

**Supplementary Table 2.** AEs considered potentially related to regorafenib with an incidence  $\geq 10\%$  (safety analysis set)

Regorafenib-related AE, n (%)	Regorafenib 72 mg/m <sup>2</sup> concomitant with VI (n=2)		Regorafenib 72 mg/m <sup>2</sup> sequential with VI (n=6)		Regorafenib 82 mg/m <sup>2</sup> sequential with VI (n=13)		Total (N=21)	
	All grades	Grade $\geq 3$	All grades	Grade $\geq 3$	All grades	Grade $\geq 3$	All grades	Grade $\geq 3$
Neutropenia <sup>a</sup>	2 (100)	2 (100)	3 (50)	3 (50)	6 (46)	5 (38)	11 (52)	10 (48)
Anemia	2 (100)	0	2 (33)	1 (17)	5 (38)	2 (15)	9 (43)	3 (14)
AST increased	2 (100)	2 (100)	3 (50)	2 (33)	4 (31)	0	9 (43)	4 (19)
ALT increased	2 (100)	2 (100)	3 (50)	2 (33)	2 (15)	1 (8)	7 (33)	5 (24)
Thrombocytopenia <sup>b</sup>	1 (50)	1 (50)	2 (33)	0	4 (31)	3 (23)	7 (33)	4 (19)
Decreased appetite	1 (50)	1 (50)	2 (33)	0	3 (23)	1 (8)	6 (29)	2 (10)
Weight decreased	1 (50)	0	1 (17)	0	4 (31)	0	6 (29)	0
Fatigue	1 (50)	0	2 (33)	0	2 (15)	0	5 (24)	0
Leukopenia <sup>c</sup>	1 (50)	1 (50)	1 (17)	1 (17)	3 (23)	0	5 (24)	2 (10)
Diarrhea	2 (100)	0	0	0	2 (15)	0	4 (19)	0
TSH increased	0	0	2 (33)	0	2 (15)	0	4 (19)	0
GGT increased	1 (50)	0	1 (17)	1 (17)	2 (15)	0	4 (19)	1 (5)
Abdominal pain	1 (50)	1 (50)	0	0	2 (15)	0	3 (14)	1 (5)
Blood bilirubin increased	1 (50)	0	1 (17)	0	1 (8)	0	3 (14)	0
Dry skin	0	0	2 (33)	0	1 (8)	0	3 (14)	0
Nausea	0	0	2 (33)	1 (17)	1 (8)	0	3 (14)	1 (5)
Proteinuria	1 (50)	0	2 (33)	0	0	0	3 (14)	0
HFSR	0	0	3 (50)	1 (17)	0	0	3 (14)	1 (5)
Rash	1 (50)	0	1 (17)	0	1 (8)	0	3 (14)	0
Rash maculopapular	0	0	1 (17)	1 (17)	2 (15)	0	3 (14)	1 (5)
Vomiting	1 (50)	1 (50)	1 (17)	0	1(8)	0	3 (14)	1 (5)
Alopecia	0	0	1 (17)	0	1 (8)	0	2 (10)	0
Erythema	0	0	0	0	2 (15)	0	2 (10)	0
Headache	1 (50)	0	0	0	1 (8)	0	2 (10)	0

Hypertension	0	0	1 (17)	0	1 (8)	0	2 (10)	0
Hypothyroidism	0	0	0	0	2 (15)	0	2 (10)	0
Lymphopenia <sup>d</sup>	1 (50)	0	1 (17)	0	0	0	2 (10)	0
Myalgia	0	0	1 (17)	0	1 (8)	0	2 (10)	0
Prothrombin time ratio increased	0	0	2 (33)	0	0	0	2 (10)	0
Stomatitis	0	0	1 (17)	0	1 (8)	0	2 (10)	0

AE, adverse event; ALT, alanine aminotransferase; AST, aspartate aminotransferase; GGT, gamma-glutamyl transferase; HFSR, hand-foot skin reaction; TSH, thyroid stimulating hormone; VI, vincristine and irinotecan; WBC, white blood cell.

Or <sup>a</sup>neutrophil count decreased; <sup>b</sup>platelet count decreased; <sup>c</sup>WBC count decreased; <sup>d</sup> lymphocyte count decreased.