

Supplementary Table 3. AEs considered potentially related to VI with an incidence $\geq 10\%$ (safety analysis set)

Drug-related AE, n (%)	Regorafenib 72 mg/m ² concomitant with VI (n=2)		Regorafenib 72 mg/m ² sequential with VI (n=6)		Regorafenib 82 mg/m ² sequential with VI (n=13)		Total (N=21)	
	All grades	Grade ≥ 3	All grades	Grade ≥ 3	All grades	Grade ≥ 3	All grades	Grade ≥ 3
Irinotecan-related AE								
Diarrhea	1 (50)	0	4 (67)	1 (17)	10 (77)	3 (23)	15 (71)	4 (19)
Neutropenia ^a	2 (100)	2 (100)	6 (100)	6 (100)	7 (54)	7 (54)	15 (71)	15 (71)
Anemia	1 (50)	0	3 (50)	1 (17)	9 (69)	5 (39)	13 (62)	6 (29)
Thrombocytopenia ^b	1 (50)	1 (50)	4 (67)	2 (33)	6 (46)	4 (31)	11 (52)	7 (33)
Vomiting	1 (50)	1 (50)	2 (33)	0	8 (62)	2 (15)	11 (52)	3 (14)
Decreased appetite	2 (100)	1 (50)	4 (67)	0	4 (31)	1 (8)	10 (48)	2 (10)
Abdominal pain	1 (50)	1 (50)	2 (33)	0	5 (39)	1 (8)	8 (38)	2 (10)
Leukopenia ^c	1 (50)	1 (50)	3 (50)	3 (50)	4 (31)	2 (15)	8 (38)	6 (29)
Nausea	0	0	3 (50)	1 (17)	5 (39)	0	8 (38)	1 (5)
AST increased	1 (50)	1 (50)	2 (33)	0	4 (31)	0	7 (33)	1 (5)
ALT increased	1 (50)	1 (50)	1 (17)	0	4 (31)	0	6 (29)	1 (5)
Alopecia	0	0	2 (33)	0	3 (23)	0	5 (24)	0
Weight decreased	1 (50)	0	1 (17)	0	3 (23)	0	5 (24)	0
Fatigue	1 (50)	0	2 (33)	0	1 (8)	0	4 (19)	0
Lethargy	0	0	2 (33)	0	2 (15)	0	4 (19)	0
Asthenia	0	0	1 (17)	0	2 (15)	1 (8)	3 (14)	1 (5)
Lymphopenia ^d	1 (50)	0	1 (17)	0	1 (8)	1 (8)	3 (14)	1 (5)
Headache	1 (50)	0	1 (17)	0	0	0	2 (10)	0
Hypokalemia	1 (50)	0	0	0	1 (8)	1 (8)	2 (10)	1 (5)
Oral pain	0	0	1 (17)	0	1 (8)	0	2 (10)	0
Pyrexia	1 (50)	0	0	0	1 (8)	0	2 (10)	0
Skin hyperpigmentation	0	0	2 (33)	0	0	0	2 (10)	0
Vincristine-related AE								
Neutropenia ^a	2 (100)	1 (50)	5 (83)	5 (83)	4 (31)	4 (31)	11 (52)	10 (48)

Anemia	0	0	1 (17)	0	7 (54)	5 (39)	8 (38)	5 (24)
Leukopenia ^c	1 (50)	0	3 (50)	3 (50)	4 (31)	2 (15)	8 (38)	5 (24)
Abdominal pain	1 (50)	1 (50)	1 (17)	0	5 (39)	1 (8)	7 (33)	2 (10)
Nausea	0	0	3 (50)	1 (17)	4 (31)	0	7 (33)	1 (5)
Vomiting	1 (50)	1 (50)	2 (33)	0	4 (31)	0	7 (33)	1 (5)
Decreased appetite	1 (50)	1 (50)	3 (50)	0	2 (15)	0	6 (29)	1 (5)
Thrombocytopenia ^b	1 (50)	1 (50)	2 (33)	1 (17)	2 (15)	1 (8)	5 (24)	3 (14)
AST increased	1 (50)	1 (50)	0	0	3 (23)	0	4 (19)	1 (5)
ALT increased	1 (50)	1 (50)	1 (17)	0	2 (15)	0	4 (19)	1 (5)
Alopecia	0	0	2 (33)	0	2 (15)	0	4 (19)	0
Fatigue	1 (50)	0	2 (33)	0	1 (8)	0	4 (19)	0
Lethargy	0	0	2 (33)	0	2 (15)	0	4 (19)	0
Constipation	1 (50)	0	1 (17)	0	1 (8)	0	3 (14)	0
Diarrhea	0	0	0	0	3 (21)	0	3 (14)	0
GGT increased	1 (50)	1 (50)	0	0	2 (15)	0	3 (14)	1 (5)
Pain in jaw	1 (5)	0	1 (17)	0	1 (8)	0	3 (14)	0
Toothache	0	0	2 (33)	0	1 (8)	0	3 (14)	0
Blood bilirubin increased	1 (50)	0	0	0	1 (8)	0	2 (10)	0
Myalgia	0	0	1 (17)	0	1 (8)	0	2 (10)	0
Headache	0	0	1 (17)	0	1 (8)	0	2 (10)	0
Oral pain	0	0	1 (16)	0	1 (8)	0	2 (10)	0
Pain in extremity	0	0	2 (33)	0	0	0	2 (10)	0
Peripheral sensory neuropathy	1 (50)	1 (50)	1 (17)	0	0	0	2 (10)	1 (5)
Skin hyperpigmentation	0	0	2 (33)	0	0	0	2 (10)	0
Weight decreased	0	0	1 (17)	0	1 (8)	0	2 (10)	0

AE, adverse event; ALT, alanine aminotransferase; AST, aspartate aminotransferase; GGT, gamma-glutamyl transferase; VI, vincristine and irinotecan; WBC, white blood cell.

^aOr neutrophil count decreased. ^bOr platelet count decreased. ^cOr WBC count decreased. ^dOr lymphocyte count decreased.