SUPPLEMENTARY TABLES

Supplementary Table S1. Eribulin mesylate dose modifications and exposure in patients with or without liver lesion involvement (safety population)

Parameter	With Liver Involvement				Without Liver Involvement			
	Normal	Liver Impairment			Normal	Liver Impairment		
	A (n=204)	B (n=210)	C (n=294)	D (n=23)	A (n=336)	B (n=82)	C (n=146)	D (n=11)
Duration of treatment								
n	204	210	294	23	336	82	146	11
Days, mean	154.74	143.29	137.23	119.70	173.03	173.09	146.36	147.73
(SD)	(125.42)	(102.81)	(99.45)	(62.81)	(182.53)	(161.23)	(137.20)	(98.73)
Number of cycles completed in study								
Median	6.0	6.0	5.0	5.0	6.0	6.5	5.0	4.0
(range)	(1.0, 41.0)	(1.0, 27.0)	(1.0, 27.0)	(1.0, 11.0)	(1.0, 65.0)	(1.0, 38.0)	(1.0, 38.0)	(2.0, 15.0)
Actual dose intensity								
n	204	210	294	22	336	82	146	11
Mean, mg/m^2/week	0.83	0.78	0.78	0.64	0.81	0.77	0.77	0.67

(SD)	(0.134)	(0.155)	(0.158)	(0.165)	(0.139)	(0.164)	(0.162)	(0.217)
Patients who received dose								
n (%)	204 (100)	210 (100)	294 (100)	23 (100)	336 (100)	82 (100)	146 (100)	11 (100)
Dose reduction								
n (%)	48 (23.5)	74 (35.2)	106 (36.1)	15 (65.2)	93 (27.7)	27 (32.9)	47 (32.2)	6 (54.6)
Dose delay								
n (%)	83 (40.7)	105 (50.0)	147 (50.0)	17 (73.9)	140 (41.7)	36 (43.9)	65 (44.5)	6 (54.6)

Group A, no liver impairment; group B, increased AST and/or ALT only; group C, any abnormality except increased bilirubin level; group D, increased bilirubin level.

ALT, alanine aminotransferase; AST, aspartate aminotransferase; SD, standard deviation.

Supplementary Table S2. TEAEs occurring in >10% of patients in any group (safety population)

TEAE, n (%)	Normal		Liver Impairment					
	Group A (n=540)		Group B (n=292)		Group C (n=440)		Group D (n=34)	
	All	Grade ≥3	All	Grade ≥3	All	Grade ≥3	All	Grade ≥3
Any TEAE	520 (96.3)	328 (60.7)	278 (95.2)	209 (71.6)	424 (96.4)	326 (74.1)	34 (100)	29 (85.3)
Neutropenia	260 (48.2)	216 (40.0)	168 (57.5)	147 (50.3)	253 (57.5)	222 (50.5)	25 (73.5)	24 (70.6)
Alopecia	204 (37.8)	0	131 (44.9)	0	183 (41.6)	0	16 (47.1)	0
Nausea	140 (25.9)	2 (0.4)	96 (32.9)	1 (0.3)	143 (32.5)	5 (1.1)	9 (26.5)	0
Leukopenia	145 (26.9)	70 (13.0)	72 (24.7)	42 (14.4)	121 (27.5)	66 (15.0)	11 (32.4)	8 (23.5)
Asthenia	96 (17.8)	20 (3.7)	56 (19.2)	16 (5.5)	101 (23.0)	30 (6.8)	10 (29.4)	3 (8.8)
Decreased appetite	89 (16.5)	0	48 (16.4)	3 (1.0)	82 (18.6)	5 (1.1)	9 (26.5)	0
Diarrhea	84 (15.6)	5 (0.9)	49 (16.8)	1 (0.3)	75 (17.1)	1 (0.2)	9 (26.5)	0
Fatigue	122 (22.6)	10 (1.9)	75 (25.7)	11 (3.8)	106 (24.1)	18 (4.1)	8 (23.5)	0
Pyrexia	84 (15.6)	1 (0.2)	52 (17.8)	0	81 (18.4)	2 (0.5)	9 (26.5)	0
Anemia	90 (16.7)	3 (0.6)	53 (18.2)	11 (3.8)	96 (21.8)	16 (3.6)	7 (20.6)	2 (5.9)
Constipation	68 (12.6)	1 (0.2)	62 (21.2)	1 (0.3)	90 (20.5)	4 (0.9)	5 (14.7)	0
Vomiting	69 (12.8)	2 (0.4)	51 (17.5)	1 (0.3)	80 (18.2)	5 (1.1)	7 (20.6)	0
Headache	80 (14.8)	4 (0.7)	56 (19.2)	2 (0.7)	79 (18.0)	2 (0.5)	4 (11.8)	0

Dyspnea	65 (12.0)	17 (3.2)	37 (12.7)	10 (3.4)	63 (14.3)	19 (4.3)	6 (17.7)	1 (2.9)
Hypokalemia	21 (3.9)	5 (0.9)	12 (4.1)	4 (1.4)	28 (6.4)	9 (2.1)	6 (17.7)	3 (8.8)
Weight, decreased	41 (7.6)	2 (0.4)	45 (15.4)	0	77 (17.5)	0	6 (17.7)	1 (2.9)
Peripheral sensory neuropathy	84 (15.6)	16 (3.0)	35 (12.0)	9 (3.1)	46 (10.5)	12 (2.7)	5 (14.7)	1 (2.9)
Hyperbilirubinemia	3 (0.6)	0	5 (1.7)	1 (0.3)	9 (2.1)	2 (0.5)	5 (14.7)	2 (5.9)
Lacrimation, increased	17 (3.2)	0	26 (8.9)	1 (0.3)	30 (6.8)	1 (0.2)	5 (14.7)	0
Stomatitis	25 (4.6)	1 (0.2)	18 (6.2)	1 (0.3)	34 (7.7)	4 (0.9)	5 (14.7)	1 (2.9)
Back pain	75 (13.9)	7 (1.3)	39 (13.4)	4 (1.4)	51 (11.6)	6 (1.4)	4 (11.8)	0
Bone pain	47 (8.7)	3 (0.6)	39 (13.4)	10 (3.4)	55 (12.5)	15 (3.4)	2 (5.9)	0
Arthralgia	66 (12.2)	5 (0.9)	33 (11.3)	1 (0.3)	42 (9.6)	1 (0.2)	2 (5.9)	0
Cough	60 (11.1)	2 (0.4)	35 (12.0)	1 (0.3)	51 (11.6)	2 (0.5)	4 (11.8)	0
Paresthesia	37 (6.9)	10 (1.9)	27 (9.3)	2 (0.7)	38 (8.6)	3 (0.7)	4 (11.8)	0
Dry mouth	21 (3.9)	0	12 (4.1)	0	19 (4.3)	0	4 (11.8)	0
Epistaxis	6 (1.1)	0	4 (1.4)	0	10 (2.3)	0	4 (11.8)	0
ALT, increased	29 (5.4)	12 (2.2)	33 (11.3)	14 (4.8)	41 (9.3)	15 (3.4)	1 (2.9)	0
Pain in extremity	56 (10.4)	2 (0.4)	32 (11.0)	1 (0.3)	45 (10.2)	5 (1.1)	0	0

Group A, no liver impairment; group B, increased AST and/or ALT only; group C, any abnormality except increased bilirubin; group D, increased bilirubin.

ALT, alanine aminotransferase; AST, aspartate aminotransferase; TEAE, treatment-emergent adverse event.

Supplementary Table S3. TEAEs leading to dose modifications (reductions, delays, or interruptions) in patients with or without liver lesion involvement and by CTCAE grade (safety population)

	With Liver Involvement				Without Liver Involvement			
	Normal	Liver Impairment			Normal	Liver Impairment		
	A	B	C	D	A	B	C	D
	(n=204)	(n=210)	(n=294)	(n=23)	(n=336)	(n=82)	(n=146)	(n=11)
Overall, n (%)								
Total	85 (41.7)	114 (54.3)	154 (52.4)	21 (91.3)	146 (43.5)	45 (54.9)	77 (52.7)	5 (45.5)
Grade 1	3 (1.5)	7 (3.3)	8 (2.7)	2 (8.7)	5 (1.5)	4 (4.9)	5 (3.4)	0
Grade 2	21 (10.3)	15 (7.1)	18 (6.1)	0	26 (7.7)	10 (12.2)	16 (11.0)	0
Grade 3	38 (18.6)	53 (25.2)	73 (24.8)	6 (26.1)	73 (21.7)	23 (28.1)	41 (28.1)	4 (36.4)
Grade 4	23 (11.3)	39 (18.6)	55 (18.7)	13 (56.5)	42 (12.5)	8 (9.8)	15 (10.3)	1 (9.1)

Group A, no liver impairment; group B, increased AST and/or ALT only; group C, any abnormality except increased bilirubin; group D, increased bilirubin.

ALT, alanine aminotransferase; AST, aspartate aminotransferase; CTCAE, Common Terminology Criteria for Adverse Events; TEAE, treatment-emergent adverse event.

Supplementary Table S4. Neutrophil/granulocyte CTCAE grade at baseline and after cycle 1 in patients with liver impairment

n (%)	Normal	Liver Impairment		
	Group A (n=540)	Group B (n=292)	Group C (n=440)	Group D (n=34)
Baseline				
n	538	286	433	34
Any grade	26 (4.8)	14 (4.9)	17 (3.9)	2 (5.9)
Grade 1	25 (4.6)	13 (4.5)	16 (3.7)	1 (2.9)
Grade 2	1 (0.2)	1 (0.3)	1 (0.2)	1 (2.9)
Cycle 1 day 8				
n	532	275	414	33
Any grade	154 (28.9)	106 (38.5)	155 (37.4)	10 (30.3)
Grade 1	68 (12.8)	35 (12.7)	49 (11.8)	2 (6.1)
Grade 2	64 (12.0)	43 (15.6)	65 (15.7)	4 (12.1)
Grade 3	16 (3.0)	17 (6.2)	27 (6.5)	1 (3.0)
Grade 4	6 (1.1)	11 (4.0)	14 (3.4)	3 (9.1)
Cycle 2 day 8				
n	507	266	393	28
Any grade	77 (15.2)	59 (22.2)	83 (21.1)	4 (14.3)
Grade 1	42 (8.3)	31 (11.7)	40 (10.2)	2 (7.1)
Grade 2	29 (5.7)	22 (8.3)	33 (8.4)	2 (7.1)
Grade 3	6 (1.2)	3 (1.1)	6 (1.5)	0
Grade 4	0	3 (1.1)	4 (1.0)	0

Cycle 3 day 8				
n	427	222	320	26
Any grade	66 (15.5)	42 (18.9)	56 (17.5)	4 (15.4)
Grade 1	38 (8.9)	21 (9.5)	27 (8.4)	3 (11.5)
Grade 2	20 (4.7)	16 (7.2)	21 (6.6)	1 (3.8)
Grade 3	7 (1.6)	4 (1.8)	6 (1.9)	0
Grade 4	1 (0.2)	1 (0.5)	2 (0.6)	0

Percentages based on the number of subjects with nonmissing data at each visit within each laboratory test.

Group A, no liver impairment; group B, increased AST and/or ALT only; group C, any abnormality except increased bilirubin; group D, increased bilirubin.

ALT, alanine aminotransferase; AST, aspartate aminotransferase; CTCAE, Common Terminology Criteria for Adverse Events.

Supplementary Table S5. Overall survival in patients with liver impairment (ITT population)

	Normal	Liver Impairment Subgroup		
	Group A (n=546)	**Group B (n=294)**	**Group C (n=443)**	**Group D (n=34)**
Median OS, months (95% CI)	17.5 (15.9–18.8)	13.2 (11.7–14.5)	12.3 (11.1–13.6)	12.3 (8.0–16.1)
OS rate (95% CI)[a]				
1 year	0.672 (0.633–0.712)	0.542 (0.485–0.599)	0.505 (0.458–0.552)	0.529 (0.362–0.739)
2 years	0.370 (0.328–0.412)	0.199 (0.151–0.248)	0.183 (0.145–0.221)	0.206 (0.070–0.342)
3 years	0.212 (0.170–0.253)	0.098 (0.055–0.141)	0.085 (0.051–0.118)	0 (NE–NE)

[a]OS rate at 1, 2, and 3 years and the 95% CIs were calculated using Kaplan–Meier estimate and Greenwood's formula.

Group A, no liver impairment; group B, increased AST and/or ALT only; group C, any abnormality except increased bilirubin; group D, increased bilirubin.

ALT, alanine aminotransferase; AST, aspartate aminotransferase; CI, confidence interval; ITT, intent to treat; NE, nonestimable; OS, overall survival.

Supplementary Table S6. Overall survival in patients with or without liver involvement (ITT population)

	With Liver Involvement				Without Liver Involvement			
	Normal	Liver Impairment			Normal	Liver Impairment		
	Group A (n=207)	Group B (n=211)	Group C (n=296)	Group D (n=23)	Group A (n=339)	Group B (n=83)	Group C (n=147)	Group D (n=11)
Overall, n (%)								
Median OS, months (95% CI)	16.0 (14.6–18.0)	11.9 (10.0–13.2)	11.6 (10.0–13.1)	9.5 (6.9–16.3)	18.6 (16.5–22.2)	18.1 (14.9–21.2)	14.5 (11.2–16.7)	12.6 (6.3–16.3)
OS rate (95% CI)[a]								
1 year	0.640 (0.574–0.706)	0.487 (0.419–0.554)	0.475 (0.418–0.532)	0.435 (0.232–0.637)	0.692 (0.643–0.742)	0.683 (0.582–0.784)	0.565 (0.484–0.686)	0.727 (0.464–0.990)
2 years	0.305 (0.238–0.371)	0.144 (0.094–0.195)	0.149 (0.105–0.192)	0.217 (0.049–0.386)	0.408 (0.354–0.461)	0.340 (0.233–0.448)	0.251 (0.178–0.324)	0.182 (0.000–0.410)
3 years	0.146 (0.084–0.208)	0.081 (0.039–0.123)	0.081 (0.044–0.119)	0 (NE–NE)	0.248 (0.193–0.303)	0.137 (0.029–0.244)	0.097 (0.034–0.161)	0 (NE–NE)

[a]OS rates at 1, 2, and 3 years and the 95% CIs were calculated using Kaplan–Meier estimate and Greenwood's formula.

Group A, no liver impairment; group B, increased AST and/or ALT only; group C, any abnormality except increased bilirubin; group D, increased bilirubin.

ALT, alanine aminotransferase; AST, aspartate aminotransferase; CI, confidence interval; ITT, intent to treat; NE, nonestimable; OS, overall survival.