.3)	1 (0.2)
4	0	0	0
5	0	0	0
>=3	0	1 (0.3)	1 (0.2)
感染	1 (2.0)	1 (0.3)	2 (0.5)
1	0	1 (0.3)	1 (0.2)
2	0	0	0
3	1 (2.0)	0	1 (0.2)
4	0	0	0
5	0	0	0
>=3	1 (2.0)	0	1 (0.2)

CTCAE = Common Terminology Criteria for Adverse Events. Adverse events of interest are presented in pre-defined event classes; each class is based on pre-specified preferred terms.
Treatment-related adverse events include adverse events that were considered by the investigator to be possibly or probably related to study drug and adverse events with missing relationship to study drug.
A subject with two or more adverse events in the same event class (or with same package insert term/preferred term) is counted only once for that event class (or package insert term/preferred term).
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Program: V:¥projects¥e7389¥iss309¥csr¥dev¥pg¥tables¥T_2_7_4_21.sas 18JUN201513:39

付録 2.7.4-21
Japanese and Non-Japanese
Treatment-Related Treatment-Emergent Adverse Events of Interest Specified in Japan by CTCAE Grade
Eribulin Treated Safety Population

Event class Package insert term or preferred term Preferred term CTCAE grade	日本人 Study 217 (N=51) n(%)	外国人 Studies 207+309 (N=353) n(%)	全体 Studies 217+207+309 (N=404) n(%)
感染症			
レンサ球菌感染	1 (2.0)	0	1 (0.2)
1	0	0	0
2	0	0	0
3	1 (2.0)	0	1 (0.2)
4	0	0	0
5	0	0	0
>=3	1 (2.0)	0	1 (0.2)
白癬感染	0	1 (0.3)	1 (0.2)
1	0	1 (0.3)	1 (0.2)
2	0	0	0
3	0	0	0
4	0	0	0
5	0	0	0
>=3	0	0	0

CTCAE = Common Terminology Criteria for Adverse Events. Adverse events of interest are presented in pre-defined event classes; each class is based on pre-specified preferred terms.
Treatment-related adverse events include adverse events that were considered by the investigator to be possibly or probably related to study drug and adverse events with missing relationship to study drug.
A subject with two or more adverse events in the same event class (or with same package insert term/preferred term) is counted only once for that event class (or package insert term/preferred term).
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付録 2.7.4-21
Japanese and Non-Japanese
Treatment-Related Treatment-Emergent Adverse Events of Interest Specified in Japan by CTCAE Grade
Eribulin Treated Safety Population

Event class Package insert term or preferred term Preferred term CTCAE grade	日本人 Study 217 (N=51) n(%)	外国人 Studies 207+309 (N=353) n(%)	全体 Studies 217+207+309 (N=404) n(%)
感染症			
感染性胸水	1 (2.0)	0	1 (0.2)
1	0	0	0
2	0	0	0
3	1 (2.0)	0	1 (0.2)
4	0	0	0
5	0	0	0
>=3	1 (2.0)	0	1 (0.2)
蓄膿	1 (2.0)	0	1 (0.2)
1	0	0	0
2	0	0	0
3	1 (2.0)	0	1 (0.2)
4	0	0	0
5	0	0	0
>=3	1 (2.0)	0	1 (0.2)

CTCAE = Common Terminology Criteria for Adverse Events. Adverse events of interest are presented in pre-defined event classes; each class is based on pre-specified preferred terms.
Treatment-related adverse events include adverse events that were considered by the investigator to be possibly or probably related to study drug and adverse events with missing relationship to study drug.
A subject with two or more adverse events in the same event class (or with same package insert term/preferred term) is counted only once for that event class (or package insert term/preferred term).
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Adverse event terms are coded using Medical Dictionary for Regulatory Activities (MedDRA) version 17.1.
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付録 2.7.4-21
Japanese and Non-Japanese
Treatment-Related Treatment-Emergent Adverse Events of Interest Specified in Japan by CTCAE Grade
Eribulin Treated Safety Population

Event class Package insert term or preferred term Preferred term CTCAE grade	日本人 Study 217 (N=51) n(%)	外国人 Studies 207+309 (N=353) n(%)	全体 Studies 217+207+309 (N=404) n(%)
感染症			
気管気管支炎	0	1 (0.3)	1 (0.2)
1	0	0	0
2	0	1 (0.3)	1 (0.2)
3	0	0	0
4	0	0	0
5	0	0	0
>=3	0	0	0
気管支炎	0	1 (0.3)	1 (0.2)
1	0	0	0
2	0	1 (0.3)	1 (0.2)
3	0	0	0
4	0	0	0
5	0	0	0
>=3	0	0	0

CTCAE = Common Terminology Criteria for Adverse Events. Adverse events of interest are presented in pre-defined event classes; each class is based on pre-specified preferred terms.
Treatment-related adverse events include adverse events that were considered by the investigator to be possibly or probably related to study drug and adverse events with missing relationship to study drug.
A subject with two or more adverse events in the same event class (or with same package insert term/preferred term) is counted only once for that event class (or package insert term/preferred term).
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Adverse event terms are coded using Medical Dictionary for Regulatory Activities (MedDRA) version 17.1.
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付録 2.7.4-21
Japanese and Non-Japanese
Treatment-Related Treatment-Emergent Adverse Events of Interest Specified in Japan by CTCAE Grade
Eribulin Treated Safety Population

Event class Package insert term or preferred term Preferred term CTCAE grade	日本人 Study 217 (N=51) n(%)	外国人 Studies 207+309 (N=353) n(%)	全体 Studies 217+207+309 (N=404) n(%)
感染症			
気道感染	0	1 (0.3)	1 (0.2)
1	0	0	0
2	0	1 (0.3)	1 (0.2)
3	0	0	0
4	0	0	0
5	0	0	0
>=3	0	0	0
気道感染	0	1 (0.3)	1 (0.2)
1	0	0	0
2	0	1 (0.3)	1 (0.2)
3	0	0	0
4	0	0	0
5	0	0	0
>=3	0	0	0

CTCAE = Common Terminology Criteria for Adverse Events. Adverse events of interest are presented in pre-defined event classes; each class is based on pre-specified preferred terms.
Treatment-related adverse events include adverse events that were considered by the investigator to be possibly or probably related to study drug and adverse events with missing relationship to study drug.
A subject with two or more adverse events in the same event class (or with same package insert term/preferred term) is counted only once for that event class (or package insert term/preferred term).
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Adverse event terms are coded using Medical Dictionary for Regulatory Activities (MedDRA) version 17.1.
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付録 2.7.4-21
Japanese and Non-Japanese
Treatment-Related Treatment-Emergent Adverse Events of Interest Specified in Japan by CTCAE Grade
Eribulin Treated Safety Population

Event class Package insert term or preferred term Preferred term CTCAE grade	日本人 Study 217 (N=51) n(%)	外国人 Studies 207+309 (N=353) n(%)	全体 Studies 217+207+309 (N=404) n(%)
感染症			
口腔感染	0	4 (1.1)	4 (1.0)
1	0	1 (0.3)	1 (0.2)
2	0	3 (0.8)	3 (0.7)
3	0	0	0
4	0	0	0
5	0	0	0
>=3	0	0	0
口腔カンジダ症	0	3 (0.8)	3 (0.7)
1	0	1 (0.3)	1 (0.2)
2	0	2 (0.6)	2 (0.5)
3	0	0	0
4	0	0	0
5	0	0	0
>=3	0	0	0

CTCAE = Common Terminology Criteria for Adverse Events. Adverse events of interest are presented in pre-defined event classes; each class is based on pre-specified preferred terms.
Treatment-related adverse events include adverse events that were considered by the investigator to be possibly or probably related to study drug and adverse events with missing relationship to study drug.
A subject with two or more adverse events in the same event class (or with same package insert term/preferred term) is counted only once for that event class (or package insert term/preferred term).
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Adverse event terms are coded using Medical Dictionary for Regulatory Activities (MedDRA) version 17.1.
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付録 2.7.4-21
Japanese and Non-Japanese
Treatment-Related Treatment-Emergent Adverse Events of Interest Specified in Japan by CTCAE Grade
Eribulin Treated Safety Population

Event class Package insert term or preferred term Preferred term CTCAE grade	日本人 Study 217 (N=51) n(%)	外国人 Studies 207+309 (N=353) n(%)	全体 Studies 217+207+309 (N=404) n(%)
感染症			
口腔ヘルペス	0	1 (0.3)	1 (0.2)
1	0	0	0
2	0	1 (0.3)	1 (0.2)
3	0	0	0
4	0	0	0
5	0	0	0
>=3	0	0	0
耳感染	0	2 (0.6)	2 (0.5)
1	0	1 (0.3)	1 (0.2)
2	0	1 (0.3)	1 (0.2)
3	0	0	0
4	0	0	0
5	0	0	0
>=3	0	0	0

CTCAE = Common Terminology Criteria for Adverse Events. Adverse events of interest are presented in pre-defined event classes; each class is based on pre-specified preferred terms.
Treatment-related adverse events include adverse events that were considered by the investigator to be possibly or probably related to study drug and adverse events with missing relationship to study drug.
A subject with two or more adverse events in the same event class (or with same package insert term/preferred term) is counted only once for that event class (or package insert term/preferred term).
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付録 2.7.4-21
Japanese and Non-Japanese
Treatment-Related Treatment-Emergent Adverse Events of Interest Specified in Japan by CTCAE Grade
Eribulin Treated Safety Population

Event class Package insert term or preferred term Preferred term CTCAE grade	日本人 Study 217 (N=51) n(%)	外国人 Studies 207+309 (N=353) n(%)	全体 Studies 217+207+309 (N=404) n(%)
感染症			
耳感染	0	2 (0.6)	2 (0.5)
1	0	1 (0.3)	1 (0.2)
2	0	1 (0.3)	1 (0.2)
3	0	0	0
4	0	0	0
5	0	0	0
>=3	0	0	0
上気道感染	6 (11.8)	4 (1.1)	10 (2.5)
1	3 (5.9)	1 (0.3)	4 (1.0)
2	3 (5.9)	2 (0.6)	5 (1.2)
3	0	1 (0.3)	1 (0.2)
4	0	0	0
5	0	0	0
>=3	0	1 (0.3)	1 (0.2)

CTCAE = Common Terminology Criteria for Adverse Events. Adverse events of interest are presented in pre-defined event classes; each class is based on pre-specified preferred terms.
Treatment-related adverse events include adverse events that were considered by the investigator to be possibly or probably related to study drug and adverse events with missing relationship to study drug.
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付録 2.7.4-21
Japanese and Non-Japanese
Treatment-Related Treatment-Emergent Adverse Events of Interest Specified in Japan by CTCAE Grade
Eribulin Treated Safety Population

Event class Package insert term or preferred term Preferred term CTCAE grade	日本人 Study 217 (N=51) n(%)	外国人 Studies 207+309 (N=353) n(%)	全体 Studies 217+207+309 (N=404) n(%)
感染症			
上気道感染	6 (11.8)	4 (1.1)	10 (2.5)
1	3 (5.9)	1 (0.3)	4 (1.0)
2	3 (5.9)	2 (0.6)	5 (1.2)
3	0	1 (0.3)	1 (0.2)
4	0	0	0
5	0	0	0
>=3	0	1 (0.3)	1 (0.2)
脊髄炎	0	1 (0.3)	1 (0.2)
1	0	0	0
2	0	1 (0.3)	1 (0.2)
3	0	0	0
4	0	0	0
5	0	0	0
>=3	0	0	0

CTCAE = Common Terminology Criteria for Adverse Events. Adverse events of interest are presented in pre-defined event classes; each class is based on pre-specified preferred terms.
Treatment-related adverse events include adverse events that were considered by the investigator to be possibly or probably related to study drug and adverse events with missing relationship to study drug.
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This table is based on adverse events data as available. Study 207 did not record laboratory abnormalities into adverse events data.

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付録 2.7.4-21
Japanese and Non-Japanese
Treatment-Related Treatment-Emergent Adverse Events of Interest Specified in Japan by CTCAE Grade
Eribulin Treated Safety Population

Event class Package insert term or preferred term Preferred term CTCAE grade	日本人 Study 217 (N=51) n(%)	外国人 Studies 207+309 (N=353) n(%)	全体 Studies 217+207+309 (N=404) n(%)
感染症			
脊髄炎	0	1 (0.3)	1 (0.2)
1	0	0	0
2	0	1 (0.3)	1 (0.2)
3	0	0	0
4	0	0	0
5	0	0	0
>=3	0	0	0
帯状疱疹	1 (2.0)	1 (0.3)	2 (0.5)
1	0	1 (0.3)	1 (0.2)
2	1 (2.0)	0	1 (0.2)
3	0	0	0
4	0	0	0
5	0	0	0
>=3	0	0	0

CTCAE = Common Terminology Criteria for Adverse Events. Adverse events of interest are presented in pre-defined event classes; each class is based on pre-specified preferred terms.
Treatment-related adverse events include adverse events that were considered by the investigator to be possibly or probably related to study drug and adverse events with missing relationship to study drug.
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付録 2.7.4-21
Japanese and Non-Japanese
Treatment-Related Treatment-Emergent Adverse Events of Interest Specified in Japan by CTCAE Grade
Eribulin Treated Safety Population

Event class Package insert term or preferred term Preferred term CTCAE grade	日本人 Study 217 (N=51) n(%)	外国人 Studies 207+309 (N=353) n(%)	全体 Studies 217+207+309 (N=404) n(%)
感染症			
帯状疱疹	1 (2.0)	1 (0.3)	2 (0.5)
1	0	1 (0.3)	1 (0.2)
2	1 (2.0)	0	1 (0.2)
3	0	0	0
4	0	0	0
5	0	0	0
>=3	0	0	0
丹毒	0	1 (0.3)	1 (0.2)
1	0	1 (0.3)	1 (0.2)
2	0	0	0
3	0	0	0
4	0	0	0
5	0	0	0
>=3	0	0	0

CTCAE = Common Terminology Criteria for Adverse Events. Adverse events of interest are presented in pre-defined event classes; each class is based on pre-specified preferred terms.
Treatment-related adverse events include adverse events that were considered by the investigator to be possibly or probably related to study drug and adverse events with missing relationship to study drug.
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付録 2.7.4-21
Japanese and Non-Japanese
Treatment-Related Treatment-Emergent Adverse Events of Interest Specified in Japan by CTCAE Grade
Eribulin Treated Safety Population

Event class Package insert term or preferred term Preferred term CTCAE grade	日本人 Study 217 (N=51) n(%)	外国人 Studies 207+309 (N=353) n(%)	全体 Studies 217+207+309 (N=404) n(%)
感染症			
丹毒	0	1 (0.3)	1 (0.2)
1	0	1 (0.3)	1 (0.2)
2	0	0	0
3	0	0	0
4	0	0	0
5	0	0	0
>=3	0	0	0
中耳炎	1 (2.0)	0	1 (0.2)
1	0	0	0
2	1 (2.0)	0	1 (0.2)
3	0	0	0
4	0	0	0
5	0	0	0
>=3	0	0	0

CTCAE = Common Terminology Criteria for Adverse Events. Adverse events of interest are presented in pre-defined event classes; each class is based on pre-specified preferred terms.
Treatment-related adverse events include adverse events that were considered by the investigator to be possibly or probably related to study drug and adverse events with missing relationship to study drug.
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Adverse event terms are coded using Medical Dictionary for Regulatory Activities (MedDRA) version 17.1.
This table is based on adverse events data as available. Study 207 did not record laboratory abnormalities into adverse events data.

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付録 2.7.4-21
Japanese and Non-Japanese
Treatment-Related Treatment-Emergent Adverse Events of Interest Specified in Japan by CTCAE Grade
Eribulin Treated Safety Population

Event class Package insert term or preferred term Preferred term CTCAE grade	日本人 Study 217 (N=51) n(%)	外国人 Studies 207+309 (N=353) n(%)	全体 Studies 217+207+309 (N=404) n(%)
感染症			
急性中耳炎	1 (2.0)	0	1 (0.2)
1	0	0	0
2	1 (2.0)	0	1 (0.2)
3	0	0	0
4	0	0	0
5	0	0	0
>=3	0	0	0
軟部組織感染	0	1 (0.3)	1 (0.2)
1	0	0	0
2	0	1 (0.3)	1 (0.2)
3	0	0	0
4	0	0	0
5	0	0	0
>=3	0	0	0

CTCAE = Common Terminology Criteria for Adverse Events. Adverse events of interest are presented in pre-defined event classes; each class is based on pre-specified preferred terms.
Treatment-related adverse events include adverse events that were considered by the investigator to be possibly or probably related to study drug and adverse events with missing relationship to study drug.
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This table is based on adverse events data as available. Study 207 did not record laboratory abnormalities into adverse events data.

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付録 2.7.4-21
Japanese and Non-Japanese
Treatment-Related Treatment-Emergent Adverse Events of Interest Specified in Japan by CTCAE Grade
Eribulin Treated Safety Population

Event class Package insert term or preferred term Preferred term CTCAE grade	日本人 Study 217 (N=51) n(%)	外国人 Studies 207+309 (N=353) n(%)	全体 Studies 217+207+309 (N=404) n(%)
感染症			
軟部組織感染	0	1 (0.3)	1 (0.2)
1	0	0	0
2	0	1 (0.3)	1 (0.2)
3	0	0	0
4	0	0	0
5	0	0	0
>=3	0	0	0
膿尿	0	1 (0.3)	1 (0.2)
1	0	1 (0.3)	1 (0.2)
2	0	0	0
3	0	0	0
4	0	0	0
5	0	0	0
>=3	0	0	0

CTCAE = Common Terminology Criteria for Adverse Events. Adverse events of interest are presented in pre-defined event classes; each class is based on pre-specified preferred terms.
Treatment-related adverse events include adverse events that were considered by the investigator to be possibly or probably related to study drug and adverse events with missing relationship to study drug.
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This table is based on adverse events data as available. Study 207 did not record laboratory abnormalities into adverse events data.

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付録 2.7.4-21
Japanese and Non-Japanese
Treatment-Related Treatment-Emergent Adverse Events of Interest Specified in Japan by CTCAE Grade
Eribulin Treated Safety Population

Event class Package insert term or preferred term Preferred term CTCAE grade	日本人 Study 217 (N=51) n(%)	外国人 Studies 207+309 (N=353) n(%)	全体 Studies 217+207+309 (N=404) n(%)
感染症			
膿尿	0	1 (0.3)	1 (0.2)
1	0	1 (0.3)	1 (0.2)
2	0	0	0
3	0	0	0
4	0	0	0
5	0	0	0
>=3	0	0	0
敗血症	0	1 (0.3)	1 (0.2)
1	0	0	0
2	0	0	0
3	0	0	0
4	0	0	0
5	0	1 (0.3)	1 (0.2)
>=3	0	1 (0.3)	1 (0.2)

CTCAE = Common Terminology Criteria for Adverse Events. Adverse events of interest are presented in pre-defined event classes; each class is based on pre-specified preferred terms.
Treatment-related adverse events include adverse events that were considered by the investigator to be possibly or probably related to study drug and adverse events with missing relationship to study drug.
A subject with two or more adverse events in the same event class (or with same package insert term/preferred term) is counted only once for that event class (or package insert term/preferred term).
A subject is counted once by the highest non-missing CTCAE grade as applicable for preferred term and event class respectively.
Adverse event terms are coded using Medical Dictionary for Regulatory Activities (MedDRA) version 17.1.
This table is based on adverse events data as available. Study 207 did not record laboratory abnormalities into adverse events data.

Program: V:¥projects¥e7389¥iss309¥csr¥dev¥pg¥tables¥T_2_7_4_21.sas 18JUN201513:39

付録 2.7.4-21
Japanese and Non-Japanese
Treatment-Related Treatment-Emergent Adverse Events of Interest Specified in Japan by CTCAE Grade
Eribulin Treated Safety Population

Event class Package insert term or preferred term Preferred term CTCAE grade	日本人 Study 217 (N=51) n(%)	外国人 Studies 207+309 (N=353) n(%)	全体 Studies 217+207+309 (N=404) n(%)
感染症			
好中球減少性敗血症	0	1 (0.3)	1 (0.2)
1	0	0	0
2	0	0	0
3	0	0	0
4	0	0	0
5	0	1 (0.3)	1 (0.2)
>=3	0	1 (0.3)	1 (0.2)
肺炎	0	6 (1.7)	6 (1.5)
1	0	0	0
2	0	0	0
3	0	6 (1.7)	6 (1.5)
4	0	0	0
5	0	0	0
>=3	0	6 (1.7)	6 (1.5)

CTCAE = Common Terminology Criteria for Adverse Events. Adverse events of interest are presented in pre-defined event classes; each class is based on pre-specified preferred terms.
Treatment-related adverse events include adverse events that were considered by the investigator to be possibly or probably related to study drug and adverse events with missing relationship to study drug.
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付録 2.7.4-21
Japanese and Non-Japanese
Treatment-Related Treatment-Emergent Adverse Events of Interest Specified in Japan by CTCAE Grade
Eribulin Treated Safety Population

Event class Package insert term or preferred term Preferred term CTCAE grade	日本人 Study 217 (N=51) n(%)	外国人 Studies 207+309 (N=353) n(%)	全体 Studies 217+207+309 (N=404) n(%)
感染症			
気管支肺炎	0	1 (0.3)	1 (0.2)
1	0	0	0
2	0	0	0
3	0	1 (0.3)	1 (0.2)
4	0	0	0
5	0	0	0
>=3	0	1 (0.3)	1 (0.2)
肺炎	0	5 (1.4)	5 (1.2)
1	0	0	0
2	0	0	0
3	0	5 (1.4)	5 (1.2)
4	0	0	0
5	0	0	0
>=3	0	5 (1.4)	5 (1.2)

CTCAE = Common Terminology Criteria for Adverse Events. Adverse events of interest are presented in pre-defined event classes; each class is based on pre-specified preferred terms.
Treatment-related adverse events include adverse events that were considered by the investigator to be possibly or probably related to study drug and adverse events with missing relationship to study drug.
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Adverse event terms are coded using Medical Dictionary for Regulatory Activities (MedDRA) version 17.1.
This table is based on adverse events data as available. Study 207 did not record laboratory abnormalities into adverse events data.

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付録 2.7.4-21
Japanese and Non-Japanese
Treatment-Related Treatment-Emergent Adverse Events of Interest Specified in Japan by CTCAE Grade
Eribulin Treated Safety Population

Event class Package insert term or preferred term Preferred term CTCAE grade	日本人 Study 217 (N=51) n(%)	外国人 Studies 207+309 (N=353) n(%)	全体 Studies 217+207+309 (N=404) n(%)
感染症			
鼻咽頭炎	7 (13.7)	6 (1.7)	13 (3.2)
1	5 (9.8)	3 (0.8)	8 (2.0)
2	2 (3.9)	1 (0.3)	3 (0.7)
3	0	2 (0.6)	2 (0.5)
4	0	0	0
5	0	0	0
>=3	0	2 (0.6)	2 (0.5)
鼻咽頭炎	6 (11.8)	3 (0.8)	9 (2.2)
1	5 (9.8)	3 (0.8)	8 (2.0)
2	1 (2.0)	0	1 (0.2)
3	0	0	0
4	0	0	0
5	0	0	0
>=3	0	0	0

CTCAE = Common Terminology Criteria for Adverse Events. Adverse events of interest are presented in pre-defined event classes; each class is based on pre-specified preferred terms.
Treatment-related adverse events include adverse events that were considered by the investigator to be possibly or probably related to study drug and adverse events with missing relationship to study drug.
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Adverse event terms are coded using Medical Dictionary for Regulatory Activities (MedDRA) version 17.1.
This table is based on adverse events data as available. Study 207 did not record laboratory abnormalities into adverse events data.

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