表 2.7.4.8-1　　治験薬の投与中止に至った有害事象の PT 別発現頻度（03 試験、P3 パート）（続き 2）

解析対象集団：Phase 3 Safety Set
Study Intervention: Any Drug

Number of Participants Evaluable for AEs	EC (N=153)		EC+mFOLFOX6 (N=232)		Control (N=229)	
	Any Grade	Grade 3 or Higher	Any Grade	Grade 3 or Higher	Any Grade	Grade 3 or Higher
Number (%) of Participants: by Preferred Term	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
腹膜炎	1 (0.7)	1 (0.7)	1 (0.4)	1 (0.4)	0	0
肺炎	0	0	1 (0.4)	1 (0.4)	2 (0.9)	2 (0.9)
肺臓炎	0	0	1 (0.4)	0	1 (0.4)	1 (0.4)
そう痒症	0	0	1 (0.4)	0	0	0
発疹	0	0	1 (0.4)	1 (0.4)	0	0
斑状丘疹状皮疹	0	0	1 (0.4)	0	0	0
敗血症性ショック	0	0	1 (0.4)	1 (0.4)	2 (0.9)	2 (0.9)
皮膚障害	0	0	1 (0.4)	1 (0.4)	0	0
顎関節症	0	0	1 (0.4)	0	0	0
嘔吐	0	0	1 (0.4)	1 (0.4)	1 (0.4)	1 (0.4)
体重減少	0	0	1 (0.4)	0	0	0
白血球数減少	0	0	1 (0.4)	0	1 (0.4)	0
腹部膨満	0	0	0	0	1 (0.4)	1 (0.4)
急性腎障害	1 (0.7)	1 (0.7)	0	0	1 (0.4)	1 (0.4)
アナフィラキシー反応	1 (0.7)	1 (0.7)	0	0	1 (0.4)	1 (0.4)
背部痛	0	0	0	0	1 (0.4)	0
二酸化炭素減少	0	0	0	0	1 (0.4)	1 (0.4)
心停止	0	0	0	0	1 (0.4)	1 (0.4)
両耳難聴	0	0	0	0	1 (0.4)	1 (0.4)
注意力障害	1 (0.7)	0	0	0	0	0
呼吸困難	0	0	0	0	1 (0.4)	1 (0.4)
腸炎	0	0	0	0	1 (0.4)	1 (0.4)
紅斑	1 (0.7)	1 (0.7)	0	0	0	0

MedDRA v27.1 coding dictionary applied.
Preferred terms are sorted in descending frequency of Any Grade EC+mFOLFOX6 column.
Other study intervention includes: irinotecan, oxaliplatin, leucovorin or levo-leucovorin, fluorouracil (bolus or infusion), capecitabine, and bevacizumab (as appropriate for the treatment group).
Permanent discontinuation of other study intervention is defined as permanent stop of all drugs.
Permanent discontinuation of any study intervention is defined as a permanent stop of encorafenib, cetuximab, or other study intervention.

表 2.7.4.8-1　　治験薬の投与中止に至った有害事象の PT 別発現頻度（03 試験、P3 パート）（続き 3）

解析対象集団：Phase 3 Safety Set
Study Intervention: Any Drug

Number of Participants Evaluable for AEs	EC (N=153)		EC+mFOLFOX6 (N=232)		Control (N=229)	
	Any Grade	Grade 3 or Higher	Any Grade	Grade 3 or Higher	Any Grade	Grade 3 or Higher
Number (%) of Participants: by Preferred Term	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
転倒	0	0	0	0	1 (0.4)	1 (0.4)
発熱性好中球減少症	0	0	0	0	1 (0.4)	1 (0.4)
全身健康状態悪化	1 (0.7)	0	0	0	3 (1.3)	2 (0.9)
歯肉出血	1 (0.7)	1 (0.7)	0	0	0	0
血便排泄	1 (0.7)	0	0	0	0	0
高アンモニア血性脳症	0	0	0	0	1 (0.4)	1 (0.4)
低カルシウム血症	1 (0.7)	1 (0.7)	0	0	0	0
低マグネシウム血症	1 (0.7)	1 (0.7)	0	0	0	0
治癒不良	0	0	0	0	1 (0.4)	1 (0.4)
輸注関連過敏反応	1 (0.7)	1 (0.7)	0	0	0	0
腸管穿孔	0	0	0	0	1 (0.4)	1 (0.4)
心筋梗塞	0	0	0	0	2 (0.9)	2 (0.9)
神経系障害	1 (0.7)	1 (0.7)	0	0	0	0
神経毒性	0	0	0	0	1 (0.4)	0
食道癌	1 (0.7)	1 (0.7)	0	0	0	0
呼吸不全	0	0	0	0	1 (0.4)	1 (0.4)
てんかん重積状態	0	0	0	0	1 (0.4)	1 (0.4)
血栓性微小血管症	0	0	0	0	1 (0.4)	1 (0.4)

MedDRA v27.1 coding dictionary applied.
Preferred terms are sorted in descending frequency of Any Grade EC+mFOLFOX6 column.
Other study intervention includes: irinotecan, oxaliplatin, leucovorin or levo-leucovorin, fluorouracil (bolus or infusion), capecitabine, and bevacizumab (as appropriate for the treatment group).
Permanent discontinuation of other study intervention is defined as permanent stop of all drugs.
Permanent discontinuation of any study intervention is defined as a permanent stop of encorafenib, cetuximab, or other study intervention.

表 2.7.4.8-1　　治験薬の投与中止に至った有害事象の PT 別発現頻度（03 試験、P3 パート）（続き 4）

解析対象集団：Phase 3 Safety Set
Study Intervention: Encorafenib

Number of Participants Evaluable for AEs	EC (N=153)		EC+mFOLFOX6 (N=232)		Control (N=229)	
	Any Grade	Grade 3 or Higher	Any Grade	Grade 3 or Higher	Any Grade	Grade 3 or Higher
Number (%) of Participants: by Preferred Term	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
有害事象発現例数	16 (10.5)	13 (8.5)	32 (13.8)	20 (8.6)	0	0
リパーゼ増加	0	0	5 (2.2)	1 (0.4)	0	0
疾患進行	2 (1.3)	2 (1.3)	3 (1.3)	3 (1.3)	0	0
無力症	0	0	2 (0.9)	1 (0.4)	0	0
過敏症	0	0	2 (0.9)	1 (0.4)	0	0
腸閉塞	2 (1.3)	2 (1.3)	2 (0.9)	2 (0.9)	0	0
末梢性感覚ニューロパチー	0	0	2 (0.9)	1 (0.4)	0	0
上腹部痛	1 (0.7)	1 (0.7)	1 (0.4)	0	0	0
腹部敗血症	0	0	1 (0.4)	1 (0.4)	0	0
貧血	0	0	1 (0.4)	1 (0.4)	0	0
関節痛	0	0	1 (0.4)	0	0	0
COVID－19	0	0	1 (0.4)	1 (0.4)	0	0
脳卒中	0	0	1 (0.4)	1 (0.4)	0	0
食欲減退	0	0	1 (0.4)	1 (0.4)	0	0
下痢	0	0	1 (0.4)	0	0	0
消化管穿孔	0	0	1 (0.4)	1 (0.4)	0	0
高リパーゼ血症	0	0	1 (0.4)	0	0	0
注入に伴う反応	2 (1.3)	1 (0.7)	1 (0.4)	0	0	0
間質性肺疾患	0	0	1 (0.4)	1 (0.4)	0	0
黄疸	0	0	1 (0.4)	1 (0.4)	0	0
関節硬直	0	0	1 (0.4)	0	0	0

MedDRA v27.1 coding dictionary applied.
Preferred terms are sorted in descending frequency of Any Grade EC+mFOLFOX6 column.
Other study intervention includes: irinotecan, oxaliplatin, leucovorin or levo-leucovorin, fluorouracil (bolus or infusion), capecitabine, and bevacizumab (as appropriate for the treatment group).
Permanent discontinuation of other study intervention is defined as permanent stop of all drugs.
Permanent discontinuation of any study intervention is defined as a permanent stop of encorafenib, cetuximab, or other study intervention.

表 2.7.4.8-1　　治験薬の投与中止に至った有害事象の PT 別発現頻度（03 試験、P3 パート）（続き 5）

解析対象集団：Phase 3 Safety Set
Study Intervention: Encorafenib

Number of Participants Evaluable for AEs	EC (N=153)		EC+mFOLFOX6 (N=232)		Control (N=229)	
	Any Grade	Grade 3 or Higher	Any Grade	Grade 3 or Higher	Any Grade	Grade 3 or Higher
Number (%) of Participants: by Preferred Term	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
ラクナ梗塞	0	0	1 (0.4)	1 (0.4)	0	0
大腸穿孔	0	0	1 (0.4)	1 (0.4)	0	0
粘膜の炎症	0	0	1 (0.4)	1 (0.4)	0	0
筋肉痛	0	0	1 (0.4)	0	0	0
悪心	0	0	1 (0.4)	0	0	0
眼窩血腫	0	0	1 (0.4)	1 (0.4)	0	0
腹膜炎	1 (0.7)	1 (0.7)	1 (0.4)	1 (0.4)	0	0
肺炎	0	0	1 (0.4)	1 (0.4)	0	0
肺臓炎	0	0	1 (0.4)	0	0	0
そう痒症	0	0	1 (0.4)	0	0	0
発疹	0	0	1 (0.4)	1 (0.4)	0	0
敗血症	0	0	1 (0.4)	1 (0.4)	0	0
敗血症性ショック	0	0	1 (0.4)	1 (0.4)	0	0
皮膚障害	0	0	1 (0.4)	1 (0.4)	0	0
顎関節症	0	0	1 (0.4)	0	0	0
嘔吐	0	0	1 (0.4)	1 (0.4)	0	0
体重減少	0	0	1 (0.4)	0	0	0
腹痛	1 (0.7)	1 (0.7)	0	0	0	0
急性腎障害	1 (0.7)	1 (0.7)	0	0	0	0
アナフィラキシー反応	1 (0.7)	1 (0.7)	0	0	0	0
全身健康状態悪化	1 (0.7)	0	0	0	0	0
歯肉出血	1 (0.7)	1 (0.7)	0	0	0	0
血便排泄	1 (0.7)	0	0	0	0	0

MedDRA v27.1 coding dictionary applied.
Preferred terms are sorted in descending frequency of Any Grade EC+mFOLFOX6 column.
Other study intervention includes: irinotecan, oxaliplatin, leucovorin or levo-leucovorin, fluorouracil (bolus or infusion), capecitabine, and bevacizumab (as appropriate for the treatment group).
Permanent discontinuation of other study intervention is defined as permanent stop of all drugs.
Permanent discontinuation of any study intervention is defined as a permanent stop of encorafenib, cetuximab, or other study intervention.

表 2.7.4.8-1　　治験薬の投与中止に至った有害事象の PT 別発現頻度（03 試験、P3 パート）（続き 6）

解析対象集団：Phase 3 Safety Set
Study Intervention: Encorafenib

Number of Participants Evaluable for AEs	EC (N=153)		EC+mFOLFOX6 (N=232)		Control (N=229)	
	Any Grade	Grade 3 or Higher	Any Grade	Grade 3 or Higher	Any Grade	Grade 3 or Higher
Number (%) of Participants: by Preferred Term	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
低カルシウム血症	1 (0.7)	1 (0.7)	0	0	0	0
低マグネシウム血症	1 (0.7)	1 (0.7)	0	0	0	0
神経系障害	1 (0.7)	1 (0.7)	0	0	0	0
食道癌	1 (0.7)	1 (0.7)	0	0	0	0

MedDRA v27.1 coding dictionary applied.
Preferred terms are sorted in descending frequency of Any Grade EC+mFOLFOX6 column.
Other study intervention includes: irinotecan, oxaliplatin, leucovorin or levo-leucovorin, fluorouracil (bolus or infusion), capecitabine, and bevacizumab (as appropriate for the treatment group).
Permanent discontinuation of other study intervention is defined as permanent stop of all drugs.
Permanent discontinuation of any study intervention is defined as a permanent stop of encorafenib, cetuximab, or other study intervention.

表 2.7.4.8-1　　治験薬の投与中止に至った有害事象の PT 別発現頻度（03 試験、P3 パート）（続き 7）

解析対象集団：Phase 3 Safety Set
Study Intervention: Cetuximab

Number of Participants Evaluable for AEs	EC (N=153)		EC+mFOLFOX6 (N=232)		Control (N=229)	
	Any Grade	Grade 3 or Higher	Any Grade	Grade 3 or Higher	Any Grade	Grade 3 or Higher
Number (%) of Participants: by Preferred Term	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
有害事象発現例数	20 (13.1)	16 (10.5)	34 (14.7)	24 (10.3)	0	0
リパーゼ増加	0	0	5 (2.2)	1 (0.4)	0	0
疾患進行	3 (2.0)	3 (2.0)	3 (1.3)	3 (1.3)	0	0
注入に伴う反応	3 (2.0)	2 (1.3)	3 (1.3)	2 (0.9)	0	0
貧血	0	0	2 (0.9)	2 (0.9)	0	0
無力症	0	0	2 (0.9)	1 (0.4)	0	0
過敏症	0	0	2 (0.9)	1 (0.4)	0	0
腸閉塞	2 (1.3)	2 (1.3)	2 (0.9)	2 (0.9)	0	0
末梢性感覚ニューロパチー	0	0	2 (0.9)	1 (0.4)	0	0
上腹部痛	1 (0.7)	1 (0.7)	1 (0.4)	0	0	0
腹部敗血症	0	0	1 (0.4)	1 (0.4)	0	0
関節痛	0	0	1 (0.4)	0	0	0
COVID－19	0	0	1 (0.4)	1 (0.4)	0	0
脳卒中	0	0	1 (0.4)	1 (0.4)	0	0
食欲減退	0	0	1 (0.4)	1 (0.4)	0	0
消化管穿孔	0	0	1 (0.4)	1 (0.4)	0	0
高リパーゼ血症	0	0	1 (0.4)	0	0	0
間質性肺疾患	0	0	1 (0.4)	1 (0.4)	0	0
黄疸	0	0	1 (0.4)	1 (0.4)	0	0
関節硬直	0	0	1 (0.4)	0	0	0
ラクナ梗塞	0	0	1 (0.4)	1 (0.4)	0	0

MedDRA v27.1 coding dictionary applied.
Preferred terms are sorted in descending frequency of Any Grade EC+mFOLFOX6 column.
Other study intervention includes: irinotecan, oxaliplatin, leucovorin or levo-leucovorin, fluorouracil (bolus or infusion), capecitabine, and bevacizumab (as appropriate for the treatment group).
Permanent discontinuation of other study intervention is defined as permanent stop of all drugs.
Permanent discontinuation of any study intervention is defined as a permanent stop of encorafenib, cetuximab, or other study intervention.

表 2.7.4.8-1　　治験薬の投与中止に至った有害事象の PT 別発現頻度（03 試験、P3 パート）（続き 8）

解析対象集団：Phase 3 Safety Set
Study Intervention: Cetuximab

Number of Participants Evaluable for AEs	EC (N=153)		EC+mFOLFOX6 (N=232)		Control (N=229)	
	Any Grade	Grade 3 or Higher	Any Grade	Grade 3 or Higher	Any Grade	Grade 3 or Higher
Number (%) of Participants: by Preferred Term	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
大腸穿孔	0	0	1 (0.4)	1 (0.4)	0	0
粘膜の炎症	0	0	1 (0.4)	1 (0.4)	0	0
筋肉痛	0	0	1 (0.4)	0	0	0
悪心	0	0	1 (0.4)	0	0	0
好中球減少症	0	0	1 (0.4)	0	0	0
眼窩血腫	0	0	1 (0.4)	1 (0.4)	0	0
爪囲炎	0	0	1 (0.4)	1 (0.4)	0	0
腹膜炎	1 (0.7)	1 (0.7)	1 (0.4)	1 (0.4)	0	0
肺炎	0	0	1 (0.4)	1 (0.4)	0	0
肺臓炎	0	0	1 (0.4)	0	0	0
そう痒症	0	0	1 (0.4)	0	0	0
発疹	0	0	1 (0.4)	1 (0.4)	0	0
斑状丘疹状皮疹	0	0	1 (0.4)	0	0	0
敗血症	0	0	1 (0.4)	1 (0.4)	0	0
敗血症性ショック	0	0	1 (0.4)	1 (0.4)	0	0
皮膚障害	0	0	1 (0.4)	1 (0.4)	0	0
顎関節症	0	0	1 (0.4)	0	0	0
嘔吐	0	0	1 (0.4)	1 (0.4)	0	0
体重減少	0	0	1 (0.4)	0	0	0
腹痛	1 (0.7)	1 (0.7)	0	0	0	0
急性腎障害	1 (0.7)	1 (0.7)	0	0	0	0
アナフィラキシー反応	1 (0.7)	1 (0.7)	0	0	0	0
注意力障害	1 (0.7)	0	0	0	0	0

MedDRA v27.1 coding dictionary applied.
Preferred terms are sorted in descending frequency of Any Grade EC+mFOLFOX6 column.
Other study intervention includes: irinotecan, oxaliplatin, leucovorin or levo-leucovorin, fluorouracil (bolus or infusion), capecitabine, and bevacizumab (as appropriate for the treatment group).
Permanent discontinuation of other study intervention is defined as permanent stop of all drugs.
Permanent discontinuation of any study intervention is defined as a permanent stop of encorafenib, cetuximab, or other study intervention.

表 2.7.4.8-1　　治験薬の投与中止に至った有害事象の PT 別発現頻度（03 試験、P3 パート）（続き 9）

解析対象集団：Phase 3 Safety Set
Study Intervention: Cetuximab

Number of Participants Evaluable for AEs	EC (N=153)		EC+mFOLFOX6 (N=232)		Control (N=229)	
	Any Grade	Grade 3 or Higher	Any Grade	Grade 3 or Higher	Any Grade	Grade 3 or Higher
Number (%) of Participants: by Preferred Term	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
紅斑	1 (0.7)	1 (0.7)	0	0	0	0
全身健康状態悪化	1 (0.7)	0	0	0	0	0
血便排泄	1 (0.7)	0	0	0	0	0
輸注関連過敏反応	1 (0.7)	1 (0.7)	0	0	0	0
神経系障害	1 (0.7)	1 (0.7)	0	0	0	0
食道癌	1 (0.7)	1 (0.7)	0	0	0	0

MedDRA v27.1 coding dictionary applied.
Preferred terms are sorted in descending frequency of Any Grade EC+mFOLFOX6 column.
Other study intervention includes: irinotecan, oxaliplatin, leucovorin or levo-leucovorin, fluorouracil (bolus or infusion), capecitabine, and bevacizumab (as appropriate for the treatment group).
Permanent discontinuation of other study intervention is defined as permanent stop of all drugs.
Permanent discontinuation of any study intervention is defined as a permanent stop of encorafenib, cetuximab, or other study intervention.

表 2.7.4.8-1　　治験薬の投与中止に至った有害事象の PT 別発現頻度（03 試験、P3 パート）（続き 10）

解析対象集団：Phase 3 Safety Set
Study Intervention: Other

Number of Participants Evaluable for AEs	EC (N=153)		EC+mFOLFOX6 (N=232)		Control (N=229)	
	Any Grade	Grade 3 or Higher	Any Grade	Grade 3 or Higher	Any Grade	Grade 3 or Higher
Number (%) of Participants: by Preferred Term	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
有害事象発現例数	0	0	48 (20.7)	27 (11.6)	40 (17.5)	36 (15.7)
無力症	0	0	6 (2.6)	1 (0.4)	1 (0.4)	0
貧血	0	0	5 (2.2)	4 (1.7)	0	0
食欲減退	0	0	3 (1.3)	2 (0.9)	0	0
疾患進行	0	0	3 (1.3)	3 (1.3)	1 (0.4)	1 (0.4)
末梢性感覚ニューロパチー	0	0	3 (1.3)	1 (0.4)	0	0
血小板数減少	0	0	3 (1.3)	0	1 (0.4)	0
尿路感染	0	0	3 (1.3)	0	1 (0.4)	1 (0.4)
疲労	0	0	2 (0.9)	0	1 (0.4)	1 (0.4)
間質性肺疾患	0	0	2 (0.9)	1 (0.4)	0	0
腸閉塞	0	0	2 (0.9)	2 (0.9)	5 (2.2)	4 (1.7)
悪心	0	0	2 (0.9)	0	1 (0.4)	1 (0.4)
好中球数減少	0	0	2 (0.9)	0	1 (0.4)	1 (0.4)
発熱	0	0	2 (0.9)	1 (0.4)	0	0
敗血症	0	0	2 (0.9)	2 (0.9)	1 (0.4)	1 (0.4)
腹痛	0	0	1 (0.4)	0	1 (0.4)	1 (0.4)
腹部敗血症	0	0	1 (0.4)	1 (0.4)	1 (0.4)	1 (0.4)
急性冠動脈症候群	0	0	1 (0.4)	1 (0.4)	0	0
関節痛	0	0	1 (0.4)	0	0	0
COVID－19	0	0	1 (0.4)	1 (0.4)	0	0
蜂巣炎	0	0	1 (0.4)	1 (0.4)	0	0

MedDRA v27.1 coding dictionary applied.
Preferred terms are sorted in descending frequency of Any Grade EC+mFOLFOX6 column.
Other study intervention includes: irinotecan, oxaliplatin, leucovorin or levo-leucovorin, fluorouracil (bolus or infusion), capecitabine, and bevacizumab (as appropriate for the treatment group).
Permanent discontinuation of other study intervention is defined as permanent stop of all drugs.
Permanent discontinuation of any study intervention is defined as a permanent stop of encorafenib, cetuximab, or other study intervention.

表 2.7.4.8-1　　治験薬の投与中止に至った有害事象の PT 別発現頻度（03 試験、P3 パート）（続き 11）

解析対象集団：Phase 3 Safety Set
Study Intervention: Other

Number of Participants Evaluable for AEs	EC (N=153)		EC+mFOLFOX6 (N=232)		Control (N=229)	
	Any Grade	Grade 3 or Higher	Any Grade	Grade 3 or Higher	Any Grade	Grade 3 or Higher
Number (%) of Participants: by Preferred Term	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
脳卒中	0	0	1 (0.4)	1 (0.4)	0	0
胸痛	0	0	1 (0.4)	0	0	0
下痢	0	0	1 (0.4)	0	1 (0.4)	1 (0.4)
消化管穿孔	0	0	1 (0.4)	1 (0.4)	1 (0.4)	1 (0.4)
注入に伴う反応	0	0	1 (0.4)	0	0	0
関節硬直	0	0	1 (0.4)	0	0	0
ラクナ梗塞	0	0	1 (0.4)	1 (0.4)	0	0
大腸穿孔	0	0	1 (0.4)	1 (0.4)	0	0
リパーゼ増加	0	0	1 (0.4)	1 (0.4)	1 (0.4)	1 (0.4)
倦怠感	0	0	1 (0.4)	0	1 (0.4)	0
粘膜の炎症	0	0	1 (0.4)	1 (0.4)	0	0
筋肉痛	0	0	1 (0.4)	0	0	0
末梢性ニューロパチー	0	0	1 (0.4)	0	1 (0.4)	0
眼窩血腫	0	0	1 (0.4)	1 (0.4)	0	0
手掌・足底発赤知覚不全症候群	0	0	1 (0.4)	0	0	0
錯感覚	0	0	1 (0.4)	1 (0.4)	0	0
末梢動脈閉塞性疾患	0	0	1 (0.4)	1 (0.4)	0	0
腹膜炎	0	0	1 (0.4)	1 (0.4)	0	0
肺炎	0	0	1 (0.4)	1 (0.4)	2 (0.9)	2 (0.9)
敗血症性ショック	0	0	1 (0.4)	1 (0.4)	2 (0.9)	2 (0.9)
皮膚障害	0	0	1 (0.4)	1 (0.4)	0	0
体重減少	0	0	1 (0.4)	0	0	0
白血球数減少	0	0	1 (0.4)	0	1 (0.4)	0

MedDRA v27.1 coding dictionary applied.
Preferred terms are sorted in descending frequency of Any Grade EC+mFOLFOX6 column.
Other study intervention includes: irinotecan, oxaliplatin, leucovorin or levo-leucovorin, fluorouracil (bolus or infusion), capecitabine, and bevacizumab (as appropriate for the treatment group).
Permanent discontinuation of other study intervention is defined as permanent stop of all drugs.
Permanent discontinuation of any study intervention is defined as a permanent stop of encorafenib, cetuximab, or other study intervention.

表 2.7.4.8-1　　治験薬の投与中止に至った有害事象の PT 別発現頻度（03 試験、P3 パート）（続き 12）

解析対象集団：Phase 3 Safety Set
Study Intervention: Other

Number of Participants Evaluable for AEs	EC (N=153)		EC+mFOLFOX6 (N=232)		Control (N=229)	
	Any Grade	Grade 3 or Higher	Any Grade	Grade 3 or Higher	Any Grade	Grade 3 or Higher
Number (%) of Participants: by Preferred Term	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
腹部膨満	0	0	0	0	1 (0.4)	1 (0.4)
急性腎障害	0	0	0	0	1 (0.4)	1 (0.4)
アナフィラキシー反応	0	0	0	0	1 (0.4)	1 (0.4)
背部痛	0	0	0	0	1 (0.4)	0
二酸化炭素減少	0	0	0	0	1 (0.4)	1 (0.4)
心停止	0	0	0	0	1 (0.4)	1 (0.4)
両耳難聴	0	0	0	0	1 (0.4)	1 (0.4)
呼吸困難	0	0	0	0	1 (0.4)	1 (0.4)
腸炎	0	0	0	0	1 (0.4)	1 (0.4)
転倒	0	0	0	0	1 (0.4)	1 (0.4)
発熱性好中球減少症	0	0	0	0	1 (0.4)	1 (0.4)
全身健康状態悪化	0	0	0	0	3 (1.3)	2 (0.9)
高アンモニア血性脳症	0	0	0	0	1 (0.4)	1 (0.4)
治癒不良	0	0	0	0	1 (0.4)	1 (0.4)
腸管穿孔	0	0	0	0	1 (0.4)	1 (0.4)
心筋梗塞	0	0	0	0	2 (0.9)	2 (0.9)
神経毒性	0	0	0	0	1 (0.4)	0
肺臓炎	0	0	0	0	1 (0.4)	1 (0.4)
呼吸不全	0	0	0	0	1 (0.4)	1 (0.4)
てんかん重積状態	0	0	0	0	1 (0.4)	1 (0.4)
血栓性微小血管症	0	0	0	0	1 (0.4)	1 (0.4)
嘔吐	0	0	0	0	1 (0.4)	1 (0.4)

MedDRA v27.1 coding dictionary applied.
Preferred terms are sorted in descending frequency of Any Grade EC+mFOLFOX6 column.
Other study intervention includes: irinotecan, oxaliplatin, leucovorin or levo-leucovorin, fluorouracil (bolus or infusion), capecitabine, and bevacizumab (as appropriate for the treatment group).
Permanent discontinuation of other study intervention is defined as permanent stop of all drugs.
Permanent discontinuation of any study intervention is defined as a permanent stop of encorafenib, cetuximab, or other study intervention.

出典［総括報告書 5.3.5.1-2（ONO-7702-03 試験、Phase3 PFS PCD）Table 14.3.1.1.2.5.1］

表 2.7.4.8-2　　治験薬の減量に至った有害事象の PT 別発現頻度（03 試験、P3 パート）

解析対象集団：Phase 3 Safety Set
Study Intervention: Any Drug

Number of Participants Evaluable for AEs	EC (N=153)		EC+mFOLFOX6 (N=232)		Control (N=229)	
	Any Grade	Grade 3 or Higher	Any Grade	Grade 3 or Higher	Any Grade	Grade 3 or Higher
Number (%) of Participants: by Preferred Term	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
有害事象発現例数	16 (10.5)	3 (2.0)	152 (65.5)	60 (25.9)	124 (54.1)	48 (21.0)
好中球数減少	0	0	28 (12.1)	17 (7.3)	25 (10.9)	15 (6.6)
好中球減少症	0	0	24 (10.3)	7 (3.0)	26 (11.4)	13 (5.7)
末梢性ニューロパチー	0	0	17 (7.3)	5 (2.2)	15 (6.6)	0
末梢性感覚ニューロパチー	0	0	14 (6.0)	1 (0.4)	17 (7.4)	3 (1.3)
血小板数減少	0	0	13 (5.6)	3 (1.3)	6 (2.6)	0
貧血	0	0	12 (5.2)	4 (1.7)	3 (1.3)	1 (0.4)
無力症	0	0	12 (5.2)	1 (0.4)	6 (2.6)	1 (0.4)
神経毒性	0	0	12 (5.2)	2 (0.9)	7 (3.1)	0
疲労	1 (0.7)	0	10 (4.3)	1 (0.4)	10 (4.4)	1 (0.4)
悪心	0	0	10 (4.3)	4 (1.7)	9 (3.9)	2 (0.9)
錯感覚	0	0	10 (4.3)	1 (0.4)	4 (1.7)	1 (0.4)
食欲減退	0	0	9 (3.9)	1 (0.4)	2 (0.9)	0
嘔吐	0	0	9 (3.9)	1 (0.4)	3 (1.3)	0
下痢	2 (1.3)	1 (0.7)	8 (3.4)	0	14 (6.1)	1 (0.4)
体重減少	0	0	8 (3.4)	1 (0.4)	2 (0.9)	0
リパーゼ増加	2 (1.3)	0	7 (3.0)	4 (1.7)	0	0
関節痛	3 (2.0)	0	6 (2.6)	0	0	0
倦怠感	1 (0.7)	1 (0.7)	5 (2.2)	0	1 (0.4)	1 (0.4)
口内炎	0	0	5 (2.2)	2 (0.9)	3 (1.3)	1 (0.4)
白血球数減少	0	0	5 (2.2)	2 (0.9)	8 (3.5)	2 (0.9)
発疹	1 (0.7)	0	4 (1.7)	0	0	0

MedDRA v27.1 coding dictionary applied.
Preferred terms are sorted in descending frequency of Any Grade EC+mFOLFOX6 column.
Other study intervention includes: irinotecan, oxaliplatin, leucovorin or levo-leucovorin, fluorouracil (bolus or infusion), capecitabine, and bevacizumab (as appropriate for the treatment group).
Dose reduction of other study intervention is defined as reduction of at least one drug.

表 2.7.4.8-2　　治験薬の減量に至った有害事象の PT 別発現頻度（03 試験、P3 パート）（続き 1）

解析対象集団：Phase 3 Safety Set
Study Intervention: Any Drug

Number of Participants Evaluable for AEs	EC (N=153)		EC+mFOLFOX6 (N=232)		Control (N=229)	
	Any Grade	Grade 3 or Higher	Any Grade	Grade 3 or Higher	Any Grade	Grade 3 or Higher
Number (%) of Participants: by Preferred Term	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
アラニンアミノトランスフェラーゼ増加	0	0	3 (1.3)	2 (0.9)	2 (0.9)	1 (0.4)
心電図 QT 延長	1 (0.7)	0	3 (1.3)	0	0	0
手掌・足底発赤知覚不全症候群	0	0	3 (1.3)	1 (0.4)	8 (3.5)	1 (0.4)
発熱	0	0	3 (1.3)	1 (0.4)	1 (0.4)	0
血小板減少症	0	0	3 (1.3)	0	4 (1.7)	1 (0.4)
血中クレアチニン増加	0	0	2 (0.9)	0	0	0
悪寒	0	0	2 (0.9)	0	0	0
ざ瘡様皮膚炎	1 (0.7)	0	2 (0.9)	1 (0.4)	0	0
味覚不全	0	0	2 (0.9)	0	0	0
粘膜の炎症	0	0	2 (0.9)	0	4 (1.7)	1 (0.4)
筋肉痛	1 (0.7)	0	2 (0.9)	0	0	0
爪囲炎	0	0	2 (0.9)	1 (0.4)	0	0
多発ニューロパチー	0	0	2 (0.9)	0	1 (0.4)	0
腹痛	0	0	1 (0.4)	0	3 (1.3)	0
急性腎障害	0	0	1 (0.4)	1 (0.4)	0	0
脱毛症	0	0	1 (0.4)	0	0	0
肛門の炎症	0	0	1 (0.4)	0	0	0
アスパラギン酸アミノトランスフェラーゼ増加	0	0	1 (0.4)	1 (0.4)	1 (0.4)	0
心房細動	0	0	1 (0.4)	1 (0.4)	0	0
胸痛	0	0	1 (0.4)	0	1 (0.4)	0
浮動性めまい	0	0	1 (0.4)	0	3 (1.3)	0
消化不良	0	0	1 (0.4)	0	0	0
鼻出血	0	0	1 (0.4)	0	0	0
発熱性好中球減少症	0	0	1 (0.4)	1 (0.4)	4 (1.7)	4 (1.7)

MedDRA v27.1 coding dictionary applied.
Preferred terms are sorted in descending frequency of Any Grade EC+mFOLFOX6 column.
Other study intervention includes: irinotecan, oxaliplatin, leucovorin or levo-leucovorin, fluorouracil (bolus or infusion), capecitabine, and bevacizumab (as appropriate for the treatment group).
Dose reduction of other study intervention is defined as reduction of at least one drug.

表 2.7.4.8-2　　治験薬の減量に至った有害事象の PT 別発現頻度（03 試験、P3 パート）（続き 2）

解析対象集団：Phase 3 Safety Set
Study Intervention: Any Drug

Number of Participants Evaluable for AEs	EC (N=153)		EC+mFOLFOX6 (N=232)		Control (N=229)	
	Any Grade	Grade 3 or Higher	Any Grade	Grade 3 or Higher	Any Grade	Grade 3 or Higher
Number (%) of Participants: by Preferred Term	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
歯肉出血	0	0	1 (0.4)	0	0	0
重度月経出血	0	0	1 (0.4)	1 (0.4)	0	0
高ビリルビン血症	0	0	1 (0.4)	1 (0.4)	0	0
高リパーゼ血症	0	0	1 (0.4)	0	0	0
高トランスアミナーゼ血症	0	0	1 (0.4)	0	0	0
感覚鈍麻	0	0	1 (0.4)	0	0	0
イレウス	0	0	1 (0.4)	0	0	0
注入に伴う反応	0	0	1 (0.4)	0	2 (0.9)	0
嗜眠	0	0	1 (0.4)	0	0	0
表皮内悪性黒色腫	0	0	1 (0.4)	1 (0.4)	0	0
肺臓炎	0	0	1 (0.4)	0	0	0
肛門周囲痛	0	0	1 (0.4)	0	0	0
肺塞栓症	0	0	1 (0.4)	1 (0.4)	0	0
腎不全	0	0	1 (0.4)	1 (0.4)	0	0
網膜剥離	0	0	1 (0.4)	1 (0.4)	0	0
皮膚変色	0	0	1 (0.4)	0	0	0
皮膚障害	0	0	1 (0.4)	0	0	0
皮膚剥脱	0	0	1 (0.4)	0	0	0
硬膜下血腫	0	0	1 (0.4)	1 (0.4)	0	0
温度変化不耐症	0	0	1 (0.4)	0	1 (0.4)	0
中毒性皮疹	0	0	1 (0.4)	1 (0.4)	0	0
霧視	0	0	1 (0.4)	0	0	0
血管性浮腫	1 (0.7)	0	0	0	0	0
不安	0	0	0	0	1 (0.4)	0

MedDRA v27.1 coding dictionary applied.
Preferred terms are sorted in descending frequency of Any Grade EC+mFOLFOX6 column.
Other study intervention includes: irinotecan, oxaliplatin, leucovorin or levo-leucovorin, fluorouracil (bolus or infusion), capecitabine, and bevacizumab (as appropriate for the treatment group).
Dose reduction of other study intervention is defined as reduction of at least one drug.

表 2.7.4.8-2　　治験薬の減量に至った有害事象の PT 別発現頻度（03 試験、P3 パート）（続き 3）

解析対象集団：Phase 3 Safety Set
Study Intervention: Any Drug

Number of Participants Evaluable for AEs	EC (N=153)		EC+mFOLFOX6 (N=232)		Control (N=229)	
	Any Grade	Grade 3 or Higher	Any Grade	Grade 3 or Higher	Any Grade	Grade 3 or Higher
Number (%) of Participants: by Preferred Term	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
関節炎	1 (0.7)	0	0	0	0	0
COVID－19	0	0	0	0	1 (0.4)	0
クロストリジウム・ディフィシレ大腸炎	0	0	0	0	1 (0.4)	1 (0.4)
大腸炎	0	0	0	0	2 (0.9)	0
便秘	0	0	0	0	1 (0.4)	0
憩室炎	0	0	0	0	1 (0.4)	1 (0.4)
薬物過敏症	0	0	0	0	1 (0.4)	0
皮膚乾燥	1 (0.7)	0	0	0	0	0
小腸炎	0	0	0	0	1 (0.4)	0
錐体外路障害	0	0	0	0	1 (0.4)	0
熱感	0	0	0	0	1 (0.4)	0
胃腸炎	0	0	0	0	1 (0.4)	1 (0.4)
肝機能異常	0	0	0	0	1 (0.4)	0
高血圧	1 (0.7)	1 (0.7)	0	0	0	0
低カリウム血症	0	0	0	0	1 (0.4)	1 (0.4)
喉頭痙攣	0	0	0	0	1 (0.4)	1 (0.4)
白血球減少症	0	0	0	0	2 (0.9)	2 (0.9)
食道痛	0	0	0	0	1 (0.4)	0
眼筋麻痺	0	0	0	0	1 (0.4)	1 (0.4)
口の錯感覚	0	0	0	0	1 (0.4)	0
蛋白尿	0	0	0	0	1 (0.4)	0
そう痒症	1 (0.7)	0	0	0	0	0
鼻漏	0	0	0	0	1 (0.4)	0

MedDRA v27.1 coding dictionary applied.
Preferred terms are sorted in descending frequency of Any Grade EC+mFOLFOX6 column.
Other study intervention includes: irinotecan, oxaliplatin, leucovorin or levo-leucovorin, fluorouracil (bolus or infusion), capecitabine, and bevacizumab (as appropriate for the treatment group).
Dose reduction of other study intervention is defined as reduction of at least one drug.

表 2.7.4.8-2　　治験薬の減量に至った有害事象の PT 別発現頻度（03 試験、P3 パート）（続き 4）

解析対象集団：Phase 3 Safety Set
Study Intervention: Any Drug

Number of Participants Evaluable for AEs	EC (N=153)		EC+mFOLFOX6 (N=232)		Control (N=229)	
	Any Grade	Grade 3 or Higher	Any Grade	Grade 3 or Higher	Any Grade	Grade 3 or Higher
Number (%) of Participants: by Preferred Term	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
上気道感染	0	0	0	0	2 (0.9)	1 (0.4)

MedDRA v27.1 coding dictionary applied.
Preferred terms are sorted in descending frequency of Any Grade EC+mFOLFOX6 column.
Other study intervention includes: irinotecan, oxaliplatin, leucovorin or levo-leucovorin, fluorouracil (bolus or infusion), capecitabine, and bevacizumab (as appropriate for the treatment group).
Dose reduction of other study intervention is defined as reduction of at least one drug.

表 2.7.4.8-2　　治験薬の減量に至った有害事象の PT 別発現頻度（03 試験、P3 パート）（続き 5）

解析対象集団：Phase 3 Safety Set
Study Intervention: Encorafenib

Number of Participants Evaluable for AEs	EC (N=153)		EC+mFOLFOX6 (N=232)		Control (N=229)	
	Any Grade	Grade 3 or Higher	Any Grade	Grade 3 or Higher	Any Grade	Grade 3 or Higher
Number (%) of Participants: by Preferred Term	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
有害事象発現例数	13 (8.5)	2 (1.3)	59 (25.4)	20 (8.6)	0	0
貧血	0	0	6 (2.6)	2 (0.9)	0	0
関節痛	3 (2.0)	0	6 (2.6)	0	0	0
リパーゼ増加	2 (1.3)	0	6 (2.6)	3 (1.3)	0	0
悪心	0	0	5 (2.2)	3 (1.3)	0	0
神経毒性	0	0	5 (2.2)	2 (0.9)	0	0
嘔吐	0	0	5 (2.2)	1 (0.4)	0	0
疲労	1 (0.7)	0	4 (1.7)	0	0	0
食欲減退	0	0	3 (1.3)	0	0	0
心電図 QT 延長	1 (0.7)	0	3 (1.3)	0	0	0
発熱	0	0	3 (1.3)	1 (0.4)	0	0
血中クレアチニン増加	0	0	2 (0.9)	0	0	0
下痢	1 (0.7)	0	2 (0.9)	0	0	0
筋肉痛	1 (0.7)	0	2 (0.9)	0	0	0
発疹	0	0	2 (0.9)	0	0	0
体重減少	0	0	2 (0.9)	0	0	0
アラニンアミノトランスフェラーゼ増加	0	0	1 (0.4)	1 (0.4)	0	0
脱毛症	0	0	1 (0.4)	0	0	0
アスパラギン酸アミノトランスフェラーゼ増加	0	0	1 (0.4)	1 (0.4)	0	0
心房細動	0	0	1 (0.4)	1 (0.4)	0	0
鼻出血	0	0	1 (0.4)	0	0	0
歯肉出血	0	0	1 (0.4)	0	0	0

MedDRA v27.1 coding dictionary applied.
Preferred terms are sorted in descending frequency of Any Grade EC+mFOLFOX6 column.
Other study intervention includes: irinotecan, oxaliplatin, leucovorin or levo-leucovorin, fluorouracil (bolus or infusion), capecitabine, and bevacizumab (as appropriate for the treatment group).
Dose reduction of other study intervention is defined as reduction of at least one drug.

表 2.7.4.8-2　　治験薬の減量に至った有害事象の PT 別発現頻度（03 試験、P3 パート）（続き 6）

解析対象集団：Phase 3 Safety Set
Study Intervention: Encorafenib

Number of Participants Evaluable for AEs	EC (N=153)		EC+mFOLFOX6 (N=232)		Control (N=229)	
	Any Grade	Grade 3 or Higher	Any Grade	Grade 3 or Higher	Any Grade	Grade 3 or Higher
Number (%) of Participants: by Preferred Term	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
重度月経出血	0	0	1 (0.4)	1 (0.4)	0	0
高ビリルビン血症	0	0	1 (0.4)	1 (0.4)	0	0
高リパーゼ血症	0	0	1 (0.4)	0	0	0
嗜眠	0	0	1 (0.4)	0	0	0
倦怠感	1 (0.7)	1 (0.7)	1 (0.4)	0	0	0
表皮内悪性黒色腫	0	0	1 (0.4)	1 (0.4)	0	0
粘膜の炎症	0	0	1 (0.4)	0	0	0
好中球減少症	0	0	1 (0.4)	1 (0.4)	0	0
好中球数減少	0	0	1 (0.4)	1 (0.4)	0	0
手掌・足底発赤知覚不全症候群	0	0	1 (0.4)	1 (0.4)	0	0
末梢性感覚ニューロパチー	0	0	1 (0.4)	0	0	0
肺臓炎	0	0	1 (0.4)	0	0	0
腎不全	0	0	1 (0.4)	1 (0.4)	0	0
網膜剥離	0	0	1 (0.4)	1 (0.4)	0	0
皮膚変色	0	0	1 (0.4)	0	0	0
皮膚障害	0	0	1 (0.4)	0	0	0
硬膜下血腫	0	0	1 (0.4)	1 (0.4)	0	0
霧視	0	0	1 (0.4)	0	0	0
血管性浮腫	1 (0.7)	0	0	0	0	0
関節炎	1 (0.7)	0	0	0	0	0
ざ瘡様皮膚炎	1 (0.7)	0	0	0	0	0
高血圧	1 (0.7)	1 (0.7)	0	0	0	0
そう痒症	1 (0.7)	0	0	0	0	0

MedDRA v27.1 coding dictionary applied.
Preferred terms are sorted in descending frequency of Any Grade EC+mFOLFOX6 column.
Other study intervention includes: irinotecan, oxaliplatin, leucovorin or levo-leucovorin, fluorouracil (bolus or infusion), capecitabine, and bevacizumab (as appropriate for the treatment group).
Dose reduction of other study intervention is defined as reduction of at least one drug.

表 2.7.4.8-2　　治験薬の減量に至った有害事象の PT 別発現頻度（03 試験、P3 パート）（続き 7）

解析対象集団：Phase 3 Safety Set
Study Intervention: Cetuximab

Number of Participants Evaluable for AEs	EC (N=153)		EC+mFOLFOX6 (N=232)		Control (N=229)	
	Any Grade	Grade 3 or Higher	Any Grade	Grade 3 or Higher	Any Grade	Grade 3 or Higher
Number (%) of Participants: by Preferred Term	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
有害事象発現例数	4 (2.6)	1 (0.7)	21 (9.1)	10 (4.3)	0	0
体重減少	0	0	6 (2.6)	1 (0.4)	0	0
食欲減退	0	0	2 (0.9)	1 (0.4)	0	0
ざ瘡様皮膚炎	0	0	2 (0.9)	1 (0.4)	0	0
好中球数減少	0	0	2 (0.9)	2 (0.9)	0	0
爪囲炎	0	0	2 (0.9)	1 (0.4)	0	0
発疹	1 (0.7)	0	2 (0.9)	0	0	0
口内炎	0	0	2 (0.9)	1 (0.4)	0	0
貧血	0	0	1 (0.4)	1 (0.4)	0	0
悪寒	0	0	1 (0.4)	0	0	0
悪心	0	0	1 (0.4)	1 (0.4)	0	0
手掌・足底発赤知覚不全症候群	0	0	1 (0.4)	0	0	0
皮膚変色	0	0	1 (0.4)	0	0	0
皮膚剥脱	0	0	1 (0.4)	0	0	0
硬膜下血腫	0	0	1 (0.4)	1 (0.4)	0	0
中毒性皮疹	0	0	1 (0.4)	1 (0.4)	0	0
下痢	1 (0.7)	1 (0.7)	0	0	0	0
皮膚乾燥	1 (0.7)	0	0	0	0	0
そう痒症	1 (0.7)	0	0	0	0	0

MedDRA v27.1 coding dictionary applied.
Preferred terms are sorted in descending frequency of Any Grade EC+mFOLFOX6 column.
Other study intervention includes: irinotecan, oxaliplatin, leucovorin or levo-leucovorin, fluorouracil (bolus or infusion), capecitabine, and bevacizumab (as appropriate for the treatment group).
Dose reduction of other study intervention is defined as reduction of at least one drug.

表 2.7.4.8-2　　治験薬の減量に至った有害事象の PT 別発現頻度（03 試験、P3 パート）（続き 8）

解析対象集団：Phase 3 Safety Set
Study Intervention: Other

Number of Participants Evaluable for AEs	EC (N=153)		EC+mFOLFOX6 (N=232)		Control (N=229)	
	Any Grade	Grade 3 or Higher	Any Grade	Grade 3 or Higher	Any Grade	Grade 3 or Higher
Number (%) of Participants: by Preferred Term	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
有害事象発現例数	0	0	139 (59.9)	48 (20.7)	124 (54.1)	48 (21.0)
好中球数減少	0	0	27 (11.6)	16 (6.9)	25 (10.9)	15 (6.6)
好中球減少症	0	0	23 (9.9)	6 (2.6)	26 (11.4)	13 (5.7)
末梢性ニューロパチー	0	0	17 (7.3)	5 (2.2)	15 (6.6)	0
末梢性感覚ニューロパチー	0	0	14 (6.0)	1 (0.4)	17 (7.4)	3 (1.3)
血小板数減少	0	0	13 (5.6)	3 (1.3)	6 (2.6)	0
無力症	0	0	12 (5.2)	1 (0.4)	6 (2.6)	1 (0.4)
錯感覚	0	0	10 (4.3)	1 (0.4)	4 (1.7)	1 (0.4)
神経毒性	0	0	9 (3.9)	1 (0.4)	7 (3.1)	0
悪心	0	0	8 (3.4)	2 (0.9)	9 (3.9)	2 (0.9)
体重減少	0	0	8 (3.4)	1 (0.4)	2 (0.9)	0
貧血	0	0	7 (3.0)	3 (1.3)	3 (1.3)	1 (0.4)
食欲減退	0	0	7 (3.0)	1 (0.4)	2 (0.9)	0
疲労	0	0	7 (3.0)	1 (0.4)	10 (4.4)	1 (0.4)
下痢	0	0	6 (2.6)	0	14 (6.1)	1 (0.4)
口内炎	0	0	5 (2.2)	1 (0.4)	3 (1.3)	1 (0.4)
白血球数減少	0	0	5 (2.2)	2 (0.9)	8 (3.5)	2 (0.9)
倦怠感	0	0	4 (1.7)	0	1 (0.4)	1 (0.4)
嘔吐	0	0	4 (1.7)	0	3 (1.3)	0
血小板減少症	0	0	3 (1.3)	0	4 (1.7)	1 (0.4)
アラニンアミノトランスフェラーゼ増加	0	0	2 (0.9)	1 (0.4)	2 (0.9)	1 (0.4)
味覚不全	0	0	2 (0.9)	0	0	0

MedDRA v27.1 coding dictionary applied.
Preferred terms are sorted in descending frequency of Any Grade EC+mFOLFOX6 column.
Other study intervention includes: irinotecan, oxaliplatin, leucovorin or levo-leucovorin, fluorouracil (bolus or infusion), capecitabine, and bevacizumab (as appropriate for the treatment group).
Dose reduction of other study intervention is defined as reduction of at least one drug.

表 2.7.4.8-2　　治験薬の減量に至った有害事象の PT 別発現頻度（03 試験、P3 パート）（続き 9）

解析対象集団：Phase 3 Safety Set
Study Intervention: Other

Number of Participants Evaluable for AEs	EC (N=153)		EC+mFOLFOX6 (N=232)		Control (N=229)	
	Any Grade	Grade 3 or Higher	Any Grade	Grade 3 or Higher	Any Grade	Grade 3 or Higher
Number (%) of Participants: by Preferred Term	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
粘膜の炎症	0	0	2 (0.9)	0	4 (1.7)	1 (0.4)
多発ニューロパチー	0	0	2 (0.9)	0	1 (0.4)	0
発疹	0	0	2 (0.9)	0	0	0
腹痛	0	0	1 (0.4)	0	3 (1.3)	0
急性腎障害	0	0	1 (0.4)	1 (0.4)	0	0
肛門の炎症	0	0	1 (0.4)	0	0	0
胸痛	0	0	1 (0.4)	0	1 (0.4)	0
悪寒	0	0	1 (0.4)	0	0	0
ざ瘡様皮膚炎	0	0	1 (0.4)	1 (0.4)	0	0
浮動性めまい	0	0	1 (0.4)	0	3 (1.3)	0
消化不良	0	0	1 (0.4)	0	0	0
発熱性好中球減少症	0	0	1 (0.4)	1 (0.4)	4 (1.7)	4 (1.7)
高トランスアミナーゼ血症	0	0	1 (0.4)	0	0	0
感覚鈍麻	0	0	1 (0.4)	0	0	0
イレウス	0	0	1 (0.4)	0	0	0
注入に伴う反応	0	0	1 (0.4)	0	2 (0.9)	0
リパーゼ増加	0	0	1 (0.4)	1 (0.4)	0	0
手掌・足底発赤知覚不全症候群	0	0	1 (0.4)	0	8 (3.5)	1 (0.4)
肛門周囲痛	0	0	1 (0.4)	0	0	0
肺塞栓症	0	0	1 (0.4)	1 (0.4)	0	0
皮膚変色	0	0	1 (0.4)	0	0	0
硬膜下血腫	0	0	1 (0.4)	1 (0.4)	0	0
温度変化不耐症	0	0	1 (0.4)	0	1 (0.4)	0
不安	0	0	0	0	1 (0.4)	0

MedDRA v27.1 coding dictionary applied.
Preferred terms are sorted in descending frequency of Any Grade EC+mFOLFOX6 column.
Other study intervention includes: irinotecan, oxaliplatin, leucovorin or levo-leucovorin, fluorouracil (bolus or infusion), capecitabine, and bevacizumab (as appropriate for the treatment group).
Dose reduction of other study intervention is defined as reduction of at least one drug.

表 2.7.4.8-2　　治験薬の減量に至った有害事象の PT 別発現頻度（03 試験、P3 パート）（続き 10）

解析対象集団：Phase 3 Safety Set
Study Intervention: Other

Number of Participants Evaluable for AEs	EC (N=153)		EC+mFOLFOX6 (N=232)		Control (N=229)	
	Any Grade	Grade 3 or Higher	Any Grade	Grade 3 or Higher	Any Grade	Grade 3 or Higher
Number (%) of Participants: by Preferred Term	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
アスパラギン酸アミノトランスフェラーゼ増加	0	0	0	0	1 (0.4)	0
COVID－19	0	0	0	0	1 (0.4)	0
クロストリジウム・ディフィシレ大腸炎	0	0	0	0	1 (0.4)	1 (0.4)
大腸炎	0	0	0	0	2 (0.9)	0
便秘	0	0	0	0	1 (0.4)	0
憩室炎	0	0	0	0	1 (0.4)	1 (0.4)
薬物過敏症	0	0	0	0	1 (0.4)	0
小腸炎	0	0	0	0	1 (0.4)	0
錐体外路障害	0	0	0	0	1 (0.4)	0
熱感	0	0	0	0	1 (0.4)	0
胃腸炎	0	0	0	0	1 (0.4)	1 (0.4)
肝機能異常	0	0	0	0	1 (0.4)	0
低カリウム血症	0	0	0	0	1 (0.4)	1 (0.4)
喉頭痙攣	0	0	0	0	1 (0.4)	1 (0.4)
白血球減少症	0	0	0	0	2 (0.9)	2 (0.9)
食道痛	0	0	0	0	1 (0.4)	0
眼筋麻痺	0	0	0	0	1 (0.4)	1 (0.4)
口の錯感覚	0	0	0	0	1 (0.4)	0
蛋白尿	0	0	0	0	1 (0.4)	0
発熱	0	0	0	0	1 (0.4)	0
鼻漏	0	0	0	0	1 (0.4)	0
上気道感染	0	0	0	0	2 (0.9)	1 (0.4)

MedDRA v27.1 coding dictionary applied.
Preferred terms are sorted in descending frequency of Any Grade EC+mFOLFOX6 column.
Other study intervention includes: irinotecan, oxaliplatin, leucovorin or levo-leucovorin, fluorouracil (bolus or infusion), capecitabine, and bevacizumab (as appropriate for the treatment group).
Dose reduction of other study intervention is defined as reduction of at least one drug.

出典［総括報告書 5.3.5.1-2（ONO-7702-03 試験、Phase3 PFS PCD）Table 14.3.1.1.4.1］

表 2.7.4.8-3　　治験薬の休薬に至った有害事象の PT 別発現頻度（03 試験、P3 パート）

解析対象集団：Phase 3 Safety Set
Study Intervention: Any Drug

Number of Participants Evaluable for AEs	EC (N=153)		EC+mFOLFOX6 (N=232)		Control (N=229)	
	Any Grade	Grade 3 or Higher	Any Grade	Grade 3 or Higher	Any Grade	Grade 3 or Higher
Number (%) of Participants: by Preferred Term	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
有害事象発現例数	63 (41.2)	30 (19.6)	212 (91.4)	165 (71.1)	168 (73.4)	87 (38.0)
好中球数減少	1 (0.7)	1 (0.7)	45 (19.4)	31 (13.4)	30 (13.1)	18 (7.9)
好中球減少症	1 (0.7)	1 (0.7)	38 (16.4)	27 (11.6)	26 (11.4)	9 (3.9)
発熱	7 (4.6)	0	35 (15.1)	4 (1.7)	6 (2.6)	0
末梢性ニューロパチー	0	0	28 (12.1)	14 (6.0)	12 (5.2)	6 (2.6)
貧血	1 (0.7)	0	27 (11.6)	17 (7.3)	5 (2.2)	1 (0.4)
COVID－19	12 (7.8)	0	26 (11.2)	0	13 (5.7)	0
末梢性感覚ニューロパチー	0	0	26 (11.2)	13 (5.6)	13 (5.7)	4 (1.7)
血小板数減少	0	0	23 (9.9)	3 (1.3)	7 (3.1)	2 (0.9)
疲労	1 (0.7)	1 (0.7)	16 (6.9)	4 (1.7)	7 (3.1)	4 (1.7)
嘔吐	2 (1.3)	1 (0.7)	16 (6.9)	4 (1.7)	7 (3.1)	1 (0.4)
無力症	3 (2.0)	1 (0.7)	15 (6.5)	6 (2.6)	5 (2.2)	1 (0.4)
下痢	4 (2.6)	0	15 (6.5)	1 (0.4)	17 (7.4)	6 (2.6)
神経毒性	0	0	15 (6.5)	12 (5.2)	6 (2.6)	0
錯感覚	0	0	15 (6.5)	8 (3.4)	6 (2.6)	3 (1.3)
血小板減少症	1 (0.7)	0	15 (6.5)	0	7 (3.1)	0
注入に伴う反応	3 (2.0)	0	12 (5.2)	1 (0.4)	6 (2.6)	0
悪心	5 (3.3)	1 (0.7)	12 (5.2)	2 (0.9)	13 (5.7)	2 (0.9)
リパーゼ増加	2 (1.3)	2 (1.3)	11 (4.7)	10 (4.3)	1 (0.4)	1 (0.4)
食欲減退	1 (0.7)	1 (0.7)	9 (3.9)	2 (0.9)	2 (0.9)	0
手掌・足底発赤知覚不全症候群	1 (0.7)	0	9 (3.9)	6 (2.6)	3 (1.3)	1 (0.4)
白血球数減少	0	0	9 (3.9)	3 (1.3)	7 (3.1)	2 (0.9)

MedDRA v27.1 coding dictionary applied.
Preferred terms are sorted in descending frequency of Any Grade EC+mFOLFOX6 column.
Other study intervention includes: irinotecan, oxaliplatin, leucovorin or levo-leucovorin, fluorouracil (bolus or infusion), capecitabine, and bevacizumab (as appropriate for the treatment group).
Dose interruption of other study intervention is defined as temporary stop of at least one drug or permanent stop of at least one (but not all) drugs.

表 2.7.4.8-3　　治験薬の休薬に至った有害事象の PT 別発現頻度（03 試験、P3 パート）（続き 1）

解析対象集団：Phase 3 Safety Set
Study Intervention: Any Drug

Number of Participants Evaluable for AEs	EC (N=153)		EC+mFOLFOX6 (N=232)		Control (N=229)	
	Any Grade	Grade 3 or Higher	Any Grade	Grade 3 or Higher	Any Grade	Grade 3 or Higher
Number (%) of Participants: by Preferred Term	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
腹痛	2 (1.3)	1 (0.7)	8 (3.4)	5 (2.2)	14 (6.1)	1 (0.4)
関節痛	0	0	8 (3.4)	4 (1.7)	0	0
薬物過敏症	1 (0.7)	0	8 (3.4)	4 (1.7)	2 (0.9)	0
口内炎	0	0	8 (3.4)	4 (1.7)	0	0
上気道感染	1 (0.7)	0	8 (3.4)	2 (0.9)	7 (3.1)	0
腸閉塞	6 (3.9)	5 (3.3)	7 (3.0)	7 (3.0)	2 (0.9)	1 (0.4)
アラニンアミノトランスフェラーゼ増加	0	0	6 (2.6)	3 (1.3)	6 (2.6)	3 (1.3)
心電図 QT 延長	1 (0.7)	0	6 (2.6)	2 (0.9)	1 (0.4)	1 (0.4)
粘膜の炎症	0	0	6 (2.6)	3 (1.3)	1 (0.4)	0
発疹	1 (0.7)	1 (0.7)	6 (2.6)	2 (0.9)	1 (0.4)	0
気道感染	0	0	6 (2.6)	0	2 (0.9)	0
尿路感染	4 (2.6)	2 (1.3)	6 (2.6)	3 (1.3)	4 (1.7)	0
アスパラギン酸アミノトランスフェラーゼ増加	1 (0.7)	0	5 (2.2)	2 (0.9)	4 (1.7)	2 (0.9)
倦怠感	2 (1.3)	0	5 (2.2)	1 (0.4)	2 (0.9)	0
上咽頭炎	2 (1.3)	0	5 (2.2)	0	2 (0.9)	0
紅斑	0	0	4 (1.7)	0	0	0
過敏症	1 (0.7)	0	4 (1.7)	2 (0.9)	4 (1.7)	2 (0.9)
低マグネシウム血症	0	0	4 (1.7)	2 (0.9)	1 (0.4)	1 (0.4)
疼痛	0	0	4 (1.7)	3 (1.3)	0	0
爪囲炎	0	0	4 (1.7)	2 (0.9)	0	0
肺塞栓症	0	0	4 (1.7)	4 (1.7)	3 (1.3)	2 (0.9)
腹水	0	0	3 (1.3)	3 (1.3)	0	0
心房細動	1 (0.7)	1 (0.7)	3 (1.3)	0	0	0
血中クレアチニン増加	2 (1.3)	1 (0.7)	3 (1.3)	0	0	0

MedDRA v27.1 coding dictionary applied.
Preferred terms are sorted in descending frequency of Any Grade EC+mFOLFOX6 column.
Other study intervention includes: irinotecan, oxaliplatin, leucovorin or levo-leucovorin, fluorouracil (bolus or infusion), capecitabine, and bevacizumab (as appropriate for the treatment group).
Dose interruption of other study intervention is defined as temporary stop of at least one drug or permanent stop of at least one (but not all) drugs.

表 2.7.4.8-3　　治験薬の休薬に至った有害事象の PT 別発現頻度（03 試験、P3 パート）（続き 2）

解析対象集団：Phase 3 Safety Set
Study Intervention: Any Drug

Number of Participants Evaluable for AEs	EC (N=153)		EC+mFOLFOX6 (N=232)		Control (N=229)	
	Any Grade	Grade 3 or Higher	Any Grade	Grade 3 or Higher	Any Grade	Grade 3 or Higher
Number (%) of Participants: by Preferred Term	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
蜂巣炎	0	0	3 (1.3)	1 (0.4)	0	0
ざ瘡様皮膚炎	1 (0.7)	0	3 (1.3)	2 (0.9)	0	0
呼吸困難	1 (0.7)	0	3 (1.3)	1 (0.4)	2 (0.9)	0
発熱性好中球減少症	0	0	3 (1.3)	3 (1.3)	4 (1.7)	4 (1.7)
高血糖	0	0	3 (1.3)	2 (0.9)	0	0
肺炎	0	0	3 (1.3)	2 (0.9)	3 (1.3)	2 (0.9)
SARS－CoV－2 検査陽性	4 (2.6)	0	3 (1.3)	0	4 (1.7)	0
敗血症	1 (0.7)	1 (0.7)	3 (1.3)	3 (1.3)	0	0
小腸閉塞	2 (1.3)	2 (1.3)	3 (1.3)	2 (0.9)	1 (0.4)	1 (0.4)
体重減少	1 (0.7)	0	3 (1.3)	0	1 (0.4)	0
腹部感染	0	0	2 (0.9)	1 (0.4)	0	0
腹部敗血症	0	0	2 (0.9)	2 (0.9)	1 (0.4)	1 (0.4)
アナフィラキシー反応	0	0	2 (0.9)	1 (0.4)	2 (0.9)	1 (0.4)
血中ビリルビン増加	1 (0.7)	0	2 (0.9)	0	1 (0.4)	0
胸痛	0	0	2 (0.9)	0	0	0
悪寒	0	0	2 (0.9)	1 (0.4)	0	0
コロナウイルス感染	0	0	2 (0.9)	0	1 (0.4)	0
咳嗽	3 (2.0)	1 (0.7)	2 (0.9)	0	1 (0.4)	0
齲歯	0	0	2 (0.9)	1 (0.4)	0	0
転倒	0	0	2 (0.9)	0	0	0
痔核	0	0	2 (0.9)	1 (0.4)	0	0
帯状疱疹	0	0	2 (0.9)	0	1 (0.4)	0
高血圧	0	0	2 (0.9)	1 (0.4)	7 (3.1)	3 (1.3)
イレウス	2 (1.3)	1 (0.7)	2 (0.9)	2 (0.9)	4 (1.7)	1 (0.4)

MedDRA v27.1 coding dictionary applied.
Preferred terms are sorted in descending frequency of Any Grade EC+mFOLFOX6 column.
Other study intervention includes: irinotecan, oxaliplatin, leucovorin or levo-leucovorin, fluorouracil (bolus or infusion), capecitabine, and bevacizumab (as appropriate for the treatment group).
Dose interruption of other study intervention is defined as temporary stop of at least one drug or permanent stop of at least one (but not all) drugs.

表 2.7.4.8-3　　治験薬の休薬に至った有害事象の PT 別発現頻度（03 試験、P3 パート）（続き 3）

解析対象集団：Phase 3 Safety Set
Study Intervention: Any Drug

Number of Participants Evaluable for AEs	EC (N=153)		EC+mFOLFOX6 (N=232)		Control (N=229)	
	Any Grade	Grade 3 or Higher	Any Grade	Grade 3 or Higher	Any Grade	Grade 3 or Higher
Number (%) of Participants: by Preferred Term	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
腸管穿孔	0	0	2 (0.9)	2 (0.9)	0	0
白血球減少症	0	0	2 (0.9)	0	1 (0.4)	0
筋肉痛	2 (1.3)	0	2 (0.9)	0	1 (0.4)	0
末梢性浮腫	1 (0.7)	0	2 (0.9)	0	0	0
四肢痛	1 (0.7)	0	2 (0.9)	1 (0.4)	1 (0.4)	0
肺臓炎	0	0	2 (0.9)	0	1 (0.4)	0
多発ニューロパチー	0	0	2 (0.9)	0	3 (1.3)	0
術後創感染	0	0	2 (0.9)	1 (0.4)	0	0
肛門周囲痛	0	0	2 (0.9)	0	0	0
腎機能障害	0	0	2 (0.9)	1 (0.4)	0	0
鼻漏	1 (0.7)	0	2 (0.9)	0	0	0
腹部膿瘍	0	0	1 (0.4)	1 (0.4)	0	0
上腹部痛	1 (0.7)	0	1 (0.4)	0	2 (0.9)	1 (0.4)
急性冠動脈症候群	0	0	1 (0.4)	1 (0.4)	0	0
急性腎障害	1 (0.7)	1 (0.7)	1 (0.4)	1 (0.4)	3 (1.3)	2 (0.9)
アミラーゼ増加	0	0	1 (0.4)	0	0	0
裂肛	0	0	1 (0.4)	1 (0.4)	0	0
肛門括約筋過緊張	0	0	1 (0.4)	1 (0.4)	0	0
吻合部瘻孔	0	0	1 (0.4)	0	0	0
狭心症	0	0	1 (0.4)	0	0	0
関節炎	1 (0.7)	1 (0.7)	1 (0.4)	0	0	0
心房粗動	0	0	1 (0.4)	1 (0.4)	0	0
心房頻脈	0	0	1 (0.4)	0	0	0
基底細胞癌	0	0	1 (0.4)	0	0	0

MedDRA v27.1 coding dictionary applied.
Preferred terms are sorted in descending frequency of Any Grade EC+mFOLFOX6 column.
Other study intervention includes: irinotecan, oxaliplatin, leucovorin or levo-leucovorin, fluorouracil (bolus or infusion), capecitabine, and bevacizumab (as appropriate for the treatment group).
Dose interruption of other study intervention is defined as temporary stop of at least one drug or permanent stop of at least one (but not all) drugs.

表 2.7.4.8-3　　治験薬の休薬に至った有害事象の PT 別発現頻度（03 試験、P3 パート）（続き 4）

解析対象集団：Phase 3 Safety Set
Study Intervention: Any Drug

Number of Participants Evaluable for AEs	EC (N=153)		EC+mFOLFOX6 (N=232)		Control (N=229)	
	Any Grade	Grade 3 or Higher	Any Grade	Grade 3 or Higher	Any Grade	Grade 3 or Higher
Number (%) of Participants: by Preferred Term	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
抱合ビリルビン増加	0	0	1 (0.4)	0	0	0
血中非抱合ビリルビン増加	0	0	1 (0.4)	0	0	0
骨痛	0	0	1 (0.4)	0	0	0
気管支炎	1 (0.7)	0	1 (0.4)	0	2 (0.9)	0
C－反応性蛋白増加	1 (0.7)	0	1 (0.4)	0	1 (0.4)	1 (0.4)
尿道結石	0	0	1 (0.4)	0	0	0
よう	0	0	1 (0.4)	0	0	0
心不全	0	0	1 (0.4)	0	0	0
心タンポナーデ	0	0	1 (0.4)	1 (0.4)	0	0
小脳梗塞	0	0	1 (0.4)	0	0	0
脳卒中	1 (0.7)	1 (0.7)	1 (0.4)	0	0	0
胸部不快感	0	0	1 (0.4)	0	0	0
慢性閉塞性肺疾患	0	0	1 (0.4)	0	0	0
大腸炎	0	0	1 (0.4)	0	2 (0.9)	1 (0.4)
挫傷	0	0	1 (0.4)	0	0	0
糖尿病性ケトアシドーシス	0	0	1 (0.4)	1 (0.4)	0	0
不快感	0	0	1 (0.4)	0	0	0
疾患進行	0	0	1 (0.4)	1 (0.4)	0	0
失見当識	0	0	1 (0.4)	0	0	0
浮動性めまい	0	0	1 (0.4)	0	0	0
十二指腸炎	0	0	1 (0.4)	0	0	0
異常感覚	0	0	1 (0.4)	0	0	0
発声障害	0	0	1 (0.4)	0	0	0
腸炎	0	0	1 (0.4)	1 (0.4)	0	0

MedDRA v27.1 coding dictionary applied.
Preferred terms are sorted in descending frequency of Any Grade EC+mFOLFOX6 column.
Other study intervention includes: irinotecan, oxaliplatin, leucovorin or levo-leucovorin, fluorouracil (bolus or infusion), capecitabine, and bevacizumab (as appropriate for the treatment group).
Dose interruption of other study intervention is defined as temporary stop of at least one drug or permanent stop of at least one (but not all) drugs.

表 2.7.4.8-3　　治験薬の休薬に至った有害事象の PT 別発現頻度（03 試験、P3 パート）（続き 5）

解析対象集団：Phase 3 Safety Set
Study Intervention: Any Drug

Number of Participants Evaluable for AEs	EC (N=153)		EC+mFOLFOX6 (N=232)		Control (N=229)	
	Any Grade	Grade 3 or Higher	Any Grade	Grade 3 or Higher	Any Grade	Grade 3 or Higher
Number (%) of Participants: by Preferred Term	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
眼の障害	0	0	1 (0.4)	0	0	0
顔面損傷	0	0	1 (0.4)	0	0	0
冷感	0	0	1 (0.4)	1 (0.4)	0	0
胃潰瘍	0	0	1 (0.4)	0	0	0
胃腸炎	0	0	1 (0.4)	0	0	0
医療機器関連胃腸合併症	0	0	1 (0.4)	1 (0.4)	0	0
胃腸出血	2 (1.3)	1 (0.7)	1 (0.4)	0	1 (0.4)	0
消化管感染	0	0	1 (0.4)	0	1 (0.4)	0
歯肉出血	1 (0.7)	0	1 (0.4)	0	0	0
痔出血	0	0	1 (0.4)	1 (0.4)	0	0
頭痛	0	0	1 (0.4)	0	0	0
重度月経出血	0	0	1 (0.4)	0	0	0
ヘリコバクター感染	0	0	1 (0.4)	0	0	0
不全片麻痺	0	0	1 (0.4)	0	0	0
肝酵素上昇	0	0	1 (0.4)	0	0	0
肝機能異常	0	0	1 (0.4)	0	1 (0.4)	0
高ビリルビン血症	0	0	1 (0.4)	1 (0.4)	0	0
高リパーゼ血症	0	0	1 (0.4)	1 (0.4)	0	0
感覚鈍麻	0	0	1 (0.4)	0	1 (0.4)	0
低カルシウム血症	0	0	1 (0.4)	0	0	0
低カリウム血症	0	0	1 (0.4)	0	0	0
低リン血症	0	0	1 (0.4)	1 (0.4)	1 (0.4)	1 (0.4)
麻痺性イレウス	0	0	1 (0.4)	1 (0.4)	0	0
免疫性腎炎	0	0	1 (0.4)	1 (0.4)	0	0

MedDRA v27.1 coding dictionary applied.
Preferred terms are sorted in descending frequency of Any Grade EC+mFOLFOX6 column.
Other study intervention includes: irinotecan, oxaliplatin, leucovorin or levo-leucovorin, fluorouracil (bolus or infusion), capecitabine, and bevacizumab (as appropriate for the treatment group).
Dose interruption of other study intervention is defined as temporary stop of at least one drug or permanent stop of at least one (but not all) drugs.

表 2.7.4.8-3　　治験薬の休薬に至った有害事象の PT 別発現頻度（03 試験、P3 パート）（続き 6）

解析対象集団：Phase 3 Safety Set
Study Intervention: Any Drug

Number of Participants Evaluable for AEs	EC (N=153)		EC+mFOLFOX6 (N=232)		Control (N=229)	
	Any Grade	Grade 3 or Higher	Any Grade	Grade 3 or Higher	Any Grade	Grade 3 or Higher
Number (%) of Participants: by Preferred Term	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
膿痂疹	0	0	1 (0.4)	0	0	0
感染	0	0	1 (0.4)	0	2 (0.9)	0
インフルエンザ	0	0	1 (0.4)	0	0	0
輸注関連過敏反応	0	0	1 (0.4)	0	0	0
注入部位裂傷	0	0	1 (0.4)	0	0	0
間質性肺疾患	0	0	1 (0.4)	0	0	0
椎間板炎	0	0	1 (0.4)	1 (0.4)	0	0
頭蓋内腫瘍出血	0	0	1 (0.4)	1 (0.4)	0	0
頚静脈血栓症	0	0	1 (0.4)	1 (0.4)	1 (0.4)	0
大腸閉塞	0	0	1 (0.4)	1 (0.4)	3 (1.3)	3 (1.3)
嗜眠	0	0	1 (0.4)	0	0	0
肝損傷	0	0	1 (0.4)	0	0	0
限局性感染	0	0	1 (0.4)	0	0	0
下部消化管出血	0	0	1 (0.4)	1 (0.4)	0	0
下気道感染	1 (0.7)	1 (0.7)	1 (0.4)	0	0	0
メラノサイト性母斑	0	0	1 (0.4)	1 (0.4)	0	0
代謝性脳症	0	0	1 (0.4)	0	0	0
気分変化	0	0	1 (0.4)	0	0	0
筋骨格痛	0	0	1 (0.4)	0	0	0
ノロウイルス感染	0	0	1 (0.4)	1 (0.4)	0	0
食道炎	0	0	1 (0.4)	0	0	0
爪甲脱落症	0	0	1 (0.4)	0	0	0
口腔感染	0	0	1 (0.4)	1 (0.4)	0	0
中咽頭カンジダ症	0	0	1 (0.4)	0	0	0

MedDRA v27.1 coding dictionary applied.
Preferred terms are sorted in descending frequency of Any Grade EC+mFOLFOX6 column.
Other study intervention includes: irinotecan, oxaliplatin, leucovorin or levo-leucovorin, fluorouracil (bolus or infusion), capecitabine, and bevacizumab (as appropriate for the treatment group).
Dose interruption of other study intervention is defined as temporary stop of at least one drug or permanent stop of at least one (but not all) drugs.

表 2.7.4.8-3　　治験薬の休薬に至った有害事象の PT 別発現頻度（03 試験、P3 パート）（続き 7）

解析対象集団：Phase 3 Safety Set
Study Intervention: Any Drug

Number of Participants Evaluable for AEs	EC (N=153)		EC+mFOLFOX6 (N=232)		Control (N=229)	
	Any Grade	Grade 3 or Higher	Any Grade	Grade 3 or Higher	Any Grade	Grade 3 or Higher
Number (%) of Participants: by Preferred Term	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
急性膵炎	0	0	1 (0.4)	1 (0.4)	0	0
心膜炎	0	0	1 (0.4)	0	0	0
腹膜炎	0	0	1 (0.4)	1 (0.4)	1 (0.4)	1 (0.4)
胸水	0	0	1 (0.4)	1 (0.4)	0	0
気縦隔症	0	0	1 (0.4)	0	0	0
多発性関節炎	0	0	1 (0.4)	1 (0.4)	0	0
直腸炎	0	0	1 (0.4)	1 (0.4)	1 (0.4)	0
蛋白尿	0	0	1 (0.4)	0	7 (3.1)	3 (1.3)
そう痒症	1 (0.7)	0	1 (0.4)	0	1 (0.4)	0
偽膜性大腸炎	0	0	1 (0.4)	0	0	0
腎盂腎炎	0	0	1 (0.4)	0	0	0
膿疱性皮疹	0	0	1 (0.4)	0	0	0
直腸出血	0	0	1 (0.4)	0	0	0
腎不全	0	0	1 (0.4)	1 (0.4)	0	0
網膜剥離	0	0	1 (0.4)	1 (0.4)	0	0
敗血症性ショック	1 (0.7)	1 (0.7)	1 (0.4)	1 (0.4)	0	0
皮膚亀裂	0	0	1 (0.4)	0	0	0
軟部組織感染	0	0	1 (0.4)	1 (0.4)	1 (0.4)	0
傾眠	0	0	1 (0.4)	0	1 (0.4)	0
脊椎痛	0	0	1 (0.4)	1 (0.4)	0	0
亜イレウス	0	0	1 (0.4)	1 (0.4)	1 (0.4)	0
上室性期外収縮	0	0	1 (0.4)	0	0	0
上室性頻脈	0	0	1 (0.4)	1 (0.4)	1 (0.4)	0
頻呼吸	0	0	1 (0.4)	0	0	0

MedDRA v27.1 coding dictionary applied.
Preferred terms are sorted in descending frequency of Any Grade EC+mFOLFOX6 column.
Other study intervention includes: irinotecan, oxaliplatin, leucovorin or levo-leucovorin, fluorouracil (bolus or infusion), capecitabine, and bevacizumab (as appropriate for the treatment group).
Dose interruption of other study intervention is defined as temporary stop of at least one drug or permanent stop of at least one (but not all) drugs.

表 2.7.4.8-3　　治験薬の休薬に至った有害事象の PT 別発現頻度（03 試験、P3 パート）（続き 8）

解析対象集団：Phase 3 Safety Set
Study Intervention: Any Drug

Number of Participants Evaluable for AEs	EC (N=153)		EC+mFOLFOX6 (N=232)		Control (N=229)	
	Any Grade	Grade 3 or Higher	Any Grade	Grade 3 or Higher	Any Grade	Grade 3 or Higher
Number (%) of Participants: by Preferred Term	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
トロポニンＴ増加	0	0	1 (0.4)	0	0	0
腫瘍出血	0	0	1 (0.4)	1 (0.4)	0	0
腫瘍性閉塞	0	0	1 (0.4)	1 (0.4)	0	0
上気道の炎症	0	0	1 (0.4)	0	0	0
血管デバイス感染	0	0	1 (0.4)	0	0	0
ウイルス感染	0	0	1 (0.4)	0	0	0
霧視	0	0	1 (0.4)	0	0	0
腹部ヘルニア	0	0	0	0	1 (0.4)	1 (0.4)
下腹部痛	1 (0.7)	0	0	0	0	0
肛門失禁	0	0	0	0	1 (0.4)	1 (0.4)
血管性浮腫	1 (0.7)	0	0	0	0	0
不安	0	0	0	0	1 (0.4)	0
菌血症	0	0	0	0	1 (0.4)	1 (0.4)
胆道閉塞	1 (0.7)	1 (0.7)	0	0	0	0
血中マグネシウム減少	1 (0.7)	0	0	0	0	0
血中リン減少	1 (0.7)	0	0	0	0	0
血圧上昇	0	0	0	0	1 (0.4)	0
徐脈	0	0	0	0	1 (0.4)	1 (0.4)
COVID－19 肺炎	0	0	0	0	1 (0.4)	0
胆嚢炎	0	0	0	0	1 (0.4)	0
クロストリジウム・ディフィシレ大腸炎	0	0	0	0	1 (0.4)	0
便秘	1 (0.7)	1 (0.7)	0	0	1 (0.4)	0
サイトカイン放出症候群	1 (0.7)	0	0	0	0	0
深部静脈血栓症	0	0	0	0	1 (0.4)	1 (0.4)

MedDRA v27.1 coding dictionary applied.
Preferred terms are sorted in descending frequency of Any Grade EC+mFOLFOX6 column.
Other study intervention includes: irinotecan, oxaliplatin, leucovorin or levo-leucovorin, fluorouracil (bolus or infusion), capecitabine, and bevacizumab (as appropriate for the treatment group).
Dose interruption of other study intervention is defined as temporary stop of at least one drug or permanent stop of at least one (but not all) drugs.

表 2.7.4.8-3　　治験薬の休薬に至った有害事象の PT 別発現頻度（03 試験、P3 パート）（続き 9）

解析対象集団：Phase 3 Safety Set
Study Intervention: Any Drug

Number of Participants Evaluable for AEs	EC (N=153)		EC+mFOLFOX6 (N=232)		Control (N=229)	
	Any Grade	Grade 3 or Higher	Any Grade	Grade 3 or Higher	Any Grade	Grade 3 or Higher
Number (%) of Participants: by Preferred Term	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
譫妄	0	0	0	0	1 (0.4)	0
医療機器関連血栓症	0	0	0	0	1 (0.4)	0
注意力障害	1 (0.7)	0	0	0	0	0
憩室炎	0	0	0	0	1 (0.4)	1 (0.4)
皮膚乾燥	1 (0.7)	0	0	0	0	0
消化不良	0	0	0	0	1 (0.4)	0
排尿困難	0	0	0	0	1 (0.4)	0
塞栓症	0	0	0	0	1 (0.4)	0
小腸炎	0	0	0	0	2 (0.9)	1 (0.4)
感染性小腸結腸炎	0	0	0	0	1 (0.4)	1 (0.4)
鼻出血	0	0	0	0	1 (0.4)	0
大腸菌性尿路感染	0	0	0	0	1 (0.4)	0
眼そう痒症	1 (0.7)	0	0	0	0	0
女性生殖器瘻	1 (0.7)	1 (0.7)	0	0	1 (0.4)	1 (0.4)
ウイルス性胃腸炎	0	0	0	0	1 (0.4)	0
胃食道逆流性疾患	0	0	0	0	1 (0.4)	0
陰部ヘルペス	0	0	0	0	1 (0.4)	0
歯肉炎	0	0	0	0	1 (0.4)	0
血尿	0	0	0	0	1 (0.4)	0
肝炎	0	0	0	0	1 (0.4)	1 (0.4)
水腎症	0	0	0	0	2 (0.9)	0
高トランスアミナーゼ血症	1 (0.7)	0	0	0	1 (0.4)	0
低ナトリウム血症	1 (0.7)	1 (0.7)	0	0	0	0
低蛋白血症	1 (0.7)	0	0	0	0	0

MedDRA v27.1 coding dictionary applied.
Preferred terms are sorted in descending frequency of Any Grade EC+mFOLFOX6 column.
Other study intervention includes: irinotecan, oxaliplatin, leucovorin or levo-leucovorin, fluorouracil (bolus or infusion), capecitabine, and bevacizumab (as appropriate for the treatment group).
Dose interruption of other study intervention is defined as temporary stop of at least one drug or permanent stop of at least one (but not all) drugs.

表 2.7.4.8-3　　治験薬の休薬に至った有害事象の PT 別発現頻度（03 試験、P3 パート）（続き 10）

解析対象集団：Phase 3 Safety Set
Study Intervention: Any Drug

Number of Participants Evaluable for AEs	EC (N=153)		EC+mFOLFOX6 (N=232)		Control (N=229)	
	Any Grade	Grade 3 or Higher	Any Grade	Grade 3 or Higher	Any Grade	Grade 3 or Higher
Number (%) of Participants: by Preferred Term	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
免疫性血小板減少症	0	0	0	0	1 (0.4)	1 (0.4)
虚血性脳梗塞	0	0	0	0	1 (0.4)	1 (0.4)
靭帯捻挫	0	0	0	0	1 (0.4)	0
リンパ球数減少	0	0	0	0	1 (0.4)	0
医療機器使用部位血栓	0	0	0	0	1 (0.4)	1 (0.4)
筋痙縮	0	0	0	0	1 (0.4)	0
心筋梗塞	2 (1.3)	2 (1.3)	0	0	0	0
心筋損傷	1 (0.7)	0	0	0	0	0
心筋炎	1 (0.7)	1 (0.7)	0	0	0	0
好中球減少性感染	0	0	0	0	1 (0.4)	0
口腔真菌感染	0	0	0	0	1 (0.4)	0
口腔咽頭痛	2 (1.3)	0	0	0	0	0
骨粗鬆症性骨折	1 (0.7)	1 (0.7)	0	0	0	0
膵炎	0	0	0	0	1 (0.4)	1 (0.4)
骨盤膿瘍	1 (0.7)	1 (0.7)	0	0	0	0
点状出血	0	0	0	0	1 (0.4)	0
咽頭紅斑	1 (0.7)	0	0	0	0	0
頻尿	1 (0.7)	0	0	0	0	0
RS ウイルス感染	0	0	0	0	1 (0.4)	0
ウイルス性気道感染	1 (0.7)	0	0	0	0	0
坐骨神経痛	0	0	0	0	1 (0.4)	0
副鼻腔炎	1 (0.7)	0	0	0	1 (0.4)	0
皮膚乳頭腫	1 (0.7)	0	0	0	0	0
脾臓梗塞	0	0	0	0	2 (0.9)	1 (0.4)

MedDRA v27.1 coding dictionary applied.
Preferred terms are sorted in descending frequency of Any Grade EC+mFOLFOX6 column.
Other study intervention includes: irinotecan, oxaliplatin, leucovorin or levo-leucovorin, fluorouracil (bolus or infusion), capecitabine, and bevacizumab (as appropriate for the treatment group).
Dose interruption of other study intervention is defined as temporary stop of at least one drug or permanent stop of at least one (but not all) drugs.

表 2.7.4.8-3　　治験薬の休薬に至った有害事象の PT 別発現頻度（03 試験、P3 パート）（続き 11）

解析対象集団：Phase 3 Safety Set
Study Intervention: Any Drug

Number of Participants Evaluable for AEs	EC (N=153)		EC+mFOLFOX6 (N=232)		Control (N=229)	
	Any Grade	Grade 3 or Higher	Any Grade	Grade 3 or Higher	Any Grade	Grade 3 or Higher
Number (%) of Participants: by Preferred Term	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
ストーマ部出血	0	0	0	0	1 (0.4)	0
ストーマ部感染	0	0	0	0	1 (0.4)	0
鎖骨下静脈血栓症	0	0	0	0	1 (0.4)	0
失神	1 (0.7)	0	0	0	0	0
温度変化不耐症	0	0	0	0	1 (0.4)	0
咽喉刺激感	1 (0.7)	0	0	0	0	0
歯牙破折	0	0	0	0	1 (0.4)	0
歯感染	0	0	0	0	1 (0.4)	0
移行上皮癌	1 (0.7)	1 (0.7)	0	0	0	0
三叉神経ニューロパチー	0	0	0	0	1 (0.4)	1 (0.4)
腫瘍熱	0	0	0	0	1 (0.4)	0
上部消化管出血	1 (0.7)	1 (0.7)	0	0	0	0
尿路性敗血症	1 (0.7)	1 (0.7)	0	0	0	0
子宮平滑筋腫	1 (0.7)	1 (0.7)	0	0	0	0
腟出血	0	0	0	0	1 (0.4)	1 (0.4)
ウイルス性上気道感染	1 (0.7)	1 (0.7)	0	0	1 (0.4)	0

MedDRA v27.1 coding dictionary applied.
Preferred terms are sorted in descending frequency of Any Grade EC+mFOLFOX6 column.
Other study intervention includes: irinotecan, oxaliplatin, leucovorin or levo-leucovorin, fluorouracil (bolus or infusion), capecitabine, and bevacizumab (as appropriate for the treatment group).
Dose interruption of other study intervention is defined as temporary stop of at least one drug or permanent stop of at least one (but not all) drugs.

表 2.7.4.8-3　　治験薬の休薬に至った有害事象の PT 別発現頻度（03 試験、P3 パート）（続き 12）

解析対象集団：Phase 3 Safety Set
Study Intervention: Encorafenib

Number of Participants Evaluable for AEs	EC (N=153)		EC+mFOLFOX6 (N=232)		Control (N=229)	
	Any Grade	Grade 3 or Higher	Any Grade	Grade 3 or Higher	Any Grade	Grade 3 or Higher
Number (%) of Participants: by Preferred Term	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
有害事象発現例数	61 (39.9)	30 (19.6)	157 (67.7)	110 (47.4)	0	0
貧血	1 (0.7)	0	21 (9.1)	13 (5.6)	0	0
発熱	7 (4.6)	0	20 (8.6)	3 (1.3)	0	0
COVID－19	10 (6.5)	0	18 (7.8)	0	0	0
好中球減少症	1 (0.7)	1 (0.7)	16 (6.9)	11 (4.7)	0	0
好中球数減少	1 (0.7)	1 (0.7)	15 (6.5)	11 (4.7)	0	0
下痢	4 (2.6)	0	12 (5.2)	1 (0.4)	0	0
疲労	1 (0.7)	1 (0.7)	11 (4.7)	4 (1.7)	0	0
嘔吐	1 (0.7)	1 (0.7)	11 (4.7)	1 (0.4)	0	0
無力症	3 (2.0)	1 (0.7)	10 (4.3)	4 (1.7)	0	0
リパーゼ増加	2 (1.3)	2 (1.3)	10 (4.3)	10 (4.3)	0	0
関節痛	0	0	8 (3.4)	4 (1.7)	0	0
悪心	5 (3.3)	1 (0.7)	8 (3.4)	2 (0.9)	0	0
腹痛	2 (1.3)	1 (0.7)	7 (3.0)	5 (2.2)	0	0
食欲減退	1 (0.7)	1 (0.7)	7 (3.0)	2 (0.9)	0	0
腸閉塞	6 (3.9)	5 (3.3)	7 (3.0)	7 (3.0)	0	0
血小板数減少	0	0	7 (3.0)	2 (0.9)	0	0
尿路感染	3 (2.0)	1 (0.7)	6 (2.6)	2 (0.9)	0	0
血小板減少症	0	0	5 (2.2)	0	0	0
心電図 QT 延長	0	0	4 (1.7)	1 (0.4)	0	0
発疹	1 (0.7)	1 (0.7)	4 (1.7)	2 (0.9)	0	0
上気道感染	0	0	4 (1.7)	1 (0.4)	0	0

MedDRA v27.1 coding dictionary applied.
Preferred terms are sorted in descending frequency of Any Grade EC+mFOLFOX6 column.
Other study intervention includes: irinotecan, oxaliplatin, leucovorin or levo-leucovorin, fluorouracil (bolus or infusion), capecitabine, and bevacizumab (as appropriate for the treatment group).
Dose interruption of other study intervention is defined as temporary stop of at least one drug or permanent stop of at least one (but not all) drugs.

表 2.7.4.8-3　　治験薬の休薬に至った有害事象の PT 別発現頻度（03 試験、P3 パート）（続き 13）

解析対象集団：Phase 3 Safety Set
Study Intervention: Encorafenib

Number of Participants Evaluable for AEs	EC (N=153)		EC+mFOLFOX6 (N=232)		Control (N=229)	
	Any Grade	Grade 3 or Higher	Any Grade	Grade 3 or Higher	Any Grade	Grade 3 or Higher
Number (%) of Participants: by Preferred Term	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
アラニンアミノトランスフェラーゼ増加	0	0	3 (1.3)	2 (0.9)	0	0
腹水	0	0	3 (1.3)	3 (1.3)	0	0
ざ瘡様皮膚炎	1 (0.7)	0	3 (1.3)	2 (0.9)	0	0
発熱性好中球減少症	0	0	3 (1.3)	3 (1.3)	0	0
高血糖	0	0	3 (1.3)	2 (0.9)	0	0
倦怠感	1 (0.7)	0	3 (1.3)	1 (0.4)	0	0
疼痛	0	0	3 (1.3)	2 (0.9)	0	0
肺炎	0	0	3 (1.3)	2 (0.9)	0	0
肺塞栓症	0	0	3 (1.3)	3 (1.3)	0	0
敗血症	1 (0.7)	1 (0.7)	3 (1.3)	3 (1.3)	0	0
小腸閉塞	1 (0.7)	1 (0.7)	3 (1.3)	2 (0.9)	0	0
口内炎	0	0	3 (1.3)	2 (0.9)	0	0
腹部敗血症	0	0	2 (0.9)	2 (0.9)	0	0
アスパラギン酸アミノトランスフェラーゼ増加	1 (0.7)	0	2 (0.9)	1 (0.4)	0	0
心房細動	1 (0.7)	1 (0.7)	2 (0.9)	0	0	0
血中クレアチニン増加	1 (0.7)	0	2 (0.9)	0	0	0
蜂巣炎	0	0	2 (0.9)	1 (0.4)	0	0
胸痛	0	0	2 (0.9)	0	0	0
悪寒	0	0	2 (0.9)	1 (0.4)	0	0
齲歯	0	0	2 (0.9)	1 (0.4)	0	0
呼吸困難	1 (0.7)	0	2 (0.9)	1 (0.4)	0	0
過敏症	0	0	2 (0.9)	1 (0.4)	0	0
高血圧	0	0	2 (0.9)	1 (0.4)	0	0
イレウス	2 (1.3)	1 (0.7)	2 (0.9)	2 (0.9)	0	0

MedDRA v27.1 coding dictionary applied.
Preferred terms are sorted in descending frequency of Any Grade EC+mFOLFOX6 column.
Other study intervention includes: irinotecan, oxaliplatin, leucovorin or levo-leucovorin, fluorouracil (bolus or infusion), capecitabine, and bevacizumab (as appropriate for the treatment group).
Dose interruption of other study intervention is defined as temporary stop of at least one drug or permanent stop of at least one (but not all) drugs.

表 2.7.4.8-3　　治験薬の休薬に至った有害事象の PT 別発現頻度（03 試験、P3 パート）（続き 14）

解析対象集団：Phase 3 Safety Set
Study Intervention: Encorafenib

Number of Participants Evaluable for AEs	EC (N=153)		EC+mFOLFOX6 (N=232)		Control (N=229)	
	Any Grade	Grade 3 or Higher	Any Grade	Grade 3 or Higher	Any Grade	Grade 3 or Higher
Number (%) of Participants: by Preferred Term	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
腸管穿孔	0	0	2 (0.9)	2 (0.9)	0	0
粘膜の炎症	0	0	2 (0.9)	2 (0.9)	0	0
筋肉痛	2 (1.3)	0	2 (0.9)	0	0	0
上咽頭炎	2 (1.3)	0	2 (0.9)	0	0	0
末梢性ニューロパチー	0	0	2 (0.9)	0	0	0
錯感覚	0	0	2 (0.9)	0	0	0
爪囲炎	0	0	2 (0.9)	2 (0.9)	0	0
肺臓炎	0	0	2 (0.9)	0	0	0
術後創感染	0	0	2 (0.9)	1 (0.4)	0	0
気道感染	0	0	2 (0.9)	0	0	0
SARS－CoV－2 検査陽性	4 (2.6)	0	2 (0.9)	0	0	0
白血球数減少	0	0	2 (0.9)	1 (0.4)	0	0
腹部膿瘍	0	0	1 (0.4)	1 (0.4)	0	0
腹部感染	0	0	1 (0.4)	1 (0.4)	0	0
上腹部痛	1 (0.7)	0	1 (0.4)	0	0	0
急性冠動脈症候群	0	0	1 (0.4)	1 (0.4)	0	0
急性腎障害	1 (0.7)	1 (0.7)	1 (0.4)	1 (0.4)	0	0
裂肛	0	0	1 (0.4)	1 (0.4)	0	0
肛門括約筋過緊張	0	0	1 (0.4)	1 (0.4)	0	0
狭心症	0	0	1 (0.4)	0	0	0
関節炎	1 (0.7)	1 (0.7)	1 (0.4)	0	0	0
心房粗動	0	0	1 (0.4)	1 (0.4)	0	0
心房頻脈	0	0	1 (0.4)	0	0	0
基底細胞癌	0	0	1 (0.4)	0	0	0

MedDRA v27.1 coding dictionary applied.
Preferred terms are sorted in descending frequency of Any Grade EC+mFOLFOX6 column.
Other study intervention includes: irinotecan, oxaliplatin, leucovorin or levo-leucovorin, fluorouracil (bolus or infusion), capecitabine, and bevacizumab (as appropriate for the treatment group).
Dose interruption of other study intervention is defined as temporary stop of at least one drug or permanent stop of at least one (but not all) drugs.

表 2.7.4.8-3　　治験薬の休薬に至った有害事象の PT 別発現頻度（03 試験、P3 パート）（続き 15）

解析対象集団：Phase 3 Safety Set
Study Intervention: Encorafenib

Number of Participants Evaluable for AEs	EC (N=153)		EC+mFOLFOX6 (N=232)		Control (N=229)	
	Any Grade	Grade 3 or Higher	Any Grade	Grade 3 or Higher	Any Grade	Grade 3 or Higher
Number (%) of Participants: by Preferred Term	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
血中ビリルビン増加	1 (0.7)	0	1 (0.4)	0	0	0
骨痛	0	0	1 (0.4)	0	0	0
気管支炎	1 (0.7)	0	1 (0.4)	0	0	0
C－反応性蛋白増加	1 (0.7)	0	1 (0.4)	0	0	0
尿道結石	0	0	1 (0.4)	0	0	0
心不全	0	0	1 (0.4)	0	0	0
小脳梗塞	0	0	1 (0.4)	0	0	0
脳卒中	1 (0.7)	1 (0.7)	1 (0.4)	0	0	0
慢性閉塞性肺疾患	0	0	1 (0.4)	0	0	0
咳嗽	2 (1.3)	1 (0.7)	1 (0.4)	0	0	0
糖尿病性ケトアシドーシス	0	0	1 (0.4)	1 (0.4)	0	0
疾患進行	0	0	1 (0.4)	1 (0.4)	0	0
浮動性めまい	0	0	1 (0.4)	0	0	0
薬物過敏症	1 (0.7)	0	1 (0.4)	1 (0.4)	0	0
発声障害	0	0	1 (0.4)	0	0	0
腸炎	0	0	1 (0.4)	1 (0.4)	0	0
紅斑	0	0	1 (0.4)	0	0	0
眼の障害	0	0	1 (0.4)	0	0	0
顔面損傷	0	0	1 (0.4)	0	0	0
転倒	0	0	1 (0.4)	0	0	0
冷感	0	0	1 (0.4)	1 (0.4)	0	0
胃潰瘍	0	0	1 (0.4)	0	0	0
胃腸炎	0	0	1 (0.4)	0	0	0
医療機器関連胃腸合併症	0	0	1 (0.4)	1 (0.4)	0	0

MedDRA v27.1 coding dictionary applied.
Preferred terms are sorted in descending frequency of Any Grade EC+mFOLFOX6 column.
Other study intervention includes: irinotecan, oxaliplatin, leucovorin or levo-leucovorin, fluorouracil (bolus or infusion), capecitabine, and bevacizumab (as appropriate for the treatment group).
Dose interruption of other study intervention is defined as temporary stop of at least one drug or permanent stop of at least one (but not all) drugs.

表 2.7.4.8-3　　治験薬の休薬に至った有害事象の PT 別発現頻度（03 試験、P3 パート）（続き 16）

解析対象集団：Phase 3 Safety Set
Study Intervention: Encorafenib

Number of Participants Evaluable for AEs	EC (N=153)		EC+mFOLFOX6 (N=232)		Control (N=229)	
	Any Grade	Grade 3 or Higher	Any Grade	Grade 3 or Higher	Any Grade	Grade 3 or Higher
Number (%) of Participants: by Preferred Term	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
胃腸出血	2 (1.3)	1 (0.7)	1 (0.4)	0	0	0
消化管感染	0	0	1 (0.4)	0	0	0
歯肉出血	1 (0.7)	0	1 (0.4)	0	0	0
痔出血	0	0	1 (0.4)	0	0	0
痔核	0	0	1 (0.4)	0	0	0
頭痛	0	0	1 (0.4)	0	0	0
重度月経出血	0	0	1 (0.4)	0	0	0
不全片麻痺	0	0	1 (0.4)	0	0	0
肝酵素上昇	0	0	1 (0.4)	0	0	0
肝機能異常	0	0	1 (0.4)	0	0	0
帯状疱疹	0	0	1 (0.4)	0	0	0
高リパーゼ血症	0	0	1 (0.4)	1 (0.4)	0	0
低カルシウム血症	0	0	1 (0.4)	0	0	0
低マグネシウム血症	0	0	1 (0.4)	1 (0.4)	0	0
低リン血症	0	0	1 (0.4)	1 (0.4)	0	0
麻痺性イレウス	0	0	1 (0.4)	1 (0.4)	0	0
免疫性腎炎	0	0	1 (0.4)	1 (0.4)	0	0
膿痂疹	0	0	1 (0.4)	0	0	0
間質性肺疾患	0	0	1 (0.4)	0	0	0
椎間板炎	0	0	1 (0.4)	1 (0.4)	0	0
頭蓋内腫瘍出血	0	0	1 (0.4)	1 (0.4)	0	0
頚静脈血栓症	0	0	1 (0.4)	1 (0.4)	0	0
大腸閉塞	0	0	1 (0.4)	1 (0.4)	0	0
限局性感染	0	0	1 (0.4)	0	0	0

MedDRA v27.1 coding dictionary applied.
Preferred terms are sorted in descending frequency of Any Grade EC+mFOLFOX6 column.
Other study intervention includes: irinotecan, oxaliplatin, leucovorin or levo-leucovorin, fluorouracil (bolus or infusion), capecitabine, and bevacizumab (as appropriate for the treatment group).
Dose interruption of other study intervention is defined as temporary stop of at least one drug or permanent stop of at least one (but not all) drugs.

表 2.7.4.8-3　　治験薬の休薬に至った有害事象の PT 別発現頻度（03 試験、P3 パート）（続き 17）

解析対象集団：Phase 3 Safety Set
Study Intervention: Encorafenib

Number of Participants Evaluable for AEs	EC (N=153)		EC+mFOLFOX6 (N=232)		Control (N=229)	
	Any Grade	Grade 3 or Higher	Any Grade	Grade 3 or Higher	Any Grade	Grade 3 or Higher
Number (%) of Participants: by Preferred Term	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
下部消化管出血	0	0	1 (0.4)	1 (0.4)	0	0
下気道感染	1 (0.7)	1 (0.7)	1 (0.4)	0	0	0
メラノサイト性母斑	0	0	1 (0.4)	1 (0.4)	0	0
代謝性脳症	0	0	1 (0.4)	0	0	0
気分変化	0	0	1 (0.4)	0	0	0
ノロウイルス感染	0	0	1 (0.4)	1 (0.4)	0	0
末梢性浮腫	1 (0.7)	0	1 (0.4)	0	0	0
食道炎	0	0	1 (0.4)	0	0	0
口腔感染	0	0	1 (0.4)	1 (0.4)	0	0
中咽頭カンジダ症	0	0	1 (0.4)	0	0	0
四肢痛	1 (0.7)	0	1 (0.4)	1 (0.4)	0	0
急性膵炎	0	0	1 (0.4)	1 (0.4)	0	0
心膜炎	0	0	1 (0.4)	0	0	0
腹膜炎	0	0	1 (0.4)	1 (0.4)	0	0
気縦隔症	0	0	1 (0.4)	0	0	0
肛門周囲痛	0	0	1 (0.4)	0	0	0
直腸炎	0	0	1 (0.4)	1 (0.4)	0	0
蛋白尿	0	0	1 (0.4)	0	0	0
偽膜性大腸炎	0	0	1 (0.4)	0	0	0
直腸出血	0	0	1 (0.4)	0	0	0
腎不全	0	0	1 (0.4)	1 (0.4)	0	0
腎機能障害	0	0	1 (0.4)	0	0	0
敗血症性ショック	1 (0.7)	1 (0.7)	1 (0.4)	1 (0.4)	0	0
傾眠	0	0	1 (0.4)	0	0	0

MedDRA v27.1 coding dictionary applied.
Preferred terms are sorted in descending frequency of Any Grade EC+mFOLFOX6 column.
Other study intervention includes: irinotecan, oxaliplatin, leucovorin or levo-leucovorin, fluorouracil (bolus or infusion), capecitabine, and bevacizumab (as appropriate for the treatment group).
Dose interruption of other study intervention is defined as temporary stop of at least one drug or permanent stop of at least one (but not all) drugs.

表 2.7.4.8-3　　治験薬の休薬に至った有害事象の PT 別発現頻度（03 試験、P3 パート）（続き 18）

解析対象集団：Phase 3 Safety Set
Study Intervention: Encorafenib

Number of Participants Evaluable for AEs	EC (N=153)		EC+mFOLFOX6 (N=232)		Control (N=229)	
	Any Grade	Grade 3 or Higher	Any Grade	Grade 3 or Higher	Any Grade	Grade 3 or Higher
Number (%) of Participants: by Preferred Term	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
脊椎痛	0	0	1 (0.4)	1 (0.4)	0	0
亜イレウス	0	0	1 (0.4)	1 (0.4)	0	0
上室性期外収縮	0	0	1 (0.4)	0	0	0
上室性頻脈	0	0	1 (0.4)	1 (0.4)	0	0
腫瘍出血	0	0	1 (0.4)	1 (0.4)	0	0
腫瘍性閉塞	0	0	1 (0.4)	1 (0.4)	0	0
上気道の炎症	0	0	1 (0.4)	0	0	0
霧視	0	0	1 (0.4)	0	0	0
体重減少	1 (0.7)	0	1 (0.4)	0	0	0
下腹部痛	1 (0.7)	0	0	0	0	0
血管性浮腫	1 (0.7)	0	0	0	0	0
胆道閉塞	1 (0.7)	1 (0.7)	0	0	0	0
血中マグネシウム減少	1 (0.7)	0	0	0	0	0
血中リン減少	1 (0.7)	0	0	0	0	0
便秘	1 (0.7)	1 (0.7)	0	0	0	0
注意力障害	1 (0.7)	0	0	0	0	0
皮膚乾燥	1 (0.7)	0	0	0	0	0
眼そう痒症	1 (0.7)	0	0	0	0	0
女性生殖器瘻	1 (0.7)	1 (0.7)	0	0	0	0
高トランスアミナーゼ血症	1 (0.7)	0	0	0	0	0
低ナトリウム血症	1 (0.7)	1 (0.7)	0	0	0	0
低蛋白血症	1 (0.7)	0	0	0	0	0
心筋梗塞	2 (1.3)	2 (1.3)	0	0	0	0
心筋炎	1 (0.7)	1 (0.7)	0	0	0	0

MedDRA v27.1 coding dictionary applied.
Preferred terms are sorted in descending frequency of Any Grade EC+mFOLFOX6 column.
Other study intervention includes: irinotecan, oxaliplatin, leucovorin or levo-leucovorin, fluorouracil (bolus or infusion), capecitabine, and bevacizumab (as appropriate for the treatment group).
Dose interruption of other study intervention is defined as temporary stop of at least one drug or permanent stop of at least one (but not all) drugs.

表 2.7.4.8-3　　治験薬の休薬に至った有害事象の PT 別発現頻度（03 試験、P3 パート）（続き 19）

解析対象集団：Phase 3 Safety Set
Study Intervention: Encorafenib

Number of Participants Evaluable for AEs	EC (N=153)		EC+mFOLFOX6 (N=232)		Control (N=229)	
	Any Grade	Grade 3 or Higher	Any Grade	Grade 3 or Higher	Any Grade	Grade 3 or Higher
Number (%) of Participants: by Preferred Term	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
口腔咽頭痛	1 (0.7)	0	0	0	0	0
骨粗鬆症性骨折	1 (0.7)	1 (0.7)	0	0	0	0
手掌・足底発赤知覚不全症候群	1 (0.7)	0	0	0	0	0
骨盤膿瘍	1 (0.7)	1 (0.7)	0	0	0	0
咽頭紅斑	1 (0.7)	0	0	0	0	0
頻尿	1 (0.7)	0	0	0	0	0
そう痒症	1 (0.7)	0	0	0	0	0
ウイルス性気道感染	1 (0.7)	0	0	0	0	0
副鼻腔炎	1 (0.7)	0	0	0	0	0
皮膚乳頭腫	1 (0.7)	0	0	0	0	0
咽喉刺激感	1 (0.7)	0	0	0	0	0
移行上皮癌	1 (0.7)	1 (0.7)	0	0	0	0
上部消化管出血	1 (0.7)	1 (0.7)	0	0	0	0
尿路性敗血症	1 (0.7)	1 (0.7)	0	0	0	0
子宮平滑筋腫	1 (0.7)	1 (0.7)	0	0	0	0
ウイルス性上気道感染	1 (0.7)	1 (0.7)	0	0	0	0

MedDRA v27.1 coding dictionary applied.
Preferred terms are sorted in descending frequency of Any Grade EC+mFOLFOX6 column.
Other study intervention includes: irinotecan, oxaliplatin, leucovorin or levo-leucovorin, fluorouracil (bolus or infusion), capecitabine, and bevacizumab (as appropriate for the treatment group).
Dose interruption of other study intervention is defined as temporary stop of at least one drug or permanent stop of at least one (but not all) drugs.

表 2.7.4.8-3　　治験薬の休薬に至った有害事象の PT 別発現頻度（03 試験、P3 パート）（続き 20）

解析対象集団：Phase 3 Safety Set
Study Intervention: Cetuximab

Number of Participants Evaluable for AEs	EC (N=153)		EC+mFOLFOX6 (N=232)		Control (N=229)	
	Any Grade	Grade 3 or Higher	Any Grade	Grade 3 or Higher	Any Grade	Grade 3 or Higher
Number (%) of Participants: by Preferred Term	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
有害事象発現例数	49 (32.0)	24 (15.7)	168 (72.4)	122 (52.6)	0	0
好中球数減少	1 (0.7)	1 (0.7)	35 (15.1)	26 (11.2)	0	0
好中球減少症	1 (0.7)	1 (0.7)	30 (12.9)	24 (10.3)	0	0
貧血	1 (0.7)	0	23 (9.9)	16 (6.9)	0	0
COVID－19	9 (5.9)	0	21 (9.1)	0	0	0
発熱	4 (2.6)	0	20 (8.6)	2 (0.9)	0	0
血小板数減少	0	0	18 (7.8)	3 (1.3)	0	0
血小板減少症	1 (0.7)	0	13 (5.6)	0	0	0
無力症	3 (2.0)	1 (0.7)	11 (4.7)	3 (1.3)	0	0
疲労	1 (0.7)	1 (0.7)	11 (4.7)	3 (1.3)	0	0
腸閉塞	5 (3.3)	4 (2.6)	7 (3.0)	6 (2.6)	0	0
腹痛	1 (0.7)	1 (0.7)	6 (2.6)	4 (1.7)	0	0
下痢	2 (1.3)	0	6 (2.6)	0	0	0
リパーゼ増加	1 (0.7)	1 (0.7)	6 (2.6)	6 (2.6)	0	0
上気道感染	1 (0.7)	0	6 (2.6)	2 (0.9)	0	0
尿路感染	3 (2.0)	2 (1.3)	6 (2.6)	2 (0.9)	0	0
食欲減退	0	0	5 (2.2)	2 (0.9)	0	0
気道感染	0	0	5 (2.2)	0	0	0
白血球数減少	0	0	5 (2.2)	2 (0.9)	0	0
注入に伴う反応	3 (2.0)	0	4 (1.7)	0	0	0
上咽頭炎	2 (1.3)	0	4 (1.7)	0	0	0
悪心	2 (1.3)	0	4 (1.7)	1 (0.4)	0	0

MedDRA v27.1 coding dictionary applied.
Preferred terms are sorted in descending frequency of Any Grade EC+mFOLFOX6 column.
Other study intervention includes: irinotecan, oxaliplatin, leucovorin or levo-leucovorin, fluorouracil (bolus or infusion), capecitabine, and bevacizumab (as appropriate for the treatment group).
Dose interruption of other study intervention is defined as temporary stop of at least one drug or permanent stop of at least one (but not all) drugs.

表 2.7.4.8-3　　治験薬の休薬に至った有害事象の PT 別発現頻度（03 試験、P3 パート）（続き 21）

解析対象集団：Phase 3 Safety Set
Study Intervention: Cetuximab

Number of Participants Evaluable for AEs	EC (N=153)		EC+mFOLFOX6 (N=232)		Control (N=229)	
	Any Grade	Grade 3 or Higher	Any Grade	Grade 3 or Higher	Any Grade	Grade 3 or Higher
Number (%) of Participants: by Preferred Term	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
爪囲炎	0	0	4 (1.7)	1 (0.4)	0	0
肺塞栓症	0	0	4 (1.7)	4 (1.7)	0	0
嘔吐	1 (0.7)	0	4 (1.7)	1 (0.4)	0	0
アラニンアミノトランスフェラーゼ増加	0	0	3 (1.3)	2 (0.9)	0	0
関節痛	0	0	3 (1.3)	2 (0.9)	0	0
腹水	0	0	3 (1.3)	3 (1.3)	0	0
アスパラギン酸アミノトランスフェラーゼ増加	1 (0.7)	0	3 (1.3)	2 (0.9)	0	0
心房細動	1 (0.7)	1 (0.7)	3 (1.3)	0	0	0
蜂巣炎	0	0	3 (1.3)	1 (0.4)	0	0
心電図 QT 延長	1 (0.7)	0	3 (1.3)	0	0	0
高血糖	0	0	3 (1.3)	2 (0.9)	0	0
低マグネシウム血症	0	0	3 (1.3)	1 (0.4)	0	0
粘膜の炎症	0	0	3 (1.3)	2 (0.9)	0	0
末梢性ニューロパチー	0	0	3 (1.3)	2 (0.9)	0	0
手掌・足底発赤知覚不全症候群	0	0	3 (1.3)	1 (0.4)	0	0
肺炎	0	0	3 (1.3)	2 (0.9)	0	0
SARS－CoV－2 検査陽性	2 (1.3)	0	3 (1.3)	0	0	0
体重減少	1 (0.7)	0	3 (1.3)	0	0	0
腹部感染	0	0	2 (0.9)	1 (0.4)	0	0
腹部敗血症	0	0	2 (0.9)	2 (0.9)	0	0
コロナウイルス感染	0	0	2 (0.9)	0	0	0
咳嗽	3 (2.0)	1 (0.7)	2 (0.9)	0	0	0
齲歯	0	0	2 (0.9)	1 (0.4)	0	0
ざ瘡様皮膚炎	1 (0.7)	0	2 (0.9)	1 (0.4)	0	0

MedDRA v27.1 coding dictionary applied.
Preferred terms are sorted in descending frequency of Any Grade EC+mFOLFOX6 column.
Other study intervention includes: irinotecan, oxaliplatin, leucovorin or levo-leucovorin, fluorouracil (bolus or infusion), capecitabine, and bevacizumab (as appropriate for the treatment group).
Dose interruption of other study intervention is defined as temporary stop of at least one drug or permanent stop of at least one (but not all) drugs.

表 2.7.4.8-3　　治験薬の休薬に至った有害事象の PT 別発現頻度（03 試験、P3 パート）（続き 22）

解析対象集団：Phase 3 Safety Set
Study Intervention: Cetuximab

Number of Participants Evaluable for AEs	EC (N=153)		EC+mFOLFOX6 (N=232)		Control (N=229)	
	Any Grade	Grade 3 or Higher	Any Grade	Grade 3 or Higher	Any Grade	Grade 3 or Higher
Number (%) of Participants: by Preferred Term	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
呼吸困難	1 (0.7)	0	2 (0.9)	1 (0.4)	0	0
発熱性好中球減少症	0	0	2 (0.9)	2 (0.9)	0	0
痔核	0	0	2 (0.9)	1 (0.4)	0	0
高血圧	0	0	2 (0.9)	1 (0.4)	0	0
腸管穿孔	0	0	2 (0.9)	2 (0.9)	0	0
白血球減少症	0	0	2 (0.9)	0	0	0
倦怠感	1 (0.7)	0	2 (0.9)	0	0	0
末梢性浮腫	1 (0.7)	0	2 (0.9)	0	0	0
錯感覚	0	0	2 (0.9)	0	0	0
肺臓炎	0	0	2 (0.9)	0	0	0
術後創感染	0	0	2 (0.9)	1 (0.4)	0	0
発疹	1 (0.7)	1 (0.7)	2 (0.9)	0	0	0
腎機能障害	0	0	2 (0.9)	1 (0.4)	0	0
鼻漏	1 (0.7)	0	2 (0.9)	0	0	0
敗血症	1 (0.7)	1 (0.7)	2 (0.9)	2 (0.9)	0	0
腹部膿瘍	0	0	1 (0.4)	1 (0.4)	0	0
上腹部痛	1 (0.7)	0	1 (0.4)	0	0	0
急性冠動脈症候群	0	0	1 (0.4)	1 (0.4)	0	0
急性腎障害	0	0	1 (0.4)	1 (0.4)	0	0
アミラーゼ増加	0	0	1 (0.4)	0	0	0
裂肛	0	0	1 (0.4)	1 (0.4)	0	0
肛門括約筋過緊張	0	0	1 (0.4)	1 (0.4)	0	0
吻合部瘻孔	0	0	1 (0.4)	0	0	0
狭心症	0	0	1 (0.4)	0	0	0

MedDRA v27.1 coding dictionary applied.
Preferred terms are sorted in descending frequency of Any Grade EC+mFOLFOX6 column.
Other study intervention includes: irinotecan, oxaliplatin, leucovorin or levo-leucovorin, fluorouracil (bolus or infusion), capecitabine, and bevacizumab (as appropriate for the treatment group).
Dose interruption of other study intervention is defined as temporary stop of at least one drug or permanent stop of at least one (but not all) drugs.

表 2.7.4.8-3　　治験薬の休薬に至った有害事象の PT 別発現頻度（03 試験、P3 パート）（続き 23）

解析対象集団：Phase 3 Safety Set
Study Intervention: Cetuximab

Number of Participants Evaluable for AEs	EC (N=153)		EC+mFOLFOX6 (N=232)		Control (N=229)	
	Any Grade	Grade 3 or Higher	Any Grade	Grade 3 or Higher	Any Grade	Grade 3 or Higher
Number (%) of Participants: by Preferred Term	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
心房粗動	0	0	1 (0.4)	1 (0.4)	0	0
心房頻脈	0	0	1 (0.4)	0	0	0
基底細胞癌	0	0	1 (0.4)	0	0	0
血中クレアチニン増加	2 (1.3)	1 (0.7)	1 (0.4)	0	0	0
骨痛	0	0	1 (0.4)	0	0	0
気管支炎	1 (0.7)	0	1 (0.4)	0	0	0
尿道結石	0	0	1 (0.4)	0	0	0
よう	0	0	1 (0.4)	0	0	0
心不全	0	0	1 (0.4)	0	0	0
心タンポナーデ	0	0	1 (0.4)	1 (0.4)	0	0
小脳梗塞	0	0	1 (0.4)	0	0	0
脳卒中	1 (0.7)	1 (0.7)	1 (0.4)	0	0	0
胸部不快感	0	0	1 (0.4)	0	0	0
胸痛	0	0	1 (0.4)	0	0	0
悪寒	0	0	1 (0.4)	1 (0.4)	0	0
慢性閉塞性肺疾患	0	0	1 (0.4)	0	0	0
大腸炎	0	0	1 (0.4)	0	0	0
糖尿病性ケトアシドーシス	0	0	1 (0.4)	1 (0.4)	0	0
不快感	0	0	1 (0.4)	0	0	0
疾患進行	0	0	1 (0.4)	1 (0.4)	0	0
失見当識	0	0	1 (0.4)	0	0	0
薬物過敏症	1 (0.7)	0	1 (0.4)	1 (0.4)	0	0
発声障害	0	0	1 (0.4)	0	0	0
腸炎	0	0	1 (0.4)	1 (0.4)	0	0

MedDRA v27.1 coding dictionary applied.
Preferred terms are sorted in descending frequency of Any Grade EC+mFOLFOX6 column.
Other study intervention includes: irinotecan, oxaliplatin, leucovorin or levo-leucovorin, fluorouracil (bolus or infusion), capecitabine, and bevacizumab (as appropriate for the treatment group).
Dose interruption of other study intervention is defined as temporary stop of at least one drug or permanent stop of at least one (but not all) drugs.

表 2.7.4.8-3　　治験薬の休薬に至った有害事象の PT 別発現頻度（03 試験、P3 パート）（続き 24）

解析対象集団：Phase 3 Safety Set
Study Intervention: Cetuximab

Number of Participants Evaluable for AEs	EC (N=153)		EC+mFOLFOX6 (N=232)		Control (N=229)	
	Any Grade	Grade 3 or Higher	Any Grade	Grade 3 or Higher	Any Grade	Grade 3 or Higher
Number (%) of Participants: by Preferred Term	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
紅斑	0	0	1 (0.4)	0	0	0
冷感	0	0	1 (0.4)	1 (0.4)	0	0
胃腸炎	0	0	1 (0.4)	0	0	0
痔出血	0	0	1 (0.4)	1 (0.4)	0	0
頭痛	0	0	1 (0.4)	0	0	0
不全片麻痺	0	0	1 (0.4)	0	0	0
肝酵素上昇	0	0	1 (0.4)	0	0	0
肝機能異常	0	0	1 (0.4)	0	0	0
帯状疱疹	0	0	1 (0.4)	0	0	0
高ビリルビン血症	0	0	1 (0.4)	1 (0.4)	0	0
高リパーゼ血症	0	0	1 (0.4)	1 (0.4)	0	0
過敏症	1 (0.7)	0	1 (0.4)	1 (0.4)	0	0
低カリウム血症	0	0	1 (0.4)	0	0	0
低リン血症	0	0	1 (0.4)	1 (0.4)	0	0
イレウス	0	0	1 (0.4)	1 (0.4)	0	0
麻痺性イレウス	0	0	1 (0.4)	1 (0.4)	0	0
免疫性腎炎	0	0	1 (0.4)	1 (0.4)	0	0
膿痂疹	0	0	1 (0.4)	0	0	0
インフルエンザ	0	0	1 (0.4)	0	0	0
輸注関連過敏反応	0	0	1 (0.4)	0	0	0
間質性肺疾患	0	0	1 (0.4)	0	0	0
椎間板炎	0	0	1 (0.4)	1 (0.4)	0	0
頭蓋内腫瘍出血	0	0	1 (0.4)	1 (0.4)	0	0
頚静脈血栓症	0	0	1 (0.4)	1 (0.4)	0	0

MedDRA v27.1 coding dictionary applied.
Preferred terms are sorted in descending frequency of Any Grade EC+mFOLFOX6 column.
Other study intervention includes: irinotecan, oxaliplatin, leucovorin or levo-leucovorin, fluorouracil (bolus or infusion), capecitabine, and bevacizumab (as appropriate for the treatment group).
Dose interruption of other study intervention is defined as temporary stop of at least one drug or permanent stop of at least one (but not all) drugs.

表 2.7.4.8-3　　治験薬の休薬に至った有害事象の PT 別発現頻度（03 試験、P3 パート）（続き 25）

解析対象集団：Phase 3 Safety Set
Study Intervention: Cetuximab

Number of Participants Evaluable for AEs	EC (N=153)		EC+mFOLFOX6 (N=232)		Control (N=229)	
	Any Grade	Grade 3 or Higher	Any Grade	Grade 3 or Higher	Any Grade	Grade 3 or Higher
Number (%) of Participants: by Preferred Term	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
大腸閉塞	0	0	1 (0.4)	1 (0.4)	0	0
嗜眠	0	0	1 (0.4)	0	0	0
限局性感染	0	0	1 (0.4)	0	0	0
下部消化管出血	0	0	1 (0.4)	1 (0.4)	0	0
下気道感染	1 (0.7)	1 (0.7)	1 (0.4)	0	0	0
代謝性脳症	0	0	1 (0.4)	0	0	0
気分変化	0	0	1 (0.4)	0	0	0
食道炎	0	0	1 (0.4)	0	0	0
爪甲脱落症	0	0	1 (0.4)	0	0	0
口腔感染	0	0	1 (0.4)	1 (0.4)	0	0
中咽頭カンジダ症	0	0	1 (0.4)	0	0	0
腹膜炎	0	0	1 (0.4)	1 (0.4)	0	0
胸水	0	0	1 (0.4)	1 (0.4)	0	0
気縦隔症	0	0	1 (0.4)	0	0	0
多発性関節炎	0	0	1 (0.4)	1 (0.4)	0	0
肛門周囲痛	0	0	1 (0.4)	0	0	0
直腸炎	0	0	1 (0.4)	1 (0.4)	0	0
そう痒症	1 (0.7)	0	1 (0.4)	0	0	0
偽膜性大腸炎	0	0	1 (0.4)	0	0	0
腎盂腎炎	0	0	1 (0.4)	0	0	0
膿疱性皮疹	0	0	1 (0.4)	0	0	0
腎不全	0	0	1 (0.4)	1 (0.4)	0	0
網膜剥離	0	0	1 (0.4)	1 (0.4)	0	0
敗血症性ショック	1 (0.7)	1 (0.7)	1 (0.4)	1 (0.4)	0	0

MedDRA v27.1 coding dictionary applied.
Preferred terms are sorted in descending frequency of Any Grade EC+mFOLFOX6 column.
Other study intervention includes: irinotecan, oxaliplatin, leucovorin or levo-leucovorin, fluorouracil (bolus or infusion), capecitabine, and bevacizumab (as appropriate for the treatment group).
Dose interruption of other study intervention is defined as temporary stop of at least one drug or permanent stop of at least one (but not all) drugs.

表 2.7.4.8-3　　治験薬の休薬に至った有害事象の PT 別発現頻度（03 試験、P3 パート）（続き 26）

解析対象集団：Phase 3 Safety Set
Study Intervention: Cetuximab

Number of Participants Evaluable for AEs	EC (N=153)		EC+mFOLFOX6 (N=232)		Control (N=229)	
	Any Grade	Grade 3 or Higher	Any Grade	Grade 3 or Higher	Any Grade	Grade 3 or Higher
Number (%) of Participants: by Preferred Term	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
小腸閉塞	2 (1.3)	2 (1.3)	1 (0.4)	1 (0.4)	0	0
軟部組織感染	0	0	1 (0.4)	1 (0.4)	0	0
傾眠	0	0	1 (0.4)	0	0	0
口内炎	0	0	1 (0.4)	1 (0.4)	0	0
亜イレウス	0	0	1 (0.4)	1 (0.4)	0	0
上室性頻脈	0	0	1 (0.4)	1 (0.4)	0	0
腫瘍出血	0	0	1 (0.4)	1 (0.4)	0	0
腫瘍性閉塞	0	0	1 (0.4)	1 (0.4)	0	0
血管デバイス感染	0	0	1 (0.4)	0	0	0
ウイルス感染	0	0	1 (0.4)	0	0	0
下腹部痛	1 (0.7)	0	0	0	0	0
血管性浮腫	1 (0.7)	0	0	0	0	0
胆道閉塞	1 (0.7)	1 (0.7)	0	0	0	0
血中ビリルビン増加	1 (0.7)	0	0	0	0	0
血中マグネシウム減少	1 (0.7)	0	0	0	0	0
血中リン減少	1 (0.7)	0	0	0	0	0
C－反応性蛋白増加	1 (0.7)	0	0	0	0	0
便秘	1 (0.7)	1 (0.7)	0	0	0	0
サイトカイン放出症候群	1 (0.7)	0	0	0	0	0
注意力障害	1 (0.7)	0	0	0	0	0
皮膚乾燥	1 (0.7)	0	0	0	0	0
胃腸出血	1 (0.7)	1 (0.7)	0	0	0	0
高トランスアミナーゼ血症	1 (0.7)	0	0	0	0	0
低ナトリウム血症	1 (0.7)	1 (0.7)	0	0	0	0

MedDRA v27.1 coding dictionary applied.
Preferred terms are sorted in descending frequency of Any Grade EC+mFOLFOX6 column.
Other study intervention includes: irinotecan, oxaliplatin, leucovorin or levo-leucovorin, fluorouracil (bolus or infusion), capecitabine, and bevacizumab (as appropriate for the treatment group).
Dose interruption of other study intervention is defined as temporary stop of at least one drug or permanent stop of at least one (but not all) drugs.

表 2.7.4.8-3　　治験薬の休薬に至った有害事象の PT 別発現頻度（03 試験、P3 パート）（続き 27）

解析対象集団：Phase 3 Safety Set
Study Intervention: Cetuximab

Number of Participants Evaluable for AEs	EC (N=153)		EC+mFOLFOX6 (N=232)		Control (N=229)	
	Any Grade	Grade 3 or Higher	Any Grade	Grade 3 or Higher	Any Grade	Grade 3 or Higher
Number (%) of Participants: by Preferred Term	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
低蛋白血症	1 (0.7)	0	0	0	0	0
筋肉痛	1 (0.7)	0	0	0	0	0
心筋梗塞	2 (1.3)	2 (1.3)	0	0	0	0
心筋損傷	1 (0.7)	0	0	0	0	0
心筋炎	1 (0.7)	1 (0.7)	0	0	0	0
口腔咽頭痛	2 (1.3)	0	0	0	0	0
骨粗鬆症性骨折	1 (0.7)	1 (0.7)	0	0	0	0
四肢痛	1 (0.7)	0	0	0	0	0
骨盤膿瘍	1 (0.7)	1 (0.7)	0	0	0	0
咽頭紅斑	1 (0.7)	0	0	0	0	0
頻尿	1 (0.7)	0	0	0	0	0
ウイルス性気道感染	1 (0.7)	0	0	0	0	0
副鼻腔炎	1 (0.7)	0	0	0	0	0
失神	1 (0.7)	0	0	0	0	0
咽喉刺激感	1 (0.7)	0	0	0	0	0
上部消化管出血	1 (0.7)	1 (0.7)	0	0	0	0
ウイルス性上気道感染	1 (0.7)	1 (0.7)	0	0	0	0

MedDRA v27.1 coding dictionary applied.
Preferred terms are sorted in descending frequency of Any Grade EC+mFOLFOX6 column.
Other study intervention includes: irinotecan, oxaliplatin, leucovorin or levo-leucovorin, fluorouracil (bolus or infusion), capecitabine, and bevacizumab (as appropriate for the treatment group).
Dose interruption of other study intervention is defined as temporary stop of at least one drug or permanent stop of at least one (but not all) drugs.

表 2.7.4.8-3　　治験薬の休薬に至った有害事象の PT 別発現頻度（03 試験、P3 パート）（続き 28）

解析対象集団：Phase 3 Safety Set
Study Intervention: Other

Number of Participants Evaluable for AEs	EC (N=153)		EC+mFOLFOX6 (N=232)		Control (N=229)	
	Any Grade	Grade 3 or Higher	Any Grade	Grade 3 or Higher	Any Grade	Grade 3 or Higher
Number (%) of Participants: by Preferred Term	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
有害事象発現例数	0	0	196 (84.5)	134 (57.8)	168 (73.4)	87 (38.0)
好中球数減少	0	0	37 (15.9)	22 (9.5)	30 (13.1)	18 (7.9)
好中球減少症	0	0	31 (13.4)	24 (10.3)	26 (11.4)	9 (3.9)
末梢性ニューロパチー	0	0	28 (12.1)	14 (6.0)	12 (5.2)	6 (2.6)
末梢性感覚ニューロパチー	0	0	26 (11.2)	13 (5.6)	13 (5.7)	4 (1.7)
発熱	0	0	25 (10.8)	1 (0.4)	6 (2.6)	0
貧血	0	0	22 (9.5)	15 (6.5)	5 (2.2)	1 (0.4)
血小板数減少	0	0	20 (8.6)	1 (0.4)	7 (3.1)	2 (0.9)
COVID－19	0	0	19 (8.2)	0	13 (5.7)	0
神経毒性	0	0	15 (6.5)	12 (5.2)	6 (2.6)	0
錯感覚	0	0	15 (6.5)	8 (3.4)	6 (2.6)	3 (1.3)
血小板減少症	0	0	15 (6.5)	0	7 (3.1)	0
疲労	0	0	11 (4.7)	3 (1.3)	7 (3.1)	4 (1.7)
無力症	0	0	10 (4.3)	3 (1.3)	5 (2.2)	1 (0.4)
注入に伴う反応	0	0	9 (3.9)	1 (0.4)	6 (2.6)	0
薬物過敏症	0	0	8 (3.4)	4 (1.7)	2 (0.9)	0
手掌・足底発赤知覚不全症候群	0	0	8 (3.4)	6 (2.6)	3 (1.3)	1 (0.4)
上気道感染	0	0	8 (3.4)	2 (0.9)	7 (3.1)	0
白血球数減少	0	0	8 (3.4)	3 (1.3)	7 (3.1)	2 (0.9)
悪心	0	0	7 (3.0)	1 (0.4)	13 (5.7)	2 (0.9)
嘔吐	0	0	7 (3.0)	3 (1.3)	7 (3.1)	1 (0.4)
腹痛	0	0	6 (2.6)	3 (1.3)	14 (6.1)	1 (0.4)

MedDRA v27.1 coding dictionary applied.
Preferred terms are sorted in descending frequency of Any Grade EC+mFOLFOX6 column.
Other study intervention includes: irinotecan, oxaliplatin, leucovorin or levo-leucovorin, fluorouracil (bolus or infusion), capecitabine, and bevacizumab (as appropriate for the treatment group).
Dose interruption of other study intervention is defined as temporary stop of at least one drug or permanent stop of at least one (but not all) drugs.

表 2.7.4.8-3　　治験薬の休薬に至った有害事象の PT 別発現頻度（03 試験、P3 パート）（続き 29）

解析対象集団：Phase 3 Safety Set
Study Intervention: Other

Number of Participants Evaluable for AEs	EC (N=153)		EC+mFOLFOX6 (N=232)		Control (N=229)	
	Any Grade	Grade 3 or Higher	Any Grade	Grade 3 or Higher	Any Grade	Grade 3 or Higher
Number (%) of Participants: by Preferred Term	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
下痢	0	0	6 (2.6)	0	17 (7.4)	6 (2.6)
腸閉塞	0	0	6 (2.6)	6 (2.6)	2 (0.9)	1 (0.4)
リパーゼ増加	0	0	6 (2.6)	5 (2.2)	1 (0.4)	1 (0.4)
気道感染	0	0	6 (2.6)	0	2 (0.9)	0
口内炎	0	0	6 (2.6)	3 (1.3)	0	0
食欲減退	0	0	5 (2.2)	1 (0.4)	2 (0.9)	0
粘膜の炎症	0	0	5 (2.2)	3 (1.3)	1 (0.4)	0
アラニンアミノトランスフェラーゼ増加	0	0	4 (1.7)	1 (0.4)	6 (2.6)	3 (1.3)
アスパラギン酸アミノトランスフェラーゼ増加	0	0	4 (1.7)	2 (0.9)	4 (1.7)	2 (0.9)
心電図 QT 延長	0	0	4 (1.7)	1 (0.4)	1 (0.4)	1 (0.4)
倦怠感	0	0	4 (1.7)	0	2 (0.9)	0
尿路感染	0	0	4 (1.7)	2 (0.9)	4 (1.7)	0
心房細動	0	0	3 (1.3)	0	0	0
蜂巣炎	0	0	3 (1.3)	1 (0.4)	0	0
呼吸困難	0	0	3 (1.3)	1 (0.4)	2 (0.9)	0
高血糖	0	0	3 (1.3)	1 (0.4)	0	0
過敏症	0	0	3 (1.3)	2 (0.9)	4 (1.7)	2 (0.9)
上咽頭炎	0	0	3 (1.3)	0	2 (0.9)	0
肺炎	0	0	3 (1.3)	2 (0.9)	3 (1.3)	2 (0.9)
肺塞栓症	0	0	3 (1.3)	3 (1.3)	3 (1.3)	2 (0.9)
SARS－CoV－2 検査陽性	0	0	3 (1.3)	0	4 (1.7)	0
体重減少	0	0	3 (1.3)	0	1 (0.4)	0
腹部敗血症	0	0	2 (0.9)	2 (0.9)	1 (0.4)	1 (0.4)
アナフィラキシー反応	0	0	2 (0.9)	1 (0.4)	2 (0.9)	1 (0.4)

MedDRA v27.1 coding dictionary applied.
Preferred terms are sorted in descending frequency of Any Grade EC+mFOLFOX6 column.
Other study intervention includes: irinotecan, oxaliplatin, leucovorin or levo-leucovorin, fluorouracil (bolus or infusion), capecitabine, and bevacizumab (as appropriate for the treatment group).
Dose interruption of other study intervention is defined as temporary stop of at least one drug or permanent stop of at least one (but not all) drugs.

表 2.7.4.8-3　　治験薬の休薬に至った有害事象の PT 別発現頻度（03 試験、P3 パート）（続き 30）

解析対象集団：Phase 3 Safety Set
Study Intervention: Other

Number of Participants Evaluable for AEs	EC (N=153)		EC+mFOLFOX6 (N=232)		Control (N=229)	
	Any Grade	Grade 3 or Higher	Any Grade	Grade 3 or Higher	Any Grade	Grade 3 or Higher
Number (%) of Participants: by Preferred Term	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
関節痛	0	0	2 (0.9)	1 (0.4)	0	0
血中クレアチニン増加	0	0	2 (0.9)	0	0	0
コロナウイルス感染	0	0	2 (0.9)	0	1 (0.4)	0
咳嗽	0	0	2 (0.9)	0	1 (0.4)	0
紅斑	0	0	2 (0.9)	0	0	0
Hemorrhoids	0	0	2 (0.9)	1 (0.4)	0	0
帯状疱疹	0	0	2 (0.9)	0	1 (0.4)	0
高血圧	0	0	2 (0.9)	1 (0.4)	7 (3.1)	3 (1.3)
腸管穿孔	0	0	2 (0.9)	2 (0.9)	0	0
白血球減少症	0	0	2 (0.9)	0	1 (0.4)	0
末梢性浮腫	0	0	2 (0.9)	0	0	0
爪囲炎	0	0	2 (0.9)	1 (0.4)	0	0
肺臓炎	0	0	2 (0.9)	0	1 (0.4)	0
多発ニューロパチー	0	0	2 (0.9)	0	3 (1.3)	0
術後創感染	0	0	2 (0.9)	1 (0.4)	0	0
発疹	0	0	2 (0.9)	0	1 (0.4)	0
鼻漏	0	0	2 (0.9)	0	0	0
腹部膿瘍	0	0	1 (0.4)	1 (0.4)	0	0
腹部感染	0	0	1 (0.4)	1 (0.4)	0	0
上腹部痛	0	0	1 (0.4)	0	2 (0.9)	1 (0.4)
急性冠動脈症候群	0	0	1 (0.4)	0	0	0
アミラーゼ増加	0	0	1 (0.4)	0	0	0
裂肛	0	0	1 (0.4)	1 (0.4)	0	0
肛門括約筋過緊張	0	0	1 (0.4)	1 (0.4)	0	0

MedDRA v27.1 coding dictionary applied.
Preferred terms are sorted in descending frequency of Any Grade EC+mFOLFOX6 column.
Other study intervention includes: irinotecan, oxaliplatin, leucovorin or levo-leucovorin, fluorouracil (bolus or infusion), capecitabine, and bevacizumab (as appropriate for the treatment group).
Dose interruption of other study intervention is defined as temporary stop of at least one drug or permanent stop of at least one (but not all) drugs.

表 2.7.4.8-3　　治験薬の休薬に至った有害事象の PT 別発現頻度（03 試験、P3 パート）（続き 31）

解析対象集団：Phase 3 Safety Set
Study Intervention: Other

Number of Participants Evaluable for AEs	EC (N=153)		EC+mFOLFOX6 (N=232)		Control (N=229)	
	Any Grade	Grade 3 or Higher	Any Grade	Grade 3 or Higher	Any Grade	Grade 3 or Higher
Number (%) of Participants: by Preferred Term	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
吻合部瘻孔	0	0	1 (0.4)	0	0	0
狭心症	0	0	1 (0.4)	0	0	0
腹水	0	0	1 (0.4)	1 (0.4)	0	0
心房粗動	0	0	1 (0.4)	1 (0.4)	0	0
心房頻脈	0	0	1 (0.4)	0	0	0
基底細胞癌	0	0	1 (0.4)	0	0	0
抱合ビリルビン増加	0	0	1 (0.4)	0	0	0
血中ビリルビン増加	0	0	1 (0.4)	0	1 (0.4)	0
血中非抱合ビリルビン増加	0	0	1 (0.4)	0	0	0
骨痛	0	0	1 (0.4)	0	0	0
気管支炎	0	0	1 (0.4)	0	2 (0.9)	0
尿道結石	0	0	1 (0.4)	0	0	0
よう	0	0	1 (0.4)	0	0	0
心不全	0	0	1 (0.4)	0	0	0
小脳梗塞	0	0	1 (0.4)	0	0	0
脳卒中	0	0	1 (0.4)	0	0	0
胸部不快感	0	0	1 (0.4)	0	0	0
胸痛	0	0	1 (0.4)	0	0	0
悪寒	0	0	1 (0.4)	1 (0.4)	0	0
慢性閉塞性肺疾患	0	0	1 (0.4)	0	0	0
大腸炎	0	0	1 (0.4)	0	2 (0.9)	1 (0.4)
挫傷	0	0	1 (0.4)	0	0	0
齲歯	0	0	1 (0.4)	0	0	0
糖尿病性ケトアシドーシス	0	0	1 (0.4)	1 (0.4)	0	0

MedDRA v27.1 coding dictionary applied.
Preferred terms are sorted in descending frequency of Any Grade EC+mFOLFOX6 column.
Other study intervention includes: irinotecan, oxaliplatin, leucovorin or levo-leucovorin, fluorouracil (bolus or infusion), capecitabine, and bevacizumab (as appropriate for the treatment group).
Dose interruption of other study intervention is defined as temporary stop of at least one drug or permanent stop of at least one (but not all) drugs.

表 2.7.4.8-3　　治験薬の休薬に至った有害事象の PT 別発現頻度（03 試験、P3 パート）（続き 32）

解析対象集団：Phase 3 Safety Set
Study Intervention: Other

Number of Participants Evaluable for AEs	EC (N=153)		EC+mFOLFOX6 (N=232)		Control (N=229)	
	Any Grade	Grade 3 or Higher	Any Grade	Grade 3 or Higher	Any Grade	Grade 3 or Higher
Number (%) of Participants: by Preferred Term	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
不快感	0	0	1 (0.4)	0	0	0
疾患進行	0	0	1 (0.4)	1 (0.4)	0	0
失見当識	0	0	1 (0.4)	0	0	0
十二指腸炎	0	0	1 (0.4)	0	0	0
異常感覚	0	0	1 (0.4)	0	0	0
発声障害	0	0	1 (0.4)	0	0	0
腸炎	0	0	1 (0.4)	1 (0.4)	0	0
転倒	0	0	1 (0.4)	0	0	0
発熱性好中球減少症	0	0	1 (0.4)	1 (0.4)	4 (1.7)	4 (1.7)
冷感	0	0	1 (0.4)	1 (0.4)	0	0
胃潰瘍	0	0	1 (0.4)	0	0	0
胃腸炎	0	0	1 (0.4)	0	0	0
医療機器関連胃腸合併症	0	0	1 (0.4)	1 (0.4)	0	0
痔出血	0	0	1 (0.4)	1 (0.4)	0	0
ヘリコバクター感染	0	0	1 (0.4)	0	0	0
不全片麻痺	0	0	1 (0.4)	0	0	0
肝酵素上昇	0	0	1 (0.4)	0	0	0
肝機能異常	0	0	1 (0.4)	0	1 (0.4)	0
高ビリルビン血症	0	0	1 (0.4)	1 (0.4)	0	0
高リパーゼ血症	0	0	1 (0.4)	1 (0.4)	0	0
感覚鈍麻	0	0	1 (0.4)	0	1 (0.4)	0
低カリウム血症	0	0	1 (0.4)	0	0	0
低マグネシウム血症	0	0	1 (0.4)	0	1 (0.4)	1 (0.4)
低リン血症	0	0	1 (0.4)	1 (0.4)	1 (0.4)	1 (0.4)

MedDRA v27.1 coding dictionary applied.
Preferred terms are sorted in descending frequency of Any Grade EC+mFOLFOX6 column.
Other study intervention includes: irinotecan, oxaliplatin, leucovorin or levo-leucovorin, fluorouracil (bolus or infusion), capecitabine, and bevacizumab (as appropriate for the treatment group).
Dose interruption of other study intervention is defined as temporary stop of at least one drug or permanent stop of at least one (but not all) drugs.

表 2.7.4.8-3　　治験薬の休薬に至った有害事象の PT 別発現頻度（03 試験、P3 パート）（続き 33）

解析対象集団：Phase 3 Safety Set
Study Intervention: Other

Number of Participants Evaluable for AEs	EC (N=153)		EC+mFOLFOX6 (N=232)		Control (N=229)	
	Any Grade	Grade 3 or Higher	Any Grade	Grade 3 or Higher	Any Grade	Grade 3 or Higher
Number (%) of Participants: by Preferred Term	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
イレウス	0	0	1 (0.4)	1 (0.4)	4 (1.7)	1 (0.4)
麻痺性イレウス	0	0	1 (0.4)	1 (0.4)	0	0
膿痂疹	0	0	1 (0.4)	0	0	0
感染	0	0	1 (0.4)	0	2 (0.9)	0
インフルエンザ	0	0	1 (0.4)	0	0	0
注入部位裂傷	0	0	1 (0.4)	0	0	0
間質性肺疾患	0	0	1 (0.4)	0	0	0
椎間板炎	0	0	1 (0.4)	1 (0.4)	0	0
頭蓋内腫瘍出血	0	0	1 (0.4)	1 (0.4)	0	0
頚静脈血栓症	0	0	1 (0.4)	1 (0.4)	1 (0.4)	0
大腸閉塞	0	0	1 (0.4)	1 (0.4)	3 (1.3)	3 (1.3)
嗜眠	0	0	1 (0.4)	0	0	0
肝損傷	0	0	1 (0.4)	0	0	0
限局性感染	0	0	1 (0.4)	0	0	0
下部消化管出血	0	0	1 (0.4)	1 (0.4)	0	0
下気道感染	0	0	1 (0.4)	0	0	0
代謝性脳症	0	0	1 (0.4)	0	0	0
気分変化	0	0	1 (0.4)	0	0	0
筋骨格痛	0	0	1 (0.4)	0	0	0
食道炎	0	0	1 (0.4)	0	0	0
爪甲脱落症	0	0	1 (0.4)	0	0	0
口腔感染	0	0	1 (0.4)	1 (0.4)	0	0
中咽頭カンジダ症	0	0	1 (0.4)	0	0	0
疼痛	0	0	1 (0.4)	1 (0.4)	0	0

MedDRA v27.1 coding dictionary applied.
Preferred terms are sorted in descending frequency of Any Grade EC+mFOLFOX6 column.
Other study intervention includes: irinotecan, oxaliplatin, leucovorin or levo-leucovorin, fluorouracil (bolus or infusion), capecitabine, and bevacizumab (as appropriate for the treatment group).
Dose interruption of other study intervention is defined as temporary stop of at least one drug or permanent stop of at least one (but not all) drugs.

表 2.7.4.8-3　　治験薬の休薬に至った有害事象の PT 別発現頻度（03 試験、P3 パート）（続き 34）

解析対象集団：Phase 3 Safety Set
Study Intervention: Other

Number of Participants Evaluable for AEs	EC (N=153)		EC+mFOLFOX6 (N=232)		Control (N=229)	
	Any Grade	Grade 3 or Higher	Any Grade	Grade 3 or Higher	Any Grade	Grade 3 or Higher
Number (%) of Participants: by Preferred Term	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
四肢痛	0	0	1 (0.4)	0	1 (0.4)	0
腹膜炎	0	0	1 (0.4)	1 (0.4)	1 (0.4)	1 (0.4)
胸水	0	0	1 (0.4)	1 (0.4)	0	0
気縦隔症	0	0	1 (0.4)	0	0	0
多発性関節炎	0	0	1 (0.4)	1 (0.4)	0	0
肛門周囲痛	0	0	1 (0.4)	0	0	0
直腸炎	0	0	1 (0.4)	1 (0.4)	1 (0.4)	0
偽膜性大腸炎	0	0	1 (0.4)	0	0	0
腎盂腎炎	0	0	1 (0.4)	0	0	0
膿疱性皮疹	0	0	1 (0.4)	0	0	0
腎不全	0	0	1 (0.4)	1 (0.4)	0	0
腎機能障害	0	0	1 (0.4)	0	0	0
網膜剥離	0	0	1 (0.4)	1 (0.4)	0	0
敗血症	0	0	1 (0.4)	1 (0.4)	0	0
皮膚亀裂	0	0	1 (0.4)	0	0	0
小腸閉塞	0	0	1 (0.4)	1 (0.4)	1 (0.4)	1 (0.4)
軟部組織感染	0	0	1 (0.4)	1 (0.4)	1 (0.4)	0
傾眠	0	0	1 (0.4)	0	1 (0.4)	0
脊椎痛	0	0	1 (0.4)	1 (0.4)	0	0
亜イレウス	0	0	1 (0.4)	1 (0.4)	1 (0.4)	0
上室性頻脈	0	0	1 (0.4)	1 (0.4)	1 (0.4)	0
頻呼吸	0	0	1 (0.4)	0	0	0
トロポニンＴ増加	0	0	1 (0.4)	0	0	0
腫瘍出血	0	0	1 (0.4)	1 (0.4)	0	0

MedDRA v27.1 coding dictionary applied.
Preferred terms are sorted in descending frequency of Any Grade EC+mFOLFOX6 column.
Other study intervention includes: irinotecan, oxaliplatin, leucovorin or levo-leucovorin, fluorouracil (bolus or infusion), capecitabine, and bevacizumab (as appropriate for the treatment group).
Dose interruption of other study intervention is defined as temporary stop of at least one drug or permanent stop of at least one (but not all) drugs.

表 2.7.4.8-3　　治験薬の休薬に至った有害事象の PT 別発現頻度（03 試験、P3 パート）（続き 35）

解析対象集団：Phase 3 Safety Set
Study Intervention: Other

Number of Participants Evaluable for AEs	EC (N=153)		EC+mFOLFOX6 (N=232)		Control (N=229)	
	Any Grade	Grade 3 or Higher	Any Grade	Grade 3 or Higher	Any Grade	Grade 3 or Higher
Number (%) of Participants: by Preferred Term	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
腫瘍性閉塞	0	0	1 (0.4)	1 (0.4)	0	0
上気道の炎症	0	0	1 (0.4)	0	0	0
血管デバイス感染	0	0	1 (0.4)	0	0	0
ウイルス感染	0	0	1 (0.4)	0	0	0
腹部ヘルニア	0	0	0	0	1 (0.4)	1 (0.4)
急性腎障害	0	0	0	0	3 (1.3)	2 (0.9)
肛門失禁	0	0	0	0	1 (0.4)	1 (0.4)
不安	0	0	0	0	1 (0.4)	0
菌血症	0	0	0	0	1 (0.4)	1 (0.4)
血圧上昇	0	0	0	0	1 (0.4)	0
徐脈	0	0	0	0	1 (0.4)	1 (0.4)
C－反応性蛋白増加	0	0	0	0	1 (0.4)	1 (0.4)
COVID－19 肺炎	0	0	0	0	1 (0.4)	0
胆嚢炎	0	0	0	0	1 (0.4)	0
クロストリジウム・ディフィシレ大腸炎	0	0	0	0	1 (0.4)	0
便秘	0	0	0	0	1 (0.4)	0
深部静脈血栓症	0	0	0	0	1 (0.4)	1 (0.4)
譫妄	0	0	0	0	1 (0.4)	0
医療機器関連血栓症	0	0	0	0	1 (0.4)	0
憩室炎	0	0	0	0	1 (0.4)	1 (0.4)
消化不良	0	0	0	0	1 (0.4)	0
排尿困難	0	0	0	0	1 (0.4)	0
塞栓症	0	0	0	0	1 (0.4)	0
小腸炎	0	0	0	0	2 (0.9)	1 (0.4)

MedDRA v27.1 coding dictionary applied.
Preferred terms are sorted in descending frequency of Any Grade EC+mFOLFOX6 column.
Other study intervention includes: irinotecan, oxaliplatin, leucovorin or levo-leucovorin, fluorouracil (bolus or infusion), capecitabine, and bevacizumab (as appropriate for the treatment group).
Dose interruption of other study intervention is defined as temporary stop of at least one drug or permanent stop of at least one (but not all) drugs.

表 2.7.4.8-3　　治験薬の休薬に至った有害事象の PT 別発現頻度（03 試験、P3 パート）（続き 36）

解析対象集団：Phase 3 Safety Set
Study Intervention: Other

Number of Participants Evaluable for AEs	EC (N=153)		EC+mFOLFOX6 (N=232)		Control (N=229)	
	Any Grade	Grade 3 or Higher	Any Grade	Grade 3 or Higher	Any Grade	Grade 3 or Higher
Number (%) of Participants: by Preferred Term	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
感染性小腸結腸炎	0	0	0	0	1 (0.4)	1 (0.4)
鼻出血	0	0	0	0	1 (0.4)	0
大腸菌性尿路感染	0	0	0	0	1 (0.4)	0
女性生殖器瘻	0	0	0	0	1 (0.4)	1 (0.4)
ウイルス性胃腸炎	0	0	0	0	1 (0.4)	0
胃腸出血	0	0	0	0	1 (0.4)	0
消化管感染	0	0	0	0	1 (0.4)	0
胃食道逆流性疾患	0	0	0	0	1 (0.4)	0
陰部ヘルペス	0	0	0	0	1 (0.4)	0
歯肉炎	0	0	0	0	1 (0.4)	0
血尿	0	0	0	0	1 (0.4)	0
肝炎	0	0	0	0	1 (0.4)	1 (0.4)
水腎症	0	0	0	0	2 (0.9)	0
高トランスアミナーゼ血症	0	0	0	0	1 (0.4)	0
免疫性血小板減少症	0	0	0	0	1 (0.4)	1 (0.4)
虚血性脳梗塞	0	0	0	0	1 (0.4)	1 (0.4)
靱帯捻挫	0	0	0	0	1 (0.4)	0
リンパ球数減少	0	0	0	0	1 (0.4)	0
医療機器使用部位血栓	0	0	0	0	1 (0.4)	1 (0.4)
筋痙縮	0	0	0	0	1 (0.4)	0
筋肉痛	0	0	0	0	1 (0.4)	0
好中球減少性感染	0	0	0	0	1 (0.4)	0
口腔真菌感染	0	0	0	0	1 (0.4)	0
膵炎	0	0	0	0	1 (0.4)	1 (0.4)

MedDRA v27.1 coding dictionary applied.
Preferred terms are sorted in descending frequency of Any Grade EC+mFOLFOX6 column.
Other study intervention includes: irinotecan, oxaliplatin, leucovorin or levo-leucovorin, fluorouracil (bolus or infusion), capecitabine, and bevacizumab (as appropriate for the treatment group).
Dose interruption of other study intervention is defined as temporary stop of at least one drug or permanent stop of at least one (but not all) drugs.

表 2.7.4.8-3　　治験薬の休薬に至った有害事象の PT 別発現頻度（03 試験、P3 パート）（続き 37）

解析対象集団：Phase 3 Safety Set
Study Intervention: Other

Number of Participants Evaluable for AEs	EC (N=153)		EC+mFOLFOX6 (N=232)		Control (N=229)	
	Any Grade	Grade 3 or Higher	Any Grade	Grade 3 or Higher	Any Grade	Grade 3 or Higher
Number (%) of Participants: by Preferred Term	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
点状出血	0	0	0	0	1 (0.4)	0
蛋白尿	0	0	0	0	7 (3.1)	3 (1.3)
そう痒症	0	0	0	0	1 (0.4)	0
RS ウイルス感染	0	0	0	0	1 (0.4)	0
坐骨神経痛	0	0	0	0	1 (0.4)	0
副鼻腔炎	0	0	0	0	1 (0.4)	0
脾臓梗塞	0	0	0	0	2 (0.9)	1 (0.4)
ストーマ部出血	0	0	0	0	1 (0.4)	0
ストーマ部感染	0	0	0	0	1 (0.4)	0
鎖骨下静脈血栓症	0	0	0	0	1 (0.4)	0
温度変化不耐症	0	0	0	0	1 (0.4)	0
歯牙破折	0	0	0	0	1 (0.4)	0
歯感染	0	0	0	0	1 (0.4)	0
三叉神経ニューロパチー	0	0	0	0	1 (0.4)	1 (0.4)
腫瘍熱	0	0	0	0	1 (0.4)	0
腟出血	0	0	0	0	1 (0.4)	1 (0.4)
ウイルス性上気道感染	0	0	0	0	1 (0.4)	0

MedDRA v27.1 coding dictionary applied.
Preferred terms are sorted in descending frequency of Any Grade EC+mFOLFOX6 column.
Other study intervention includes: irinotecan, oxaliplatin, leucovorin or levo-leucovorin, fluorouracil (bolus or infusion), capecitabine, and bevacizumab (as appropriate for the treatment group).
Dose interruption of other study intervention is defined as temporary stop of at least one drug or permanent stop of at least one (but not all) drugs.

出典［総括報告書 5.3.5.1-2（ONO-7702-03 試験、Phase 3 PFS PCD）Table 14.3.1.1.3.1］

表 2.7.4.8-4　　エンコラフェニブの注目すべき有害事象の概要（03 試験、SLI パート）

解析対象集団：Safety Lead-in Safety Set

Adverse Event Category	EC+mFOLFOX6 (N=27) n (%)	EC+FOLFIRI (N=30) n (%)
Number (%) of Participants with AESIs (All Causality)		
Any AESIs	20 (74.1)	13 (43.3)
AESIs with Maximum CTCAE Grade 3 or 4	11 (40.7)	5 (16.7)
AESIs with Maximum CTCAE Grade 5	0 (0.0)	0 (0.0)
Any Serious AESIs	2 (7.4)	0 (0.0)
Number (%) of Participants with AESIs Related to Any Study Intervention		
Treatment-related AESIs	19 (70.4)	11 (36.7)
Treatment-related AESIs with Maximum CTCAE Grade 3 or 4	11 (40.7)	4 (13.3)
Treatment-related AESIs with Maximum CTCAE Grade 5	0 (0.0)	0 (0.0)
Treatment-related Serious AESIs	1 (3.7)	0 (0.0)

MedDRA v26.1 coding dictionary applied.
AE must be treatment-emergent to be included in this table.

出典［総括報告書 5.3.5.1-1（ONO-7702-03 試験、Phase 3 ORR PCD）Table 14.3.1.5.1.2］

表 2.7.4.8-5　　エンコラフェニブの注目すべき有害事象のカテゴリー・PT 別発現頻度（03 試験、SLI パート）

解析対象集団：Safety Lead-in Safety Set

Number of Participants Evaluable for AEs	EC+mFOLFOX6 (N=27)			
	Any Grade	Grade 3	Grade 4	Grade 5
Number (%) of Participants: by GROUPING and Preferred Term	n (%)	n (%)	n (%)	n (%)
特に注目すべき有害事象発現例数	20 (74.1)	8 (29.6)	3 (11.1)	0
骨髄抑制	20 (74.1)	8 (29.6)	3 (11.1)	0
好中球減少症	7 (25.9)	2 (7.4)	1 (3.7)	0
好中球数減少	7 (25.9)	5 (18.5)	1 (3.7)	0
貧血	6 (22.2)	2 (7.4)	0	0
血小板数減少	5 (18.5)	0	0	0
血小板減少症	5 (18.5)	0	0	0
発熱性好中球減少症	1 (3.7)	0	1 (3.7)	0
ヘモグロビン減少	1 (3.7)	0	0	0
QT 延長	2 (7.4)	2 (7.4)	0	0
心電図 QT 延長	1 (3.7)	1 (3.7)	0	0
失神	1 (3.7)	1 (3.7)	0	0

(@@) Denotes AE terms that were not coded by the MedDRA dictionary.
MedDRA v26.1 coding dictionary applied.
Grouping and preferred terms are sorted in descending frequency of Any Grade EC+mFOLFOX6 column.

表 2.7.4.8-5　　エンコラフェニブの注目すべき有害事象のカテゴリー・PT 別発現頻度（03 試験、SLI パート）（続き）

解析対象集団：Safety Lead-in Safety Set

Number of Participants Evaluable for AEs	EC+FOLFIRI (N=30)			
	Any Grade	Grade 3	Grade 4	Grade 5
Number (%) of Participants: by GROUPING and Preferred Term	n (%)	n (%)	n (%)	n (%)
特に注目すべき有害事象発現例数	13 (43.3)	3 (10.0)	2 (6.7)	0
骨髄抑制	11 (36.7)	2 (6.7)	2 (6.7)	0
好中球減少症	2 (6.7)	0	1 (3.3)	0
好中球数減少	5 (16.7)	0	1 (3.3)	0
貧血	6 (20.0)	3 (10.0)	0	0
血小板数減少	0	0	0	0
血小板減少症	0	0	0	0
発熱性好中球減少症	0	0	0	0
ヘモグロビン減少	0	0	0	0
QT 延長	2 (6.7)	1 (3.3)	0	0
心電図 QT 延長	2 (6.7)	1 (3.3)	0	0
失神	0	0	0	0

(@@) Denotes AE terms that were not coded by the MedDRA dictionary.
MedDRA v26.1 coding dictionary applied.
Grouping and preferred terms are sorted in descending frequency of Any Grade EC+mFOLFOX6 column.

出典［総括報告書 5.3.5.1-1（ONO-7702-03 試験、Phase 3 ORR PCD）Table 14.3.1.5.2.2］

表 2.7.4.8-6　　治験薬と関連のあるエンコラフェニブの注目すべき有害事象のカテゴリー・PT 別発現頻度（03 試験、SLI パート）

解析対象集団：Safety Lead-in Safety Set

Number of Participants Evaluable for AEs	EC+mFOLFOX6 (N=27)			
	Any Grade	Grade 3	Grade 4	Grade 5
Number (%) of Participants: by GROUPING and Preferred Term	n (%)	n (%)	n (%)	n (%)
特に注目すべき有害事象発現例数	19 (70.4)	8 (29.6)	3 (11.1)	0
骨髄抑制	19 (70.4)	8 (29.6)	3 (11.1)	0
好中球減少症	7 (25.9)	2 (7.4)	1 (3.7)	0
好中球数減少	7 (25.9)	5 (18.5)	1 (3.7)	0
貧血	5 (18.5)	2 (7.4)	0	0
血小板数減少	5 (18.5)	0	0	0
血小板減少症	5 (18.5)	0	0	0
発熱性好中球減少症	1 (3.7)	0	1 (3.7)	0
ヘモグロビン減少	1 (3.7)	0	0	0
QT 延長	1 (3.7)	1 (3.7)	0	0
失神	1 (3.7)	1 (3.7)	0	0
心電図 QT 延長	0	0	0	0

(@@) Denotes AE terms that were not coded by the MedDRA dictionary.
MedDRA v26.1 coding dictionary applied.
Grouping and preferred terms are sorted in descending frequency of Any Grade EC+mFOLFOX6 column.

表 2.7.4.8-6　　治験薬と関連のあるエンコラフェニブの注目すべき有害事象のカテゴリー・PT 別発現頻度（03 試験、SLI パート）（続き）

解析対象集団：Safety Lead-in Safety Set

Number of Participants Evaluable for AEs	EC+FOLFIRI (N=30)			
	Any Grade	Grade 3	Grade 4	Grade 5
Number (%) of Participants: by GROUPING and Preferred Term	n (%)	n (%)	n (%)	n (%)
特に注目すべき有害事象発現例数	11 (36.7)	2 (6.7)	2 (6.7)	0
骨髄抑制	10 (33.3)	2 (6.7)	2 (6.7)	0
好中球減少症	2 (6.7)	0	1 (3.3)	0
好中球数減少	5 (16.7)	0	1 (3.3)	0
貧血	5 (16.7)	3 (10.0)	0	0
血小板数減少	0	0	0	0
血小板減少症	0	0	0	0
発熱性好中球減少症	0	0	0	0
ヘモグロビン減少	0	0	0	0
QT 延長	1 (3.3)	0	0	0
失神	0	0	0	0
心電図 QT 延長	1 (3.3)	0	0	0

(@@) Denotes AE terms that were not coded by the MedDRA dictionary.
MedDRA v26.1 coding dictionary applied.
Grouping and preferred terms are sorted in descending frequency of Any Grade EC+mFOLFOX6 column.

出典［総括報告書 5.3.5.1-1（ONO-7702-03 試験、Phase 3 ORR PCD）Table 14.3.1.5.4.2］

表 2.7.4.8-7　　重篤なエンコラフェニブの注目すべき有害事象のカテゴリー・PT 別発現頻度（03 試験、SLI パート）

解析対象集団：Safety Lead-in Safety Set

Number of Participants Evaluable for AEs	EC+mFOLFOX6 (N=27)		EC+FOLFIRI (N=30)	
	Any Grade	Grade 3 or Higher	Any Grade	Grade 3 or Higher
Number (%) of Participants: by GROUPING and Preferred Term	n (%)	n (%)	n (%)	n (%)
特に注目すべき有害事象発現例数	2 (7.4)	2 (7.4)	0	0
QT 延長	2 (7.4)	2 (7.4)	0	0
心電図 QT 延長	1 (3.7)	1 (3.7)	0	0
失神	1 (3.7)	1 (3.7)	0	0
骨髄抑制	1 (3.7)	1 (3.7)	0	0
発熱性好中球減少症	1 (3.7)	1 (3.7)	0	0

(@@) Denotes AE terms that were not coded by the MedDRA dictionary.
MedDRA v26.1 coding dictionary applied.
Grouping and preferred terms are sorted in descending frequency of Any Grade EC+mFOLFOX6 column.
出典［総括報告書 5.3.5.1-1（ONO-7702-03 試験、Phase 3 ORR PCD）Table 14.3.1.5.3.2］