Dossier zur Nutzenbewertung gemäß § 35a SGB V

Encorafenib (Braftovi®)

Pierre Fabre Pharma GmbH

Modul 4A – Anhang 4-G

Encorafenib in Kombination mit Cetuximab und FOLFOX zur Erstlinienbehandlung erwachsener Patienten mit metastasiertem Kolorektalkarzinom mit einer BRAF-V600E-Mutation

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Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Disposition Events Summary
Full Analysis Set

	EC+FOLFOX (N=236) n (%)	Control 1 (N=243) n (%)
Disposition phase: Treatment		
Entered	236 (100.0)	243 (100.0)
Any reason for discontinuation	169 (71.6)	227 (93.4)
Adverse event	17 (7.2)	26 (10.7)
Death	9 (3.8)	10 (4.1)
Progressive disease	101 (42.8)	118 (48.6)
Withdrawal by subject	17 (7.2)	37 (15.2)
Global deterioration of health status	10 (4.2)	9 (3.7)
Other	15 (6.4)	27 (11.1)
Ongoing	67 (28.4)	16 (6.6)
Disposition phase: Long-term follow-up		
Entered	169 (71.6)	227 (93.4)
Any reason for discontinuation	104 (44.1)	164 (67.5)
Death	94 (39.8)	143 (58.8)
Withdrawal by subject	8 (3.4)	19 (7.8)
Lost to follow-Up	2 (0.8)	2 (0.8)
Ongoing	65 (27.5)	63 (25.9)

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Demographic and Disease Characteristics
Full Analysis Set

		EC+FOLFOX (N=236)	Control 1 (N=243)
Age - Group (Years), n (%)	18 - < 65	150 (63.6)	139 (57.2)
	65 - < 75	70 (29.7)	80 (32.9)
	>= 75	16 (6.8)	24 (9.9)
Age (Years)	n (missing)	236 (0)	243 (0)
	Mean (SD)	57.95 (12.707)	59.38 (12.890)
	Median	60.00	62.00
	Q1, Q3	48.50, 68.00	50.00, 69.00
	Min, Max	24.0, 81.0	28.0, 84.0
Sex, n (%)	Male	123 (52.1)	119 (49.0)
	Female	113 (47.9)	124 (51.0)
Race, n (%)	Black or African American	0	1 (0.4)
	Asian	88 (37.3)	91 (37.4)
	White	141 (59.7)	144 (59.3)
	Not reported	7 (3.0)	5 (2.1)
	Multiracial	0	2 (0.8)
Region, n (%)	Europe	109 (46.2)	111 (45.7)
	USA/Canada	15 (6.4)	19 (7.8)
	Rest of World	112 (47.5)	113 (46.5)
Ethnicity, n (%)	Hispanic or Latino	28 (11.9)	30 (12.3)
	Not Hispanic or Latino	187 (79.2)	201 (82.7)
	Not reported	21 (8.9)	12 (4.9)
Body Site, n (%)	Colon, Ascending	78 (33.1)	72 (29.6)
	Colon, Descending	18 (7.6)	16 (6.6)
	Colon, Rectosigmoid + Colon, Sigmoid	47 (19.9)	48 (19.8)
	Colon, Transverse	39 (16.5)	35 (14.4)
	Colon, Hepatic Flexure	9 (3.8)	14 (5.8)
	Rectum	24 (10.2)	27 (11.1)
	Cecum	20 (8.5)	24 (9.9)
	Colon, Splenic Flexure	1 (0.4)	7 (2.9)
Side of Tumor, n (%)	Left	90 (38.1)	98 (40.3)
	Right	146 (61.9)	145 (59.7)
Stage at Initial Diagnosis, n (%)	Stage I	3 (1.3)	2 (0.8)
	Stage II	13 (5.5)	10 (4.1)
	Stage III	38 (16.1)	45 (18.5)
	Stage IV	182 (77.1)	186 (76.5)
Primary Tumor Resection, n (%)	Completely Resected	116 (49.2)	110 (45.3)
	Partially Resected	14 (5.9)	11 (4.5)
	No Resection	106 (44.9)	122 (50.2)
Number of Organs Involved, n (%)	<= 2	119 (50.4)	127 (52.3)
	>= 3	117 (49.6)	116 (47.7)
Presence of Liver Metastases, n (%)	Yes	147 (62.3)	160 (65.8)
	No	89 (37.7)	83 (34.2)

Age at Screening (years) as reported on CRF.

		EC+FOLFOX (N=236)	Control 1 (N=243)
Time Since Initial Diagnosis (Months)	n (missing)	236 (0)	243 (0)
	Mean (SD)	6.81 (13.183)	7.26 (15.506)
	Median	1.94	1.84
	Q1, Q3	1.33, 3.60	1.28, 3.45
	Min, Max	0.3, 112.5	0.4, 123.9
Time Since Recurrence/Metastatic (Months)	n (missing)	235 (1)	241 (2)
	Mean (SD)	2.26 (3.701)	2.03 (2.974)
	Median	1.54	1.51
	Q1, Q3	1.02, 2.23	1.05, 2.04
	Min, Max	0.0, 40.0	0.1, 33.9
ECOG-PS at Randomization, n (%)	0	131 (55.5)	136 (56.0)
	1	105 (44.5)	107 (44.0)
ECOG-PS at Baseline, n (%)	0	128 (54.2)	131 (53.9)
	1	104 (44.1)	98 (40.3)
	Missing	4 (1.7)	14 (5.8)
BRAF V600E Status, Tumor Tissue (Central), n (%)	Detected	226 (95.8)	224 (92.2)
	Indeterminate	0	1 (0.4)
	Not Detected	4 (1.7)	2 (0.8)
	Not Available	6 (2.5)	16 (6.6)
BRAF V600E Status (Local), n (%)	Detected	222 (94.1)	219 (90.1)
	Not Available	14 (5.9)	24 (9.9)
BRAF V600E Status Central vs. Local, n (%)	Detected vs. Detected	216 (91.5)	214 (88.1)
	Detected vs. Not Available	10 (4.2)	10 (4.1)
	Indeterminate vs. Detected	0	1 (0.4)
	Not Detected vs. Detected	4 (1.7)	2 (0.8)
	Not Available vs. Detected	2 (0.8)	2 (0.8)
	Not Available vs. Not Available	4 (1.7)	14 (5.8)
KRAS Mutation Status (Local), n (%)	Not Detected	231 (97.9)	229 (94.2)
	Not Available	5 (2.1)	14 (5.8)
NRAS Mutation Status (Local), n (%)	Not Detected	230 (97.5)	229 (94.2)
	Not Available	6 (2.5)	14 (5.8)
MSI/MMR Status (Local), n (%)	MSI-H/dMMR	1 (0.4)	0
	MSS/pMMR	229 (97.0)	227 (93.4)
	Not Available	6 (2.5)	16 (6.6)
CEA at Baseline - Group (ug/L), n (%)	<= 5	64 (27.1)	63 (25.9)
	> 5	167 (70.8)	163 (67.1)
	Missing	5 (2.1)	17 (7.0)
CEA at Baseline (ug/L)	n (missing)	230 (6)	226 (17)
	Mean (SD)	149.91 (547.713)	225.99 (912.458)
	Median	13.60	17.35
	Q1, Q3	4.60, 67.16	4.50, 94.60
	Min, Max	0.5, 6236.0	0.5, 11132.0
CRP at Baseline - Group (mg/L), n (%)	<= 10	125 (53.0)	118 (48.6)
	> 10	105 (44.5)	108 (44.4)
	Missing	6 (2.5)	17 (7.0)

Age at Screening (years) as reported on CRF.

		___EC+FOLFOX (N=236)___	___Control 1 (N=243)___
CRP at Baseline (mg/L)	n (missing)	229 (7)	225 (18)
	Mean (SD)	23.72 (36.094)	29.49 (44.052)
	Median	8.20	8.50
	Q1, Q3	2.50, 29.90	2.20, 38.30
	Min, Max	0.2, 208.8	0.2, 284.3

Age at Screening (years) as reported on CRF.

		EC+FOLFOX (N=232)
Treatment duration of regime EC+FOLFOX (Weeks)	n (missing)	232 (0)
	Mean (SD)	55.45 (35.413)
	Median	49.79
	Q1, Q3	26.07, 79.50
	Min, Max	1.3, 161.9
Cetuximab	n (missing)	232 (0)
	Mean (SD)	53.81 (36.180)
	Median	49.07
	Q1, Q3	23.93, 77.50
	Min, Max	1.3, 160.7
Encorafenib	n (missing)	232 (0)
	Mean (SD)	54.31 (36.208)
	Median	49.43
	Q1, Q3	23.86, 78.07
	Min, Max	0.4, 161.9
Fluorouracil	n (missing)	232 (0)
	Mean (SD)	46.73 (34.142)
	Median	37.50
	Q1, Q3	20.07, 68.14
	Min, Max	1.3, 160.7
Leucovorin	n (missing)	232 (0)
	Mean (SD)	46.53 (34.378)
	Median	36.71
	Q1, Q3	19.86, 68.14
	Min, Max	1.3, 160.7
Oxaliplatin	n (missing)	232 (0)
	Mean (SD)	23.25 (15.964)
	Median	21.29
	Q1, Q3	15.29, 27.07
	Min, Max	1.3, 141.1

Cetuximab: Defined as time from the date of first cetuximab dose to the date of last cetuximab dose + 14.
Encorafenib: Defined as time from the date of first encorafenib dose to the date of last encorafenib dose + 1.
Fluorouracil: Defined as time from the date of first fluorouracil dose to the date of last fluorouracil dose + 14 for bolus. Defined as time from the date of first fluorouracil dose to the date of last fluorouracil dose + 12 for infusion. Use maximum time of bolus and infusion.
Leucovorin: Defined as time from the date of first leucovorin dose to the date of last leucovorin dose + 14.
Oxaliplatin: Defined as time from the date of first oxaliplatin dose to the date of last oxaliplatin dose + 14.
Division by 7 for day-to-week calculation.

		Control 1 (N=229)
Treatment duration of regime CAPOX (Weeks)	n	6
	Mean (SD)	7.88 (5.906)
	Median	5.86
	Q1, Q3	3.00, 11.71
	Min, Max	2.9, 18.0
Capecitabine	n	6
	Mean (SD)	7.83 (5.897)
	Median	5.79
	Q1, Q3	3.00, 11.57
	Min, Max	2.9, 18.0
Oxaliplatin	n	6
	Mean (SD)	7.43 (6.201)
	Median	4.50
	Q1, Q3	3.00, 11.71
	Min, Max	2.9, 18.0

Capecitabine: Defined as time from the date of first capecitabine dose to the date of last capecitabine dose + 7.
Oxaliplatin: Defined as time from the date of first oxaliplatin dose to the date of last oxaliplatin dose + 21.
Division by 7 for day-to-week calculation.

		Control 1 (N=229)
Treatment duration of regime CAPOX+Bevacizumab (Weeks)	n	41
	Mean (SD)	32.46 (27.585)
	Median	25.00
	Q1, Q3	13.14, 42.86
	Min, Max	3.0, 130.9
Bevacizumab	n	41
	Mean (SD)	30.62 (25.082)
	Median	21.71
	Q1, Q3	13.00, 42.86
	Min, Max	3.0, 98.3
Capecitabine	n	41
	Mean (SD)	31.81 (27.706)
	Median	22.71
	Q1, Q3	13.14, 42.86
	Min, Max	2.7, 130.9
Oxaliplatin	n	41
	Mean (SD)	19.15 (15.953)
	Median	17.71
	Q1, Q3	12.71, 21.71
	Min, Max	3.0, 98.3

Bevacizumab: Defined as time from the date of first bevacizumab dose to the date of last bevacizumab dose + 21.
Capecitabine: Defined as time from the date of first capecitabine dose to the date of last capecitabine dose + 7.
Oxaliplatin: Defined as time from the date of first oxaliplatin dose to the date of last oxaliplatin dose + 21.
Division by 7 for day-to-week calculation.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Duration of regime CAPOX and CAPOX+Bevacizumab
Safety Analysis Set

		Control 1 (N=229)
Treatment duration of regime CAPOX and CAPOX+Bevacizumab (Weeks)	n	47
	Mean (SD)	29.32 (27.096)
	Median	21.14
	Q1, Q3	9.00, 39.57
	Min, Max	2.9, 130.9
Bevacizumab	n	41
	Mean (SD)	30.62 (25.082)
	Median	21.71
	Q1, Q3	13.00, 42.86
	Min, Max	3.0, 98.3
Capecitabine	n	47
	Mean (SD)	28.75 (27.142)
	Median	18.00
	Q1, Q3	8.86, 39.57
	Min, Max	2.7, 130.9
Oxaliplatin	n	47
	Mean (SD)	17.65 (15.527)
	Median	16.43
	Q1, Q3	7.00, 21.43
	Min, Max	2.9, 98.3

Bevacizumab: Defined as time from the date of first bevacizumab dose to the date of last bevacizumab dose + 21.
Capecitabine: Defined as time from the date of first capecitabine dose to the date of last capecitabine dose + 7.
Oxaliplatin: Defined as time from the date of first oxaliplatin dose to the date of last oxaliplatin dose + 21.
Division by 7 for day-to-week calculation.

		Control 1 (N=229)
Treatment duration of regime FOLFOXIRI (Weeks)	n	8
	Mean (SD)	35.57 (27.321)
	Median	29.00
	Q1, Q3	15.86, 48.00
	Min, Max	7.0, 91.9
Fluorouracil	n	8
	Mean (SD)	35.57 (27.321)
	Median	29.00
	Q1, Q3	15.86, 48.00
	Min, Max	7.0, 91.9
Irinotecan	n	8
	Mean (SD)	29.20 (28.594)
	Median	21.00
	Q1, Q3	11.36, 37.50
	Min, Max	2.0, 91.9
Leucovorin	n	7
	Mean (SD)	33.08 (28.513)
	Median	26.00
	Q1, Q3	15.71, 43.00
	Min, Max	7.0, 91.9
Oxaliplatin	n	8
	Mean (SD)	20.48 (8.492)
	Median	20.57
	Q1, Q3	14.86, 26.50
	Min, Max	7.0, 33.0

Fluorouracil: Defined as time from the date of first fluorouracil dose to the date of last fluorouracil dose + 14 for bolus. Defined as time from the date of first fluorouracil dose to the date of last fluorouracil dose + 12 for infusion. Use maximum time of bolus and infusion.
Irinotecan: Defined as time from the date of first irinotecan dose to the date of last irinotecan dose + 14.
Leucovorin: Defined as time from the date of first leucovorin dose to the date of last leucovorin dose + 14.
Oxaliplatin: Defined as time from the date of first oxaliplatin dose to the date of last oxaliplatin dose + 14.
Division by 7 for day-to-week calculation.

		Control 1 (N=229)
Treatment duration of regime FOLFOXIRI+Bevacizumab (Weeks)	n	59
	Mean (SD)	38.98 (27.492)
	Median	33.00
	Q1, Q3	21.00, 48.86
	Min, Max	4.0, 150.0
Bevacizumab	n	59
	Mean (SD)	36.65 (27.573)
	Median	31.29
	Q1, Q3	18.00, 44.86
	Min, Max	2.0, 150.0
Fluorouracil	n	59
	Mean (SD)	38.95 (27.500)
	Median	33.00
	Q1, Q3	20.86, 48.86
	Min, Max	3.9, 150.0
Irinotecan	n	59
	Mean (SD)	35.80 (27.465)
	Median	30.14
	Q1, Q3	17.71, 42.86
	Min, Max	4.0, 150.0
Leucovorin	n	58
	Mean (SD)	38.78 (27.696)
	Median	32.43
	Q1, Q3	21.00, 44.86
	Min, Max	4.0, 150.0
Oxaliplatin	n	59
	Mean (SD)	24.10 (15.965)
	Median	21.71
	Q1, Q3	13.14, 30.14
	Min, Max	4.0, 97.0

Bevacizumab: Defined as time from the date of first bevacizumab dose to the date of last bevacizumab dose + 14.
Fluorouracil: Defined as time from the date of first fluorouracil dose to the date of last fluorouracil dose + 14 for bolus. Defined as time from the date of first fluorouracil dose to the date of last fluorouracil dose + 12 for infusion. Use maximum time of bolus and infusion.
Irinotecan: Defined as time from the date of first irinotecan dose to the date of last irinotecan dose + 14.
Leucovorin: Defined as time from the date of first leucovorin dose to the date of last leucovorin dose + 14.
Oxaliplatin: Defined as time from the date of first oxaliplatin dose to the date of last oxaliplatin dose + 14.
Division by 7 for day-to-week calculation.

		Control 1 (N=229)
Treatment duration of regime FOLFOXIRI and FOLFOXIRI+Bevacizumab (Weeks)	n	67
	Mean (SD)	38.57 (27.287)
	Median	32.00
	Q1, Q3	20.57, 48.86
	Min, Max	4.0, 150.0
Bevacizumab	n	59
	Mean (SD)	36.65 (27.573)
	Median	31.29
	Q1, Q3	18.00, 44.86
	Min, Max	2.0, 150.0
Fluorouracil	n	67
	Mean (SD)	38.55 (27.294)
	Median	32.00
	Q1, Q3	20.43, 48.86
	Min, Max	3.9, 150.0
Irinotecan	n	67
	Mean (SD)	35.01 (27.464)
	Median	30.00
	Q1, Q3	16.00, 42.86
	Min, Max	2.0, 150.0
Leucovorin	n	65
	Mean (SD)	38.17 (27.615)
	Median	31.86
	Q1, Q3	20.57, 43.00
	Min, Max	4.0, 150.0
Oxaliplatin	n	67
	Mean (SD)	23.67 (15.265)
	Median	21.71
	Q1, Q3	13.71, 30.00
	Min, Max	4.0, 97.0

Bevacizumab: Defined as time from the date of first bevacizumab dose to the date of last bevacizumab dose + 14.
Fluorouracil: Defined as time from the date of first fluorouracil dose to the date of last fluorouracil dose + 14 for bolus. Defined as time from the date of first fluorouracil dose to the date of last fluorouracil dose + 12 for infusion. Use maximum time of bolus and infusion.
Irinotecan: Defined as time from the date of first irinotecan dose to the date of last irinotecan dose + 14.
Leucovorin: Defined as time from the date of first leucovorin dose to the date of last leucovorin dose + 14.
Oxaliplatin: Defined as time from the date of first oxaliplatin dose to the date of last oxaliplatin dose + 14.
Division by 7 for day-to-week calculation.

		Control 1 (N=229)
Treatment duration of regime FOLFOX (Weeks)	n	18
	Mean (SD)	19.52 (13.601)
	Median	16.00
	Q1, Q3	10.00, 30.29
	Min, Max	2.0, 54.9
Fluorouracil	n	18
	Mean (SD)	19.41 (13.671)
	Median	16.00
	Q1, Q3	10.00, 30.29
	Min, Max	2.0, 54.9
Leucovorin	n	18
	Mean (SD)	17.80 (13.176)
	Median	13.93
	Q1, Q3	9.00, 22.86
	Min, Max	2.0, 54.9
Oxaliplatin	n	18
	Mean (SD)	16.25 (8.309)
	Median	16.00
	Q1, Q3	10.00, 24.00
	Min, Max	2.0, 31.0

Fluorouracil: Defined as time from the date of first fluorouracil dose to the date of last fluorouracil dose + 14 for bolus. Defined as time from the date of first fluorouracil dose to the date of last fluorouracil dose + 12 for infusion. Use maximum time of bolus and infusion.
Leucovorin: Defined as time from the date of first leucovorin dose to the date of last leucovorin dose + 14.
Oxaliplatin: Defined as time from the date of first oxaliplatin dose to the date of last oxaliplatin dose + 14.
Division by 7 for day-to-week calculation.

		Control 1 (N=229)
Treatment duration of regime FOLFOX+Bevacizumab (Weeks)	n	97
	Mean (SD)	28.42 (22.262)
	Median	25.86
	Q1, Q3	10.86, 35.86
	Min, Max	2.0, 115.6
Bevacizumab	n	97
	Mean (SD)	27.35 (22.485)
	Median	24.86
	Q1, Q3	10.00, 32.00
	Min, Max	2.0, 115.6
Fluorouracil	n	97
	Mean (SD)	28.42 (22.256)
	Median	25.86
	Q1, Q3	10.86, 35.86
	Min, Max	2.0, 115.4
Leucovorin	n	97
	Mean (SD)	27.52 (20.389)
	Median	25.86
	Q1, Q3	10.86, 35.86
	Min, Max	2.0, 87.0
Oxaliplatin	n	97
	Mean (SD)	19.71 (12.401)
	Median	19.86
	Q1, Q3	10.29, 26.00
	Min, Max	2.0, 71.4

Bevacizumab: Defined as time from the date of first bevacizumab dose to the date of last bevacizumab dose + 14.
Fluorouracil: Defined as time from the date of first fluorouracil dose to the date of last fluorouracil dose + 14 for bolus. Defined as time from the date of first fluorouracil dose to the date of last fluorouracil dose + 12 for infusion. Use maximum time of bolus and infusion.
Leucovorin: Defined as time from the date of first leucovorin dose to the date of last leucovorin dose + 14.
Oxaliplatin: Defined as time from the date of first oxaliplatin dose to the date of last oxaliplatin dose + 14.
Division by 7 for day-to-week calculation.

		Control 1 (N=229)
Treatment duration of regime FOLFOX and FOLFOX+Bevacizumab (Weeks)	n	115
	Mean (SD)	27.03 (21.342)
	Median	24.14
	Q1, Q3	10.29, 34.00
	Min, Max	2.0, 115.6
Bevacizumab	n	97
	Mean (SD)	27.35 (22.485)
	Median	24.86
	Q1, Q3	10.00, 32.00
	Min, Max	2.0, 115.6
Fluorouracil	n	115
	Mean (SD)	27.01 (21.350)
	Median	24.14
	Q1, Q3	10.29, 34.00
	Min, Max	2.0, 115.4
Leucovorin	n	115
	Mean (SD)	26.00 (19.711)
	Median	24.00
	Q1, Q3	10.00, 33.00
	Min, Max	2.0, 87.0
Oxaliplatin	n	115
	Mean (SD)	19.17 (11.891)
	Median	19.00
	Q1, Q3	10.00, 25.43
	Min, Max	2.0, 71.4

Bevacizumab: Defined as time from the date of first bevacizumab dose to the date of last bevacizumab dose + 14.
Fluorouracil: Defined as time from the date of first fluorouracil dose to the date of last fluorouracil dose + 14 for bolus. Defined as time from the date of first fluorouracil dose to the date of last fluorouracil dose + 12 for infusion. Use maximum time of bolus and infusion.
Leucovorin: Defined as time from the date of first leucovorin dose to the date of last leucovorin dose + 14.
Oxaliplatin: Defined as time from the date of first oxaliplatin dose to the date of last oxaliplatin dose + 14.
Division by 7 for day-to-week calculation.

		EC+FOLFOX (N=232)	Control 1 (N=229)
Treatment duration of all regimens (Weeks)	n (missing)	232 (0)	229 (0)
	Mean (SD)	55.45 (35.413)	30.88 (24.834)
	Median	49.79	25.86
	Q1, Q3	26.07, 79.50	13.14, 39.00
	Min, Max	1.3, 161.9	2.0, 150.0

Defined as time from the date of first drug dose to the date of last drug dose + 1/+ 7/+ 14/+ 21.
Division by 7 for day-to-week calculation.

		EC+FOLFOX (N=236)	Control 1 (N=243)
Overall Survival Follow-up duration (Months)	n (missing)	236 (0)	243 (0)
	Mean (SD)	17.73 (7.810)	13.91 (7.884)
	Median	18.14	13.50
	Q1, Q3	12.67, 22.85	8.38, 18.66
	Min, Max	0.2, 37.3	0.0, 35.0

Defined as the time from randomization to the date of death due to any cause. Patients last known to be alive will be censored at the date of last contact.
Division by 30.4375 for day-to-month calculation.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Follow-up Duration of Progression Free Survival
Full Analysis Set

		EC+FOLFOX (N=236)	Control 1 (N=243)
PFS based on BICR Assessment Follow-up duration (Months)	n (missing)	236 (0)	243 (0)
	Mean (SD)	10.76 (7.660)	6.28 (5.560)
	Median	9.76	5.36
	Q1, Q3	5.27, 15.41	2.40, 8.48
	Min, Max	0.0, 36.8	0.0, 34.4

Please refer to table 4 and table 5 in the statistical analysis plan for details regarding censoring.
Division by 30.4375 for day-to-month calculation.

		EC+FOLFOX (N=236)	Control 1 (N=243)
Duration of Objective Response based on BICR Assessment Follow-up duration (Months)	n (missing)	155 (81)	91 (152)
	Mean (SD)	10.70 (6.818)	7.36 (5.936)
	Median	9.20	5.52
	Q1, Q3	5.42, 15.11	2.79, 10.84
	Min, Max	1.3, 35.2	1.0, 32.9

Please refer to table 4 and table 5 in the statistical analysis plan for details regarding censoring.
Division by 30.4375 for day-to-month calculation.
Including only patients having complete response or partial response.

		EC+FOLFOX (N=236)	Control 1 (N=243)
Time to first deterioration of at least 10 points - EOR01-Global QOL Follow-up duration (Months)	n (missing)	219 (17)	222 (21)
	Mean (SD)	7.06 (6.660)	4.82 (5.146)
	Median	4.37	2.96
	Q1, Q3	1.61, 11.24	1.48, 6.08
	Min, Max	0.0, 35.3	0.0, 34.4
Time to first improvement of at least 10 points - EOR01-Global QOL Follow-up duration (Months)	n (missing)	219 (17)	222 (21)
	Mean (SD)	8.19 (7.571)	5.06 (4.528)
	Median	5.55	4.14
	Q1, Q3	1.74, 13.04	1.54, 7.29
	Min, Max	0.0, 34.3	0.0, 24.6
Time to first deterioration of at least 10 points - EOR01-Physical Functioning Follow-up duration (Months)	n (missing)	219 (17)	222 (21)
	Mean (SD)	7.40 (7.442)	5.51 (5.483)
	Median	4.21	4.17
	Q1, Q3	1.58, 11.27	1.61, 7.16
	Min, Max	0.0, 32.0	0.0, 34.4
Time to first improvement of at least 10 points - EOR01-Physical Functioning Follow-up duration (Months)	n (missing)	219 (17)	222 (21)
	Mean (SD)	9.73 (7.856)	5.31 (4.689)
	Median	8.08	4.17
	Q1, Q3	2.92, 14.03	1.64, 7.72
	Min, Max	0.0, 34.5	0.0, 24.6
Time to first deterioration of at least 10 points - EOR01-Role Functioning Follow-up duration (Months)	n (missing)	219 (17)	222 (21)
	Mean (SD)	5.96 (6.239)	4.54 (4.805)
	Median	3.12	2.84
	Q1, Q3	1.51, 9.23	1.48, 5.78
	Min, Max	0.0, 29.1	0.0, 29.3
Time to first improvement of at least 10 points - EOR01-Role Functioning Follow-up duration (Months)	n (missing)	219 (17)	222 (21)
	Mean (SD)	8.51 (7.869)	5.10 (4.928)
	Median	5.88	4.14
	Q1, Q3	1.87, 13.27	1.51, 7.10
	Min, Max	0.0, 34.5	0.0, 34.4
Time to first deterioration of at least 10 points - EOR01-Emotional Functioning Follow-up duration (Months)	n (missing)	219 (17)	222 (21)
	Mean (SD)	9.45 (7.424)	5.70 (5.408)
	Median	7.66	4.44
	Q1, Q3	3.52, 13.86	1.71, 7.39
	Min, Max	0.0, 35.3	0.0, 34.4
Time to first improvement of at least 10 points - EOR01-Emotional Functioning Follow-up duration (Months)	n (missing)	219 (17)	222 (21)
	Mean (SD)	7.02 (7.153)	5.04 (5.039)
	Median	4.21	3.27
	Q1, Q3	1.61, 11.07	1.58, 6.77
	Min, Max	0.0, 34.3	0.0, 34.4
Time to first deterioration of at least 10 points - EOR01-Cognitive Functioning Follow-up duration (Months)	n (missing)	219 (17)	222 (21)
	Mean (SD)	6.67 (6.553)	4.61 (4.405)
	Median	4.17	2.94
	Q1, Q3	1.61, 9.76	1.51, 6.57
	Min, Max	0.0, 35.3	0.0, 24.6

Defined as the time from the date of randomization to the date of last assessment.
Division by 30.4375 for day-to-month calculation.

		EC+FOLFOX (N=236)	Control 1 (N=243)
Time to first improvement of at least 10 points - EOR01-Cognitive Functioning Follow-up duration (Months)	n (missing)	219 (17)	222 (21)
	Mean (SD)	9.79 (8.260)	5.76 (5.380)
	Median	7.95	4.45
	Q1, Q3	2.76, 14.09	1.68, 8.15
	Min, Max	0.0, 35.3	0.0, 34.4
Time to first deterioration of at least 10 points - EOR01-Social Functioning Follow-up duration (Months)	n (missing)	219 (17)	222 (21)
	Mean (SD)	6.60 (6.727)	4.83 (4.683)
	Median	3.88	3.10
	Q1, Q3	1.58, 9.79	1.51, 6.44
	Min, Max	0.0, 29.1	0.0, 29.3
Time to first improvement of at least 10 points - EOR01-Social Functioning Follow-up duration (Months)	n (missing)	219 (17)	222 (21)
	Mean (SD)	8.50 (7.856)	5.26 (5.209)
	Median	5.59	3.88
	Q1, Q3	2.04, 13.27	1.54, 7.13
	Min, Max	0.0, 34.3	0.0, 34.4
Time to first deterioration of at least 10 points - EOR01-Fatigue Follow-up duration (Months)	n (missing)	219 (17)	222 (21)
	Mean (SD)	5.23 (5.824)	4.58 (4.938)
	Median	2.56	2.76
	Q1, Q3	1.48, 6.97	1.48, 5.88
	Min, Max	0.0, 27.9	0.0, 29.3
Time to first improvement of at least 10 points - EOR01-Fatigue Follow-up duration (Months)	n (missing)	219 (17)	222 (21)
	Mean (SD)	8.02 (7.329)	5.09 (4.558)
	Median	5.72	4.16
	Q1, Q3	2.07, 11.33	1.51, 7.26
	Min, Max	0.0, 34.3	0.0, 24.6
Time to first deterioration of at least 10 points - EOR01-Nausea and Vomiting Follow-up duration (Months)	n (missing)	219 (17)	222 (21)
	Mean (SD)	6.99 (7.126)	4.52 (4.443)
	Median	3.88	2.89
	Q1, Q3	1.58, 10.94	1.48, 6.01
	Min, Max	0.0, 34.3	0.0, 24.6
Time to first improvement of at least 10 points - EOR01-Nausea and Vomiting Follow-up duration (Months)	n (missing)	219 (17)	222 (21)
	Mean (SD)	10.84 (8.062)	6.25 (5.532)
	Median	9.72	5.47
	Q1, Q3	4.14, 17.05	2.27, 8.31
	Min, Max	0.0, 35.3	0.0, 34.4
Time to first deterioration of at least 10 points - EOR01-Pain Follow-up duration (Months)	n (missing)	219 (17)	222 (21)
	Mean (SD)	7.38 (6.481)	5.22 (5.148)
	Median	5.49	4.17
	Q1, Q3	2.10, 11.01	1.58, 7.06
	Min, Max	0.0, 29.1	0.0, 34.4
Time to first improvement of at least 10 points - EOR01-Pain Follow-up duration (Months)	n (missing)	219 (17)	222 (21)
	Mean (SD)	7.16 (7.788)	5.05 (5.218)
	Median	3.22	3.10
	Q1, Q3	1.51, 11.30	1.48, 6.77
	Min, Max	0.0, 34.5	0.0, 34.4

Defined as the time from the date of randomization to the date of last assessment.
Division by 30.4375 for day-to-month calculation.

		EC+FOLFOX (N=236)	Control 1 (N=243)
Time to first deterioration of at least 10 points - EOR01-Dyspnoea Follow-up duration (Months)	n (missing)	219 (17)	222 (21)
	Mean (SD)	8.00 (7.260)	5.39 (5.133)
	Median	5.52	4.19
	Q1, Q3	1.68, 12.48	1.64, 7.29
	Min, Max	0.0, 29.8	0.0, 34.4
Time to first improvement of at least 10 points - EOR01-Dyspnoea Follow-up duration (Months)	n (missing)	219 (17)	222 (21)
	Mean (SD)	10.37 (8.101)	6.12 (5.614)
	Median	8.67	4.80
	Q1, Q3	3.48, 16.69	2.00, 8.34
	Min, Max	0.0, 35.3	0.0, 34.4
Time to first deterioration of at least 10 points - EOR01-Insomnia Follow-up duration (Months)	n (missing)	219 (17)	222 (21)
	Mean (SD)	8.59 (7.382)	5.39 (5.336)
	Median	6.51	4.16
	Q1, Q3	2.17, 13.83	1.68, 7.06
	Min, Max	0.0, 32.0	0.0, 34.4
Time to first improvement of at least 10 points - EOR01-Insomnia Follow-up duration (Months)	n (missing)	219 (17)	222 (21)
	Mean (SD)	8.12 (7.891)	5.29 (4.720)
	Median	5.39	4.17
	Q1, Q3	1.64, 12.71	1.61, 7.36
	Min, Max	0.0, 35.3	0.0, 24.6
Time to first deterioration of at least 10 points - EOR01-Appetite Loss Follow-up duration (Months)	n (missing)	219 (17)	222 (21)
	Mean (SD)	6.21 (6.329)	5.02 (5.237)
	Median	3.25	3.02
	Q1, Q3	1.58, 9.69	1.48, 6.67
	Min, Max	0.0, 32.0	0.0, 34.4
Time to first improvement of at least 10 points - EOR01-Appetite Loss Follow-up duration (Months)	n (missing)	219 (17)	222 (21)
	Mean (SD)	9.55 (8.295)	5.55 (4.842)
	Median	6.93	4.45
	Q1, Q3	2.37, 13.96	1.71, 7.75
	Min, Max	0.0, 35.3	0.0, 24.6
Time to first deterioration of at least 10 points - EOR01-Constipation Follow-up duration (Months)	n (missing)	219 (17)	222 (21)
	Mean (SD)	8.41 (7.145)	5.25 (4.788)
	Median	5.91	4.32
	Q1, Q3	2.10, 13.73	1.64, 7.06
	Min, Max	0.0, 32.0	0.0, 29.3
Time to first improvement of at least 10 points - EOR01-Constipation Follow-up duration (Months)	n (missing)	219 (17)	222 (21)
	Mean (SD)	10.14 (8.357)	5.97 (5.513)
	Median	8.31	4.62
	Q1, Q3	2.37, 16.72	1.81, 8.48
	Min, Max	0.0, 35.3	0.0, 34.4
Time to first deterioration of at least 10 points - EOR01-Diarrhea Follow-up duration (Months)	n (missing)	219 (17)	222 (21)
	Mean (SD)	8.78 (6.940)	4.58 (4.726)
	Median	7.69	2.86
	Q1, Q3	2.73, 13.27	1.48, 6.05
	Min, Max	0.0, 32.0	0.0, 29.3

Defined as the time from the date of randomization to the date of last assessment.
Division by 30.4375 for day-to-month calculation.

		EC+FOLFOX (N=236)	Control 1 (N=243)
Time to first improvement of at least 10 points - EOR01-Diarrhea Follow-up duration (Months)	n (missing)	219 (17)	222 (21)
	Mean (SD)	9.80 (7.967)	6.21 (5.473)
	Median	8.15	5.14
	Q1, Q3	2.56, 15.18	1.97, 8.54
	Min, Max	0.0, 34.5	0.0, 34.4
Time to first deterioration of at least 10 points - EOR01-Financial Difficulties Follow-up duration (Months)	n (missing)	219 (17)	222 (21)
	Mean (SD)	8.60 (7.641)	5.81 (5.481)
	Median	5.88	4.35
	Q1, Q3	2.33, 12.48	1.91, 7.79
	Min, Max	0.0, 32.4	0.0, 34.4
Time to first improvement of at least 10 points - EOR01-Financial Difficulties Follow-up duration (Months)	n (missing)	219 (17)	222 (21)
	Mean (SD)	10.01 (8.108)	5.73 (5.170)
	Median	8.34	4.71
	Q1, Q3	2.76, 15.18	1.87, 7.72
	Min, Max	0.0, 35.3	0.0, 34.4

Defined as the time from the date of randomization to the date of last assessment.
Division by 30.4375 for day-to-month calculation.

		EC+FOLFOX (N=236)	Control 1 (N=243)
Time to first deterioration of at least 15 percent - EQ5D02-EQ-VAS Score Follow-up duration (Months)	n (missing)	215 (21)	217 (26)
	Mean (SD)	8.67 (6.863)	5.84 (5.480)
	Median	6.93	4.60
	Q1, Q3	2.92, 13.73	1.87, 7.79
	Min, Max	0.0, 35.3	0.0, 34.4
Time to first improvement of at least 15 percent - EQ5D02-EQ-VAS Score Follow-up duration (Months)	n (missing)	215 (21)	217 (26)
	Mean (SD)	9.48 (8.110)	5.76 (5.120)
	Median	7.13	4.63
	Q1, Q3	2.76, 14.00	1.87, 7.85
	Min, Max	0.0, 34.5	0.0, 34.4

Defined as the time from the date of randomization to the date of last assessment.
Division by 30.4375 for day-to-month calculation.

		EC+FOLFOX (N=236)	Control 1 (N=243)
Time to first deterioration of at least 15 percent - PGIS01 - Colorectal Cancer Follow-up duration (Months)	n (missing)	219 (17)	222 (21)
	Mean (SD)	8.38 (7.152)	5.49 (5.494)
	Median	5.91	4.14
	Q1, Q3	2.79, 12.45	1.64, 7.13
	Min, Max	0.0, 35.3	0.0, 34.4
Time to first improvement of at least 15 percent - PGIS01 - Colorectal Cancer Follow-up duration (Months)	n (missing)	219 (17)	222 (21)
	Mean (SD)	7.10 (7.716)	4.55 (4.667)
	Median	3.48	2.86
	Q1, Q3	1.51, 11.04	1.48, 6.05
	Min, Max	0.0, 34.5	0.0, 34.4

Defined as the time from the date of randomization to the date of last assessment.
Division by 30.4375 for day-to-month calculation.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Follow-up Duration of PGIC
Full Analysis Set

		EC+FOLFOX (N=236)	Control 1 (N=243)
Time to first deterioration of at least 15 percent - PGI01-Change Follow-up duration (Months)	n (missing)	212 (24)	202 (41)
	Mean (SD)	7.07 (6.835)	5.16 (5.307)
	Median	4.58	2.89
	Q1, Q3	1.54, 10.15	1.51, 7.10
	Min, Max	0.5, 35.3	0.5, 34.4
Time to first improvement of at least 15 percent - PGI01-Change Follow-up duration (Months)	n (missing)	212 (24)	202 (41)
	Mean (SD)	5.82 (5.460)	4.57 (3.528)
	Median	3.56	3.47
	Q1, Q3	2.02, 8.26	1.84, 6.08
	Min, Max	0.6, 32.4	0.7, 21.7

Defined as the time from the date of randomization to the date of last assessment.
Division by 30.4375 for day-to-month calculation.

		EC+FOLFOX (N=232)	Control 1 (N=229)
Safety Follow-up duration (Months)	n (missing)	232 (0)	229 (0)
	Mean (SD)	13.41 (8.247)	7.57 (5.756)
	Median	12.17	6.44
	Q1, Q3	6.46, 18.97	3.58, 9.43
	Min, Max	0.3, 38.1	0.8, 35.1

Defined as the time from the date of first dose to the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
Division by 30.4375 for day-to-month calculation.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
All Subsequent Systemic Anticancer Treatment
Full Analysis Set

Drug Category Drug	EC+FOLFOX (N=236) n (%)	Control 1 (N=243) n (%)
Any Subsequent Systemic Anticancer Treatment	108 (45.8)	139 (57.2)
FOLFIRI +/- Combination	57 (24.2)	40 (16.5)
FLUOROURACIL	37 (15.7)	32 (13.2)
IRINOTECAN	31 (13.1)	24 (9.9)
BEVACIZUMAB	32 (13.6)	16 (6.6)
FOLINIC ACID	17 (7.2)	13 (5.3)
CALCIUM FOLINATE;FLUOROURACIL;IRINOTECAN HYDROCHLORIDE	19 (8.1)	7 (2.9)
CALCIUM FOLINATE	8 (3.4)	6 (2.5)
IRINOTECAN HYDROCHLORIDE	5 (2.1)	8 (3.3)
AFLIBERCEPT	8 (3.4)	3 (1.2)
CALCIUM LEVOFOLINATE	2 (0.8)	8 (3.3)
RAMUCIRUMAB	0 (0.0)	5 (2.1)
LEVOFOLINIC ACID	2 (0.8)	2 (0.8)
CETUXIMAB	1 (0.4)	1 (0.4)
AFLIBERCEPT BETA	1 (0.4)	0 (0.0)
BEVACIZUMAB ADCD	0 (0.0)	1 (0.4)
CAPECITABINE	1 (0.4)	0 (0.0)
FLUOROURACIL;FOLINIC ACID;IRINOTECAN	1 (0.4)	0 (0.0)
FLUOROURACIL;IRINOTECAN	0 (0.0)	1 (0.4)
FOLIC ACID	1 (0.4)	0 (0.0)
IRINOTECAN HYDROCHLORIDE TRIHYDRATE	1 (0.4)	0 (0.0)
RALTITREXED	1 (0.4)	0 (0.0)
TIPIRACIL HYDROCHLORIDE;TRIFLURIDINE	1 (0.4)	0 (0.0)
TISLELIZUMAB	0 (0.0)	1 (0.4)
BRAF Inhibitor +/- Combination	19 (8.1)	100 (41.2)
CETUXIMAB	16 (6.8)	90 (37.0)
ENCORAFENIB	16 (6.8)	81 (33.3)
BINIMETINIB	5 (2.1)	14 (5.8)
DABRAFENIB	1 (0.4)	7 (2.9)
IRINOTECAN	1 (0.4)	7 (2.9)
PANITUMUMAB	1 (0.4)	7 (2.9)
VEMURAFENIB	2 (0.8)	6 (2.5)
DABRAFENIB MESILATE	2 (0.8)	3 (1.2)
TRAMETINIB	1 (0.4)	4 (1.6)
FLUOROURACIL	1 (0.4)	2 (0.8)
BEVACIZUMAB	0 (0.0)	2 (0.8)
CALCIUM FOLINATE;FLUOROURACIL;IRINOTECAN HYDROCHLORIDE	0 (0.0)	2 (0.8)
TISLELIZUMAB	0 (0.0)	2 (0.8)
AFLIBERCEPT	0 (0.0)	1 (0.4)
AZENOSERTIB	1 (0.4)	0 (0.0)
BEVACIZUMAB;CALCIUM FOLINATE;FLUOROURACIL;IRINOTECAN HYDROCHLORIDE	1 (0.4)	0 (0.0)
CALCIUM FOLINATE	1 (0.4)	0 (0.0)
CETUXIMAB;ENCORAFENIB	0 (0.0)	1 (0.4)
CETUXIMAB;FLUOROURACIL;FOLINIC ACID;IRINOTECAN	1 (0.4)	0 (0.0)
INVESTIGATIONAL DRUG	0 (0.0)	1 (0.4)
IRINOTECAN HYDROCHLORIDE	1 (0.4)	0 (0.0)
NIVOLUMAB	0 (0.0)	1 (0.4)
OXALIPLATIN	0 (0.0)	1 (0.4)
RINETERKIB	0 (0.0)	1 (0.4)
RO 7276389	0 (0.0)	1 (0.4)
TRAMETINIB DIMETHYL SULFOXIDE	1 (0.4)	0 (0.0)
TUNLAMETINIB	0 (0.0)	1 (0.4)
Single Agent Chemotherapy +/- Combination	17 (7.2)	19 (7.8)
CAPECITABINE	10 (4.2)	11 (4.5)
BEVACIZUMAB	9 (3.8)	9 (3.7)
IRINOTECAN	4 (1.7)	3 (1.2)

WHODD GLOBALB3 MAR2024 coding dictionary applied.
Drug category is determined by medical review of all subsequent anticancer systemic treatment before database lock.

Drug Category Drug	EC+FOLFOX (N=236) n (%)	Control 1 (N=243) n (%)
FLUOROURACIL	1 (0.4)	4 (1.6)
FOLINIC ACID	1 (0.4)	3 (1.2)
IRINOTECAN HYDROCHLORIDE	2 (0.8)	1 (0.4)
BEVACIZUMAB BVZR	0 (0.0)	1 (0.4)
BEVACIZUMAB;CAPECITABINE	0 (0.0)	1 (0.4)
BEVACIZUMAB;FLUOROURACIL	0 (0.0)	1 (0.4)
CISPLATIN	1 (0.4)	0 (0.0)
GEMCITABINE HYDROCHLORIDE	1 (0.4)	0 (0.0)
GIMERACIL;OTERACIL POTASSIUM;TEGAFUR	1 (0.4)	0 (0.0)
HSTC 810	0 (0.0)	1 (0.4)
MITOMYCIN	1 (0.4)	0 (0.0)
OTERACIL POTASSIUM	0 (0.0)	1 (0.4)
RAMUCIRUMAB	0 (0.0)	1 (0.4)
CAPIRI +/- Combination	11 (4.7)	2 (0.8)
CAPECITABINE	11 (4.7)	1 (0.4)
BEVACIZUMAB	10 (4.2)	1 (0.4)
IRINOTECAN	9 (3.8)	1 (0.4)
IRINOTECAN HYDROCHLORIDE	2 (0.8)	0 (0.0)
CAPECITABINE;IRINOTECAN	0 (0.0)	1 (0.4)
FOLFOX +/- Combination	10 (4.2)	11 (4.5)
BEVACIZUMAB	7 (3.0)	8 (3.3)
FLUOROURACIL	7 (3.0)	8 (3.3)
OXALIPLATIN	7 (3.0)	8 (3.3)
FLUOROURACIL;FOLINIC ACID;OXALIPLATIN	3 (1.3)	3 (1.2)
FOLINIC ACID	2 (0.8)	2 (0.8)
CALCIUM FOLINATE	1 (0.4)	2 (0.8)
CALCIUM LEVOFOLINATE	2 (0.8)	1 (0.4)
CETUXIMAB	1 (0.4)	0 (0.0)
Trifluridine/Tipiracil +/- VEGF Inhibitor	10 (4.2)	14 (5.8)
BEVACIZUMAB	9 (3.8)	13 (5.3)
TIPIRACIL HYDROCHLORIDE;TRIFLURIDINE	5 (2.1)	12 (4.9)
TIPIRACIL;TRIFLURIDINE	4 (1.7)	1 (0.4)
TIPIRACIL	1 (0.4)	1 (0.4)
TRIFLURIDINE	1 (0.4)	1 (0.4)
FRUQUINTINIB	0 (0.0)	1 (0.4)
SINTILIMAB	0 (0.0)	1 (0.4)
Other	8 (3.4)	7 (2.9)
BEVACIZUMAB	4 (1.7)	2 (0.8)
CETUXIMAB	1 (0.4)	3 (1.2)
RALTITREXED	2 (0.8)	2 (0.8)
INVESTIGATIONAL DRUG	1 (0.4)	1 (0.4)
IRINOTECAN	1 (0.4)	1 (0.4)
OXALIPLATIN	0 (0.0)	1 (0.4)
FOLFOXIRI +/- Combination	3 (1.3)	7 (2.9)
FLUOROURACIL	2 (0.8)	6 (2.5)
OXALIPLATIN	2 (0.8)	6 (2.5)
BEVACIZUMAB	1 (0.4)	6 (2.5)
IRINOTECAN	2 (0.8)	5 (2.1)
CALCIUM FOLINATE	1 (0.4)	1 (0.4)
FOLINIC ACID	0 (0.0)	2 (0.8)
BEVACIZUMAB;FLUOROURACIL;FOLINIC ACID;IRINOTECAN;OXALIPLATIN	0 (0.0)	1 (0.4)
CALCIUM FOLINATE;FLUOROURACIL;IRINOTECAN HYDROCHLORIDE	1 (0.4)	0 (0.0)
CALCIUM FOLINATE;FLUOROURACIL;IRINOTECAN HYDROCHLORIDE;OXALIPLATIN	0 (0.0)	1 (0.4)
CALCIUM LEVOFOLINATE	0 (0.0)	1 (0.4)
FLUOROURACIL;FOLINIC ACID;OXALIPLATIN	1 (0.4)	0 (0.0)

WHODD GLOBALB3 MAR2024 coding dictionary applied.
Drug category is determined by medical review of all subsequent anticancer systemic treatment before database lock.

Drug Category Drug	EC+FOLFOX (N=236) n (%)	Control 1 (N=243) n (%)
IRINOTECAN HYDROCHLORIDE	0 (0.0)	1 (0.4)
LEVOFOLINIC ACID	1 (0.4)	0 (0.0)
Regorafenib	3 (1.3)	4 (1.6)
REGORAFENIB	3 (1.3)	4 (1.6)
ENVAFOLIMAB	1 (0.4)	0 (0.0)
KN046	1 (0.4)	0 (0.0)
PEMBROLIZUMAB	0 (0.0)	1 (0.4)
SINTILIMAB	0 (0.0)	1 (0.4)
CAPOX +/- Combination	2 (0.8)	2 (0.8)
BEVACIZUMAB	2 (0.8)	2 (0.8)
CAPECITABINE	2 (0.8)	2 (0.8)
OXALIPLATIN	2 (0.8)	2 (0.8)
Fruquintinib	1 (0.4)	3 (1.2)
FRUQUINTINIB	1 (0.4)	3 (1.2)
RALTITREXED	0 (0.0)	1 (0.4)
Immunotherapy	1 (0.4)	3 (1.2)
BALSTILIMAB	0 (0.0)	1 (0.4)
BEVACIZUMAB	1 (0.4)	0 (0.0)
BOTENSILIMAB	0 (0.0)	1 (0.4)
CHIDAMIDE	1 (0.4)	0 (0.0)
INVESTIGATIONAL DRUG	0 (0.0)	1 (0.4)
IRINOTECAN	0 (0.0)	1 (0.4)
OXALIPLATIN	0 (0.0)	1 (0.4)
PENPULIMAB	0 (0.0)	1 (0.4)
SINTILIMAB	1 (0.4)	0 (0.0)
ZIMBERELIMAB	0 (0.0)	1 (0.4)

WHODD GLOBALB3 MAR2024 coding dictionary applied.
Drug category is determined by medical review of all subsequent anticancer systemic treatment before database lock.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
First Subsequent Systemic Anticancer Treatment
Full Analysis Set

Drug Category Drug	EC+FOLFOX (N=236) n (%)	Control 1 (N=243) n (%)
Any Subsequent Systemic Anticancer Treatment	108 (45.8)	139 (57.2)
FOLFIRI +/- Combination	54 (22.9)	21 (8.6)
FLUOROURACIL	21 (8.9)	13 (5.3)
BEVACIZUMAB	15 (6.4)	2 (0.8)
CALCIUM FOLINATE;FLUOROURACIL;IRINOTECAN HYDROCHLORIDE	8 (3.4)	1 (0.4)
AFLIBERCEPT	5 (2.1)	3 (1.2)
CALCIUM FOLINATE	2 (0.8)	1 (0.4)
CALCIUM LEVOFOLINATE	1 (0.4)	0 (0.0)
FLUOROURACIL;FOLINIC ACID;IRINOTECAN	1 (0.4)	0 (0.0)
FLUOROURACIL;IRINOTECAN	0 (0.0)	1 (0.4)
FOLIC ACID	1 (0.4)	0 (0.0)
BRAF Inhibitor +/- Combination	10 (4.2)	83 (34.2)
CETUXIMAB	3 (1.3)	59 (24.3)
BINIMETINIB	1 (0.4)	9 (3.7)
ENCORAFENIB	3 (1.3)	7 (2.9)
BEVACIZUMAB	0 (0.0)	1 (0.4)
BEVACIZUMAB;CALCIUM FOLINATE;FLUOROURACIL;IRINOTECAN HYDROCHLORIDE	1 (0.4)	0 (0.0)
CETUXIMAB;ENCORAFENIB	0 (0.0)	1 (0.4)
CETUXIMAB;FLUOROURACIL;FOLINIC ACID;IRINOTECAN	1 (0.4)	0 (0.0)
DABRAFENIB	0 (0.0)	1 (0.4)
FLUOROURACIL	1 (0.4)	0 (0.0)
INVESTIGATIONAL DRUG	0 (0.0)	1 (0.4)
PANITUMUMAB	0 (0.0)	1 (0.4)
RINETERKIB	0 (0.0)	1 (0.4)
RO 7276389	0 (0.0)	1 (0.4)
VEMURAFENIB	0 (0.0)	1 (0.4)
Single Agent Chemotherapy +/- Combination	15 (6.4)	10 (4.1)
BEVACIZUMAB	6 (2.5)	5 (2.1)
CAPECITABINE	5 (2.1)	2 (0.8)
FLUOROURACIL	0 (0.0)	3 (1.2)
IRINOTECAN	2 (0.8)	0 (0.0)
CISPLATIN	1 (0.4)	0 (0.0)
GEMCITABINE HYDROCHLORIDE	1 (0.4)	0 (0.0)
CAPIRI +/- Combination	11 (4.7)	1 (0.4)
BEVACIZUMAB	9 (3.8)	0 (0.0)
CAPECITABINE	1 (0.4)	0 (0.0)
CAPECITABINE;IRINOTECAN	0 (0.0)	1 (0.4)
IRINOTECAN HYDROCHLORIDE	1 (0.4)	0 (0.0)
FOLFOX +/- Combination	7 (3.0)	10 (4.1)
BEVACIZUMAB	5 (2.1)	7 (2.9)
FLUOROURACIL	0 (0.0)	3 (1.2)
FLUOROURACIL;FOLINIC ACID;OXALIPLATIN	2 (0.8)	0 (0.0)
Trifluridine/Tipiracil +/- VEGF Inhibitor	2 (0.8)	0 (0.0)
BEVACIZUMAB	1 (0.4)	0 (0.0)
TIPIRACIL;TRIFLURIDINE	1 (0.4)	0 (0.0)
Other	5 (2.1)	5 (2.1)
BEVACIZUMAB	3 (1.3)	1 (0.4)
INVESTIGATIONAL DRUG	1 (0.4)	1 (0.4)
RALTITREXED	1 (0.4)	1 (0.4)
CETUXIMAB	0 (0.0)	1 (0.4)
OXALIPLATIN	0 (0.0)	1 (0.4)

WHODD GLOBALB3 MAR2024 coding dictionary applied.
Drug category is determined by medical review of all subsequent anticancer systemic treatment before database lock.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
First Subsequent Systemic Anticancer Treatment
Full Analysis Set

Drug Category Drug	EC+FOLFOX (N=236) n (%)	Control 1 (N=243) n (%)
FOLFOXIRI +/- Combination	2 (0.8)	5 (2.1)
FLUOROURACIL	0 (0.0)	3 (1.2)
BEVACIZUMAB	0 (0.0)	1 (0.4)
BEVACIZUMAB;FLUOROURACIL;FOLINIC ACID;IRINOTECAN;OXALIPLATIN	0 (0.0)	1 (0.4)
CALCIUM FOLINATE	1 (0.4)	0 (0.0)
FLUOROURACIL;FOLINIC ACID;OXALIPLATIN	1 (0.4)	0 (0.0)
Regorafenib	0 (0.0)	1 (0.4)
REGORAFENIB	0 (0.0)	1 (0.4)
CAPOX +/- Combination	2 (0.8)	2 (0.8)
BEVACIZUMAB	2 (0.8)	2 (0.8)
Fruquintinib	0 (0.0)	1 (0.4)
RALTITREXED	0 (0.0)	1 (0.4)

WHODD GLOBALB3 MAR2024 coding dictionary applied.
Drug category is determined by medical review of all subsequent anticancer systemic treatment before database lock.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Concomitant Medication
Safety Analysis Set

ATC 2	EC+FOLFOX (N=232) n (%)	Control 1 (N=229) n (%)
ANY CONCOMITANT MEDICATION	232 (100.0)	229 (100.0)
STOMATOLOGICAL PREPARATIONS	222 (95.7)	209 (91.3)
ANTIEMETICS AND ANTINAUSEANTS	220 (94.8)	213 (93.0)
OPHTHALMOLOGICALS	220 (94.8)	218 (95.2)
CORTICOSTEROIDS, DERMATOLOGICAL PREPARATIONS	218 (94.0)	204 (89.1)
CORTICOSTEROIDS FOR SYSTEMIC USE	216 (93.1)	201 (87.8)
OTOLOGICALS	214 (92.2)	207 (90.4)
VASOPROTECTIVES	214 (92.2)	204 (89.1)
NASAL PREPARATIONS	212 (91.4)	205 (89.5)
OPHTHALMOLOGICAL AND OTOLOGICAL PREPARATIONS	208 (89.7)	195 (85.2)
DRUGS FOR OBSTRUCTIVE AIRWAY DISEASES	204 (87.9)	189 (82.5)
ANTIPRURITICS, INCL. ANTIHISTAMINES, ANESTHETICS, ETC.	191 (82.3)	98 (42.8)
ANTIHISTAMINES FOR SYSTEMIC USE	188 (81.0)	95 (41.5)
ANALGESICS	170 (73.3)	160 (69.9)
DRUGS FOR ACID RELATED DISORDERS	169 (72.8)	166 (72.5)
ANTIBACTERIALS FOR SYSTEMIC USE	165 (71.1)	108 (47.2)
PSYCHOLEPTICS	150 (64.7)	121 (52.8)
ANTIDIARRHEALS, INTESTINAL ANTIINFLAMMATORY/ANTIINFECTIVE AGENTS	143 (61.6)	133 (58.1)
ANTIBIOTICS AND CHEMOTHERAPEUTICS FOR DERMATOLOGICAL USE	140 (60.3)	62 (27.1)
DRUGS FOR FUNCTIONAL GASTROINTESTINAL DISORDERS	138 (59.5)	145 (63.3)
DRUGS FOR CONSTIPATION	130 (56.0)	119 (52.0)
OTHER DERMATOLOGICAL PREPARATIONS	127 (54.7)	104 (45.4)
BLOOD SUBSTITUTES AND PERFUSION SOLUTIONS	124 (53.4)	111 (48.5)
ANTIINFLAMMATORY AND ANTIRHEUMATIC PRODUCTS	117 (50.4)	90 (39.3)
TOPICAL PRODUCTS FOR JOINT AND MUSCULAR PAIN	117 (50.4)	96 (41.9)
MINERAL SUPPLEMENTS	116 (50.0)	92 (40.2)
ANTI-ACNE PREPARATIONS	112 (48.3)	41 (17.9)
HOMEOPATHIC PREPARATION	110 (47.4)	73 (31.9)
ANTITHROMBOTIC AGENTS	109 (47.0)	89 (38.9)
ANTIANEMIC PREPARATIONS	100 (43.1)	46 (20.1)
CARDIAC THERAPY	97 (41.8)	89 (38.9)
THROAT PREPARATIONS	93 (40.1)	76 (33.2)
GYNECOLOGICAL ANTIINFECTIVES AND ANTISEPTICS	91 (39.2)	66 (28.8)
ALL OTHER THERAPEUTIC PRODUCTS	86 (37.1)	77 (33.6)
OTHER GYNECOLOGICALS	82 (35.3)	86 (37.6)
UROLOGICALS	82 (35.3)	75 (32.8)
ANTIEPILEPTICS	81 (34.9)	57 (24.9)
COUGH AND COLD PREPARATIONS	79 (34.1)	57 (24.9)
IMMUNOSTIMULANTS	75 (32.3)	83 (36.2)
EMOLLIENTS AND PROTECTIVES	70 (30.2)	54 (23.6)
LIPID MODIFYING AGENTS	68 (29.3)	46 (20.1)
VITAMINS	68 (29.3)	61 (26.6)
BILE AND LIVER THERAPY	66 (28.4)	56 (24.5)
AGENTS ACTING ON THE RENIN-ANGIOTENSIN SYSTEM	59 (25.4)	65 (28.4)
MEDICATED DRESSINGS	57 (24.6)	29 (12.7)
OTHER ALIMENTARY TRACT AND METABOLISM PRODUCTS	57 (24.6)	46 (20.1)
ANESTHETICS	54 (23.3)	42 (18.3)
DIURETICS	53 (22.8)	41 (17.9)
UNSPECIFIED HERBAL AND TRADITIONAL MEDICINE	53 (22.8)	36 (15.7)
ALL OTHER NON-THERAPEUTIC PRODUCTS	52 (22.4)	35 (15.3)
GENERAL NUTRIENTS	51 (22.0)	37 (16.2)
OTHER NERVOUS SYSTEM DRUGS	49 (21.1)	44 (19.2)
PREPARATIONS FOR TREATMENT OF WOUNDS AND ULCERS	49 (21.1)	39 (17.0)
ANTIHEMORRHAGICS	44 (19.0)	27 (11.8)
PSYCHOANALEPTICS	44 (19.0)	29 (12.7)
ANTI-PARKINSON DRUGS	41 (17.7)	26 (11.4)
ANTIFUNGALS FOR DERMATOLOGICAL USE	40 (17.2)	26 (11.4)
DRUGS USED IN DIABETES	39 (16.8)	27 (11.8)
BETA BLOCKING AGENTS	36 (15.5)	33 (14.4)
DIAGNOSTIC AGENTS	36 (15.5)	17 (7.4)

WHODD GLOBALB3 MAR2024 coding dictionary applied.
Only medications are listed with a prevalence of >= 5% in one of the two treatment arms.

ATC 2	EC+FOLFOX (N=232) n (%)	Control 1 (N=229) n (%)
CALCIUM CHANNEL BLOCKERS	35 (15.1)	49 (21.4)
ANTIPROTOZOALS	34 (14.7)	26 (11.4)
MUSCLE RELAXANTS	31 (13.4)	18 (7.9)
ANTINEOPLASTIC AGENTS	27 (11.6)	16 (7.0)
SEX HORMONES AND MODULATORS OF THE GENITAL SYSTEM	27 (11.6)	19 (8.3)
ANTIVIRALS FOR SYSTEMIC USE	25 (10.8)	24 (10.5)
ENDOCRINE THERAPY	25 (10.8)	18 (7.9)
ANTIHYPERTENSIVES	24 (10.3)	15 (6.6)
APPETITE STIMULANTS	23 (9.9)	13 (5.7)
VACCINES	22 (9.5)	13 (5.7)
ANTIMYCOTICS FOR SYSTEMIC USE	21 (9.1)	16 (7.0)
THYROID THERAPY	20 (8.6)	13 (5.7)
ANTISEPTICS AND DISINFECTANTS	17 (7.3)	5 (2.2)
OTHER RESPIRATORY SYSTEM PRODUCTS	17 (7.3)	8 (3.5)
DIGESTIVES, INCL. ENZYMES	11 (4.7)	12 (5.2)
**Uncoded ATC Level 2 Text	6 (2.6)	12 (5.2)

WHODD GLOBALB3 MAR2024 coding dictionary applied.
Only medications are listed with a prevalence of >= 5% in one of the two treatment arms.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Overall Survival (Months)
Full Analysis Set

	EC+FOLFOX (N=236)	Control 1 (N=243)
Number of subjects with events, n (%)	94 (39.8)	148 (60.9)
Number of censored subjects, n (%)	142 (60.2)	95 (39.1)
Kaplan-Meier estimates of Time to Event (Months) [1]		
25%-ile (95% CI)	14.7 (11.9, 17.9)	9.8 (8.6, 11.2)
Median (95% CI)	30.3 (21.7, NE)	15.1 (13.7, 17.7)
75%-ile (95% CI)	NE (NE, NE)	25.2 (22.9, NE)
Stratified analysis [2]		
Hazard Ratio (95% CI) [3]	0.49 (0.38, 0.63)	
p-value [4]	<.0001	

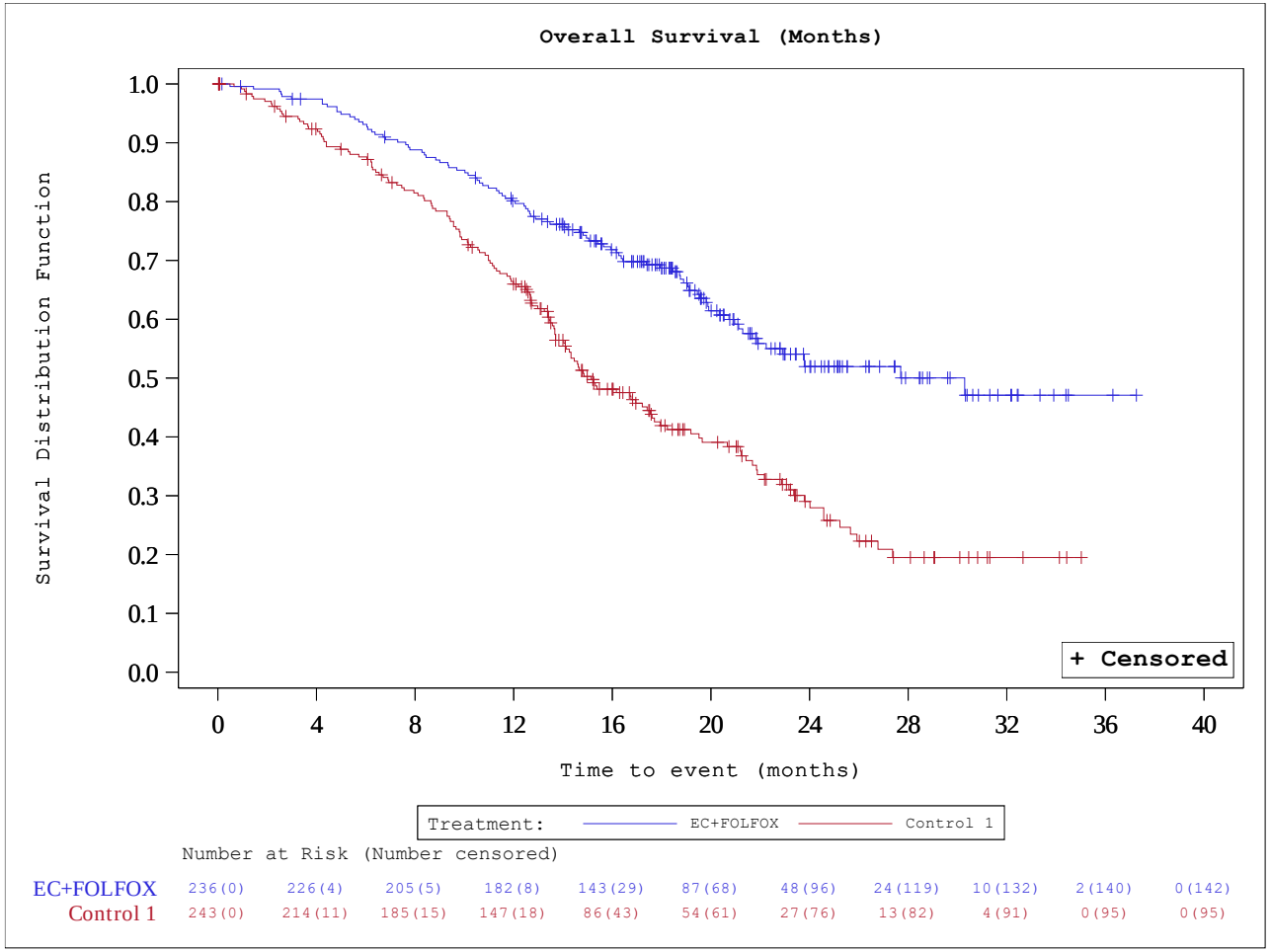
[1] Based on the Brookmeyer and Crowley method.
[2] Stratified by ECOG PS by Randomization and Geographic Region by Randomization.
[3] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[4] P-value from 2-sided log-rank test.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Overall Survival (Months) - Subgroup analysis
Full Analysis Set

Subgroup Level	EC+FOLFOX (N=236) n/ N (%)	EC+FOLFOX (N=236) Median (95% CI)[1]	Control 1 (N=243) n/ N (%)	Control 1 (N=243) Median (95% CI)[1]	Unstratified analysis Hazard Ratio (95% CI)[2]	Unstratified analysis p-Value[3]	Interaction p-Value[4]
Age (Years)							0.5132
< 65	56/ 150 (37.3)	NE (21.3, NE)	85/ 139 (61.2)	15.1 (13.7, 17.9)	0.44 (0.31, 0.62)	<.0001	
>= 65	38/ 86 (44.2)	27.7 (19.8, NE)	63/ 104 (60.6)	14.5 (12.7, 21.4)	0.54 (0.36, 0.82)	0.0028	
Sex							0.1048
Male	54/ 123 (43.9)	22.2 (19.5, NE)	71/ 119 (59.7)	15.2 (13.5, 21.7)	0.59 (0.42, 0.84)	0.0035	
Female	40/ 113 (35.4)	30.3 (23.8, NE)	77/ 124 (62.1)	14.6 (13.6, 17.7)	0.38 (0.26, 0.56)	<.0001	
Region							0.3908
Europe	46/ 109 (42.2)	30.3 (19.8, NE)	63/ 111 (56.8)	17.4 (14.1, 21.8)	0.55 (0.37, 0.80)	0.0016	
USA/Canada	7/ 15 (46.7)	20.7 (16.2, NE)	10/ 19 (52.6)	23.4 (12.7, 25.9)	0.70 (0.27, 1.86)	0.4756	
Rest of World	41/ 112 (36.6)	27.7 (21.9, NE)	75/ 113 (66.4)	14.0 (13.2, 16.2)	0.40 (0.27, 0.59)	<.0001	
ECOG-PS at Randomization							0.4073
0	42/ 131 (32.1)	NE (23.8, NE)	76/ 136 (55.9)	17.4 (14.5, 21.4)	0.42 (0.29, 0.62)	<.0001	
1	52/ 105 (49.5)	20.3 (17.9, NE)	72/ 107 (67.3)	13.6 (11.7, 16.7)	0.54 (0.38, 0.77)	0.0006	
Number of Organs Involved							0.2463
<= 2	32/ 119 (26.9)	NE (30.3, NE)	66/ 127 (52.0)	20.7 (16.2, 24.0)	0.39 (0.25, 0.59)	<.0001	
>= 3	62/ 117 (53.0)	19.1 (16.2, 22.2)	82/ 116 (70.7)	13.2 (11.4, 14.7)	0.52 (0.38, 0.73)	0.0001	
Presence of Liver Metastases							0.0448
Yes	73/ 147 (49.7)	21.0 (18.5, 27.7)	104/ 160 (65.0)	14.3 (12.7, 16.7)	0.58 (0.43, 0.78)	0.0003	
No	21/ 89 (23.6)	NE (30.3, NE)	44/ 83 (53.0)	21.2 (14.0, 23.4)	0.31 (0.18, 0.52)	<.0001	
Side of Tumor							0.9445
Left	38/ 90 (42.2)	30.3 (20.3, NE)	62/ 98 (63.3)	14.6 (13.4, 17.7)	0.48 (0.32, 0.72)	0.0003	
Right	56/ 146 (38.4)	27.7 (21.3, NE)	86/ 145 (59.3)	15.3 (13.7, 21.4)	0.49 (0.35, 0.68)	<.0001	

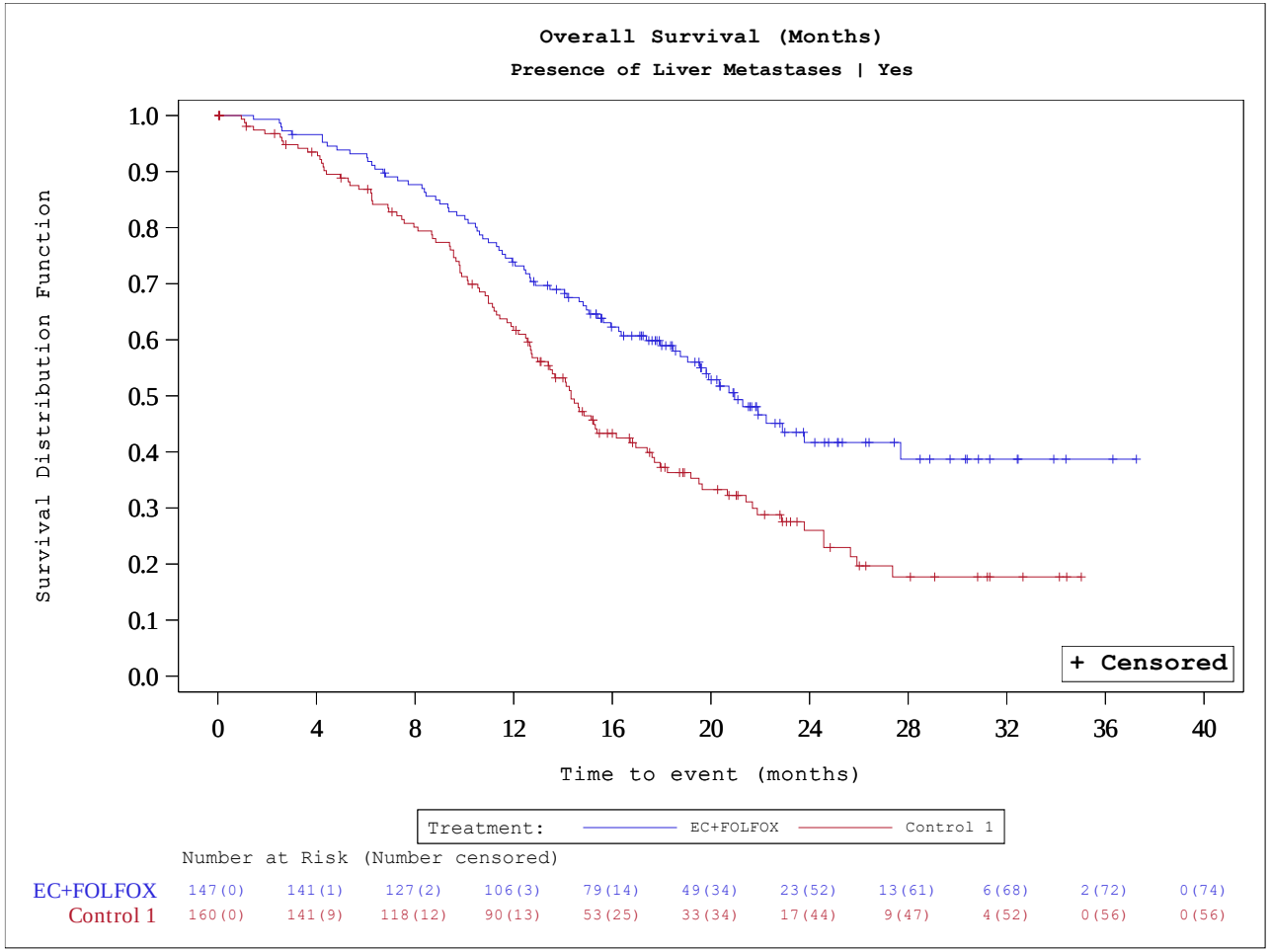
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.
[4] P-Value for interaction from Cox proportional hazards model using ties=exact option with treatment, subgroup and treatment*subgroup interaction as covariates.
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Kaplan Meier Plot of Overall Survival (Months)
Full Analysis Set



Kaplan-Meier Plots for subgroups only created if p-value for interaction < 0.05.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Kaplan Meier Plot of Overall Survival (Months)
Full Analysis Set



Kaplan-Meier Plots for subgroups only created if p-value for interaction < 0.05.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
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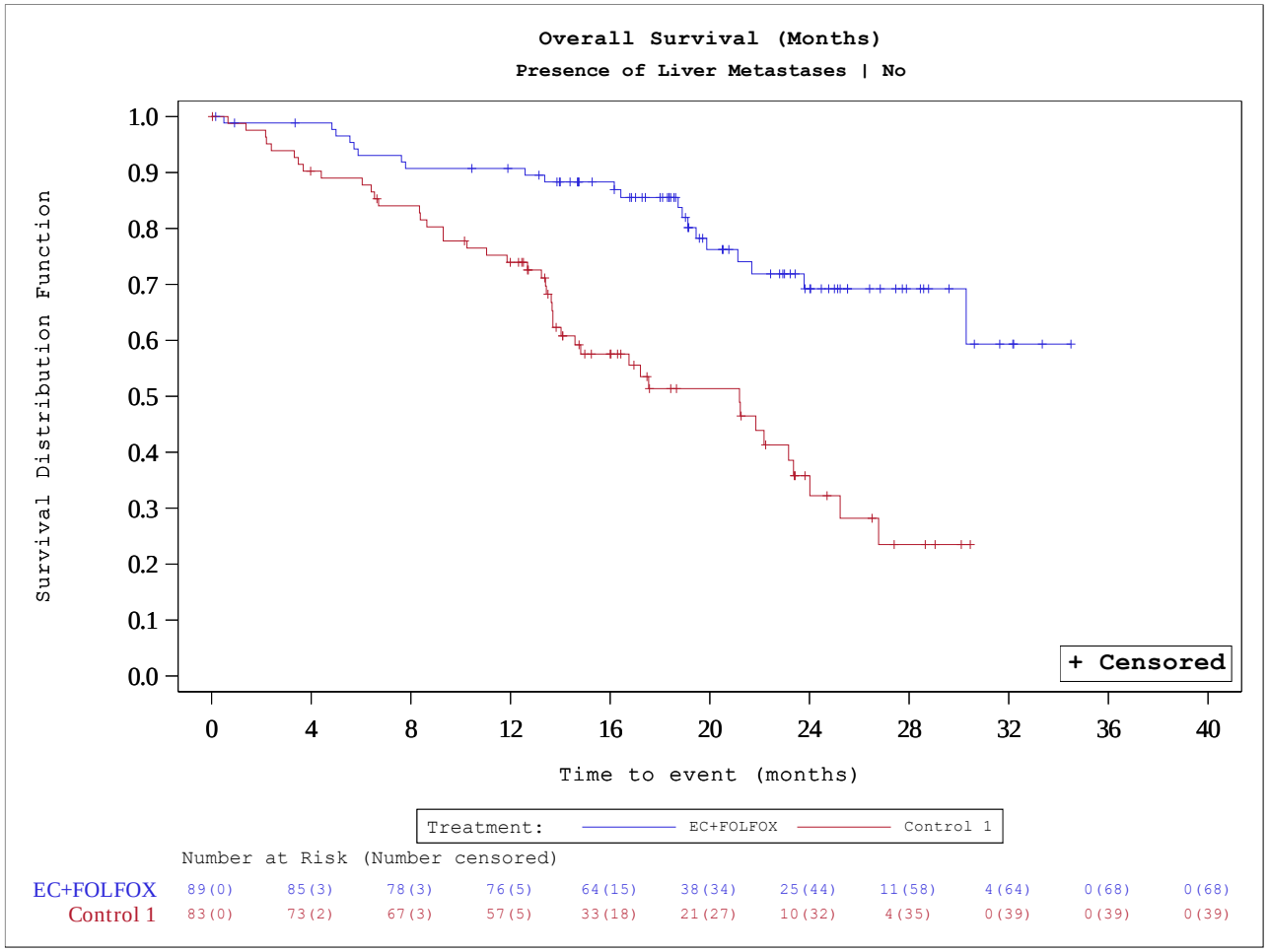
Kaplan Meier Plot of Overall Survival (Months)
Full Analysis Set



Kaplan-Meier Plots for subgroups only created if p-value for interaction < 0.05.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
PFS based on BICR Assessment (Months)
Full Analysis Set

	EC+FOLFOX (N=236)	Control 1 (N=243)
Number of subjects with events, n (%)	122 (51.7)	132 (54.3)
Number of censored subjects, n (%)	114 (48.3)	111 (45.7)
Kaplan-Meier estimates of Time to Event (Months) [1]		
25%-ile (95% CI)	7.2 (6.2, 8.4)	4.2 (3.9, 5.3)
Median (95% CI)	12.8 (11.2, 15.9)	7.1 (6.8, 8.5)
75%-ile (95% CI)	32.9 (20.0, NE)	13.6 (11.1, 19.7)
Stratified analysis [2]		
Hazard Ratio (95% CI) [3]	0.53 (0.41, 0.68)	
p-value [4]	<.0001	

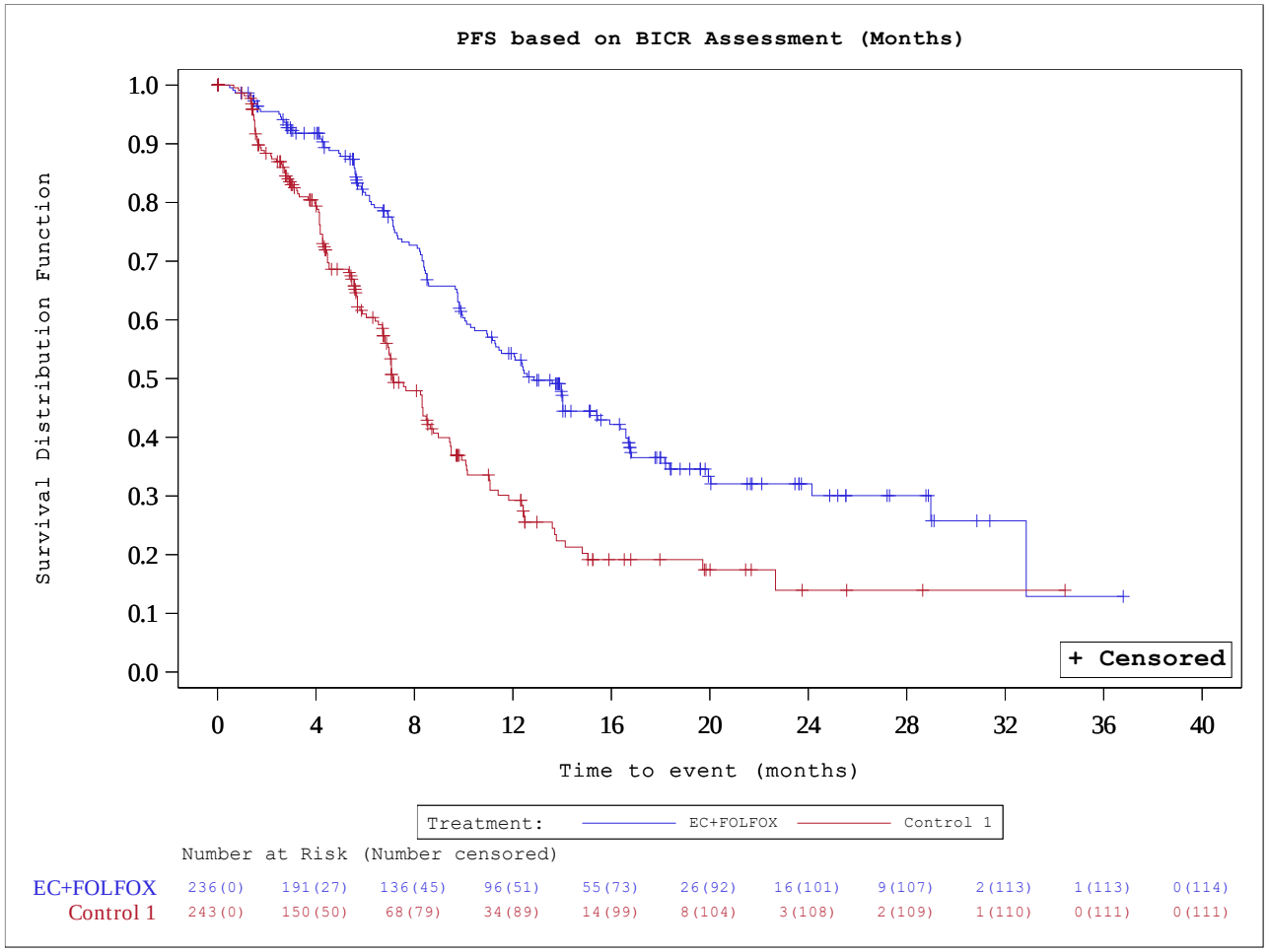
[1] Based on the Brookmeyer and Crowley method.
[2] Stratified by ECOG PS by Randomization and Geographic Region by Randomization.
[3] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[4] P-value from 2-sided log-rank test.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
PFS based on BICR Assessment (Months) - Subgroup analysis
Full Analysis Set

Subgroup Level	EC+FOLFOX (N=236) n/ N (%)	EC+FOLFOX (N=236) Median (95% CI)[1]	Control 1 (N=243) n/ N (%)	Control 1 (N=243) Median (95% CI)[1]	Unstratified analysis Hazard Ratio (95% CI)[2]	Unstratified analysis p-Value[3]	Interaction p-Value[4]
Age (Years)							0.9292
< 65	78/ 150 (52.0)	12.4 (10.1, 15.4)	71/ 139 (51.1)	7.1 (6.7, 9.5)	0.51 (0.37, 0.71)	<.0001	
>= 65	44/ 86 (51.2)	14.0 (11.0, 19.9)	61/ 104 (58.7)	7.6 (5.8, 9.4)	0.51 (0.34, 0.75)	0.0006	
Sex							0.6977
Male	59/ 123 (48.0)	15.4 (10.0, 18.2)	63/ 119 (52.9)	7.1 (6.0, 9.5)	0.50 (0.35, 0.72)	0.0001	
Female	63/ 113 (55.8)	12.4 (10.3, 14.0)	69/ 124 (55.6)	8.2 (6.4, 9.4)	0.53 (0.37, 0.75)	0.0002	
Region							0.1655
Europe	54/ 109 (49.5)	14.0 (11.3, 18.4)	60/ 111 (54.1)	7.1 (5.8, 8.5)	0.41 (0.28, 0.60)	<.0001	
USA/Canada	11/ 15 (73.3)	11.4 (5.8, 15.4)	8/ 19 (42.1)	9.5 (6.7, NE)	1.04 (0.41, 2.62)	0.9306	
Rest of World	57/ 112 (50.9)	11.5 (9.8, 16.6)	64/ 113 (56.6)	8.2 (6.5, 9.9)	0.55 (0.38, 0.80)	0.0013	
ECOG-PS at Randomization							0.1789
0	60/ 131 (45.8)	15.9 (12.4, 24.1)	74/ 136 (54.4)	8.3 (7.0, 9.5)	0.43 (0.30, 0.61)	<.0001	
1	62/ 105 (59.0)	11.3 (8.5, 14.0)	58/ 107 (54.2)	6.8 (5.7, 8.5)	0.63 (0.44, 0.90)	0.0110	
Number of Organs Involved							0.1128
<= 2	52/ 119 (43.7)	15.9 (12.6, 32.9)	66/ 127 (52.0)	7.7 (6.5, 9.4)	0.40 (0.28, 0.58)	<.0001	
>= 3	70/ 117 (59.8)	9.8 (8.4, 14.0)	66/ 116 (56.9)	7.1 (6.0, 9.5)	0.64 (0.45, 0.90)	0.0088	
Presence of Liver Metastases							0.0684
Yes	87/ 147 (59.2)	11.0 (8.6, 12.8)	86/ 160 (53.8)	7.1 (6.7, 8.3)	0.60 (0.44, 0.81)	0.0007	
No	35/ 89 (39.3)	18.4 (14.0, 32.9)	46/ 83 (55.4)	8.3 (6.4, 11.0)	0.36 (0.23, 0.57)	<.0001	
Side of Tumor							0.6238
Left	51/ 90 (56.7)	11.2 (8.5, 16.7)	53/ 98 (54.1)	7.0 (5.7, 8.3)	0.49 (0.33, 0.73)	0.0003	
Right	71/ 146 (48.6)	14.0 (11.4, 16.6)	79/ 145 (54.5)	8.3 (6.8, 10.1)	0.52 (0.37, 0.72)	<.0001	

[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.
[4] P-Value for interaction from Cox proportional hazards model using ties=exact option with treatment, subgroup and treatment*subgroup interaction as covariates.
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Kaplan Meier Plot of PFS based on BICR Assessment (Months)
Full Analysis Set



Kaplan-Meier Plots for subgroups only created if p-value for interaction < 0.05.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Duration of Objective Response based on BICR Assessment (Months)
Full Analysis Set

	EC+FOLFOX (N=155)	Control 1 (N=91)
Number of subjects with events, n (%)	74 (47.7)	38 (41.8)
Number of censored subjects, n (%)	81 (52.3)	53 (58.2)
Kaplan-Meier estimates of Time to Event (Months) [1]		
25%-ile (95% CI)	7.1 (6.6, 8.4)	5.6 (4.3, 7.6)
Median (95% CI)	13.9 (10.9, 18.5)	10.8 (7.6, 13.4)
75%-ile (95% CI)	27.6 (22.6, NE)	19.8 (12.7, NE)
Stratified analysis [2]		
Hazard Ratio (95% CI) [3]	0.73 (0.49, 1.10)	
p-value [4]	0.1344	

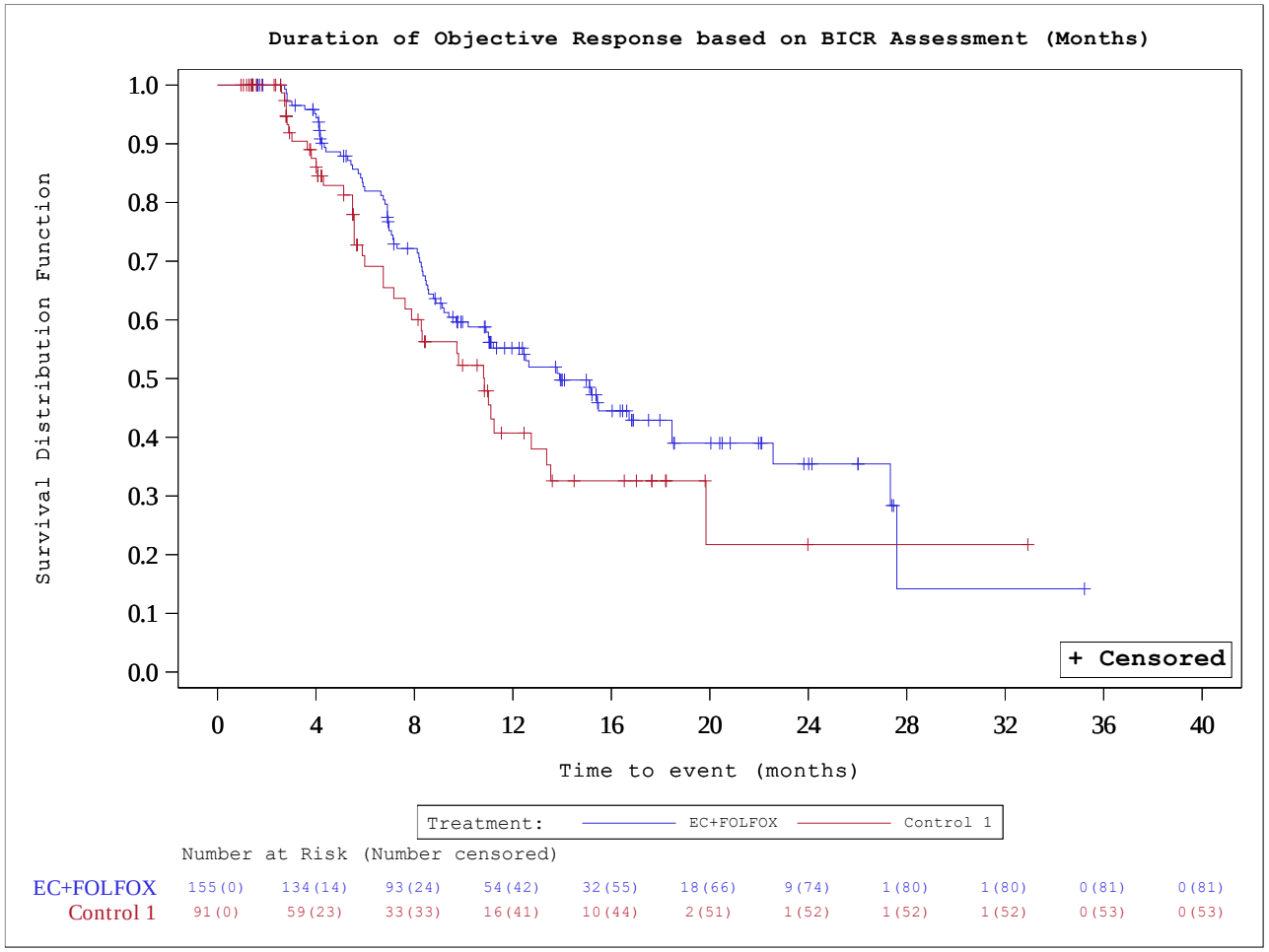
[1] Based on the Brookmeyer and Crowley method.
[2] Stratified by ECOG PS by Randomization and Geographic Region by Randomization.
[3] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[4] P-value from 2-sided log-rank test.
Including only patients having complete response or partial response.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Duration of Objective Response based on BICR Assessment (Months) - Subgroup analysis
Full Analysis Set

Subgroup Level	EC+FOLFOX (N=155) n/ N (%)	EC+FOLFOX (N=155) Median (95% CI)[1]	Control 1 (N=91) n/ N (%)	Control 1 (N=91) Median (95% CI)[1]	Unstratified analysis Hazard Ratio (95% CI)[2]	Unstratified analysis p-Value[3]	Interaction p-Value[4]
Age (Years)							0.7743
< 65	50/ 100 (50.0)	12.5 (8.8, 18.5)	18/ 50 (36.0)	9.8 (7.9, 13.5)	0.75 (0.43, 1.30)	0.3046	
>= 65	24/ 55 (43.6)	15.2 (10.9, 27.3)	20/ 41 (48.8)	10.8 (5.9, 19.8)	0.66 (0.36, 1.20)	0.1685	
Sex							0.4762
Male	38/ 82 (46.3)	15.5 (8.6, 27.6)	20/ 42 (47.6)	8.3 (5.9, 13.5)	0.64 (0.37, 1.09)	0.1004	
Female	36/ 73 (49.3)	13.8 (10.2, 18.5)	18/ 49 (36.7)	11.0 (8.3, 19.8)	0.78 (0.44, 1.37)	0.3871	
Region							0.6377
Europe	36/ 76 (47.4)	15.1 (9.7, 27.6)	16/ 37 (43.2)	11.0 (6.7, 19.8)	0.69 (0.38, 1.26)	0.2250	
USA/Canada	6/ 8 (75.0)	9.3 (4.2, NE)	3/ 8 (37.5)	NE (5.1, NE)	1.49 (0.37, 5.96)	0.5737	
Rest of World	32/ 71 (45.1)	15.4 (8.9, 27.3)	19/ 46 (41.3)	9.8 (7.2, 13.5)	0.60 (0.34, 1.06)	0.0773	
ECOG-PS at Randomization							0.8571
0	40/ 89 (44.9)	18.5 (9.7, 27.6)	21/ 52 (40.4)	11.1 (7.2, NE)	0.69 (0.40, 1.17)	0.1705	
1	34/ 66 (51.5)	12.6 (8.9, 16.7)	17/ 39 (43.6)	9.7 (5.6, 19.8)	0.74 (0.41, 1.33)	0.3139	
Number of Organs Involved							0.3460
<= 2	28/ 77 (36.4)	27.3 (12.5, NE)	17/ 46 (37.0)	11.2 (7.2, NE)	0.58 (0.32, 1.06)	0.0759	
>= 3	46/ 78 (59.0)	9.2 (7.3, 15.4)	21/ 45 (46.7)	9.7 (6.7, 12.7)	0.83 (0.50, 1.40)	0.4919	
Presence of Liver Metastases							0.0661
Yes	56/ 100 (56.0)	10.2 (8.4, 13.9)	27/ 62 (43.5)	9.8 (6.7, 13.5)	0.91 (0.57, 1.44)	0.6846	
No	18/ 55 (32.7)	27.3 (27.3, 27.6)	11/ 29 (37.9)	11.0 (7.6, NE)	0.41 (0.19, 0.89)	0.0206	
Side of Tumor							0.0442
Left	31/ 60 (51.7)	15.1 (8.3, 27.3)	17/ 36 (47.2)	6.7 (5.1, 9.7)	0.44 (0.24, 0.81)	0.0071	
Right	43/ 95 (45.3)	13.8 (10.2, 27.6)	21/ 55 (38.2)	12.7 (10.8, NE)	0.91 (0.54, 1.54)	0.7270	

[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.
[4] P-Value for interaction from Cox proportional hazards model using ties=exact option with treatment, subgroup and treatment*subgroup interaction as covariates.
Including only patients having complete response or partial response.
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Kaplan Meier Plot of Duration of Objective Response based on BICR Assessment (Months)
Full Analysis Set



Kaplan-Meier Plots for subgroups only created if p-value for interaction < 0.05.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
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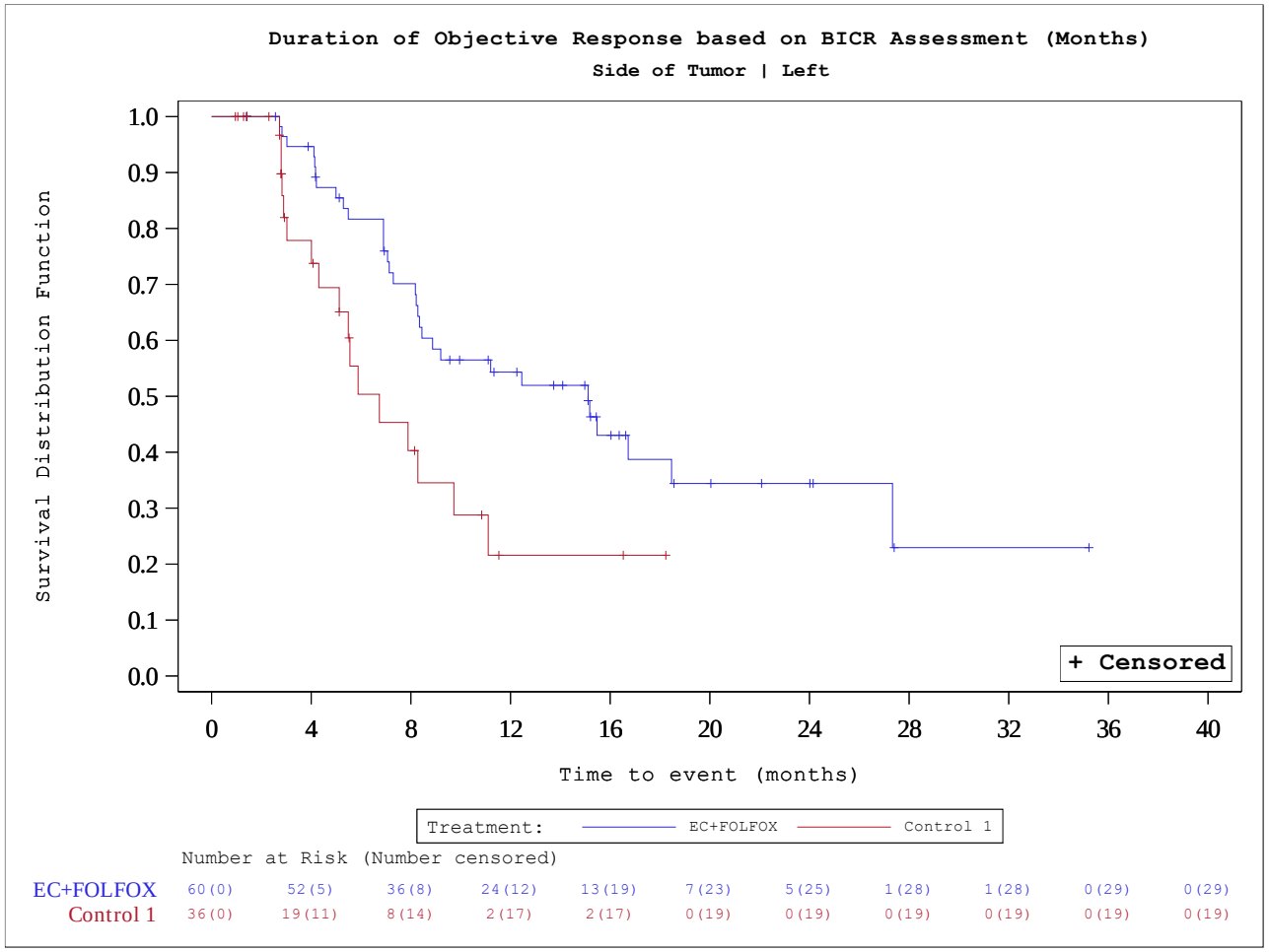
Kaplan Meier Plot of Duration of Objective Response based on BICR Assessment (Months)
Full Analysis Set



Kaplan-Meier Plots for subgroups only created if p-value for interaction < 0.05.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
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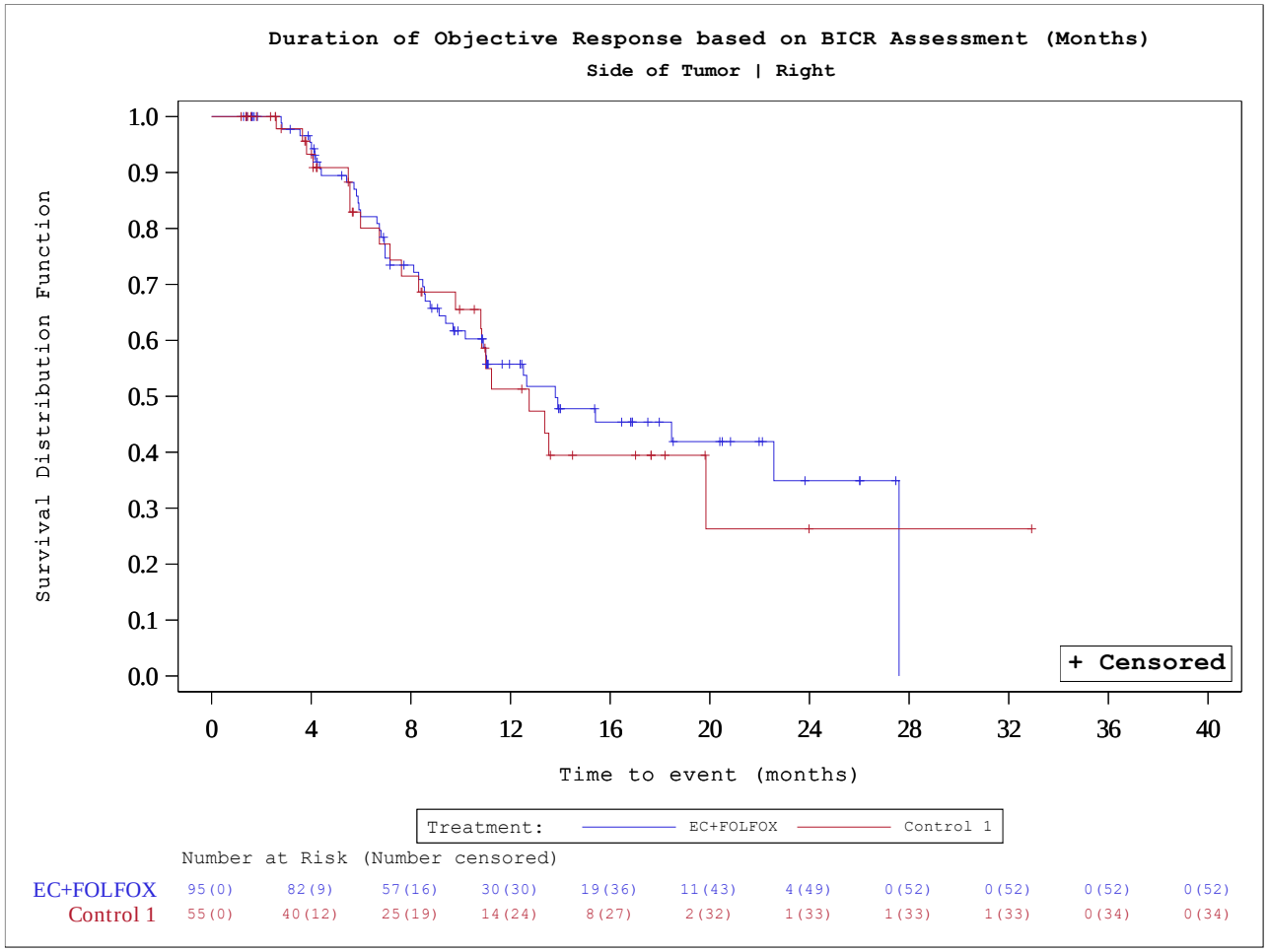
Kaplan Meier Plot of Duration of Objective Response based on BICR Assessment (Months)
Full Analysis Set



Kaplan-Meier Plots for subgroups only created if p-value for interaction < 0.05.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Time to first deterioration of at least 10 points - EOR01-Global QOL (Months)
Full Analysis Set

	EC+FOLFOX (N=219)	Control 1 (N=222)
Number of subjects with events, n (%)	121 (55.3)	95 (42.8)
Number of censored subjects, n (%)	98 (44.7)	127 (57.2)
Kaplan-Meier estimates of Time to Event (Months) [1]		
25%-ile (95% CI)	2.0 (1.6, 2.9)	1.8 (1.6, 2.8)
Median (95% CI)	5.8 (4.4, 9.8)	6.1 (4.3, NE)
75%-ile (95% CI)	NE (23.0, NE)	NE (NE, NE)
Stratified analysis [2]		
Hazard Ratio (95% CI) [3]	1.07 (0.81, 1.40)	
p-value [4]	0.6430	

[1] Based on the Brookmeyer and Crowley method.
[2] Stratified by ECOG PS by Randomization and Geographic Region by Randomization.
[3] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[4] P-value from 2-sided log-rank test.
Including only patients from the full analysis set who completed a baseline (last PRO assessment prior to or on the first dose of study treatment) and at least 1 post-baseline PRO assessment.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Time to first deterioration of at least 10 points - EOR01-Global QOL (Months) - Subgroup analysis
Full Analysis Set

Subgroup Level	EC+FOLFOX (N=219) n/ N (%)	EC+FOLFOX (N=219) Median (95% CI)[1]	Control 1 (N=222) n/ N (%)	Control 1 (N=222) Median (95% CI)[1]	Unstratified analysis Hazard Ratio (95% CI)[2]	Unstratified analysis p-Value[3]	Interaction p-Value[4]
Age (Years)							0.7076
< 65	72/ 139 (51.8)	6.9 (4.4, 15.3)	52/ 127 (40.9)	8.5 (4.3, NE)	1.03 (0.72, 1.47)	0.8822	
>= 65	49/ 80 (61.3)	5.6 (3.8, 8.1)	43/ 95 (45.3)	5.6 (2.9, NE)	1.12 (0.74, 1.70)	0.5854	
Sex							0.3647
Male	62/ 114 (54.4)	5.9 (4.7, 10.6)	45/ 108 (41.7)	8.5 (4.4, NE)	1.17 (0.79, 1.72)	0.4353	
Female	59/ 105 (56.2)	5.5 (4.0, 19.0)	50/ 114 (43.9)	5.8 (2.9, NE)	0.95 (0.65, 1.38)	0.7881	
Region							0.6623
Europe	54/ 104 (51.9)	8.8 (4.4, NE)	34/ 100 (34.0)	12.7 (5.8, NE)	1.14 (0.74, 1.76)	0.5572	
USA/Canada	5/ 8 (62.5)	3.8 (1.6, NE)	4/ 14 (28.6)	NE (1.8, NE)	1.90 (0.51, 7.12)	0.3207	
Rest of World	62/ 107 (57.9)	5.6 (4.2, 6.9)	57/ 108 (52.8)	4.2 (2.8, 8.5)	0.98 (0.68, 1.40)	0.8948	
ECOG-PS at Randomization							0.1501
0	65/ 123 (52.8)	5.8 (4.3, 19.0)	61/ 124 (49.2)	4.4 (3.1, 8.5)	0.91 (0.64, 1.30)	0.6054	
1	56/ 96 (58.3)	5.6 (4.3, 10.2)	34/ 98 (34.7)	12.7 (5.6, NE)	1.31 (0.85, 2.01)	0.2135	
Number of Organs Involved							0.1223
<= 2	71/ 110 (64.5)	4.3 (2.9, 5.7)	52/ 115 (45.2)	5.5 (4.0, NE)	1.32 (0.92, 1.89)	0.1261	
>= 3	50/ 109 (45.9)	10.2 (5.8, NE)	43/ 107 (40.2)	7.1 (3.7, NE)	0.81 (0.54, 1.23)	0.3270	
Presence of Liver Metastases							0.0582
Yes	69/ 135 (51.1)	7.1 (5.5, 19.0)	67/ 142 (47.2)	5.6 (3.1, 12.7)	0.86 (0.62, 1.21)	0.3996	
No	52/ 84 (61.9)	4.7 (3.9, 7.2)	28/ 80 (35.0)	NE (4.8, NE)	1.51 (0.95, 2.40)	0.0781	
Side of Tumor							0.4269
Left	40/ 83 (48.2)	8.8 (5.6, NE)	34/ 86 (39.5)	8.5 (4.3, NE)	0.90 (0.57, 1.42)	0.6423	
Right	81/ 136 (59.6)	4.4 (3.8, 7.1)	61/ 136 (44.9)	5.8 (3.1, NE)	1.17 (0.84, 1.63)	0.3607	

[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.
[4] P-Value for interaction from Cox proportional hazards model using ties=exact option with treatment, subgroup and treatment*subgroup interaction as covariates.
Including only patients from the full analysis set who completed a baseline (last PRO assessment prior to or on the first dose of study treatment) and at least 1 post-baseline PRO assessment.
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Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
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Datacut: 06JAN2025
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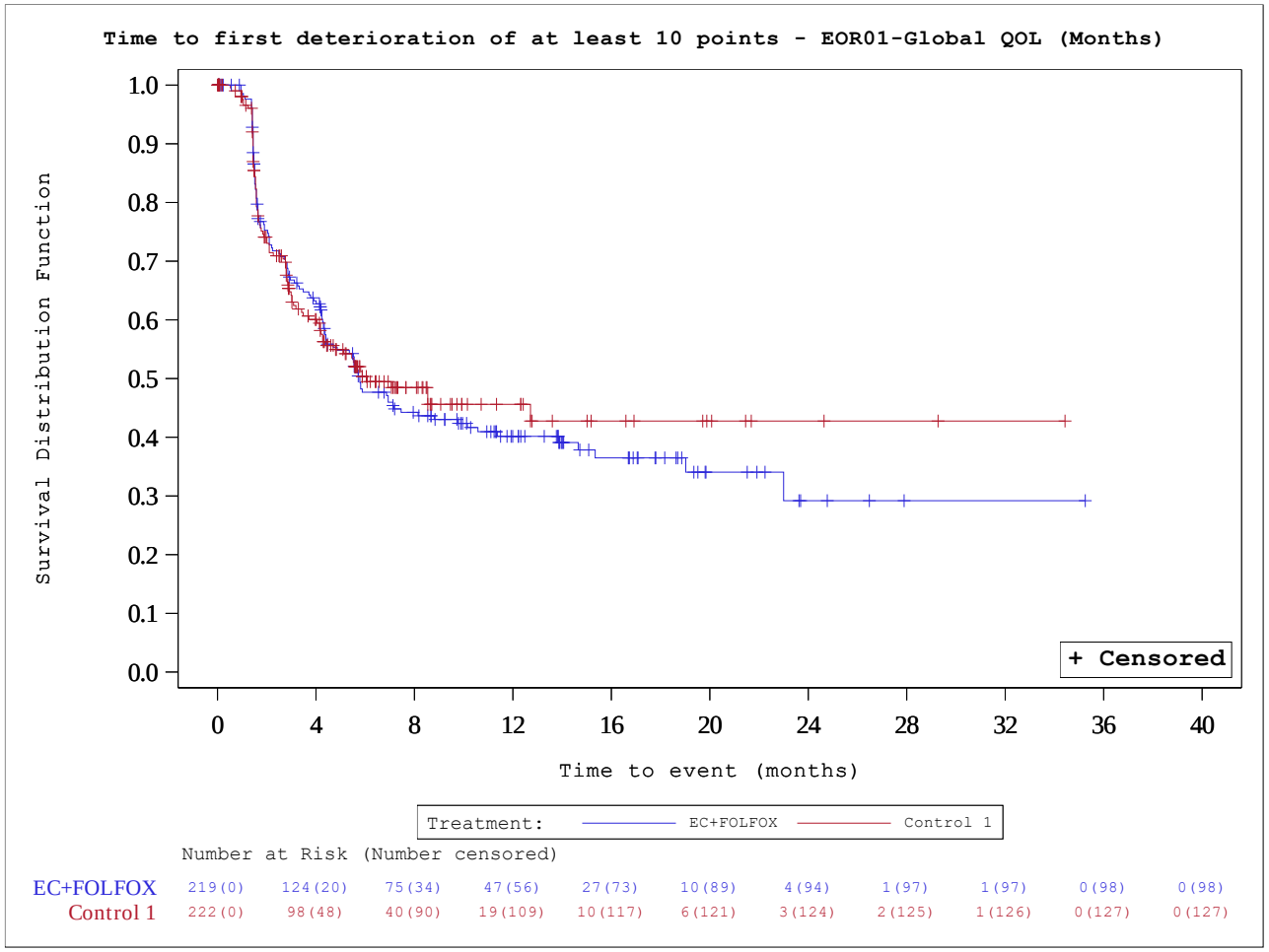
Full Analysis Set



Kaplan-Meier Plots for subgroups only created if p-value for interaction < 0.05.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
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Time to first improvement of at least 10 points - EOR01-Global QOL (Months)
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	EC+FOLFOX (N=219)	Control 1 (N=222)
Number of subjects with events, n (%)	96 (43.8)	72 (32.4)
Number of censored subjects, n (%)	123 (56.2)	150 (67.6)
Kaplan-Meier estimates of Time to Event (Months) [1]		
25%-ile (95% CI)	2.9 (1.9, 4.1)	2.9 (1.9, 4.3)
Median (95% CI)	15.0 (8.3, NE)	NE (8.3, NE)
75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
Stratified analysis [2]		
Hazard Ratio (95% CI) [3]	1.05 (0.77, 1.44)	
p-value [4]	0.7369	

[1] Based on the Brookmeyer and Crowley method.
[2] Stratified by ECOG PS by Randomization and Geographic Region by Randomization.
[3] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio > 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[4] P-value from 2-sided log-rank test.
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Time to first improvement of at least 10 points - EOR01-Global QOL (Months) - Subgroup analysis
Full Analysis Set

Subgroup Level	EC+FOLFOX (N=219) n/ N (%)	EC+FOLFOX (N=219) Median (95% CI)[1]	Control 1 (N=222) n/ N (%)	Control 1 (N=222) Median (95% CI)[1]	Unstratified analysis Hazard Ratio (95% CI)[2]	Unstratified analysis p-Value[3]	Interaction p-Value[4]
Age (Years)							0.6430
< 65	64/ 139 (46.0)	12.7 (7.0, NE)	41/ 127 (32.3)	NE (7.2, NE)	1.14 (0.77, 1.70)	0.5066	
>= 65	32/ 80 (40.0)	15.3 (8.1, NE)	31/ 95 (32.6)	NE (6.0, NE)	0.99 (0.60, 1.63)	0.9672	
Sex							0.4349
Male	45/ 114 (39.5)	23.7 (7.6, NE)	37/ 108 (34.3)	NE (7.1, NE)	1.01 (0.65, 1.56)	0.9766	
Female	51/ 105 (48.6)	8.8 (6.8, 18.3)	35/ 114 (30.7)	NE (7.2, NE)	1.19 (0.77, 1.83)	0.4383	
Region							0.5640
Europe	46/ 104 (44.2)	15.3 (6.8, NE)	27/ 100 (27.0)	NE (8.3, NE)	1.24 (0.77, 1.99)	0.3898	
USA/Canada	2/ 8 (25.0)	NE (2.8, NE)	1/ 14 (7.1)	NE (NE , NE)	2.45 (0.22, 27.04)	0.4495	
Rest of World	48/ 107 (44.9)	14.3 (5.7, NE)	44/ 108 (40.7)	8.3 (5.8, NE)	0.93 (0.61, 1.41)	0.7325	
ECOG-PS at Randomization							0.7318
0	47/ 123 (38.2)	23.7 (8.5, NE)	36/ 124 (29.0)	NE (8.3, NE)	1.01 (0.65, 1.57)	0.9764	
1	49/ 96 (51.0)	7.6 (3.9, 18.3)	36/ 98 (36.7)	NE (4.2, NE)	1.16 (0.75, 1.79)	0.5018	
Number of Organs Involved							0.0570
<= 2	42/ 110 (38.2)	23.7 (14.3, NE)	41/ 115 (35.7)	NE (7.1, NE)	0.79 (0.51, 1.22)	0.2925	
>= 3	54/ 109 (49.5)	7.6 (4.1, 15.3)	31/ 107 (29.0)	NE (7.0, NE)	1.50 (0.96, 2.34)	0.0727	
Presence of Liver Metastases							0.4321
Yes	64/ 135 (47.4)	8.5 (4.6, NE)	47/ 142 (33.1)	NE (7.0, NE)	1.20 (0.82, 1.76)	0.3383	
No	32/ 84 (38.1)	23.7 (12.7, NE)	25/ 80 (31.3)	NE (7.2, NE)	0.92 (0.54, 1.56)	0.7519	
Side of Tumor							0.5662
Left	43/ 83 (51.8)	7.5 (3.7, NE)	28/ 86 (32.6)	NE (5.8, NE)	1.26 (0.78, 2.04)	0.3437	
Right	53/ 136 (39.0)	18.3 (8.8, NE)	44/ 136 (32.4)	NE (7.8, NE)	0.97 (0.65, 1.46)	0.8878	

[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio > 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.
[4] P-Value for interaction from Cox proportional hazards model using ties=exact option with treatment, subgroup and treatment*subgroup interaction as covariates.
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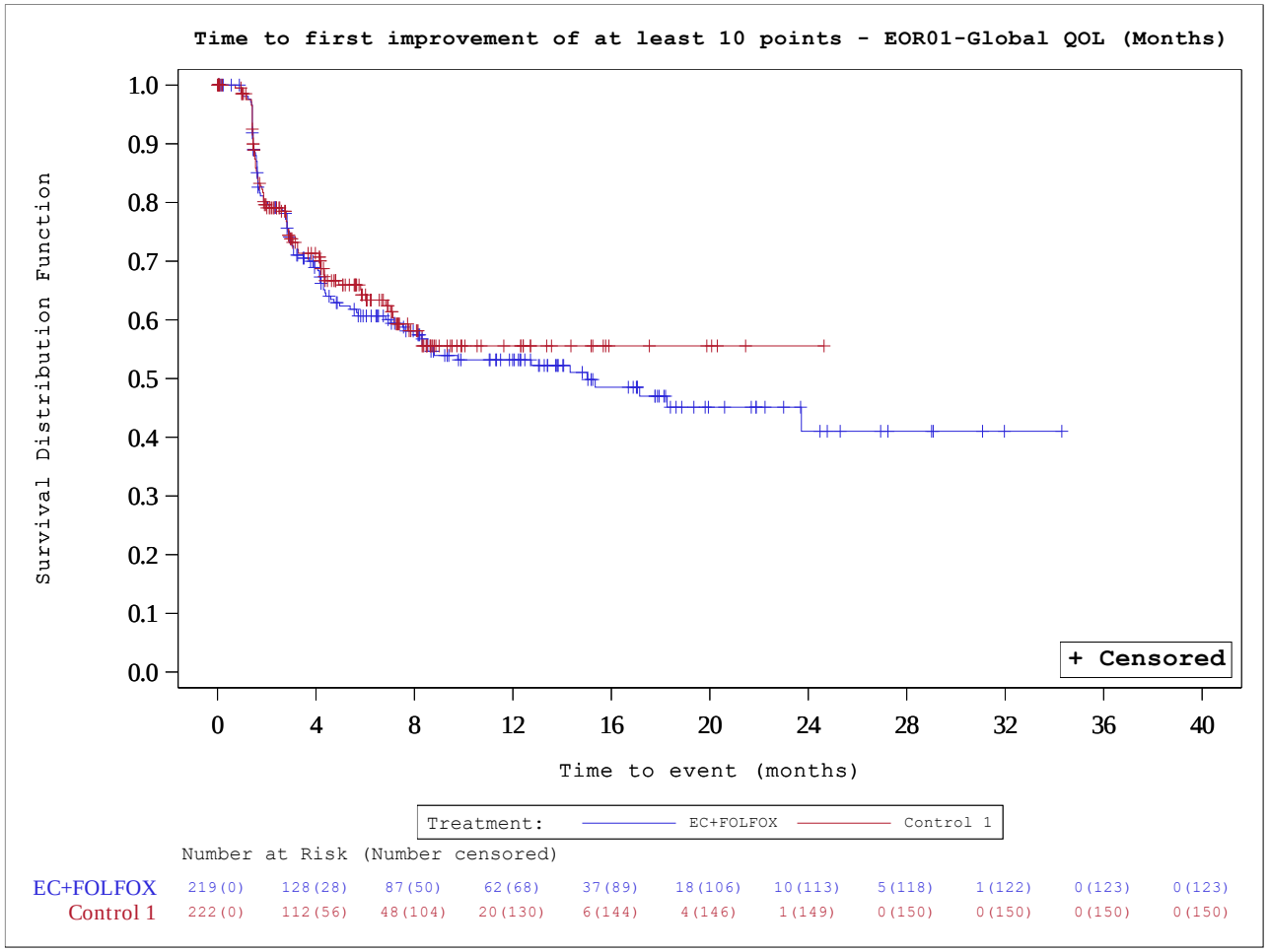

Kaplan-Meier Plots for subgroups only created if p-value for interaction < 0.05.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
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Time to first deterioration of at least 10 points - EOR01-Physical Functioning (Months)
Full Analysis Set

	EC+FOLFOX (N=219)	Control 1 (N=222)
Number of subjects with events, n (%)	128 (58.4)	86 (38.7)
Number of censored subjects, n (%)	91 (41.6)	136 (61.3)
Kaplan-Meier estimates of Time to Event (Months) [1]		
25%-ile (95% CI)	1.7 (1.6, 2.3)	2.9 (1.9, 3.7)
Median (95% CI)	5.8 (4.2, 8.0)	10.1 (6.7, NE)
75%-ile (95% CI)	29.8 (20.5, NE)	NE (NE, NE)
Stratified analysis [2]		
Hazard Ratio (95% CI) [3]	1.34 (1.01, 1.76)	
p-value [4]	0.0398	

[1] Based on the Brookmeyer and Crowley method.
[2] Stratified by ECOG PS by Randomization and Geographic Region by Randomization.
[3] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[4] P-value from 2-sided log-rank test.
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Time to first deterioration of at least 10 points - EOR01-Physical Functioning (Months) - Subgroup analysis
Full Analysis Set

Subgroup Level	EC+FOLFOX (N=219) n/ N (%)	EC+FOLFOX (N=219) Median (95% CI)[1]	Control 1 (N=222) n/ N (%)	Control 1 (N=222) Median (95% CI)[1]	Unstratified analysis Hazard Ratio (95% CI)[2]	Unstratified analysis p-Value[3]	Interaction p-Value[4]
Age (Years)							0.8834
< 65	79/ 139 (56.8)	6.4 (5.5, 11.2)	46/ 127 (36.2)	11.8 (7.0, NE)	1.34 (0.93, 1.94)	0.1127	
>= 65	49/ 80 (61.3)	3.3 (2.3, 9.7)	40/ 95 (42.1)	7.7 (4.4, NE)	1.43 (0.94, 2.19)	0.0935	
Sex							0.0130
Male	71/ 114 (62.3)	5.7 (3.3, 7.3)	36/ 108 (33.3)	NE (7.0, NE)	1.90 (1.27, 2.85)	0.0015	
Female	57/ 105 (54.3)	7.1 (4.2, 20.5)	50/ 114 (43.9)	5.8 (3.1, NE)	0.98 (0.67, 1.44)	0.9180	
Region							0.8583
Europe	59/ 104 (56.7)	6.9 (4.3, 23.0)	35/ 100 (35.0)	10.1 (6.1, NE)	1.29 (0.84, 1.97)	0.2408	
USA/Canada	4/ 8 (50.0)	NE (1.6, NE)	3/ 14 (21.4)	NE (4.8, NE)	2.06 (0.46, 9.24)	0.3370	
Rest of World	65/ 107 (60.7)	5.6 (2.9, 9.7)	48/ 108 (44.4)	8.5 (4.4, NE)	1.37 (0.94, 1.99)	0.1000	
ECOG-PS at Randomization							0.6230
0	73/ 123 (59.3)	6.9 (3.7, 10.3)	52/ 124 (41.9)	8.5 (5.5, NE)	1.28 (0.89, 1.83)	0.1810	
1	55/ 96 (57.3)	5.7 (3.0, 11.2)	34/ 98 (34.7)	10.1 (7.0, NE)	1.48 (0.96, 2.28)	0.0719	
Number of Organs Involved							0.4133
<= 2	75/ 110 (68.2)	5.6 (3.2, 7.9)	47/ 115 (40.9)	8.5 (5.1, NE)	1.49 (1.03, 2.16)	0.0321	
>= 3	53/ 109 (48.6)	6.4 (4.2, NE)	39/ 107 (36.4)	10.1 (6.7, NE)	1.22 (0.80, 1.84)	0.3580	
Presence of Liver Metastases							0.6323
Yes	82/ 135 (60.7)	5.7 (2.9, 7.3)	58/ 142 (40.8)	8.5 (5.6, NE)	1.44 (1.03, 2.02)	0.0326	
No	46/ 84 (54.8)	7.9 (4.2, 20.5)	28/ 80 (35.0)	NE (5.5, NE)	1.26 (0.79, 2.03)	0.3338	
Side of Tumor							0.9198
Left	47/ 83 (56.6)	7.1 (4.0, 11.3)	30/ 86 (34.9)	NE (6.1, NE)	1.39 (0.88, 2.21)	0.1598	
Right	81/ 136 (59.6)	5.7 (3.3, 9.7)	56/ 136 (41.2)	8.5 (5.1, NE)	1.34 (0.95, 1.89)	0.0953	

[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.
[4] P-Value for interaction from Cox proportional hazards model using ties=exact option with treatment, subgroup and treatment*subgroup interaction as covariates.
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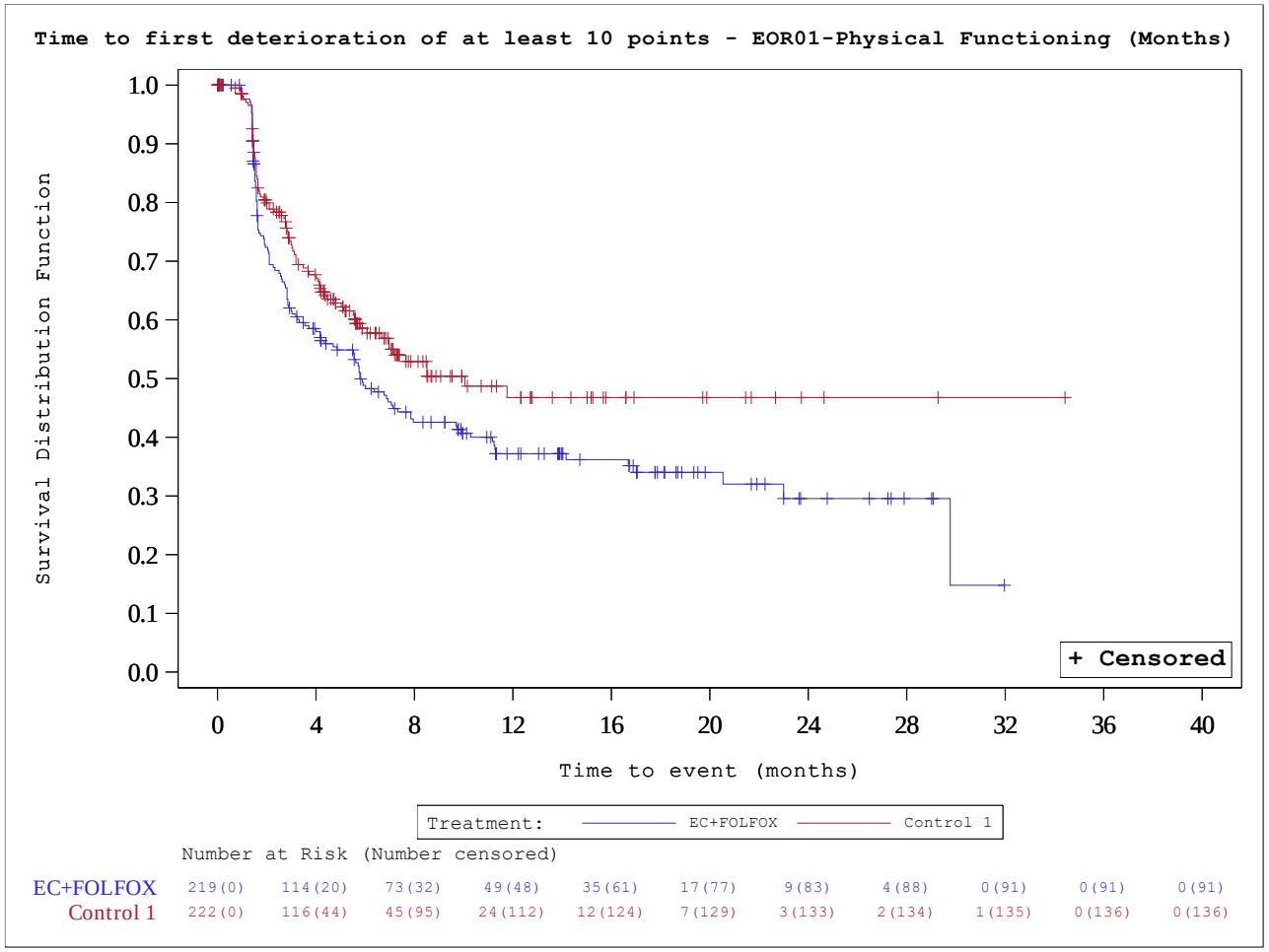

Kaplan-Meier Plots for subgroups only created if p-value for interaction < 0.05.

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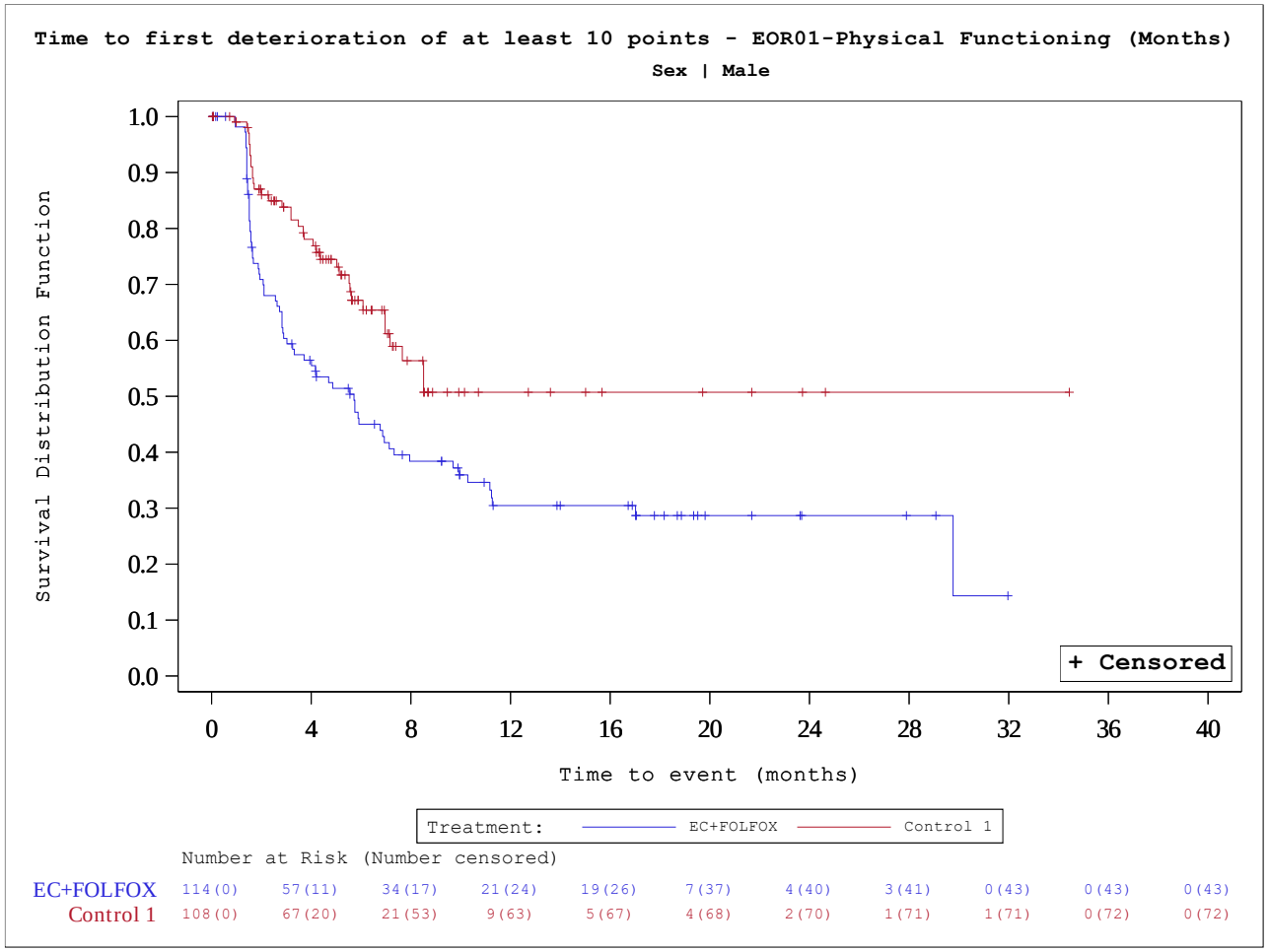

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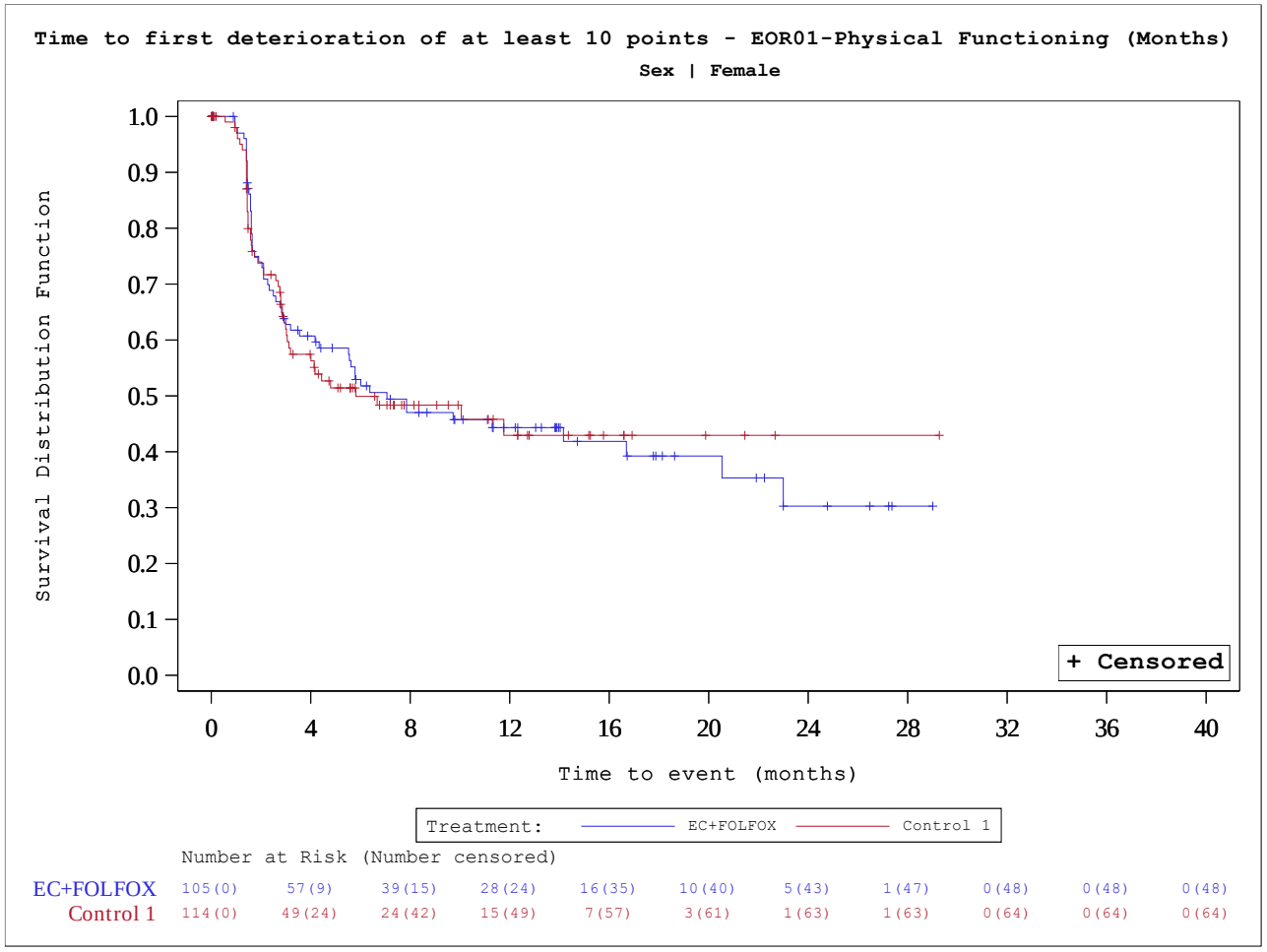

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	EC+FOLFOX (N=219)	Control 1 (N=222)
Number of subjects with events, n (%)	61 (27.9)	59 (26.6)
Number of censored subjects, n (%)	158 (72.1)	163 (73.4)
Kaplan-Meier estimates of Time to Event (Months) [1]		
25%-ile (95% CI)	5.7 (4.4, 11.3)	3.3 (2.8, 7.0)
Median (95% CI)	NE (NE, NE)	NE (13.0, NE)
75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
Stratified analysis [2]		
Hazard Ratio (95% CI) [3]	0.77 (0.54, 1.11)	
p-value [4]	0.1592	

[1] Based on the Brookmeyer and Crowley method.
[2] Stratified by ECOG PS by Randomization and Geographic Region by Randomization.
[3] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio > 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[4] P-value from 2-sided log-rank test.
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Full Analysis Set

Subgroup Level	EC+FOLFOX (N=219) n/ N (%)	EC+FOLFOX (N=219) Median (95% CI)[1]	Control 1 (N=222) n/ N (%)	Control 1 (N=222) Median (95% CI)[1]	Unstratified analysis Hazard Ratio (95% CI)[2]	Unstratified analysis p-Value[3]	Interaction p-Value[4]
Age (Years)							0.3510
< 65	45/ 139 (32.4)	NE (NE , NE)	35/ 127 (27.6)	NE (13.0, NE)	0.85 (0.54, 1.33)	0.4733	
>= 65	16/ 80 (20.0)	NE (NE , NE)	24/ 95 (25.3)	NE (NE , NE)	0.66 (0.35, 1.25)	0.1960	
Sex							0.0421
Male	25/ 114 (21.9)	NE (NE , NE)	33/ 108 (30.6)	NE (9.7, NE)	0.56 (0.33, 0.94)	0.0273	
Female	36/ 105 (34.3)	NE (13.0, NE)	26/ 114 (22.8)	NE (13.0, NE)	1.12 (0.67, 1.86)	0.6670	
Region							0.0541
Europe	38/ 104 (36.5)	NE (11.3, NE)	22/ 100 (22.0)	NE (NE , NE)	1.23 (0.72, 2.09)	0.4427	
USA/Canada	1/ 8 (12.5)	NE (10.8, NE)	2/ 14 (14.3)	NE (NE , NE)	0.40 (0.04, 4.63)	0.4531	
Rest of World	22/ 107 (20.6)	NE (NE , NE)	35/ 108 (32.4)	NE (9.7, NE)	0.50 (0.29, 0.85)	0.0092	
ECOG-PS at Randomization							0.3416
0	32/ 123 (26.0)	NE (NE , NE)	27/ 124 (21.8)	NE (13.0, NE)	0.89 (0.53, 1.50)	0.6642	
1	29/ 96 (30.2)	NE (NE , NE)	32/ 98 (32.7)	NE (6.5, NE)	0.68 (0.41, 1.12)	0.1308	
Number of Organs Involved							0.0912
<= 2	23/ 110 (20.9)	NE (NE , NE)	32/ 115 (27.8)	NE (13.0, NE)	0.52 (0.30, 0.90)	0.0174	
>= 3	38/ 109 (34.9)	NE (8.8, NE)	27/ 107 (25.2)	NE (NE , NE)	1.09 (0.66, 1.78)	0.7458	
Presence of Liver Metastases							0.5869
Yes	39/ 135 (28.9)	NE (NE , NE)	36/ 142 (25.4)	NE (NE , NE)	0.87 (0.55, 1.38)	0.5667	
No	22/ 84 (26.2)	NE (NE , NE)	23/ 80 (28.8)	13.0 (9.7, NE)	0.66 (0.36, 1.19)	0.1628	
Side of Tumor							0.0694
Left	27/ 83 (32.5)	NE (NE , NE)	17/ 86 (19.8)	NE (NE , NE)	1.27 (0.69, 2.34)	0.4395	
Right	34/ 136 (25.0)	NE (NE , NE)	42/ 136 (30.9)	NE (13.0, NE)	0.60 (0.38, 0.95)	0.0289	

[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio > 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
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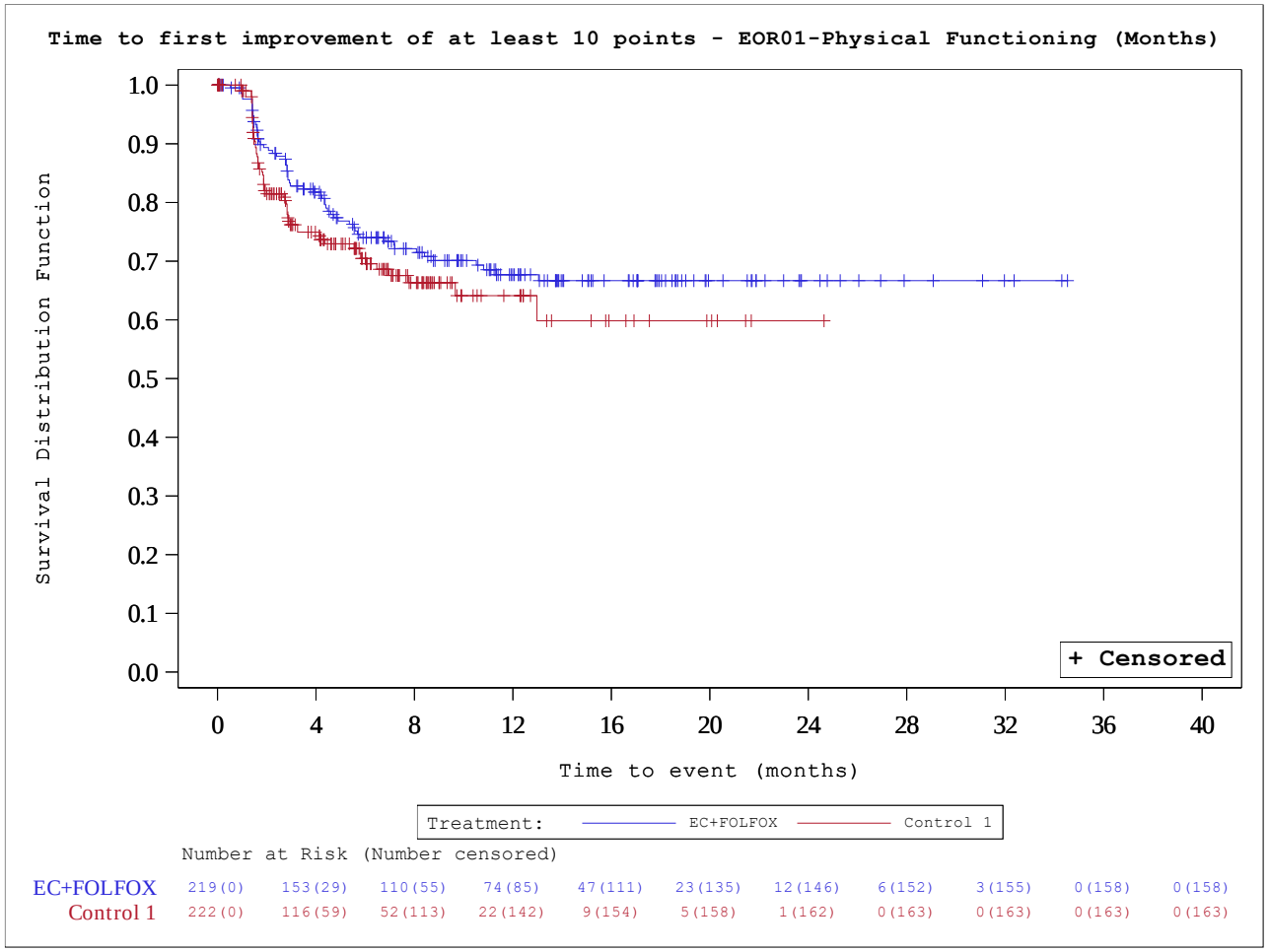

Kaplan-Meier Plots for subgroups only created if p-value for interaction < 0.05.

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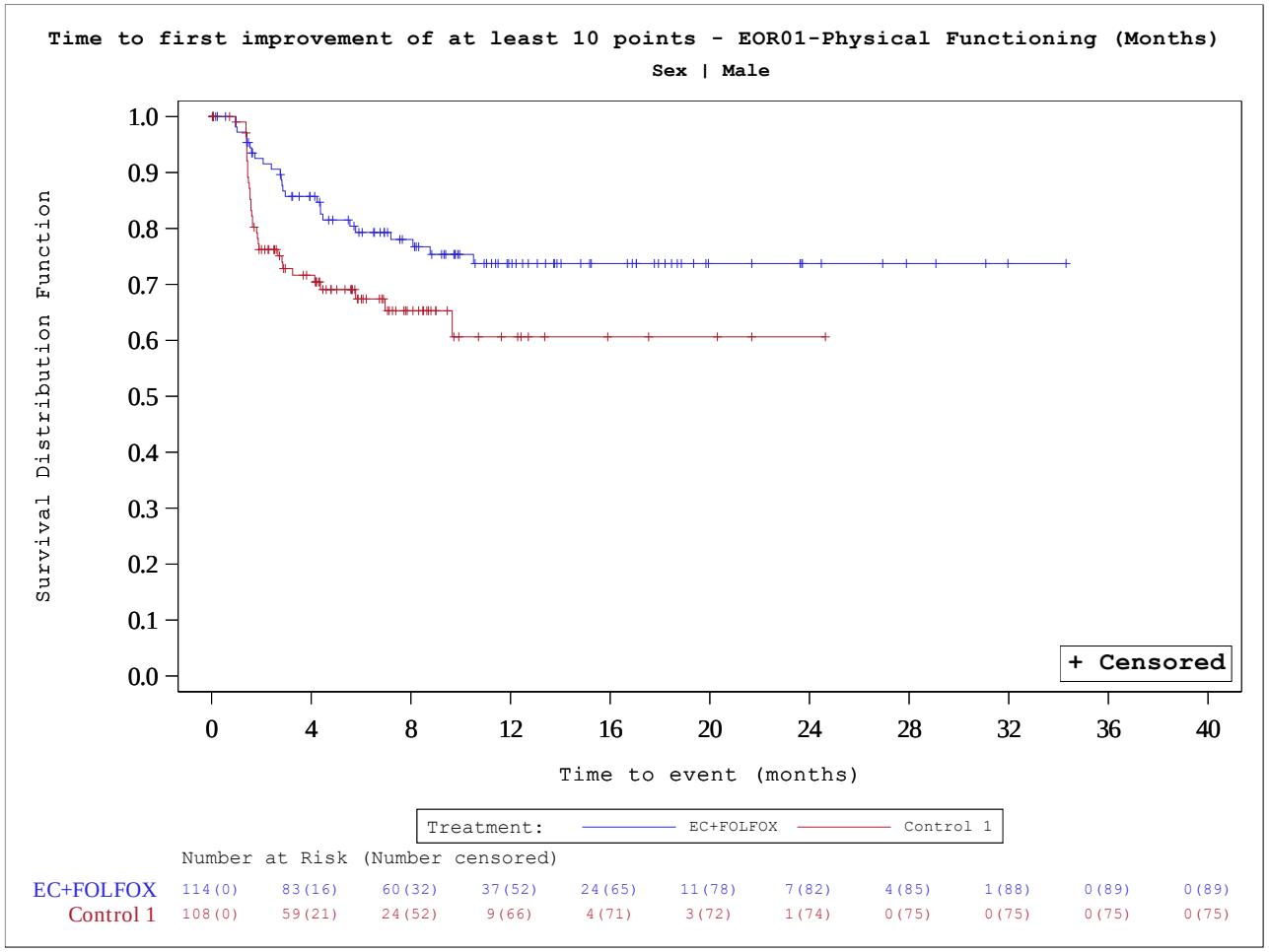

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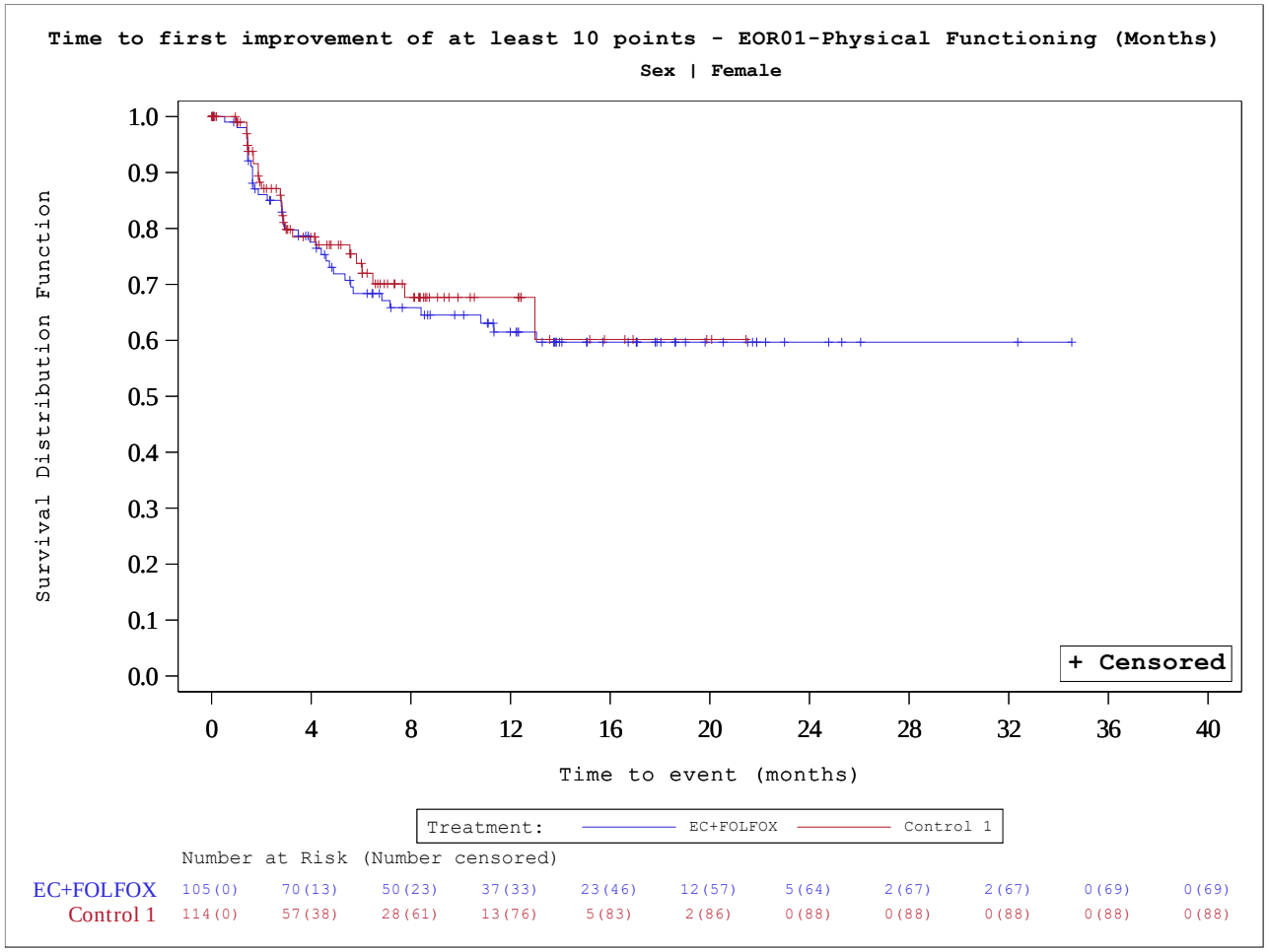
Kaplan Meier Plot of Time to first improvement of at least 10 points - EOR01-Physical Functioning (Months)
Full Analysis Set



Kaplan-Meier Plots for subgroups only created if p-value for interaction < 0.05.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Time to first deterioration of at least 10 points - EOR01-Role Functioning (Months)
Full Analysis Set

	EC+FOLFOX (N=219)	Control 1 (N=222)
Number of subjects with events, n (%)	140 (63.9)	117 (52.7)
Number of censored subjects, n (%)	79 (36.1)	105 (47.3)
Kaplan-Meier estimates of Time to Event (Months) [1]		
25%-ile (95% CI)	1.6 (1.5, 1.7)	1.6 (1.5, 1.9)
Median (95% CI)	4.2 (2.9, 5.9)	4.3 (3.2, 6.7)
75%-ile (95% CI)	17.9 (11.1, NE)	NE (9.7, NE)
Stratified analysis [2]		
Hazard Ratio (95% CI) [3]	1.03 (0.81, 1.32)	
p-value [4]	0.7945	

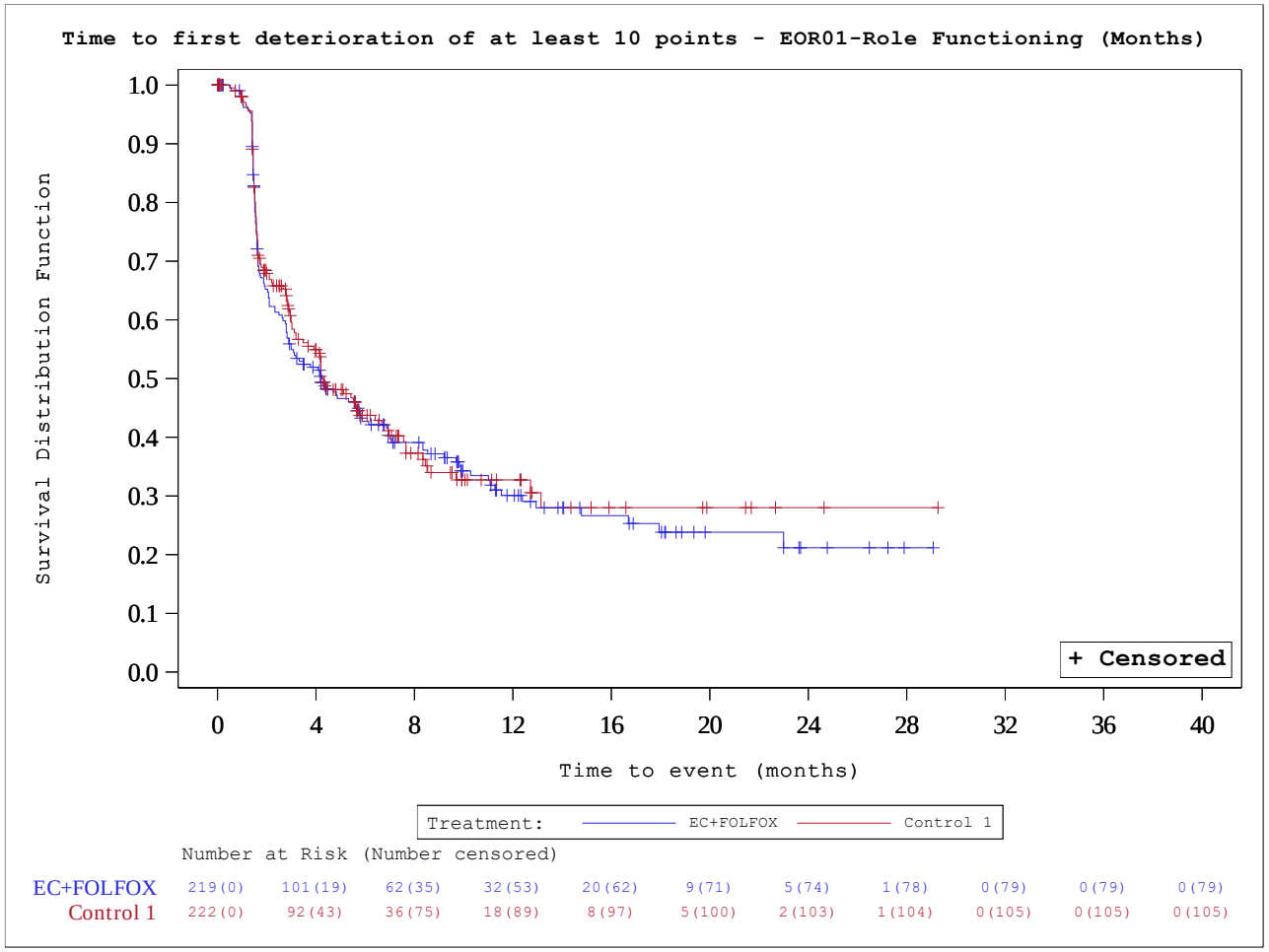
[1] Based on the Brookmeyer and Crowley method.
[2] Stratified by ECOG PS by Randomization and Geographic Region by Randomization.
[3] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[4] P-value from 2-sided log-rank test.
Including only patients from the full analysis set who completed a baseline (last PRO assessment prior to or on the first dose of study treatment) and at least 1 post-baseline PRO assessment.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Time to first deterioration of at least 10 points - EOR01-Role Functioning (Months) - Subgroup analysis
Full Analysis Set

Subgroup Level	EC+FOLFOX (N=219) n/ N (%)	EC+FOLFOX (N=219) Median (95% CI)[1]	Control 1 (N=222) n/ N (%)	Control 1 (N=222) Median (95% CI)[1]	Unstratified analysis Hazard Ratio (95% CI)[2]	Unstratified analysis p-Value[3]	Interaction p-Value[4]
Age (Years)							0.8593
< 65	87/ 139 (62.6)	4.9 (2.8, 7.1)	65/ 127 (51.2)	4.2 (3.0, 9.7)	1.04 (0.75, 1.44)	0.7979	
>= 65	53/ 80 (66.3)	3.1 (2.1, 5.7)	52/ 95 (54.7)	5.1 (3.0, 7.6)	1.08 (0.74, 1.60)	0.6794	
Sex							0.8471
Male	71/ 114 (62.3)	5.6 (3.3, 7.1)	58/ 108 (53.7)	5.6 (3.5, 7.7)	1.00 (0.70, 1.42)	0.9986	
Female	69/ 105 (65.7)	2.9 (2.3, 5.7)	59/ 114 (51.8)	4.2 (2.9, 6.7)	1.10 (0.77, 1.56)	0.5982	
Region							0.1476
Europe	67/ 104 (64.4)	4.2 (2.5, 8.3)	45/ 100 (45.0)	6.9 (3.2, 8.5)	1.17 (0.80, 1.71)	0.4258	
USA/Canada	6/ 8 (75.0)	1.9 (1.4, NE)	4/ 14 (28.6)	NE (3.0, NE)	2.94 (0.82, 10.53)	0.0814	
Rest of World	67/ 107 (62.6)	4.8 (2.8, 7.1)	68/ 108 (63.0)	4.2 (2.8, 5.5)	0.88 (0.62, 1.23)	0.4499	
ECOG-PS at Randomization							0.9250
0	80/ 123 (65.0)	3.3 (2.1, 6.9)	69/ 124 (55.6)	4.2 (2.8, 6.7)	1.05 (0.76, 1.45)	0.7706	
1	60/ 96 (62.5)	4.8 (3.0, 9.2)	48/ 98 (49.0)	5.1 (3.7, 7.7)	1.04 (0.71, 1.52)	0.8414	
Number of Organs Involved							0.3071
<= 2	76/ 110 (69.1)	3.3 (2.0, 5.7)	70/ 115 (60.9)	4.1 (2.7, 5.1)	0.97 (0.70, 1.34)	0.8369	
>= 3	64/ 109 (58.7)	4.9 (3.0, 9.7)	47/ 107 (43.9)	7.0 (3.9, 12.7)	1.19 (0.82, 1.74)	0.3558	
Presence of Liver Metastases							0.7237
Yes	84/ 135 (62.2)	4.2 (2.8, 6.9)	75/ 142 (52.8)	4.4 (3.2, 7.6)	1.08 (0.79, 1.48)	0.6236	
No	56/ 84 (66.7)	4.8 (2.7, 7.1)	42/ 80 (52.5)	4.2 (2.8, 7.7)	1.00 (0.67, 1.50)	0.9881	
Side of Tumor							0.8015
Left	51/ 83 (61.4)	4.9 (2.8, 7.1)	41/ 86 (47.7)	5.8 (2.9, 12.7)	1.12 (0.74, 1.69)	0.6046	
Right	89/ 136 (65.4)	3.8 (2.7, 6.1)	76/ 136 (55.9)	4.2 (3.0, 5.7)	1.02 (0.75, 1.39)	0.8828	

[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.
[4] P-Value for interaction from Cox proportional hazards model using ties=exact option with treatment, subgroup and treatment*subgroup interaction as covariates.
Including only patients from the full analysis set who completed a baseline (last PRO assessment prior to or on the first dose of study treatment) and at least 1 post-baseline PRO assessment.
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Kaplan Meier Plot of Time to first deterioration of at least 10 points - EOR01-Role Functioning (Months)
Full Analysis Set



Kaplan-Meier Plots for subgroups only created if p-value for interaction < 0.05.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Time to first improvement of at least 10 points - EOR01-Role Functioning (Months)
Full Analysis Set

	EC+FOLFOX (N=219)	Control 1 (N=222)
Number of subjects with events, n (%)	85 (38.8)	66 (29.7)
Number of censored subjects, n (%)	134 (61.2)	156 (70.3)
Kaplan-Meier estimates of Time to Event (Months) [1]		
25%-ile (95% CI)	2.8 (1.9, 4.2)	2.9 (1.9, 5.6)
Median (95% CI)	24.6 (13.4, NE)	NE (11.1, NE)
75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
Stratified analysis [2]		
Hazard Ratio (95% CI) [3]	1.04 (0.75, 1.44)	
p-value [4]	0.8417	

[1] Based on the Brookmeyer and Crowley method.
[2] Stratified by ECOG PS by Randomization and Geographic Region by Randomization.
[3] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio > 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[4] P-value from 2-sided log-rank test.
Including only patients from the full analysis set who completed a baseline (last PRO assessment prior to or on the first dose of study treatment) and at least 1 post-baseline PRO assessment.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Time to first improvement of at least 10 points - EOR01-Role Functioning (Months) - Subgroup analysis
Full Analysis Set

Subgroup Level	EC+FOLFOX (N=219) n/ N (%)	EC+FOLFOX (N=219) Median (95% CI)[1]	Control 1 (N=222) n/ N (%)	Control 1 (N=222) Median (95% CI)[1]	Unstratified analysis Hazard Ratio (95% CI)[2]	Unstratified analysis p-Value[3]	Interaction p-Value[4]
Age (Years)							0.5821
< 65	58/ 139 (41.7)	14.0 (9.7, NE)	38/ 127 (29.9)	NE (11.1, NE)	1.12 (0.74, 1.69)	0.5900	
>= 65	27/ 80 (33.8)	NE (24.6, NE)	28/ 95 (29.5)	NE (10.4, NE)	0.98 (0.57, 1.67)	0.9340	
Sex							0.9778
Male	41/ 114 (36.0)	NE (NE , NE)	33/ 108 (30.6)	NE (NE , NE)	1.12 (0.71, 1.78)	0.6167	
Female	44/ 105 (41.9)	24.6 (9.7, NE)	33/ 114 (28.9)	NE (10.4, NE)	0.99 (0.62, 1.58)	0.9761	
Region							0.1598
Europe	48/ 104 (46.2)	13.4 (4.7, NE)	29/ 100 (29.0)	NE (6.0, NE)	1.29 (0.81, 2.06)	0.2801	
USA/Canada	4/ 8 (50.0)	9.7 (2.8, NE)	2/ 14 (14.3)	NE (NE , NE)	2.45 (0.45, 13.42)	0.2938	
Rest of World	33/ 107 (30.8)	NE (14.0, NE)	35/ 108 (32.4)	NE (11.1, NE)	0.79 (0.49, 1.27)	0.3304	
ECOG-PS at Randomization							0.7824
0	41/ 123 (33.3)	NE (24.6, NE)	33/ 124 (26.6)	NE (11.1, NE)	1.01 (0.64, 1.61)	0.9594	
1	44/ 96 (45.8)	13.4 (4.5, NE)	33/ 98 (33.7)	NE (6.3, NE)	1.12 (0.71, 1.76)	0.6296	
Number of Organs Involved							0.2931
<= 2	41/ 110 (37.3)	NE (14.0, NE)	37/ 115 (32.2)	NE (10.4, NE)	0.90 (0.57, 1.41)	0.6378	
>= 3	44/ 109 (40.4)	13.7 (5.6, NE)	29/ 107 (27.1)	NE (5.9, NE)	1.28 (0.80, 2.05)	0.3029	
Presence of Liver Metastases							0.4635
Yes	50/ 135 (37.0)	NE (13.4, NE)	44/ 142 (31.0)	NE (6.3, NE)	0.96 (0.64, 1.45)	0.8537	
No	35/ 84 (41.7)	24.6 (6.4, NE)	22/ 80 (27.5)	NE (10.4, NE)	1.27 (0.74, 2.18)	0.3755	
Side of Tumor							0.5981
Left	34/ 83 (41.0)	24.6 (7.2, NE)	27/ 86 (31.4)	NE (5.8, NE)	0.96 (0.57, 1.59)	0.8594	
Right	51/ 136 (37.5)	NE (12.7, NE)	39/ 136 (28.7)	NE (10.4, NE)	1.14 (0.75, 1.74)	0.5218	

[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio > 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.
[4] P-Value for interaction from Cox proportional hazards model using ties=exact option with treatment, subgroup and treatment*subgroup interaction as covariates.
Including only patients from the full analysis set who completed a baseline (last PRO assessment prior to or on the first dose of study treatment) and at least 1 post-baseline PRO assessment.
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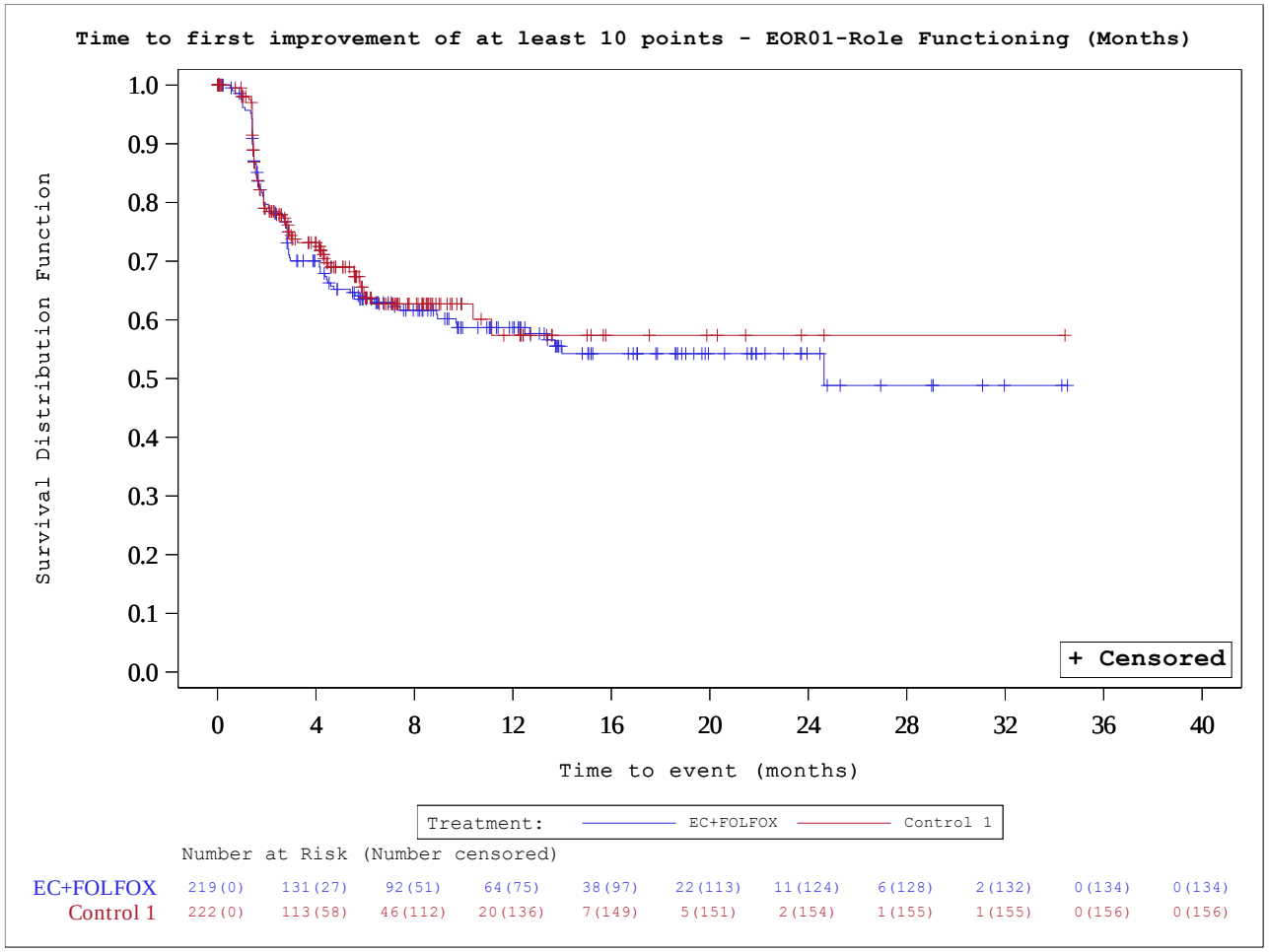
Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Kaplan Meier Plot of Time to first improvement of at least 10 points - EOR01-Role Functioning (Months)
Full Analysis Set



Kaplan-Meier Plots for subgroups only created if p-value for interaction < 0.05.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Time to first deterioration of at least 10 points - EOR01-Emotional Functioning (Months)
Full Analysis Set

	EC+FOLFOX (N=219)	Control 1 (N=222)
Number of subjects with events, n (%)	85 (38.8)	63 (28.4)
Number of censored subjects, n (%)	134 (61.2)	159 (71.6)
Kaplan-Meier estimates of Time to Event (Months) [1]		
25%-ile (95% CI)	5.4 (4.2, 7.1)	4.4 (2.8, 6.6)
Median (95% CI)	19.0 (13.9, NE)	NE (12.3, NE)
75%-ile (95% CI)	NE (25.7, NE)	NE (NE, NE)
Stratified analysis [2]		
Hazard Ratio (95% CI) [3]	0.93 (0.67, 1.30)	
p-value [4]	0.6901	

[1] Based on the Brookmeyer and Crowley method.
[2] Stratified by ECOG PS by Randomization and Geographic Region by Randomization.
[3] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[4] P-value from 2-sided log-rank test.
Including only patients from the full analysis set who completed a baseline (last PRO assessment prior to or on the first dose of study treatment) and at least 1 post-baseline PRO assessment.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Time to first deterioration of at least 10 points - EOR01-Emotional Functioning (Months) - Subgroup analysis
Full Analysis Set

Subgroup Level	EC+FOLFOX (N=219) n/ N (%)	EC+FOLFOX (N=219) Median (95% CI)[1]	Control 1 (N=222) n/ N (%)	Control 1 (N=222) Median (95% CI)[1]	Unstratified analysis Hazard Ratio (95% CI)[2]	Unstratified analysis p-Value[3]	Interaction p-Value[4]
Age (Years)							0.0268
< 65	61/ 139 (43.9)	15.4 (8.8, NE)	31/ 127 (24.4)	NE (13.9, NE)	1.27 (0.82, 1.97)	0.2820	
>= 65	24/ 80 (30.0)	25.7 (15.7, NE)	32/ 95 (33.7)	8.5 (6.3, NE)	0.58 (0.33, 0.99)	0.0436	
Sex							0.8598
Male	41/ 114 (36.0)	NE (12.9, NE)	30/ 108 (27.8)	NE (12.3, NE)	0.99 (0.61, 1.59)	0.9536	
Female	44/ 105 (41.9)	19.0 (11.1, 25.7)	33/ 114 (28.9)	NE (6.9, NE)	0.91 (0.57, 1.44)	0.6855	
Region							0.3905
Europe	42/ 104 (40.4)	21.4 (12.9, NE)	21/ 100 (21.0)	NE (NE , NE)	1.23 (0.72, 2.09)	0.4472	
USA/Canada	2/ 8 (25.0)	NE (4.2, NE)	4/ 14 (28.6)	NE (4.8, NE)	0.60 (0.11, 3.30)	0.5545	
Rest of World	41/ 107 (38.3)	15.4 (11.1, NE)	38/ 108 (35.2)	13.9 (6.9, NE)	0.81 (0.52, 1.27)	0.3598	
ECOG-PS at Randomization							0.5174
0	47/ 123 (38.2)	21.4 (13.9, NE)	33/ 124 (26.6)	NE (12.3, NE)	1.03 (0.66, 1.62)	0.8821	
1	38/ 96 (39.6)	17.0 (11.0, NE)	30/ 98 (30.6)	NE (6.3, NE)	0.83 (0.51, 1.35)	0.4612	
Number of Organs Involved							0.3411
<= 2	49/ 110 (44.5)	15.7 (12.9, NE)	42/ 115 (36.5)	8.5 (6.6, NE)	0.86 (0.56, 1.30)	0.4748	
>= 3	36/ 109 (33.0)	21.4 (11.5, NE)	21/ 107 (19.6)	NE (13.9, NE)	1.15 (0.67, 1.99)	0.6052	
Presence of Liver Metastases							0.0533
Yes	55/ 135 (40.7)	19.0 (11.1, 25.7)	35/ 142 (24.6)	NE (13.9, NE)	1.19 (0.78, 1.83)	0.4247	
No	30/ 84 (35.7)	21.4 (15.4, NE)	28/ 80 (35.0)	12.3 (6.6, NE)	0.65 (0.39, 1.11)	0.1113	
Side of Tumor							0.9830
Left	31/ 83 (37.3)	20.3 (11.1, NE)	22/ 86 (25.6)	NE (7.8, NE)	0.92 (0.53, 1.60)	0.7671	
Right	54/ 136 (39.7)	19.0 (13.4, NE)	41/ 136 (30.1)	NE (13.9, NE)	0.97 (0.65, 1.47)	0.9007	

[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.
[4] P-Value for interaction from Cox proportional hazards model using ties=exact option with treatment, subgroup and treatment*subgroup interaction as covariates.
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Encorafenib (PF-07263896) Protocol C4221015
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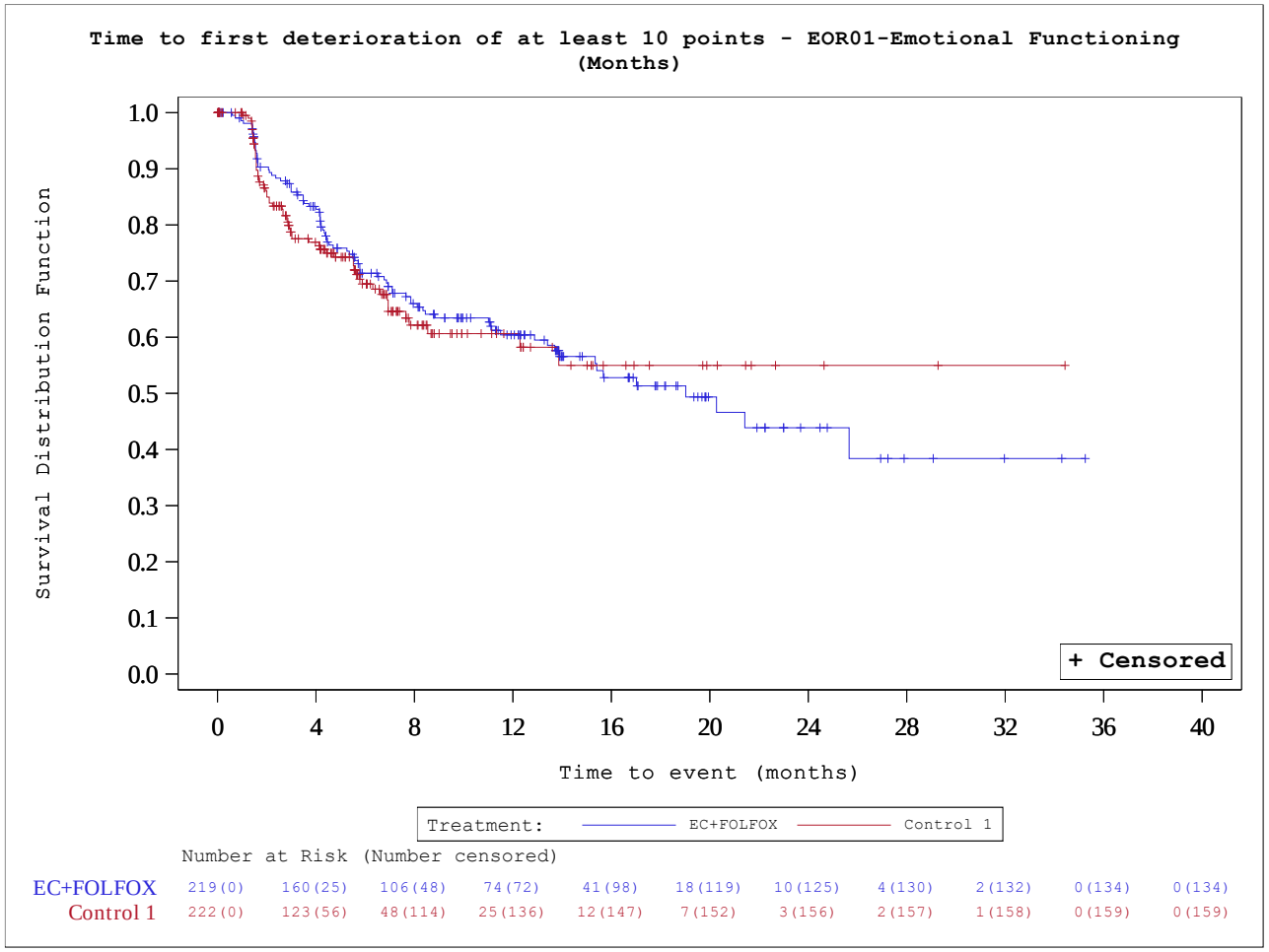
Full Analysis Set



Kaplan-Meier Plots for subgroups only created if p-value for interaction < 0.05.

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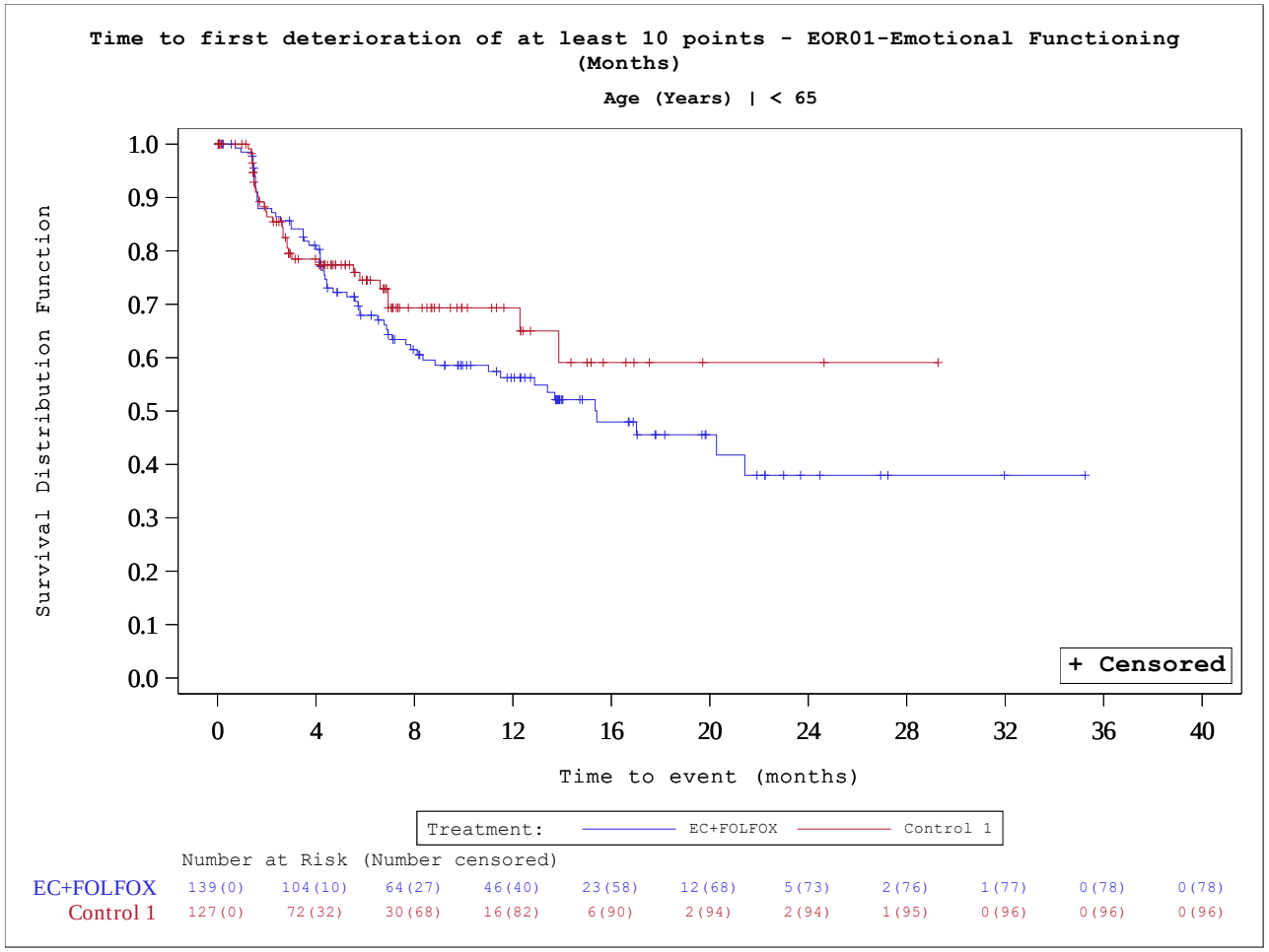

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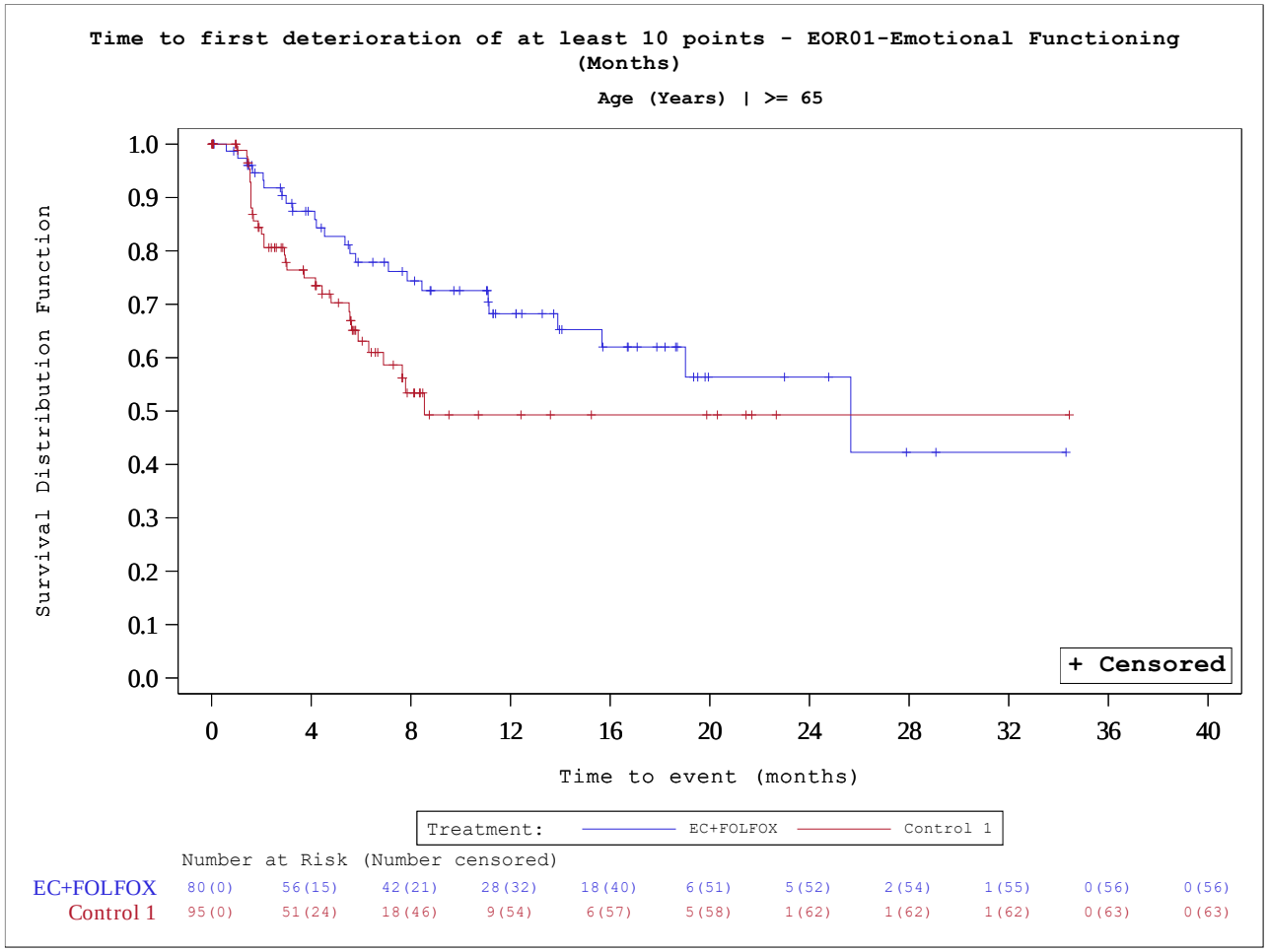

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Encorafenib (PF-07263896) Protocol C4221015
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Datacut: 06JAN2025
Time to first improvement of at least 10 points - EOR01-Emotional Functioning (Months)
Full Analysis Set

	EC+FOLFOX (N=219)	Control 1 (N=222)
Number of subjects with events, n (%)	110 (50.2)	77 (34.7)
Number of censored subjects, n (%)	109 (49.8)	145 (65.3)
Kaplan-Meier estimates of Time to Event (Months) [1]		
25%-ile (95% CI)	1.7 (1.6, 2.3)	2.7 (1.8, 3.3)
Median (95% CI)	6.4 (4.2, 16.8)	NE (8.6, NE)
75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
Stratified analysis [2]		
Hazard Ratio (95% CI) [3]	1.31 (0.97, 1.75)	
p-value [4]	0.0744	

[1] Based on the Brookmeyer and Crowley method.
[2] Stratified by ECOG PS by Randomization and Geographic Region by Randomization.
[3] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio > 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[4] P-value from 2-sided log-rank test.
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Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Time to first improvement of at least 10 points - EOR01-Emotional Functioning (Months) - Subgroup analysis
Full Analysis Set

Subgroup Level	EC+FOLFOX (N=219) n/ N (%)	EC+FOLFOX (N=219) Median (95% CI)[1]	Control 1 (N=222) n/ N (%)	Control 1 (N=222) Median (95% CI)[1]	Unstratified analysis Hazard Ratio (95% CI)[2]	Unstratified analysis p-Value[3]	Interaction p-Value[4]
Age (Years)							0.6018
< 65	69/ 139 (49.6)	8.1 (4.1, NE)	45/ 127 (35.4)	NE (5.6, NE)	1.26 (0.87, 1.84)	0.2243	
>= 65	41/ 80 (51.3)	5.9 (4.2, NE)	32/ 95 (33.7)	NE (6.3, NE)	1.44 (0.90, 2.28)	0.1262	
Sex							0.6587
Male	55/ 114 (48.2)	7.0 (4.2, NE)	33/ 108 (30.6)	NE (NE , NE)	1.46 (0.95, 2.25)	0.0818	
Female	55/ 105 (52.4)	5.6 (2.5, NE)	44/ 114 (38.6)	8.6 (4.4, NE)	1.24 (0.84, 1.86)	0.2847	
Region							0.1499
Europe	63/ 104 (60.6)	4.2 (2.3, 6.0)	33/ 100 (33.0)	9.5 (5.8, NE)	1.69 (1.11, 2.58)	0.0136	
USA/Canada	3/ 8 (37.5)	NE (2.8, NE)	2/ 14 (14.3)	NE (NE , NE)	2.13 (0.35, 12.77)	0.3985	
Rest of World	44/ 107 (41.1)	NE (7.0, NE)	42/ 108 (38.9)	NE (5.4, NE)	0.97 (0.63, 1.48)	0.8701	
ECOG-PS at Randomization							0.6220
0	60/ 123 (48.8)	6.4 (4.2, NE)	44/ 124 (35.5)	NE (5.8, NE)	1.26 (0.85, 1.86)	0.2452	
1	50/ 96 (52.1)	5.9 (3.1, 14.1)	33/ 98 (33.7)	9.5 (5.6, NE)	1.42 (0.91, 2.20)	0.1232	
Number of Organs Involved							0.0142
<= 2	50/ 110 (45.5)	14.1 (5.6, NE)	48/ 115 (41.7)	9.5 (4.4, NE)	0.92 (0.62, 1.37)	0.6855	
>= 3	60/ 109 (55.0)	4.2 (2.8, 8.3)	29/ 107 (27.1)	NE (NE , NE)	2.01 (1.29, 3.14)	0.0015	
Presence of Liver Metastases							0.4355
Yes	71/ 135 (52.6)	4.9 (3.4, 16.8)	48/ 142 (33.8)	NE (6.3, NE)	1.47 (1.02, 2.12)	0.0388	
No	39/ 84 (46.4)	11.1 (4.2, NE)	29/ 80 (36.3)	NE (4.4, NE)	1.12 (0.69, 1.83)	0.6396	
Side of Tumor							0.6434
Left	39/ 83 (47.0)	11.1 (3.9, NE)	24/ 86 (27.9)	NE (NE , NE)	1.50 (0.90, 2.50)	0.1217	
Right	71/ 136 (52.2)	5.4 (4.2, 11.3)	53/ 136 (39.0)	9.5 (5.4, NE)	1.26 (0.88, 1.80)	0.1981	

[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio > 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.
[4] P-Value for interaction from Cox proportional hazards model using ties=exact option with treatment, subgroup and treatment*subgroup interaction as covariates.
Including only patients from the full analysis set who completed a baseline (last PRO assessment prior to or on the first dose of study treatment) and at least 1 post-baseline PRO assessment.
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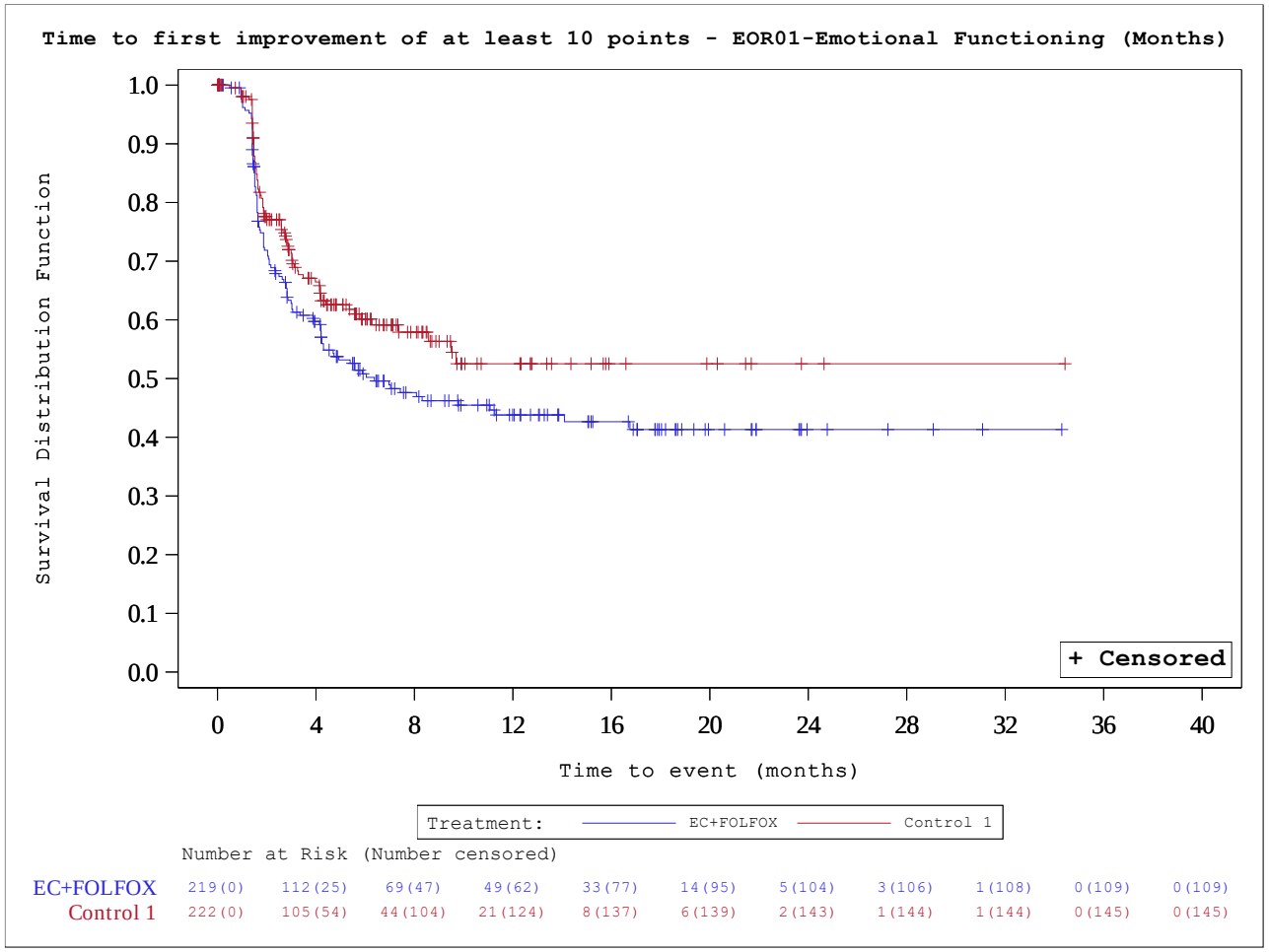
Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Kaplan Meier Plot of Time to first improvement of at least 10 points - EOR01-Emotional Functioning (Months)
Full Analysis Set



Kaplan-Meier Plots for subgroups only created if p-value for interaction < 0.05.

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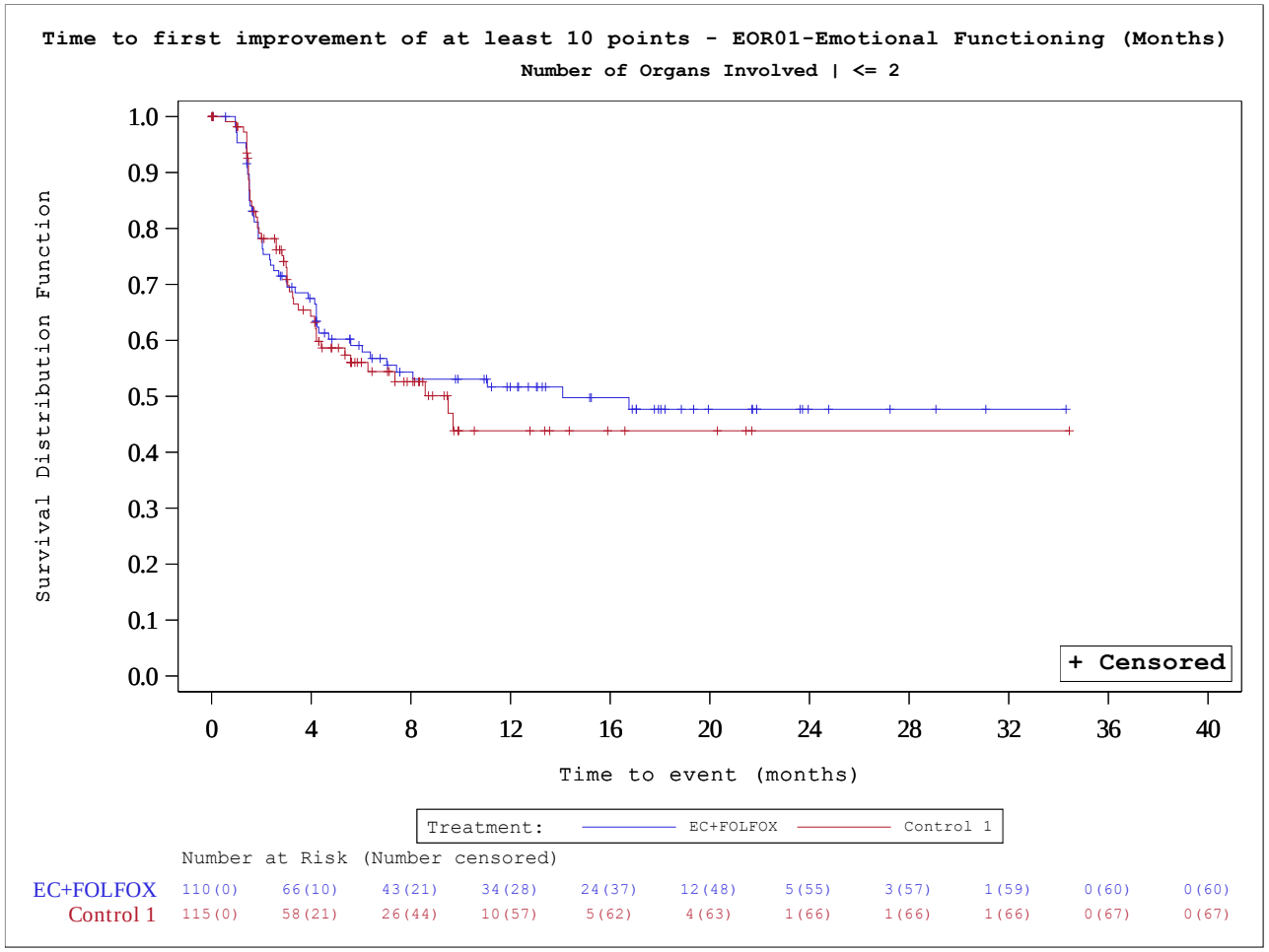

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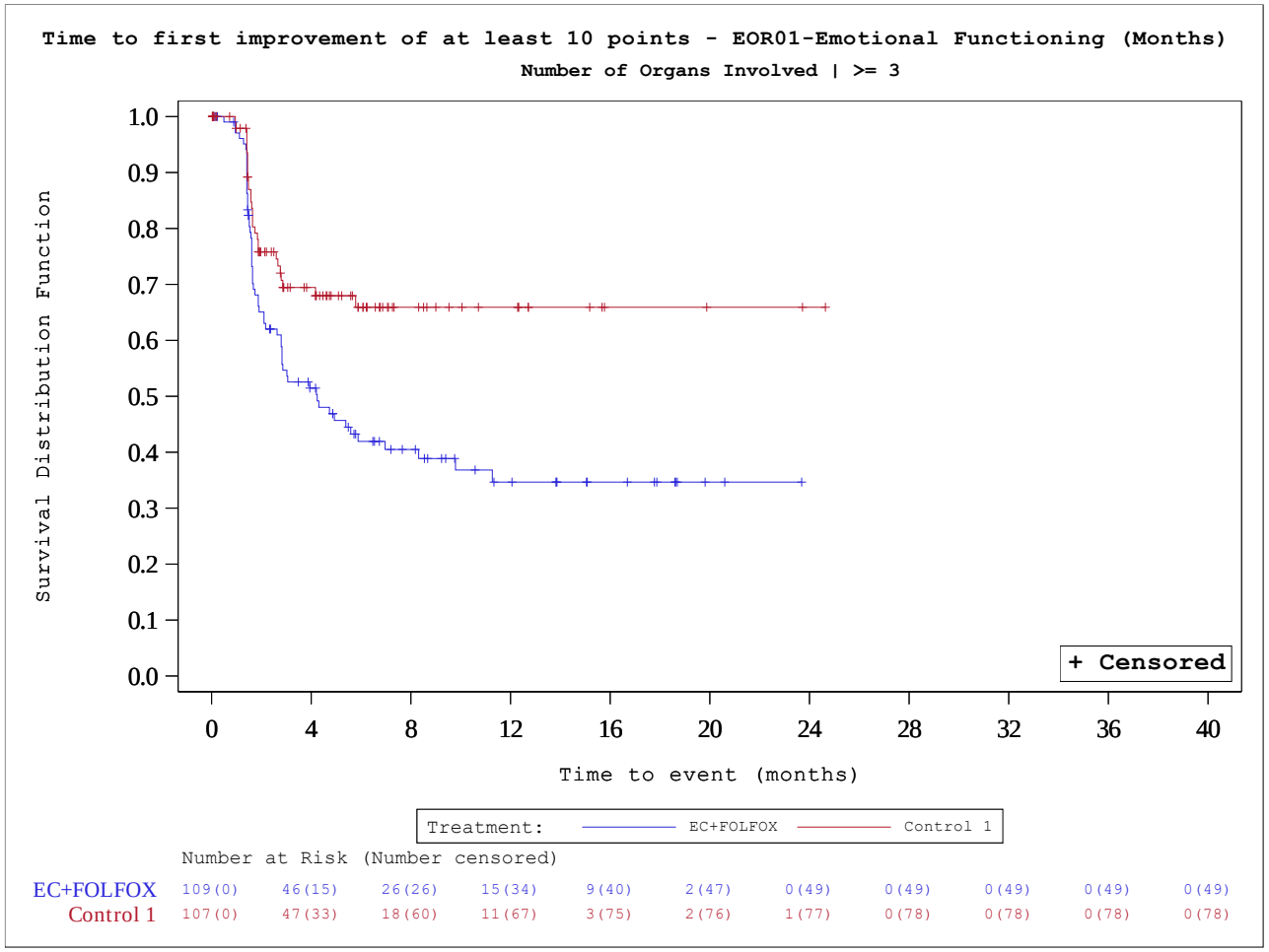

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Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Time to first deterioration of at least 10 points - EOR01-Cognitive Functioning (Months)
Full Analysis Set

	EC+FOLFOX (N=219)	Control 1 (N=222)
Number of subjects with events, n (%)	132 (60.3)	101 (45.5)
Number of censored subjects, n (%)	87 (39.7)	121 (54.5)
Kaplan-Meier estimates of Time to Event (Months) [1]		
25%-ile (95% CI)	2.1 (1.6, 2.9)	2.1 (1.6, 2.8)
Median (95% CI)	5.7 (4.2, 7.0)	6.7 (5.1, 8.3)
75%-ile (95% CI)	24.2 (13.1, NE)	NE (21.1, NE)
Stratified analysis [2]		
Hazard Ratio (95% CI) [3]	1.06 (0.81, 1.38)	
p-value [4]	0.6579	

[1] Based on the Brookmeyer and Crowley method.
[2] Stratified by ECOG PS by Randomization and Geographic Region by Randomization.
[3] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[4] P-value from 2-sided log-rank test.
Including only patients from the full analysis set who completed a baseline (last PRO assessment prior to or on the first dose of study treatment) and at least 1 post-baseline PRO assessment.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Time to first deterioration of at least 10 points - EOR01-Cognitive Functioning (Months) - Subgroup analysis
Full Analysis Set

Subgroup Level	EC+FOLFOX (N=219) n/ N (%)	EC+FOLFOX (N=219) Median (95% CI)[1]	Control 1 (N=222) n/ N (%)	Control 1 (N=222) Median (95% CI)[1]	Unstratified analysis Hazard Ratio (95% CI)[2]	Unstratified analysis p-Value[3]	Interaction p-Value[4]
Age (Years)							0.7220
< 65	86/ 139 (61.9)	5.8 (4.2, 7.5)	55/ 127 (43.3)	7.1 (4.4, 11.3)	1.12 (0.80, 1.57)	0.5161	
>= 65	46/ 80 (57.5)	5.3 (3.8, 8.0)	46/ 95 (48.4)	5.8 (4.3, 7.8)	1.04 (0.69, 1.57)	0.8530	
Sex							0.3942
Male	66/ 114 (57.9)	5.8 (4.3, 8.8)	47/ 108 (43.5)	6.9 (5.5, NE)	1.18 (0.81, 1.72)	0.3968	
Female	66/ 105 (62.9)	5.6 (3.5, 7.5)	54/ 114 (47.4)	5.8 (2.8, 9.1)	0.96 (0.67, 1.37)	0.8132	
Region							0.2705
Europe	59/ 104 (56.7)	7.0 (4.2, 11.0)	31/ 100 (31.0)	21.1 (8.3, NE)	1.35 (0.87, 2.10)	0.1679	
USA/Canada	5/ 8 (62.5)	7.1 (1.6, NE)	4/ 14 (28.6)	NE (4.1, NE)	1.67 (0.44, 6.42)	0.4477	
Rest of World	68/ 107 (63.6)	5.3 (3.0, 6.2)	66/ 108 (61.1)	5.5 (2.9, 6.7)	0.90 (0.64, 1.26)	0.5224	
ECOG-PS at Randomization							0.1344
0	68/ 123 (55.3)	6.8 (4.3, 10.6)	60/ 124 (48.4)	5.9 (4.4, 7.8)	0.90 (0.64, 1.28)	0.5610	
1	64/ 96 (66.7)	4.8 (3.5, 6.2)	41/ 98 (41.8)	7.1 (4.3, 21.1)	1.31 (0.88, 1.95)	0.1715	
Number of Organs Involved							0.2030
<= 2	70/ 110 (63.6)	4.7 (3.1, 7.0)	63/ 115 (54.8)	5.5 (4.0, 6.9)	0.95 (0.67, 1.34)	0.7678	
>= 3	62/ 109 (56.9)	5.8 (4.3, 8.3)	38/ 107 (35.5)	11.3 (6.9, NE)	1.30 (0.87, 1.95)	0.1979	
Presence of Liver Metastases							0.9730
Yes	78/ 135 (57.8)	5.8 (4.0, 8.3)	64/ 142 (45.1)	6.7 (4.4, 8.3)	1.08 (0.77, 1.50)	0.6571	
No	54/ 84 (64.3)	5.7 (4.2, 7.1)	37/ 80 (46.3)	7.2 (3.5, 9.7)	1.05 (0.69, 1.61)	0.8020	
Side of Tumor							0.7329
Left	48/ 83 (57.8)	7.5 (5.3, 10.6)	33/ 86 (38.4)	7.8 (5.9, NE)	1.12 (0.71, 1.74)	0.6318	
Right	84/ 136 (61.8)	4.4 (3.5, 6.1)	68/ 136 (50.0)	5.6 (4.0, 7.2)	1.06 (0.77, 1.46)	0.7232	

[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.
[4] P-Value for interaction from Cox proportional hazards model using ties=exact option with treatment, subgroup and treatment*subgroup interaction as covariates.
Including only patients from the full analysis set who completed a baseline (last PRO assessment prior to or on the first dose of study treatment) and at least 1 post-baseline PRO assessment.
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Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
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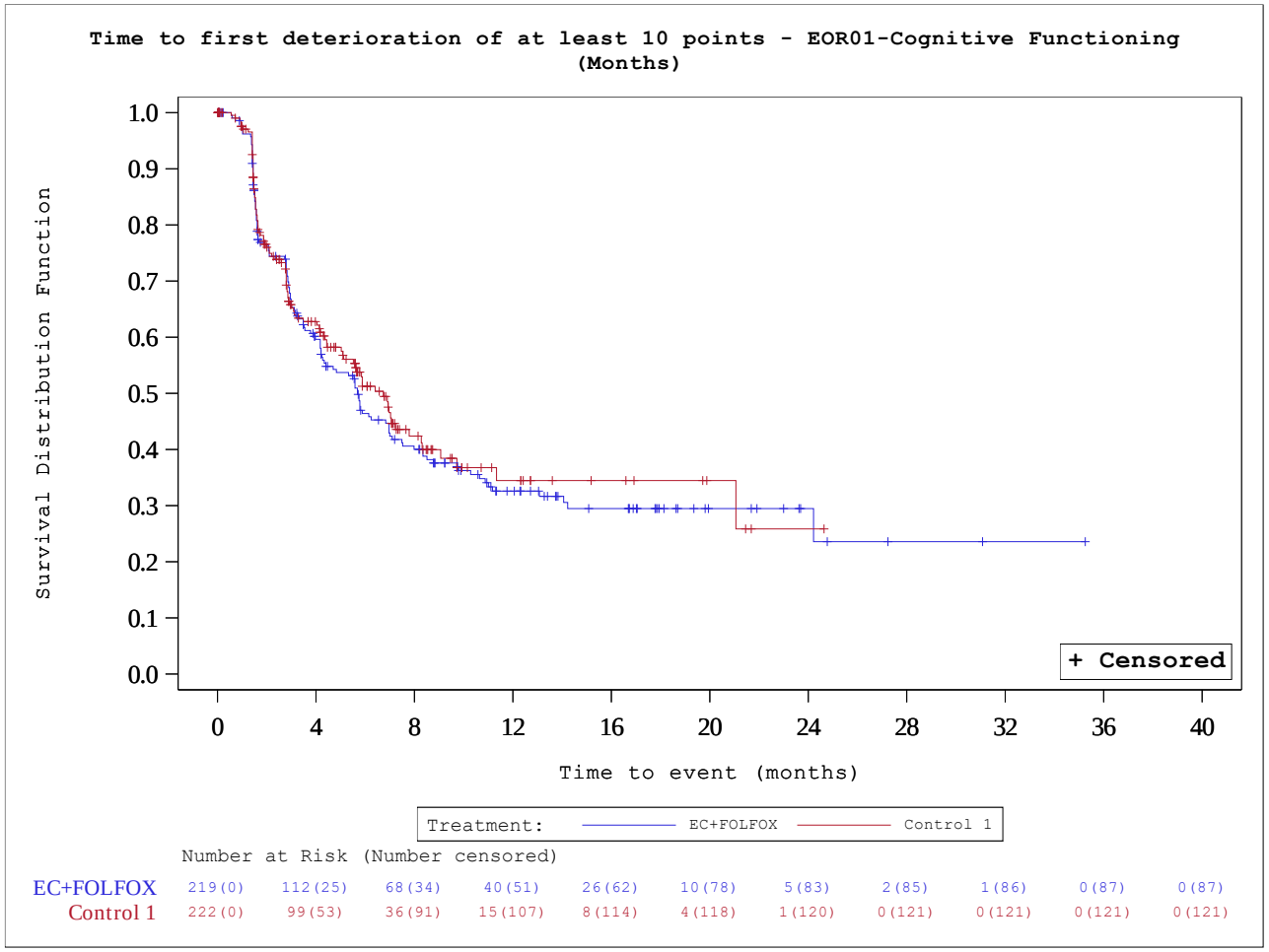
Full Analysis Set



Kaplan-Meier Plots for subgroups only created if p-value for interaction < 0.05.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Time to first improvement of at least 10 points - EOR01-Cognitive Functioning (Months)
Full Analysis Set

	EC+FOLFOX (N=219)	Control 1 (N=222)
Number of subjects with events, n (%)	66 (30.1)	50 (22.5)
Number of censored subjects, n (%)	153 (69.9)	172 (77.5)
Kaplan-Meier estimates of Time to Event (Months) [1]		
25%-ile (95% CI)	4.3 (3.0, 11.3)	5.6 (3.0, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
Stratified analysis [2]		
Hazard Ratio (95% CI) [3]	1.07 (0.74, 1.55)	
p-value [4]	0.7254	

[1] Based on the Brookmeyer and Crowley method.
[2] Stratified by ECOG PS by Randomization and Geographic Region by Randomization.
[3] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio > 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[4] P-value from 2-sided log-rank test.
Including only patients from the full analysis set who completed a baseline (last PRO assessment prior to or on the first dose of study treatment) and at least 1 post-baseline PRO assessment.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Time to first improvement of at least 10 points - EOR01-Cognitive Functioning (Months) - Subgroup analysis
Full Analysis Set

Subgroup Level	EC+FOLFOX (N=219) n/ N (%)	EC+FOLFOX (N=219) Median (95% CI)[1]	Control 1 (N=222) n/ N (%)	Control 1 (N=222) Median (95% CI)[1]	Unstratified analysis Hazard Ratio (95% CI)[2]	Unstratified analysis p-Value[3]	Interaction p-Value[4]
Age (Years)							0.7480
< 65	40/ 139 (28.8)	NE (NE , NE)	25/ 127 (19.7)	NE (NE , NE)	1.19 (0.72, 1.97)	0.4971	
>= 65	26/ 80 (32.5)	NE (14.1, NE)	25/ 95 (26.3)	NE (11.1, NE)	1.03 (0.59, 1.79)	0.9144	
Sex							0.7309
Male	32/ 114 (28.1)	NE (NE , NE)	25/ 108 (23.1)	NE (NE , NE)	1.04 (0.62, 1.77)	0.8702	
Female	34/ 105 (32.4)	NE (NE , NE)	25/ 114 (21.9)	NE (NE , NE)	1.15 (0.68, 1.94)	0.5979	
Region							0.5197
Europe	34/ 104 (32.7)	NE (NE , NE)	19/ 100 (19.0)	NE (NE , NE)	1.27 (0.72, 2.23)	0.4128	
USA/Canada	3/ 8 (37.5)	NE (2.8, NE)	2/ 14 (14.3)	NE (NE , NE)	2.01 (0.34, 12.07)	0.4354	
Rest of World	29/ 107 (27.1)	NE (NE , NE)	29/ 108 (26.9)	NE (NE , NE)	0.90 (0.54, 1.52)	0.6999	
ECOG-PS at Randomization							0.4521
0	36/ 123 (29.3)	NE (NE , NE)	25/ 124 (20.2)	NE (NE , NE)	1.26 (0.75, 2.10)	0.3790	
1	30/ 96 (31.3)	NE (14.1, NE)	25/ 98 (25.5)	NE (11.1, NE)	0.92 (0.54, 1.57)	0.7536	
Number of Organs Involved							0.9906
<= 2	33/ 110 (30.0)	NE (NE , NE)	26/ 115 (22.6)	NE (NE , NE)	1.06 (0.63, 1.78)	0.8280	
>= 3	33/ 109 (30.3)	NE (NE , NE)	24/ 107 (22.4)	NE (NE , NE)	1.11 (0.66, 1.89)	0.6899	
Presence of Liver Metastases							0.1999
Yes	38/ 135 (28.1)	NE (NE , NE)	35/ 142 (24.6)	NE (NE , NE)	0.92 (0.58, 1.46)	0.7304	
No	28/ 84 (33.3)	NE (14.1, NE)	15/ 80 (18.8)	NE (NE , NE)	1.49 (0.79, 2.80)	0.2158	
Side of Tumor							0.3615
Left	25/ 83 (30.1)	NE (NE , NE)	22/ 86 (25.6)	NE (NE , NE)	0.93 (0.52, 1.65)	0.7998	
Right	41/ 136 (30.1)	NE (NE , NE)	28/ 136 (20.6)	NE (NE , NE)	1.22 (0.75, 1.98)	0.4231	

[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio > 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.
[4] P-Value for interaction from Cox proportional hazards model using ties=exact option with treatment, subgroup and treatment*subgroup interaction as covariates.
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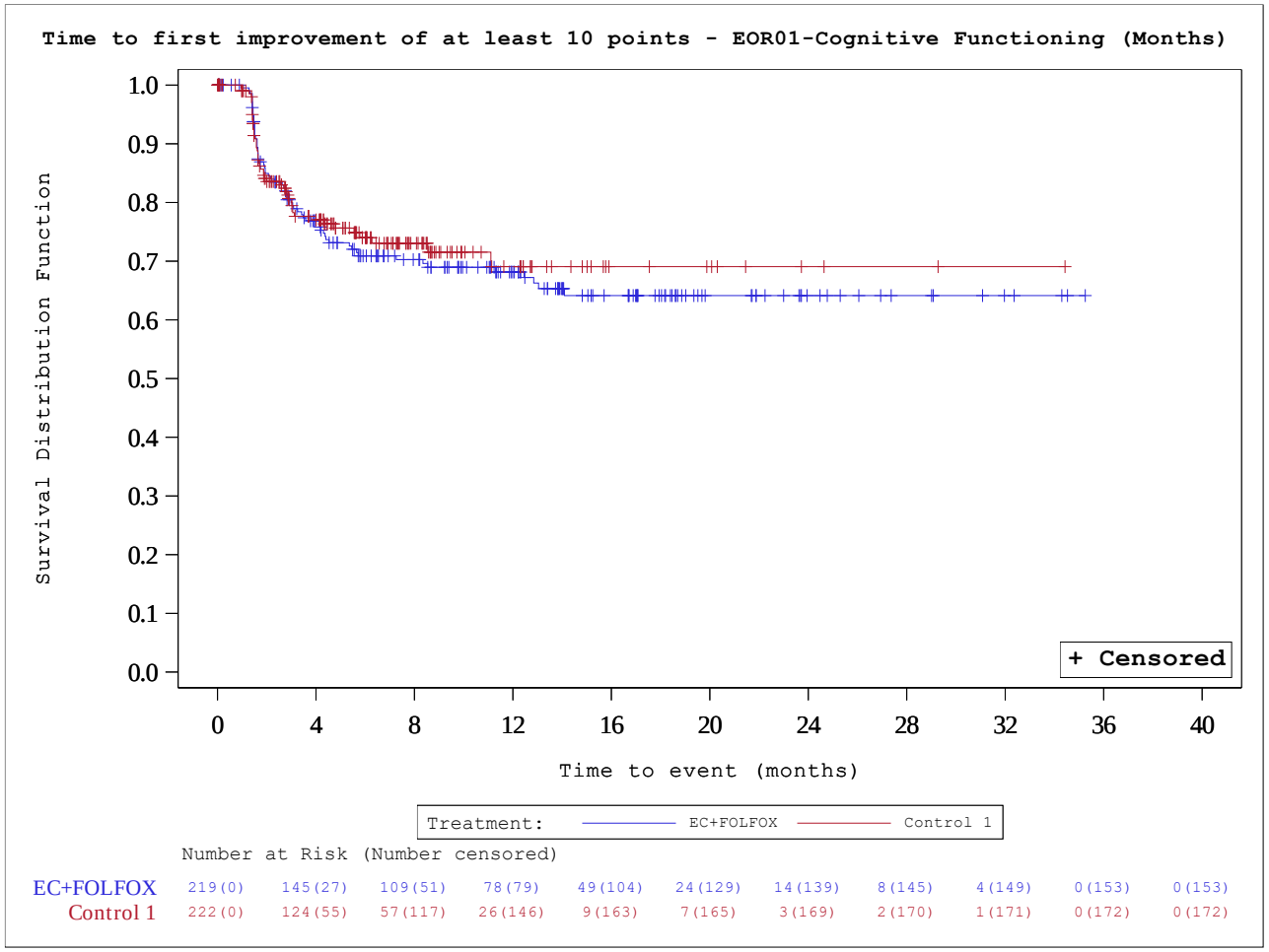

Kaplan-Meier Plots for subgroups only created if p-value for interaction < 0.05.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
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Time to first deterioration of at least 10 points - EOR01-Social Functioning (Months)
Full Analysis Set

	EC+FOLFOX (N=219)	Control 1 (N=222)
Number of subjects with events, n (%)	123 (56.2)	101 (45.5)
Number of censored subjects, n (%)	96 (43.8)	121 (54.5)
Kaplan-Meier estimates of Time to Event (Months) [1]		
25%-ile (95% CI)	1.7 (1.6, 2.3)	2.0 (1.6, 2.8)
Median (95% CI)	5.5 (4.1, 7.0)	5.7 (4.5, 12.3)
75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
Stratified analysis [2]		
Hazard Ratio (95% CI) [3]	1.09 (0.83, 1.42)	
p-value [4]	0.5349	

[1] Based on the Brookmeyer and Crowley method.
[2] Stratified by ECOG PS by Randomization and Geographic Region by Randomization.
[3] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[4] P-value from 2-sided log-rank test.
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Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
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Time to first deterioration of at least 10 points - EOR01-Social Functioning (Months) - Subgroup analysis
Full Analysis Set

Subgroup Level	EC+FOLFOX (N=219) n/ N (%)	EC+FOLFOX (N=219) Median (95% CI)[1]	Control 1 (N=222) n/ N (%)	Control 1 (N=222) Median (95% CI)[1]	Unstratified analysis Hazard Ratio (95% CI)[2]	Unstratified analysis p-Value[3]	Interaction p-Value[4]
Age (Years)							0.3989
< 65	80/ 139 (57.6)	5.5 (3.0, 7.1)	56/ 127 (44.1)	7.0 (4.4, NE)	1.22 (0.87, 1.72)	0.2611	
>= 65	43/ 80 (53.8)	5.6 (4.1, 13.9)	45/ 95 (47.4)	5.5 (3.3, 12.6)	0.95 (0.62, 1.45)	0.8093	
Sex							0.4447
Male	63/ 114 (55.3)	5.6 (3.9, 7.1)	49/ 108 (45.4)	7.0 (5.1, 12.3)	1.22 (0.84, 1.78)	0.2926	
Female	60/ 105 (57.1)	5.5 (3.4, 11.3)	52/ 114 (45.6)	4.8 (3.3, NE)	1.00 (0.69, 1.46)	0.9819	
Region							0.9487
Europe	60/ 104 (57.7)	5.6 (3.5, 8.5)	40/ 100 (40.0)	7.4 (3.3, NE)	1.12 (0.75, 1.67)	0.5873	
USA/Canada	3/ 8 (37.5)	NE (1.6, NE)	3/ 14 (21.4)	NE (4.8, NE)	1.53 (0.31, 7.63)	0.5978	
Rest of World	60/ 107 (56.1)	4.4 (3.0, 7.1)	58/ 108 (53.7)	5.5 (4.0, 9.7)	1.06 (0.74, 1.53)	0.7552	
ECOG-PS at Randomization							0.1714
0	70/ 123 (56.9)	5.6 (3.4, 8.5)	65/ 124 (52.4)	5.1 (3.3, 7.3)	0.94 (0.67, 1.32)	0.7345	
1	53/ 96 (55.2)	4.4 (3.5, 9.9)	36/ 98 (36.7)	12.6 (4.7, NE)	1.39 (0.91, 2.12)	0.1311	
Number of Organs Involved							0.6097
<= 2	67/ 110 (60.9)	4.3 (2.8, 7.0)	55/ 115 (47.8)	5.5 (3.3, NE)	1.21 (0.84, 1.72)	0.3110	
>= 3	56/ 109 (51.4)	6.9 (4.3, 11.3)	46/ 107 (43.0)	7.0 (4.4, 12.6)	1.02 (0.69, 1.50)	0.9339	
Presence of Liver Metastases							0.4526
Yes	76/ 135 (56.3)	5.5 (3.5, 8.4)	70/ 142 (49.3)	4.8 (3.3, 9.7)	1.03 (0.74, 1.42)	0.8817	
No	47/ 84 (56.0)	5.8 (3.3, 9.8)	31/ 80 (38.8)	12.3 (5.1, NE)	1.28 (0.81, 2.02)	0.2823	
Side of Tumor							0.9299
Left	50/ 83 (60.2)	4.3 (2.8, 7.0)	40/ 86 (46.5)	5.5 (2.9, NE)	1.13 (0.75, 1.72)	0.5577	
Right	73/ 136 (53.7)	5.8 (4.1, 11.3)	61/ 136 (44.9)	7.2 (4.8, 12.6)	1.07 (0.76, 1.51)	0.6885	

[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.
[4] P-Value for interaction from Cox proportional hazards model using ties=exact option with treatment, subgroup and treatment*subgroup interaction as covariates.
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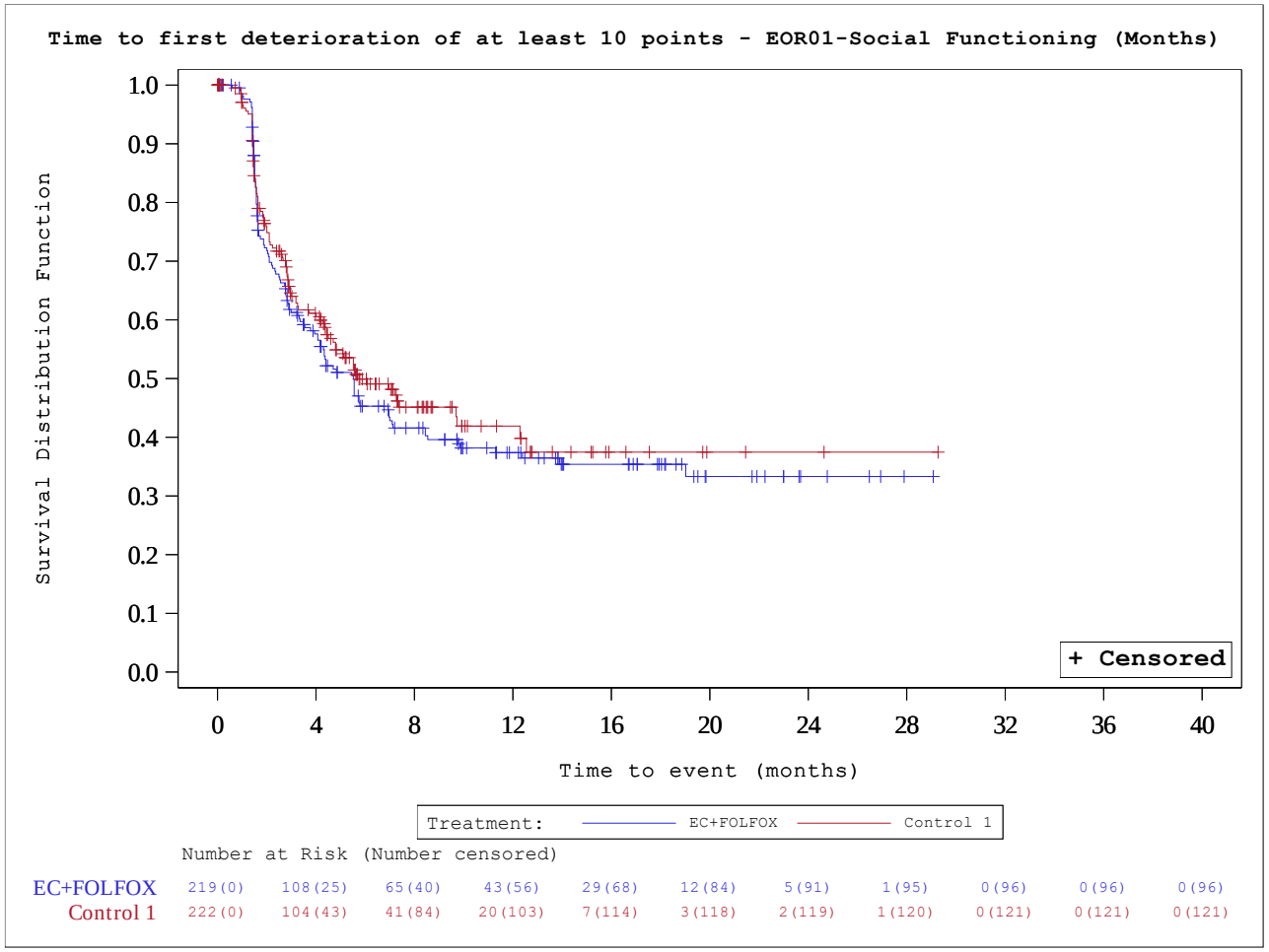

Kaplan-Meier Plots for subgroups only created if p-value for interaction < 0.05.

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Time to first improvement of at least 10 points - EOR01-Social Functioning (Months)
Full Analysis Set

	EC+FOLFOX (N=219)	Control 1 (N=222)
Number of subjects with events, n (%)	89 (40.6)	71 (32.0)
Number of censored subjects, n (%)	130 (59.4)	151 (68.0)
Kaplan-Meier estimates of Time to Event (Months) [1]		
25%-ile (95% CI)	2.9 (2.6, 4.1)	2.9 (1.7, 5.4)
Median (95% CI)	NE (8.4, NE)	NE (9.1, NE)
75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
Stratified analysis [2]		
Hazard Ratio (95% CI) [3]	1.00 (0.73, 1.38)	
p-value [4]	0.9942	

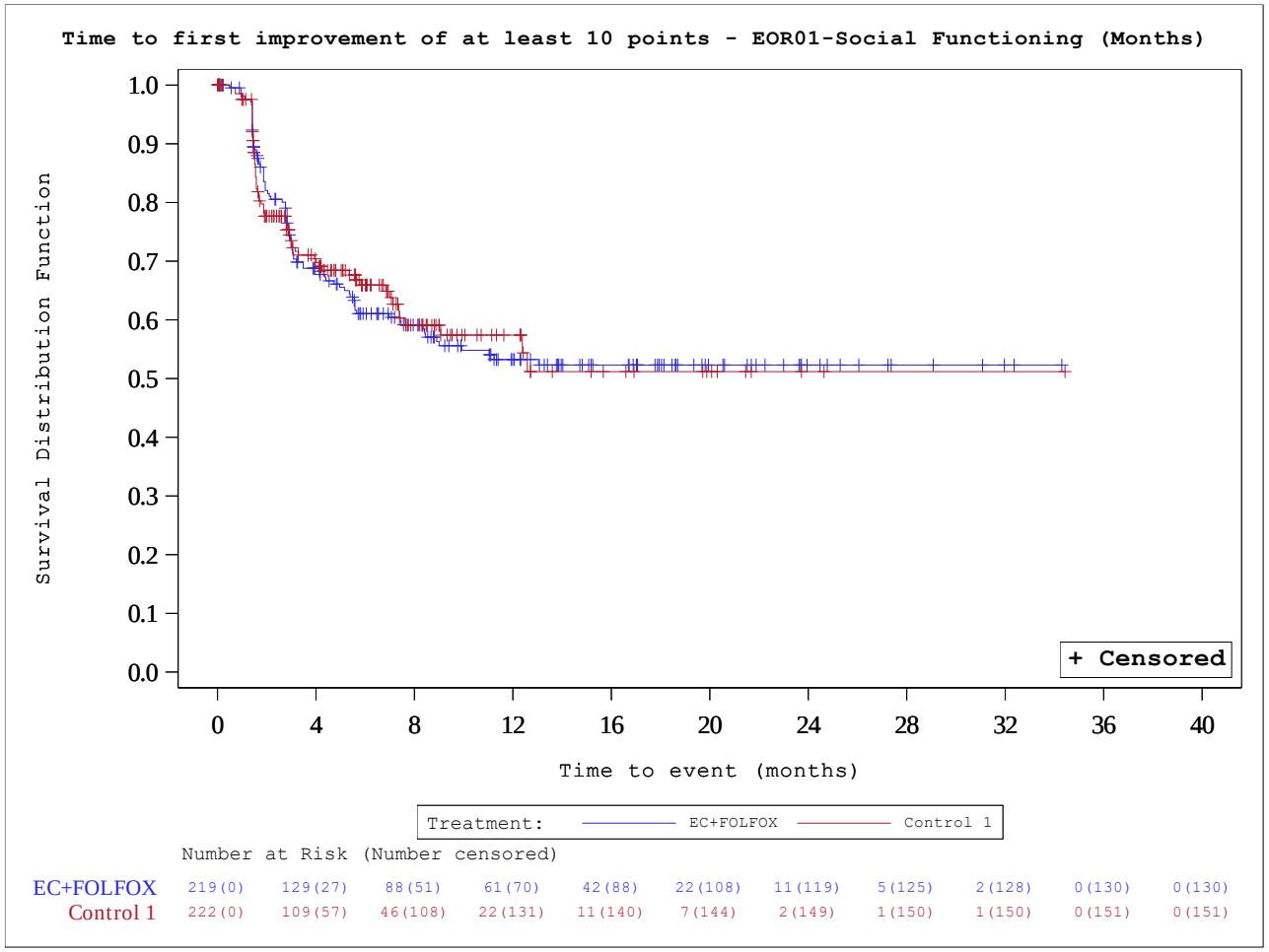
[1] Based on the Brookmeyer and Crowley method.
[2] Stratified by ECOG PS by Randomization and Geographic Region by Randomization.
[3] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio > 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[4] P-value from 2-sided log-rank test.
Including only patients from the full analysis set who completed a baseline (last PRO assessment prior to or on the first dose of study treatment) and at least 1 post-baseline PRO assessment.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Time to first improvement of at least 10 points - EOR01-Social Functioning (Months) - Subgroup analysis
Full Analysis Set

Subgroup Level	EC+FOLFOX (N=219) n/ N (%)	EC+FOLFOX (N=219) Median (95% CI)[1]	Control 1 (N=222) n/ N (%)	Control 1 (N=222) Median (95% CI)[1]	Unstratified analysis Hazard Ratio (95% CI)[2]	Unstratified analysis p-Value[3]	Interaction p-Value[4]
Age (Years)							0.9392
< 65	58/ 139 (41.7)	NE (8.4, NE)	41/ 127 (32.3)	12.6 (9.1, NE)	0.99 (0.66, 1.48)	0.9564	
>= 65	31/ 80 (38.8)	NE (4.2, NE)	30/ 95 (31.6)	NE (7.4, NE)	1.10 (0.66, 1.81)	0.7188	
Sex							0.9433
Male	45/ 114 (39.5)	NE (7.5, NE)	36/ 108 (33.3)	NE (12.4, NE)	1.07 (0.69, 1.66)	0.7656	
Female	44/ 105 (41.9)	NE (7.4, NE)	35/ 114 (30.7)	12.6 (7.4, NE)	0.98 (0.63, 1.53)	0.9304	
Region							0.0280
Europe	49/ 104 (47.1)	9.0 (5.0, NE)	24/ 100 (24.0)	NE (NE , NE)	1.61 (0.99, 2.62)	0.0549	
USA/Canada	4/ 8 (50.0)	NE (2.8, NE)	3/ 14 (21.4)	12.6 (NE , NE)	1.32 (0.29, 6.02)	0.7314	
Rest of World	36/ 107 (33.6)	NE (11.2, NE)	44/ 108 (40.7)	7.4 (6.8, NE)	0.65 (0.42, 1.02)	0.0608	
ECOG-PS at Randomization							0.9685
0	46/ 123 (37.4)	NE (8.9, NE)	37/ 124 (29.8)	NE (9.1, NE)	1.02 (0.66, 1.58)	0.9328	
1	43/ 96 (44.8)	11.0 (4.7, NE)	34/ 98 (34.7)	NE (5.4, NE)	1.02 (0.65, 1.61)	0.9119	
Number of Organs Involved							0.0330
<= 2	42/ 110 (38.2)	NE (11.0, NE)	44/ 115 (38.3)	9.1 (7.0, NE)	0.73 (0.47, 1.12)	0.1467	
>= 3	47/ 109 (43.1)	8.4 (5.2, NE)	27/ 107 (25.2)	NE (12.6, NE)	1.51 (0.94, 2.43)	0.0828	
Presence of Liver Metastases							0.0956
Yes	57/ 135 (42.2)	11.2 (7.0, NE)	40/ 142 (28.2)	NE (9.1, NE)	1.26 (0.84, 1.90)	0.2545	
No	32/ 84 (38.1)	NE (9.0, NE)	31/ 80 (38.8)	12.4 (5.4, NE)	0.73 (0.44, 1.20)	0.2089	
Side of Tumor							0.7339
Left	32/ 83 (38.6)	NE (8.4, NE)	23/ 86 (26.7)	NE (7.4, NE)	1.11 (0.65, 1.91)	0.7012	
Right	57/ 136 (41.9)	13.0 (7.0, NE)	48/ 136 (35.3)	12.6 (7.4, NE)	0.98 (0.67, 1.45)	0.9350	

[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio > 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.
[4] P-Value for interaction from Cox proportional hazards model using ties=exact option with treatment, subgroup and treatment*subgroup interaction as covariates.
Including only patients from the full analysis set who completed a baseline (last PRO assessment prior to or on the first dose of study treatment) and at least 1 post-baseline PRO assessment.
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Kaplan Meier Plot of Time to first improvement of at least 10 points - EOR01-Social Functioning (Months)
Full Analysis Set



Kaplan-Meier Plots for subgroups only created if p-value for interaction < 0.05.

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Encorafenib (PF-07263896) Protocol C4221015
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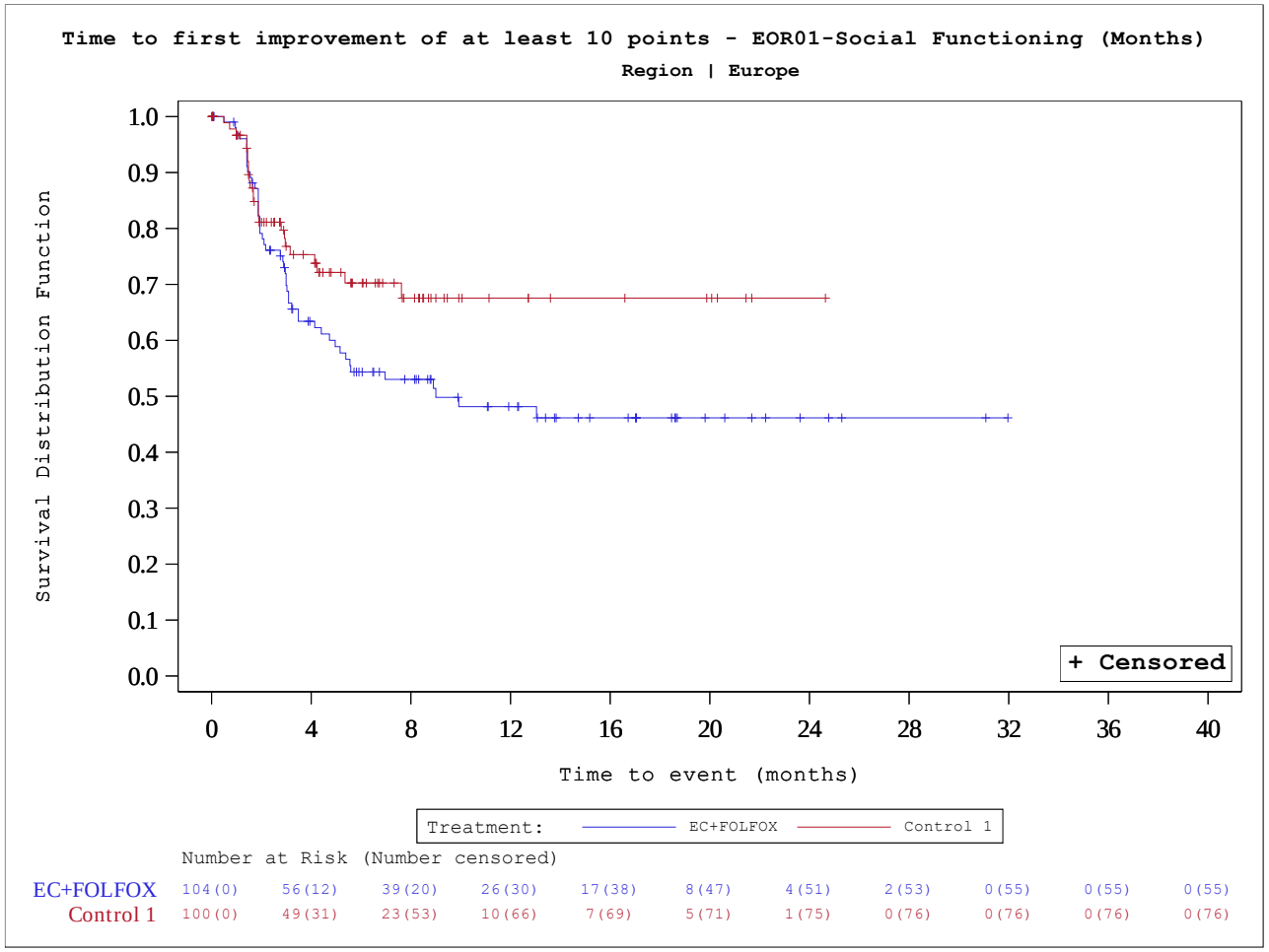

Kaplan-Meier Plots for subgroups only created if p-value for interaction < 0.05.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
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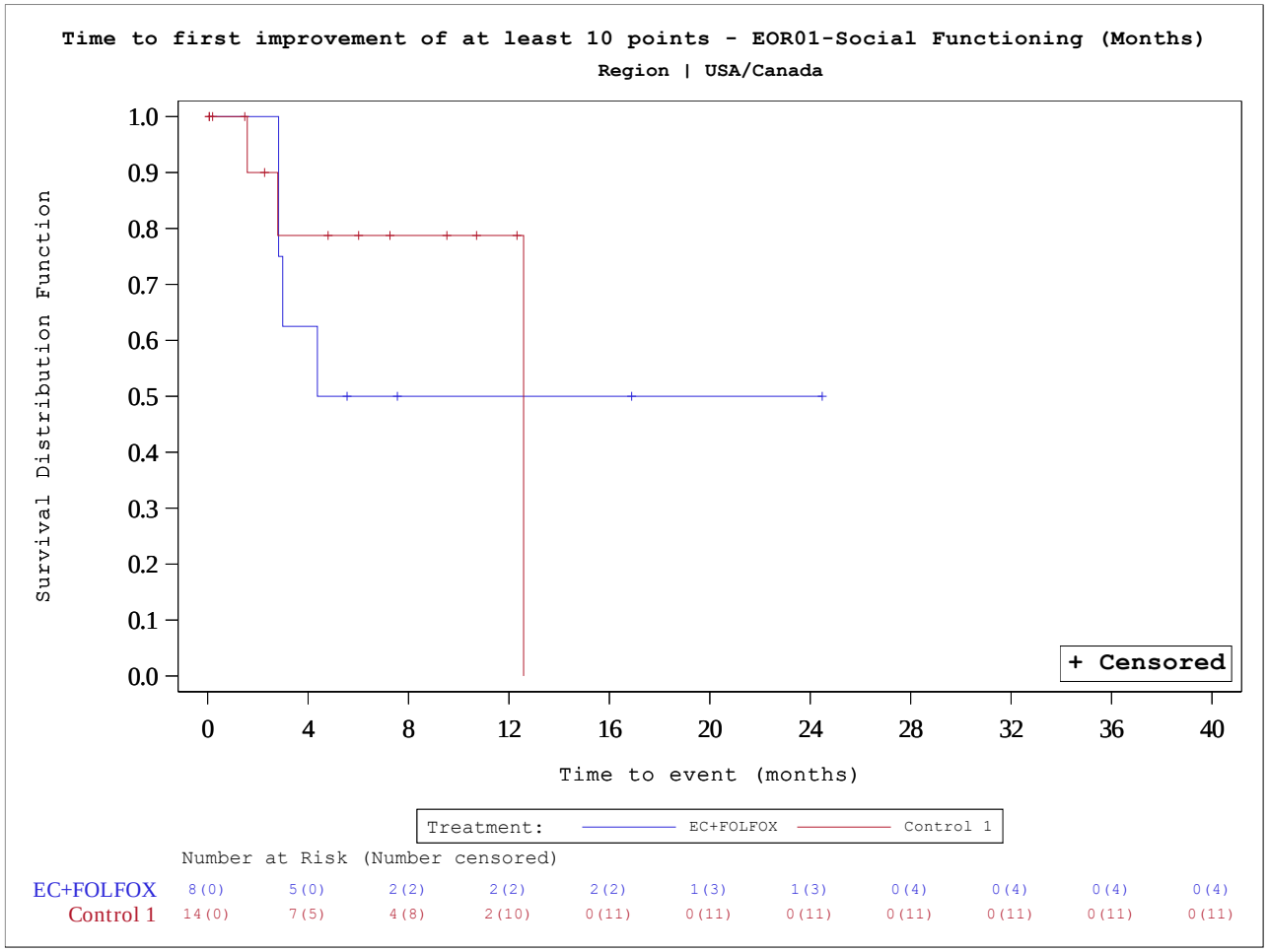

Kaplan-Meier Plots for subgroups only created if p-value for interaction < 0.05.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
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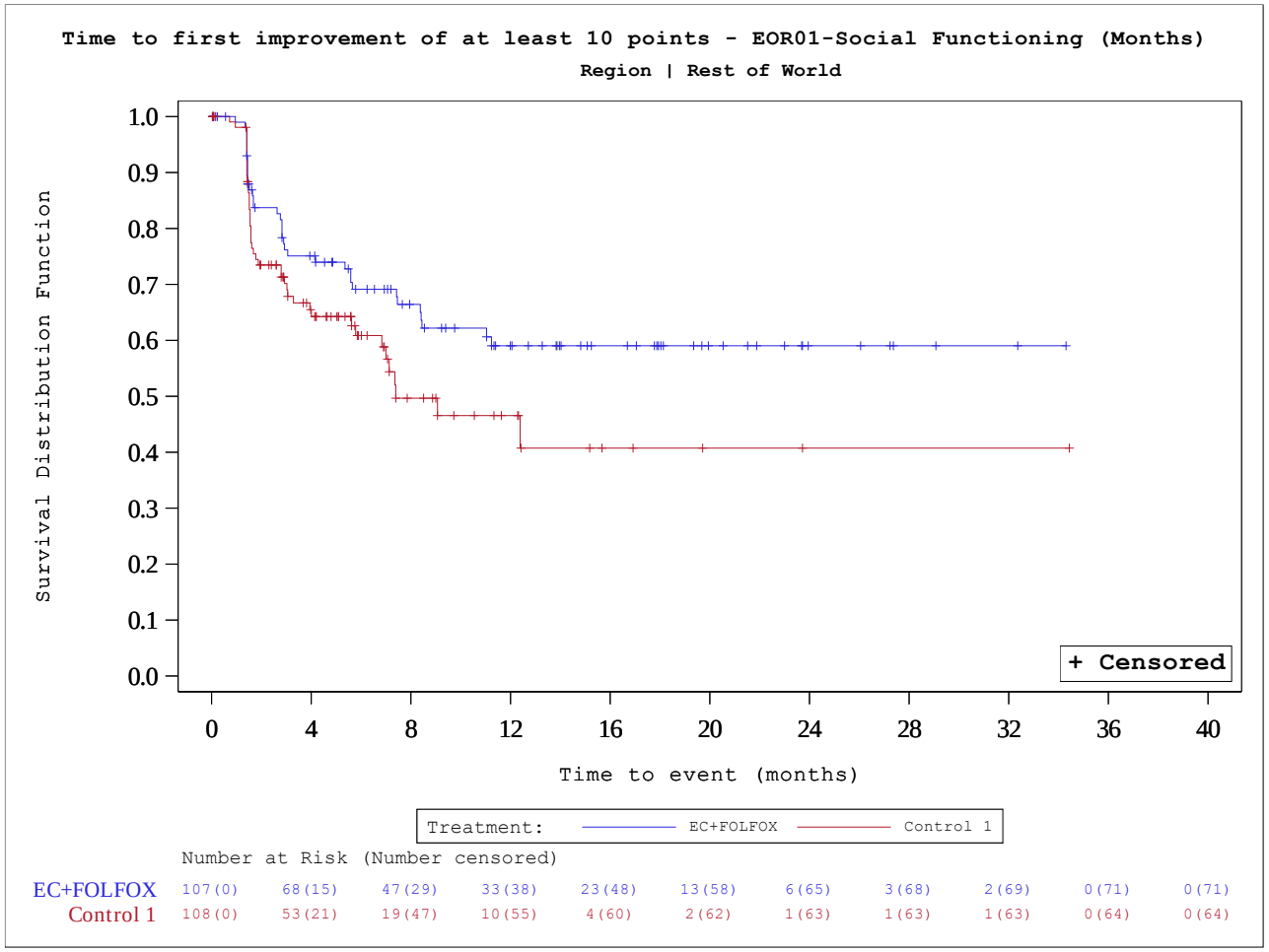

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Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
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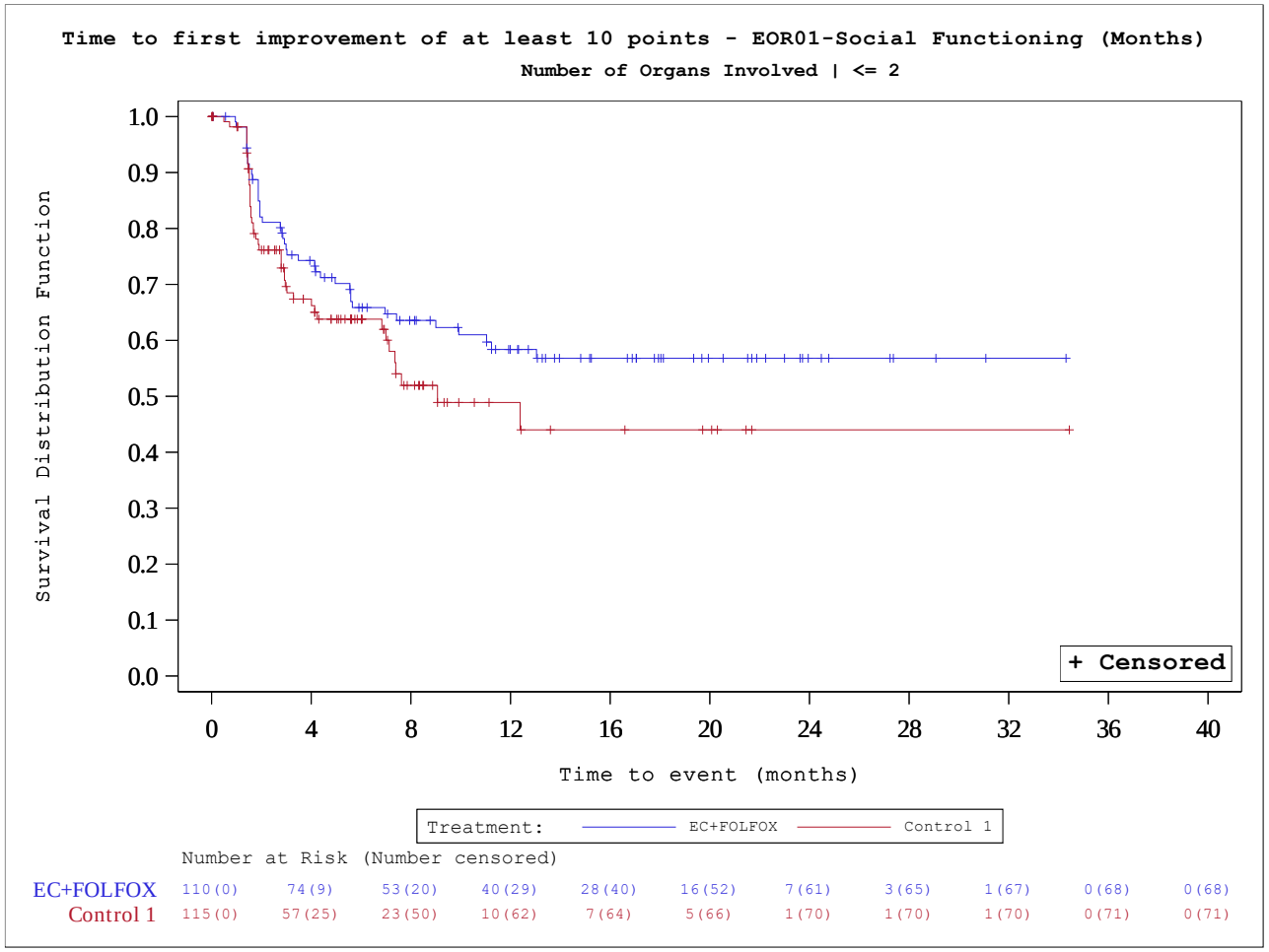

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Encorafenib (PF-07263896) Protocol C4221015
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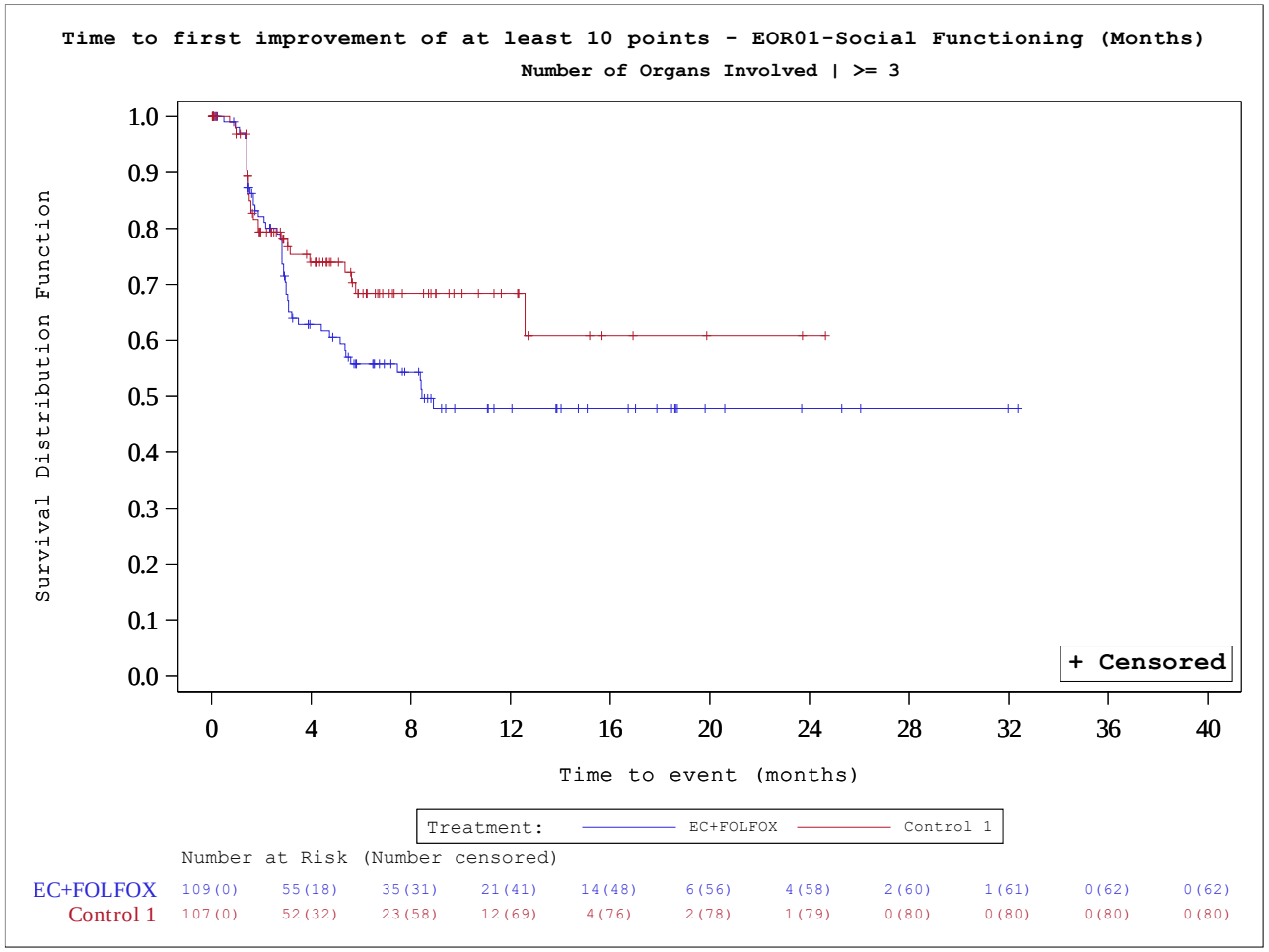


Kaplan-Meier Plots for subgroups only created if p-value for interaction < 0.05.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Time to first deterioration of at least 10 points - EOR01-Fatigue (Months)
Full Analysis Set

	EC+FOLFOX (N=219)	Control 1 (N=222)
Number of subjects with events, n (%)	151 (68.9)	111 (50.0)
Number of censored subjects, n (%)	68 (31.1)	111 (50.0)
Kaplan-Meier estimates of Time to Event (Months) [1]		
25%-ile (95% CI)	1.5 (1.5, 1.6)	1.6 (1.5, 1.9)
Median (95% CI)	2.8 (2.1, 4.0)	4.5 (3.0, 6.9)
75%-ile (95% CI)	13.9 (7.0, NE)	NE (12.7, NE)
Stratified analysis [2]		
Hazard Ratio (95% CI) [3]	1.33 (1.04, 1.71)	
p-value [4]	0.0221	

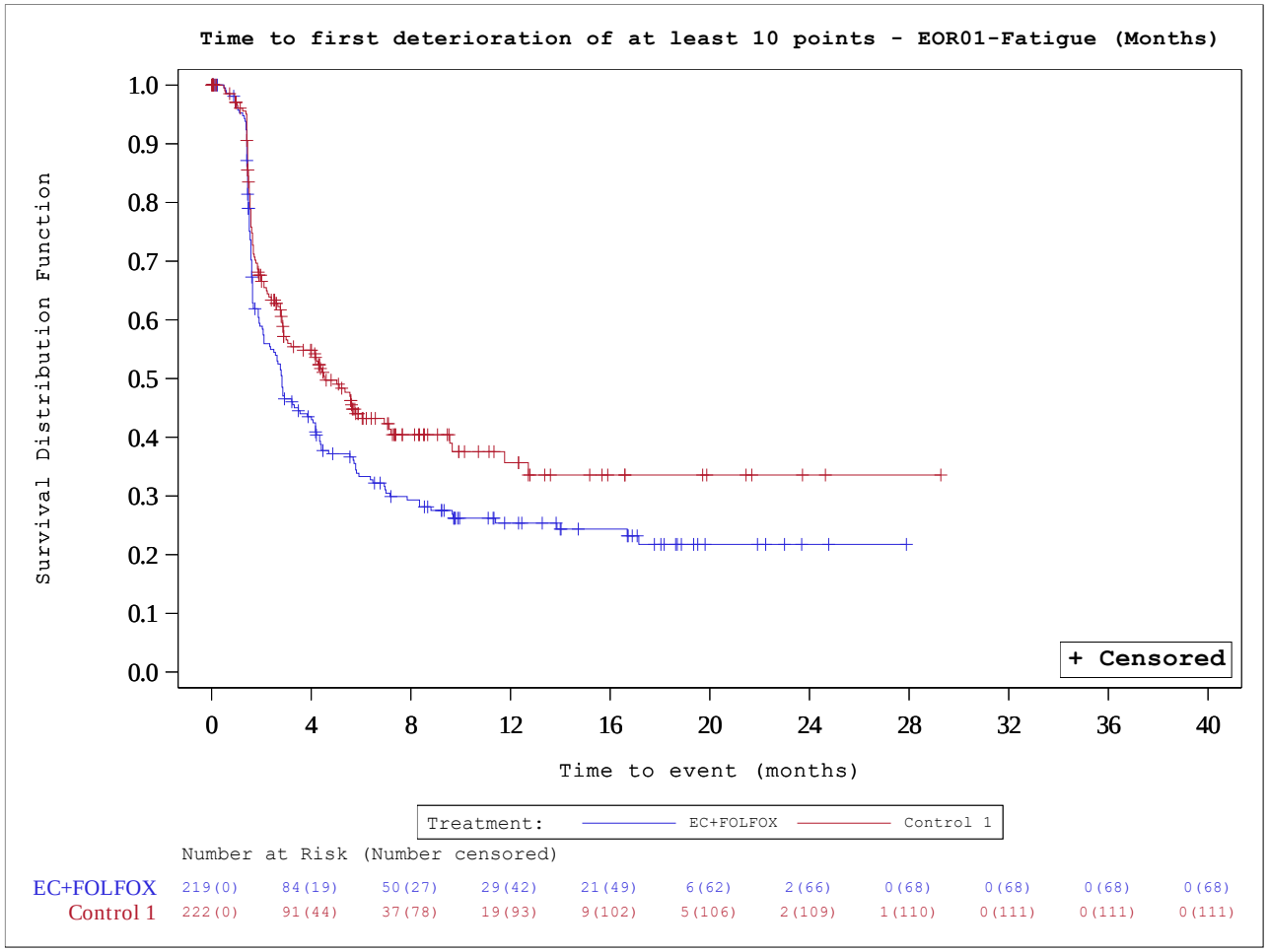
[1] Based on the Brookmeyer and Crowley method.
[2] Stratified by ECOG PS by Randomization and Geographic Region by Randomization.
[3] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[4] P-value from 2-sided log-rank test.
Including only patients from the full analysis set who completed a baseline (last PRO assessment prior to or on the first dose of study treatment) and at least 1 post-baseline PRO assessment.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Time to first deterioration of at least 10 points - EOR01-Fatigue (Months) - Subgroup analysis
Full Analysis Set

Subgroup Level	EC+FOLFOX (N=219) n/ N (%)	EC+FOLFOX (N=219) Median (95% CI)[1]	Control 1 (N=222) n/ N (%)	Control 1 (N=222) Median (95% CI)[1]	Unstratified analysis Hazard Ratio (95% CI)[2]	Unstratified analysis p-Value[3]	Interaction p-Value[4]
Age (Years)							0.7133
< 65	97/ 139 (69.8)	2.8 (1.9, 4.4)	64/ 127 (50.4)	4.3 (2.8, 11.8)	1.30 (0.94, 1.78)	0.1107	
>= 65	54/ 80 (67.5)	2.8 (2.0, 3.8)	47/ 95 (49.5)	5.4 (2.9, 9.6)	1.44 (0.97, 2.14)	0.0660	
Sex							0.8753
Male	78/ 114 (68.4)	2.9 (1.9, 4.4)	55/ 108 (50.9)	5.1 (2.8, 7.1)	1.39 (0.98, 1.96)	0.0607	
Female	73/ 105 (69.5)	2.8 (2.0, 3.5)	56/ 114 (49.1)	4.4 (2.9, 9.7)	1.32 (0.93, 1.87)	0.1197	
Region							0.5470
Europe	71/ 104 (68.3)	4.0 (2.4, 5.7)	45/ 100 (45.0)	5.6 (4.2, 12.7)	1.33 (0.92, 1.94)	0.1297	
USA/Canada	6/ 8 (75.0)	2.4 (1.6, NE)	4/ 14 (28.6)	NE (2.6, NE)	2.68 (0.75, 9.61)	0.1157	
Rest of World	74/ 107 (69.2)	2.6 (1.6, 2.9)	62/ 108 (57.4)	3.1 (2.4, 5.7)	1.31 (0.93, 1.84)	0.1219	
ECOG-PS at Randomization							0.4176
0	86/ 123 (69.9)	2.8 (2.0, 4.3)	67/ 124 (54.0)	3.2 (2.3, 5.7)	1.24 (0.90, 1.71)	0.1884	
1	65/ 96 (67.7)	2.8 (1.7, 4.2)	44/ 98 (44.9)	6.9 (4.1, 12.7)	1.50 (1.02, 2.20)	0.0374	
Number of Organs Involved							0.6607
<= 2	84/ 110 (76.4)	1.9 (1.6, 2.9)	64/ 115 (55.7)	4.2 (2.6, 5.7)	1.46 (1.05, 2.02)	0.0239	
>= 3	67/ 109 (61.5)	4.1 (2.8, 5.9)	47/ 107 (43.9)	5.8 (3.1, 12.7)	1.27 (0.87, 1.84)	0.2149	
Presence of Liver Metastases							0.8796
Yes	92/ 135 (68.1)	2.8 (2.1, 4.1)	73/ 142 (51.4)	4.5 (3.0, 6.9)	1.33 (0.97, 1.81)	0.0732	
No	59/ 84 (70.2)	2.6 (1.7, 4.4)	38/ 80 (47.5)	5.4 (2.0, NE)	1.40 (0.93, 2.11)	0.1028	
Side of Tumor							0.5578
Left	53/ 83 (63.9)	3.2 (1.6, 6.5)	41/ 86 (47.7)	5.0 (2.4, 12.7)	1.23 (0.82, 1.86)	0.3163	
Right	98/ 136 (72.1)	2.8 (2.1, 3.5)	70/ 136 (51.5)	4.4 (2.9, 9.6)	1.43 (1.05, 1.94)	0.0220	

[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.
[4] P-Value for interaction from Cox proportional hazards model using ties=exact option with treatment, subgroup and treatment*subgroup interaction as covariates.
Including only patients from the full analysis set who completed a baseline (last PRO assessment prior to or on the first dose of study treatment) and at least 1 post-baseline PRO assessment.
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Kaplan Meier Plot of Time to first deterioration of at least 10 points - EOR01-Fatigue (Months)
Full Analysis Set



Kaplan-Meier Plots for subgroups only created if p-value for interaction < 0.05.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Time to first improvement of at least 10 points - EOR01-Fatigue (Months)
Full Analysis Set

	EC+FOLFOX (N=219)	Control 1 (N=222)
Number of subjects with events, n (%)	97 (44.3)	77 (34.7)
Number of censored subjects, n (%)	122 (55.7)	145 (65.3)
Kaplan-Meier estimates of Time to Event (Months) [1]		
25%-ile (95% CI)	3.0 (2.6, 4.2)	2.9 (1.8, 4.3)
Median (95% CI)	11.1 (8.1, NE)	12.4 (8.4, NE)
75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
Stratified analysis [2]		
Hazard Ratio (95% CI) [3]	0.99 (0.73, 1.33)	
p-value [4]	0.9341	

[1] Based on the Brookmeyer and Crowley method.
[2] Stratified by ECOG PS by Randomization and Geographic Region by Randomization.
[3] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio > 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[4] P-value from 2-sided log-rank test.
Including only patients from the full analysis set who completed a baseline (last PRO assessment prior to or on the first dose of study treatment) and at least 1 post-baseline PRO assessment.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Time to first improvement of at least 10 points - EOR01-Fatigue (Months) - Subgroup analysis
Full Analysis Set

Subgroup Level	EC+FOLFOX (N=219) n/ N (%)	EC+FOLFOX (N=219) Median (95% CI)[1]	Control 1 (N=222) n/ N (%)	Control 1 (N=222) Median (95% CI)[1]	Unstratified analysis Hazard Ratio (95% CI)[2]	Unstratified analysis p-Value[3]	Interaction p-Value[4]
Age (Years)							0.4029
< 65	69/ 139 (49.6)	8.3 (5.6, NE)	46/ 127 (36.2)	12.4 (5.9, NE)	1.09 (0.75, 1.59)	0.6308	
>= 65	28/ 80 (35.0)	24.6 (9.5, NE)	31/ 95 (32.6)	12.4 (6.7, NE)	0.81 (0.48, 1.37)	0.4345	
Sex							0.9264
Male	50/ 114 (43.9)	8.5 (5.4, NE)	41/ 108 (38.0)	12.4 (6.5, NE)	1.02 (0.67, 1.55)	0.9187	
Female	47/ 105 (44.8)	12.3 (8.3, NE)	36/ 114 (31.6)	NE (8.4, NE)	0.99 (0.64, 1.54)	0.9733	
Region							0.4303
Europe	46/ 104 (44.2)	24.6 (5.0, NE)	31/ 100 (31.0)	10.0 (6.5, NE)	1.11 (0.70, 1.76)	0.6435	
USA/Canada	3/ 8 (37.5)	NE (5.6, NE)	1/ 14 (7.1)	NE (NE , NE)	3.09 (0.32, 29.74)	0.3031	
Rest of World	48/ 107 (44.9)	9.8 (8.1, NE)	45/ 108 (41.7)	12.4 (5.3, NE)	0.87 (0.58, 1.32)	0.5285	
ECOG-PS at Randomization							0.1151
0	54/ 123 (43.9)	9.8 (7.1, NE)	37/ 124 (29.8)	NE (12.4, NE)	1.26 (0.82, 1.91)	0.2883	
1	43/ 96 (44.8)	11.1 (6.9, NE)	40/ 98 (40.8)	8.4 (3.8, NE)	0.78 (0.50, 1.20)	0.2653	
Number of Organs Involved							0.4224
<= 2	46/ 110 (41.8)	24.6 (8.3, NE)	42/ 115 (36.5)	12.4 (6.7, NE)	0.88 (0.57, 1.34)	0.5385	
>= 3	51/ 109 (46.8)	8.5 (5.2, NE)	35/ 107 (32.7)	NE (5.9, NE)	1.16 (0.75, 1.78)	0.5007	
Presence of Liver Metastases							0.1268
Yes	60/ 135 (44.4)	9.5 (7.1, NE)	56/ 142 (39.4)	9.0 (4.3, NE)	0.86 (0.59, 1.23)	0.4098	
No	37/ 84 (44.0)	12.5 (6.2, NE)	21/ 80 (26.3)	NE (10.0, NE)	1.38 (0.80, 2.37)	0.2483	
Side of Tumor							0.9191
Left	42/ 83 (50.6)	8.3 (4.6, NE)	30/ 86 (34.9)	12.4 (4.3, NE)	1.03 (0.64, 1.65)	0.9035	
Right	55/ 136 (40.4)	NE (8.3, NE)	47/ 136 (34.6)	12.4 (8.4, NE)	0.98 (0.66, 1.46)	0.9382	

[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio > 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.
[4] P-Value for interaction from Cox proportional hazards model using ties=exact option with treatment, subgroup and treatment*subgroup interaction as covariates.
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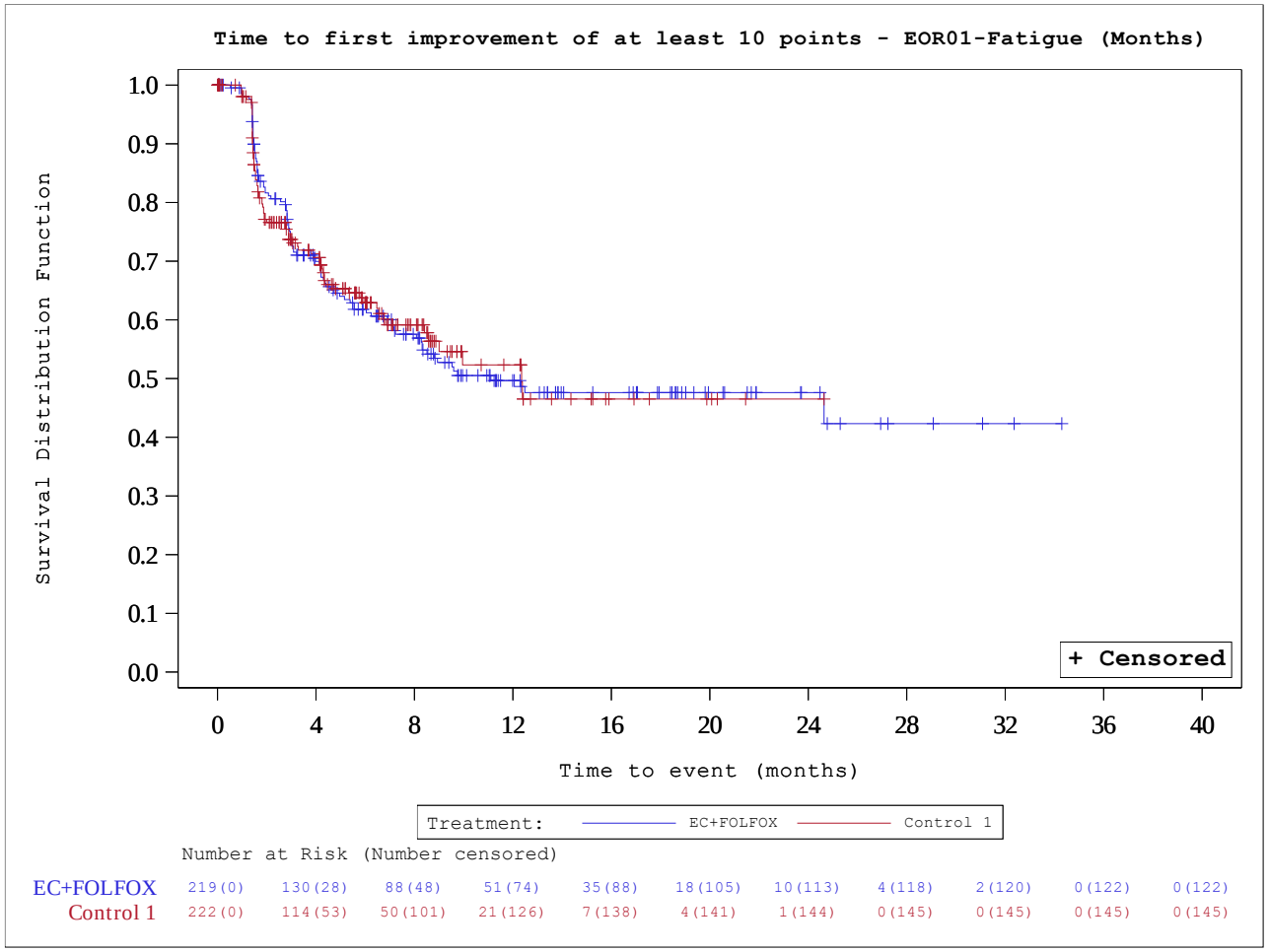
Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Kaplan Meier Plot of Time to first improvement of at least 10 points - EOR01-Fatigue (Months)
Full Analysis Set



Kaplan-Meier Plots for subgroups only created if p-value for interaction < 0.05.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Time to first deterioration of at least 10 points - EOR01-Nausea and Vomiting (Months)
Full Analysis Set

	EC+FOLFOX (N=219)	Control 1 (N=222)
Number of subjects with events, n (%)	115 (52.5)	98 (44.1)
Number of censored subjects, n (%)	104 (47.5)	124 (55.9)
Kaplan-Meier estimates of Time to Event (Months) [1]		
25%-ile (95% CI)	1.6 (1.5, 2.1)	1.7 (1.6, 2.8)
Median (95% CI)	6.9 (3.9, 15.2)	5.9 (4.2, 11.6)
75%-ile (95% CI)	NE (20.0, NE)	NE (12.9, NE)
Stratified analysis [2]		
Hazard Ratio (95% CI) [3]	0.97 (0.73, 1.27)	
p-value [4]	0.7969	

[1] Based on the Brookmeyer and Crowley method.
[2] Stratified by ECOG PS by Randomization and Geographic Region by Randomization.
[3] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[4] P-value from 2-sided log-rank test.
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Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Time to first deterioration of at least 10 points - EOR01-Nausea and Vomiting (Months) - Subgroup analysis
Full Analysis Set

Subgroup Level	EC+FOLFOX (N=219) n/ N (%)	EC+FOLFOX (N=219) Median (95% CI)[1]	Control 1 (N=222) n/ N (%)	Control 1 (N=222) Median (95% CI)[1]	Unstratified analysis Hazard Ratio (95% CI)[2]	Unstratified analysis p-Value[3]	Interaction p-Value[4]
Age (Years)							0.2454
< 65	80/ 139 (57.6)	4.7 (2.9, 9.8)	57/ 127 (44.9)	5.6 (4.0, 12.9)	1.11 (0.79, 1.57)	0.5484	
>= 65	35/ 80 (43.8)	15.2 (3.9, NE)	41/ 95 (43.2)	5.9 (2.9, NE)	0.80 (0.51, 1.26)	0.3410	
Sex							0.8717
Male	50/ 114 (43.9)	16.7 (4.7, NE)	43/ 108 (39.8)	11.2 (5.6, NE)	0.98 (0.65, 1.48)	0.9139	
Female	65/ 105 (61.9)	3.8 (2.8, 8.5)	55/ 114 (48.2)	4.1 (2.9, 10.0)	1.01 (0.70, 1.46)	0.9569	
Region							0.0135
Europe	53/ 104 (51.0)	4.9 (3.7, NE)	33/ 100 (33.0)	11.6 (5.4, NE)	1.33 (0.86, 2.06)	0.2013	
USA/Canada	6/ 8 (75.0)	2.2 (1.4, NE)	2/ 14 (14.3)	NE (NE , NE)	5.89 (1.18, 29.35)	0.0144	
Rest of World	56/ 107 (52.3)	8.5 (3.9, 20.0)	63/ 108 (58.3)	4.0 (2.8, 5.6)	0.70 (0.49, 1.02)	0.0585	
ECOG-PS at Randomization							0.5849
0	65/ 123 (52.8)	7.2 (3.7, 20.0)	58/ 124 (46.8)	5.6 (3.2, 11.6)	0.92 (0.64, 1.31)	0.6243	
1	50/ 96 (52.1)	5.8 (2.9, NE)	40/ 98 (40.8)	5.9 (3.9, NE)	1.09 (0.72, 1.66)	0.6748	
Number of Organs Involved							0.4402
<= 2	61/ 110 (55.5)	4.8 (3.0, 20.0)	57/ 115 (49.6)	5.6 (2.9, 11.2)	0.90 (0.62, 1.30)	0.5825	
>= 3	54/ 109 (49.5)	6.9 (4.0, NE)	41/ 107 (38.3)	10.0 (4.1, NE)	1.12 (0.74, 1.68)	0.5917	
Presence of Liver Metastases							0.5120
Yes	64/ 135 (47.4)	11.4 (4.0, 20.0)	62/ 142 (43.7)	5.6 (3.2, NE)	0.93 (0.65, 1.32)	0.6711	
No	51/ 84 (60.7)	4.7 (2.9, 9.8)	36/ 80 (45.0)	8.5 (4.1, NE)	1.11 (0.72, 1.72)	0.6242	
Side of Tumor							0.2064
Left	41/ 83 (49.4)	8.5 (3.7, NE)	39/ 86 (45.3)	5.2 (2.2, NE)	0.81 (0.52, 1.25)	0.3432	
Right	74/ 136 (54.4)	4.9 (3.3, 19.0)	59/ 136 (43.4)	5.9 (4.1, NE)	1.14 (0.81, 1.61)	0.4722	

[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.
[4] P-Value for interaction from Cox proportional hazards model using ties=exact option with treatment, subgroup and treatment*subgroup interaction as covariates.
Including only patients from the full analysis set who completed a baseline (last PRO assessment prior to or on the first dose of study treatment) and at least 1 post-baseline PRO assessment.
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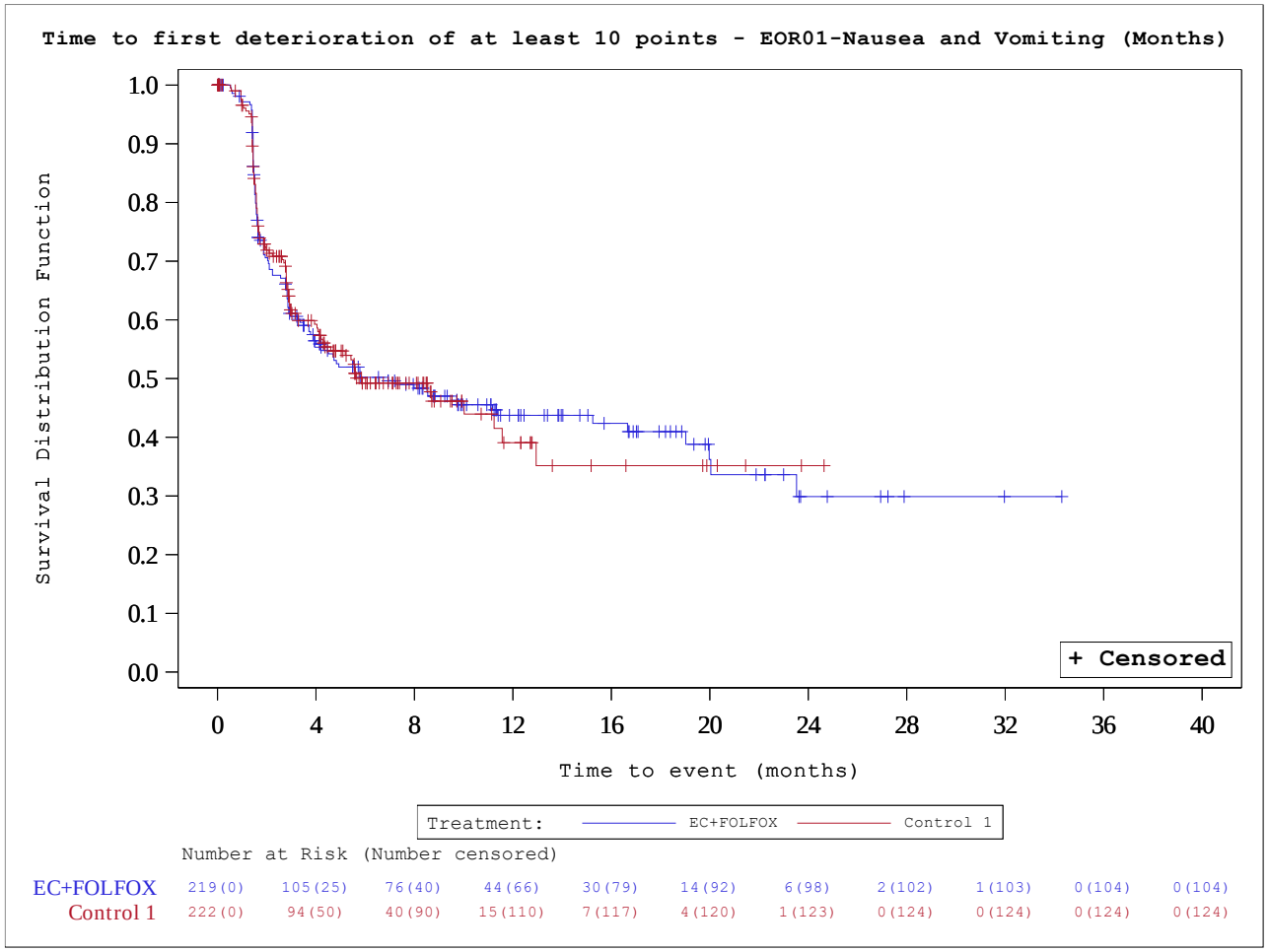
Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Kaplan Meier Plot of Time to first deterioration of at least 10 points - EOR01-Nausea and Vomiting (Months)
Full Analysis Set



Kaplan-Meier Plots for subgroups only created if p-value for interaction < 0.05.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
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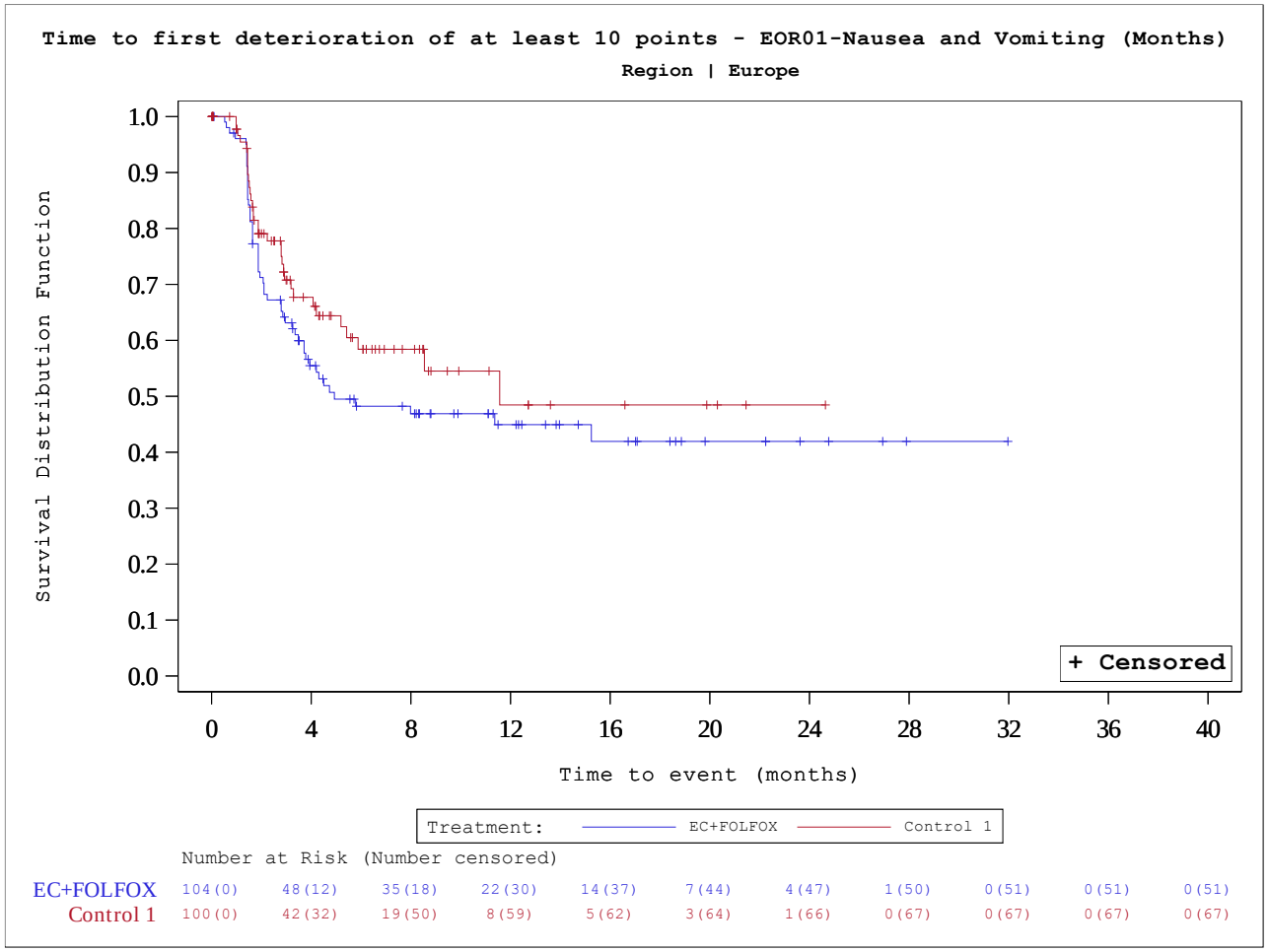
Full Analysis Set



Kaplan-Meier Plots for subgroups only created if p-value for interaction < 0.05.

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Encorafenib (PF-07263896) Protocol C4221015
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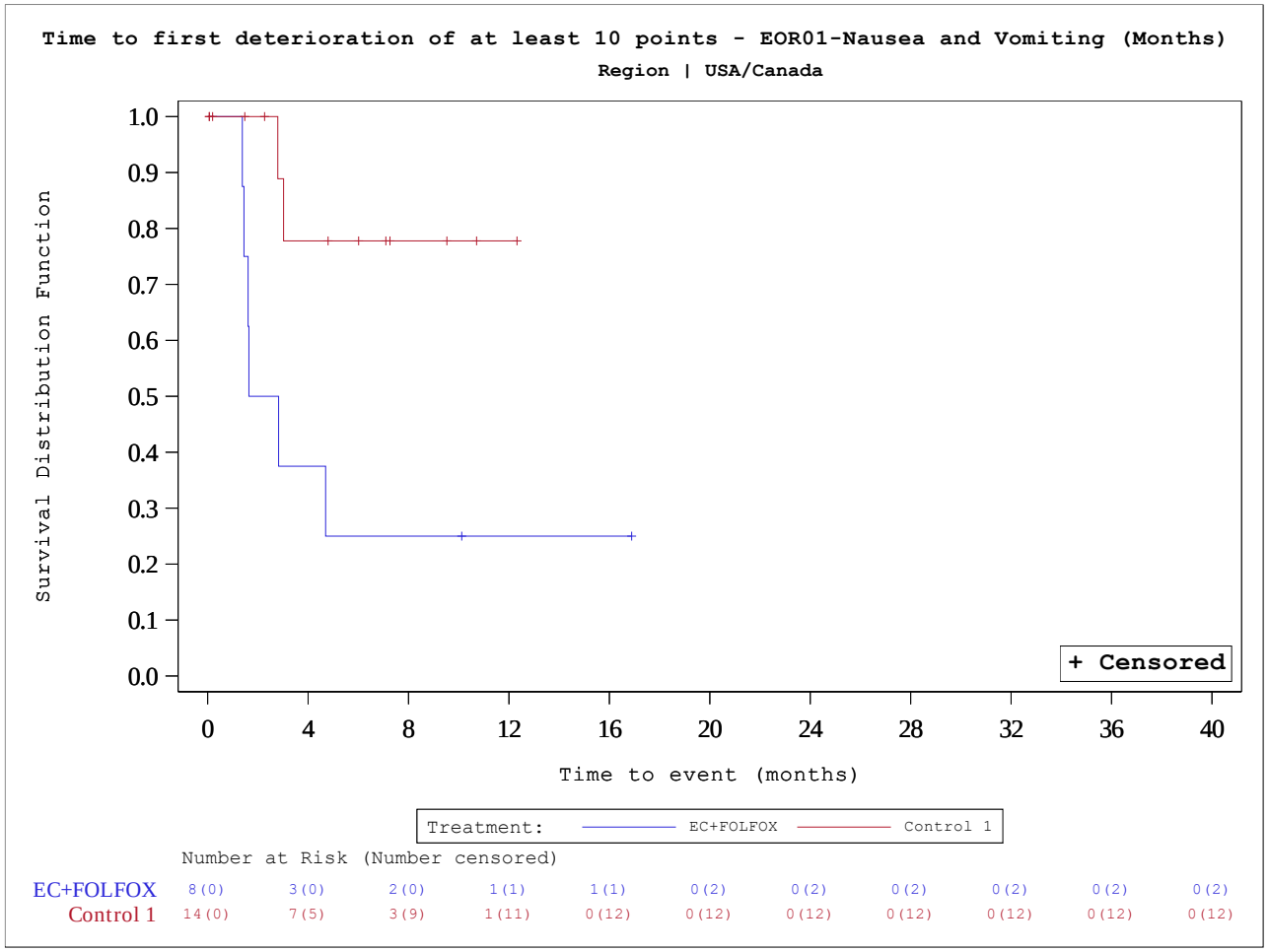

Kaplan-Meier Plots for subgroups only created if p-value for interaction < 0.05.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
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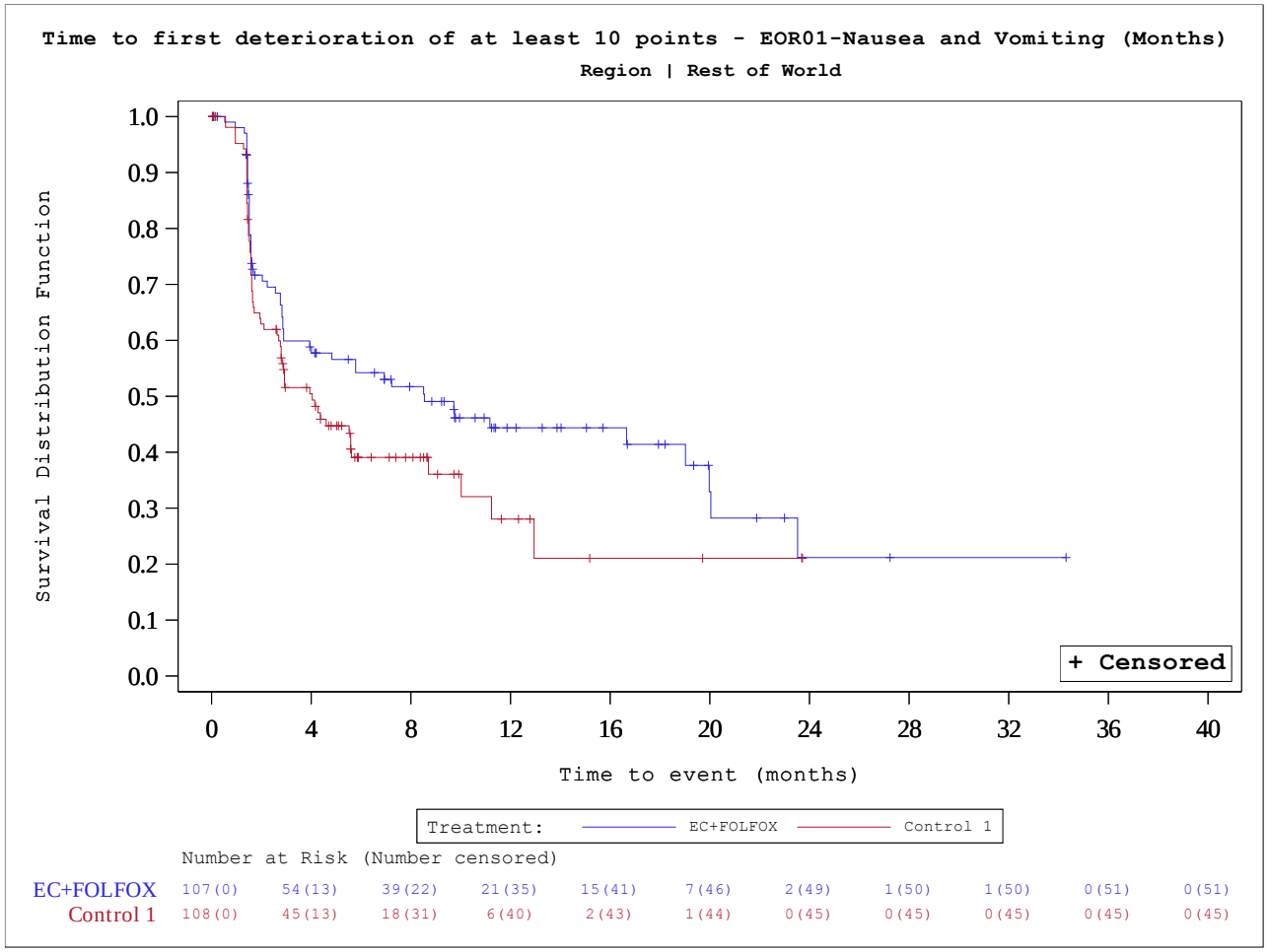
Full Analysis Set



Kaplan-Meier Plots for subgroups only created if p-value for interaction < 0.05.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Time to first improvement of at least 10 points - EOR01-Nausea and Vomiting (Months)
Full Analysis Set

	EC+FOLFOX (N=219)	Control 1 (N=222)
Number of subjects with events, n (%)	31 (14.2)	30 (13.5)
Number of censored subjects, n (%)	188 (85.8)	192 (86.5)
Kaplan-Meier estimates of Time to Event (Months) [1]		
25%-ile (95% CI)	NE (NE, NE)	NE (8.5, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
Stratified analysis [2]		
Hazard Ratio (95% CI) [3]	0.86 (0.52, 1.42)	
p-value [4]	0.5482	

[1] Based on the Brookmeyer and Crowley method.
[2] Stratified by ECOG PS by Randomization and Geographic Region by Randomization.
[3] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio > 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[4] P-value from 2-sided log-rank test.
Including only patients from the full analysis set who completed a baseline (last PRO assessment prior to or on the first dose of study treatment) and at least 1 post-baseline PRO assessment.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Time to first improvement of at least 10 points - EOR01-Nausea and Vomiting (Months) - Subgroup analysis
Full Analysis Set

Subgroup Level	EC+FOLFOX (N=219) n/ N (%)	EC+FOLFOX (N=219) Median (95% CI)[1]	Control 1 (N=222) n/ N (%)	Control 1 (N=222) Median (95% CI)[1]	Unstratified analysis Hazard Ratio (95% CI)[2]	Unstratified analysis p-Value[3]	Interaction p-Value[4]
Age (Years)							0.3124
< 65	25/ 139 (18.0)	NE (NE , NE)	19/ 127 (15.0)	NE (NE , NE)	0.98 (0.54, 1.79)	0.9583	
>= 65	6/ 80 (7.5)	NE (NE , NE)	11/ 95 (11.6)	NE (NE , NE)	0.52 (0.19, 1.41)	0.1916	
Sex							0.8888
Male	13/ 114 (11.4)	NE (NE , NE)	13/ 108 (12.0)	NE (NE , NE)	0.86 (0.40, 1.86)	0.6999	
Female	18/ 105 (17.1)	NE (NE , NE)	17/ 114 (14.9)	NE (NE , NE)	0.87 (0.45, 1.69)	0.6737	
Region							0.1883
Europe	14/ 104 (13.5)	NE (NE , NE)	6/ 100 (6.0)	NE (NE , NE)	1.84 (0.71, 4.79)	0.2042	
USA/Canada	1/ 8 (12.5)	NE (NE , NE)	0/ 14 (0.0)	NE (NE , NE)	NE		
Rest of World	16/ 107 (15.0)	NE (NE , NE)	24/ 108 (22.2)	NE (14.4, NE)	0.57 (0.30, 1.08)	0.0798	
ECOG-PS at Randomization							0.7865
0	15/ 123 (12.2)	NE (NE , NE)	14/ 124 (11.3)	NE (NE , NE)	0.91 (0.44, 1.90)	0.8125	
1	16/ 96 (16.7)	NE (NE , NE)	16/ 98 (16.3)	NE (NE , NE)	0.80 (0.40, 1.60)	0.5243	
Number of Organs Involved							0.1790
<= 2	14/ 110 (12.7)	NE (NE , NE)	19/ 115 (16.5)	NE (NE , NE)	0.60 (0.30, 1.21)	0.1494	
>= 3	17/ 109 (15.6)	NE (NE , NE)	11/ 107 (10.3)	NE (NE , NE)	1.30 (0.61, 2.78)	0.4975	
Presence of Liver Metastases							0.8017
Yes	18/ 135 (13.3)	NE (NE , NE)	19/ 142 (13.4)	NE (NE , NE)	0.82 (0.43, 1.57)	0.5516	
No	13/ 84 (15.5)	NE (NE , NE)	11/ 80 (13.8)	NE (NE , NE)	0.94 (0.42, 2.10)	0.8748	
Side of Tumor							0.3715
Left	13/ 83 (15.7)	NE (NE , NE)	9/ 86 (10.5)	NE (NE , NE)	1.24 (0.53, 2.90)	0.6236	
Right	18/ 136 (13.2)	NE (NE , NE)	21/ 136 (15.4)	NE (NE , NE)	0.71 (0.38, 1.34)	0.2879	

[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio > 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.
[4] P-Value for interaction from Cox proportional hazards model using ties=exact option with treatment, subgroup and treatment*subgroup interaction as covariates.
Including only patients from the full analysis set who completed a baseline (last PRO assessment prior to or on the first dose of study treatment) and at least 1 post-baseline PRO assessment.
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Pierre Fabre Pharma GmbH: Final
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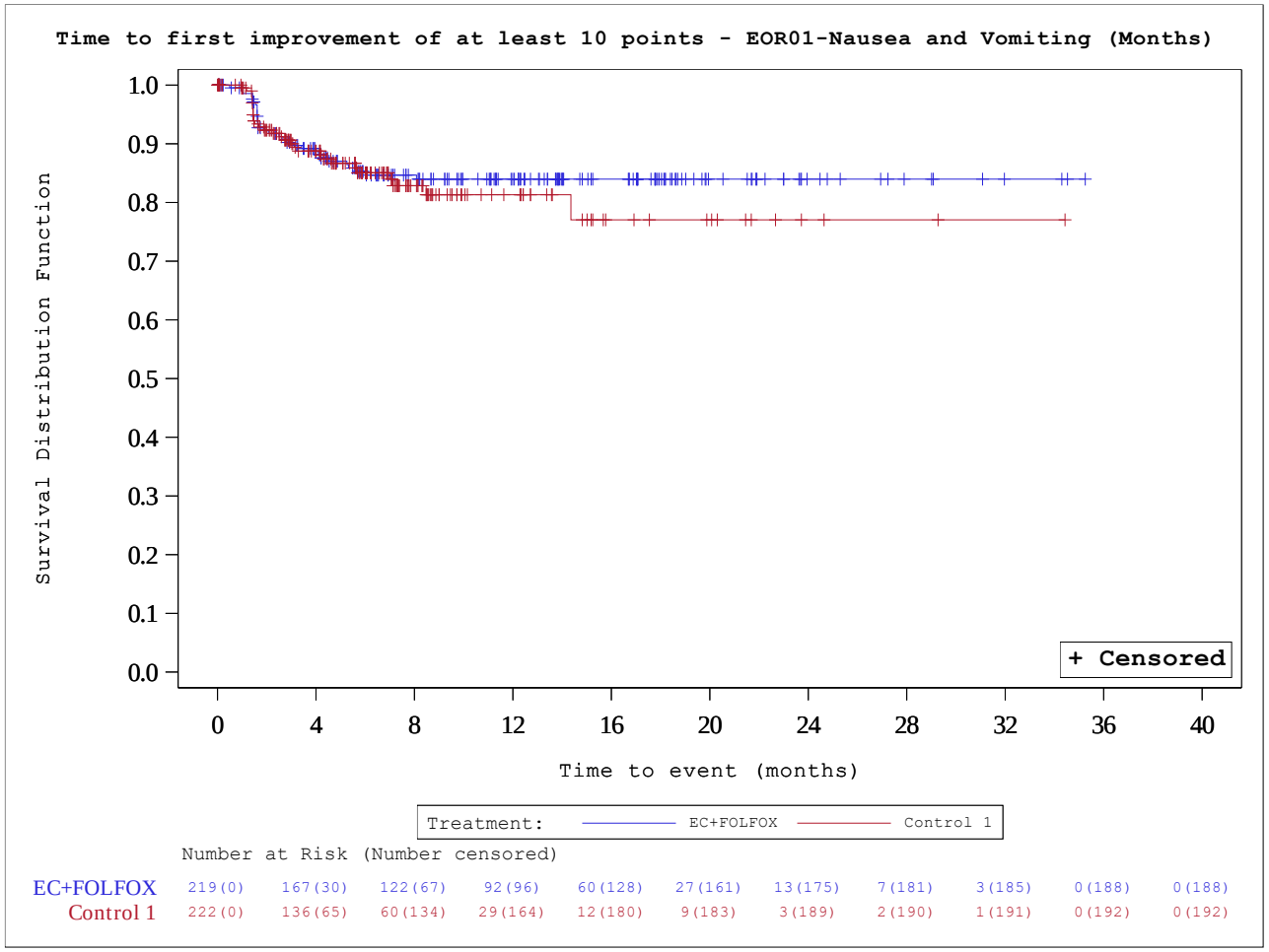
Kaplan Meier Plot of Time to first improvement of at least 10 points - EOR01-Nausea and Vomiting (Months)
Full Analysis Set



Kaplan-Meier Plots for subgroups only created if p-value for interaction < 0.05.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Time to first deterioration of at least 10 points - EOR01-Pain (Months)
Full Analysis Set

	EC+FOLFOX (N=219)	Control 1 (N=222)
Number of subjects with events, n (%)	125 (57.1)	93 (41.9)
Number of censored subjects, n (%)	94 (42.9)	129 (58.1)
Kaplan-Meier estimates of Time to Event (Months) [1]		
25%-ile (95% CI)	2.9 (2.6, 3.9)	2.9 (2.1, 4.0)
Median (95% CI)	8.1 (6.4, 9.9)	7.2 (5.6, 13.6)
75%-ile (95% CI)	20.5 (16.7, NE)	NE (NE, NE)
Stratified analysis [2]		
Hazard Ratio (95% CI) [3]	0.99 (0.75, 1.30)	
p-value [4]	0.9366	

[1] Based on the Brookmeyer and Crowley method.
[2] Stratified by ECOG PS by Randomization and Geographic Region by Randomization.
[3] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[4] P-value from 2-sided log-rank test.
Including only patients from the full analysis set who completed a baseline (last PRO assessment prior to or on the first dose of study treatment) and at least 1 post-baseline PRO assessment.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Time to first deterioration of at least 10 points - EOR01-Pain (Months) - Subgroup analysis
Full Analysis Set

Subgroup Level	EC+FOLFOX (N=219) n/ N (%)	EC+FOLFOX (N=219) Median (95% CI)[1]	Control 1 (N=222) n/ N (%)	Control 1 (N=222) Median (95% CI)[1]	Unstratified analysis Hazard Ratio (95% CI)[2]	Unstratified analysis p-Value[3]	Interaction p-Value[4]
Age (Years)							0.6300
< 65	79/ 139 (56.8)	8.3 (6.4, 11.2)	50/ 127 (39.4)	7.2 (5.8, NE)	1.08 (0.76, 1.55)	0.6701	
>= 65	46/ 80 (57.5)	7.8 (4.2, 11.3)	43/ 95 (45.3)	7.6 (4.4, 13.6)	0.98 (0.64, 1.49)	0.9224	
Sex							0.1090
Male	64/ 114 (56.1)	7.5 (5.6, 9.7)	42/ 108 (38.9)	7.7 (5.9, NE)	1.27 (0.86, 1.88)	0.2332	
Female	61/ 105 (58.1)	8.8 (5.8, 13.7)	51/ 114 (44.7)	5.8 (4.2, 9.6)	0.84 (0.57, 1.22)	0.3613	
Region							0.5334
Europe	61/ 104 (58.7)	8.3 (7.3, 11.1)	40/ 100 (40.0)	7.0 (5.3, 13.6)	0.94 (0.63, 1.41)	0.7627	
USA/Canada	5/ 8 (62.5)	3.8 (1.6, NE)	3/ 14 (21.4)	NE (2.8, NE)	2.30 (0.55, 9.66)	0.2413	
Rest of World	59/ 107 (55.1)	8.0 (5.5, 14.8)	50/ 108 (46.3)	7.1 (5.3, NE)	1.01 (0.69, 1.48)	0.9503	
ECOG-PS at Randomization							0.3046
0	72/ 123 (58.5)	7.8 (5.7, 11.1)	48/ 124 (38.7)	8.5 (5.9, NE)	1.18 (0.81, 1.70)	0.3847	
1	53/ 96 (55.2)	8.8 (5.6, 13.4)	45/ 98 (45.9)	5.6 (4.4, 9.6)	0.87 (0.58, 1.30)	0.4931	
Number of Organs Involved							0.6936
<= 2	75/ 110 (68.2)	5.7 (4.2, 8.3)	55/ 115 (47.8)	6.9 (4.5, 13.6)	1.12 (0.79, 1.59)	0.5249	
>= 3	50/ 109 (45.9)	11.0 (7.8, 16.7)	38/ 107 (35.5)	8.5 (5.9, NE)	0.93 (0.61, 1.43)	0.7532	
Presence of Liver Metastases							0.4560
Yes	72/ 135 (53.3)	9.6 (7.3, 11.7)	59/ 142 (41.5)	7.1 (5.6, NE)	0.94 (0.66, 1.33)	0.7228	
No	53/ 84 (63.1)	6.4 (4.2, 9.9)	34/ 80 (42.5)	7.6 (5.3, NE)	1.22 (0.79, 1.88)	0.3791	
Side of Tumor							0.3849
Left	44/ 83 (53.0)	8.3 (6.9, 14.1)	36/ 86 (41.9)	6.9 (5.2, NE)	0.87 (0.56, 1.36)	0.5354	
Right	81/ 136 (59.6)	8.0 (5.6, 9.9)	57/ 136 (41.9)	8.3 (5.6, NE)	1.13 (0.80, 1.59)	0.4799	

[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.
[4] P-Value for interaction from Cox proportional hazards model using ties=exact option with treatment, subgroup and treatment*subgroup interaction as covariates.
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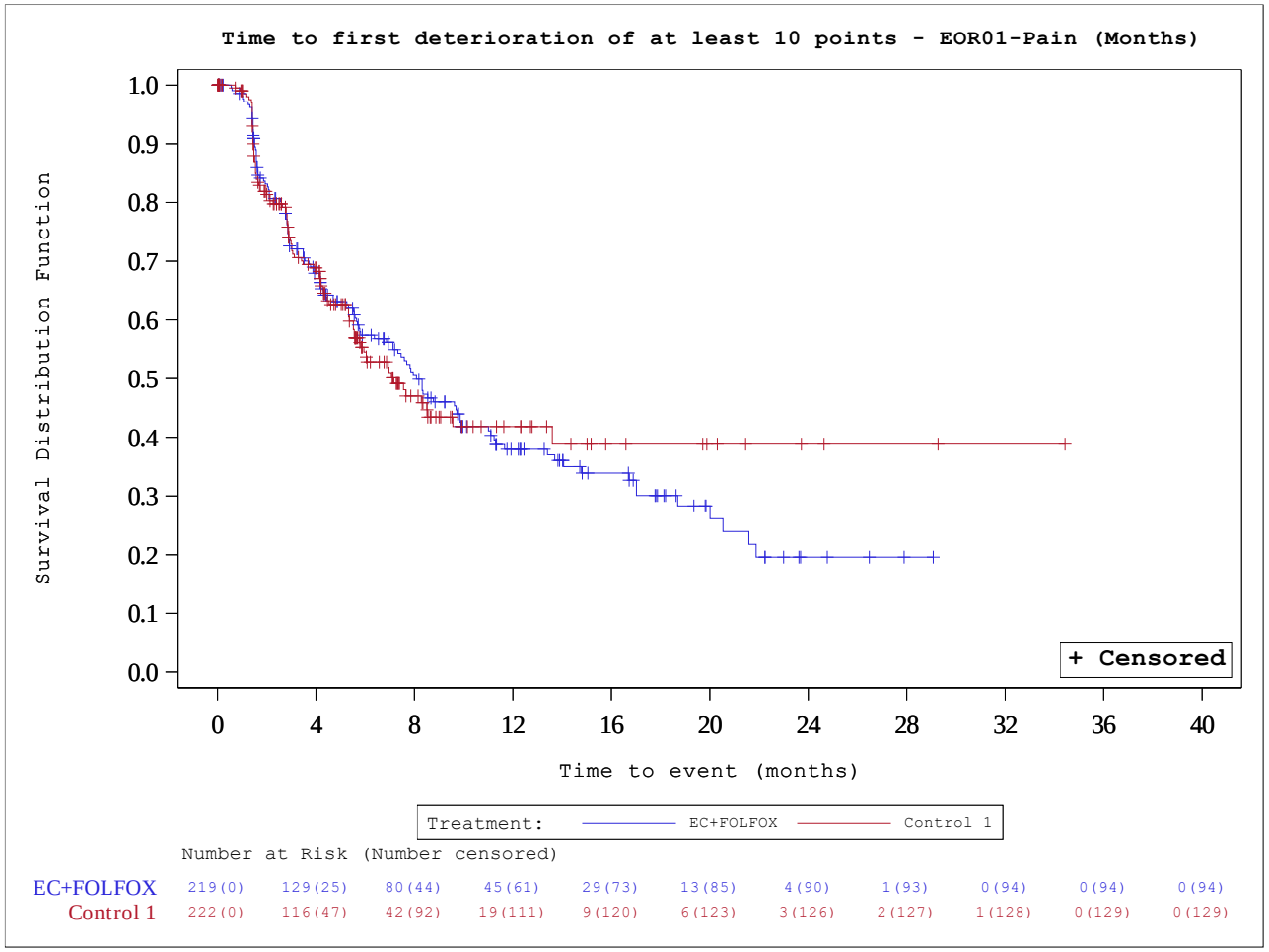
Kaplan Meier Plot of Time to first deterioration of at least 10 points - EOR01-Pain (Months)
Full Analysis Set



Kaplan-Meier Plots for subgroups only created if p-value for interaction < 0.05.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
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Time to first improvement of at least 10 points - EOR01-Pain (Months)
Full Analysis Set

	EC+FOLFOX (N=219)	Control 1 (N=222)
Number of subjects with events, n (%)	104 (47.5)	75 (33.8)
Number of censored subjects, n (%)	115 (52.5)	147 (66.2)
Kaplan-Meier estimates of Time to Event (Months) [1]		
25%-ile (95% CI)	1.6 (1.5, 1.6)	1.9 (1.6, 3.0)
Median (95% CI)	8.3 (3.3, NE)	NE (8.2, NE)
75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
Stratified analysis [2]		
Hazard Ratio (95% CI) [3]	1.36 (1.01, 1.83)	
p-value [4]	0.0427	

[1] Based on the Brookmeyer and Crowley method.
[2] Stratified by ECOG PS by Randomization and Geographic Region by Randomization.
[3] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio > 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[4] P-value from 2-sided log-rank test.
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Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
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Time to first improvement of at least 10 points - EOR01-Pain (Months) - Subgroup analysis
Full Analysis Set

Subgroup Level	EC+FOLFOX (N=219) n/ N (%)	EC+FOLFOX (N=219) Median (95% CI)[1]	Control 1 (N=222) n/ N (%)	Control 1 (N=222) Median (95% CI)[1]	Unstratified analysis Hazard Ratio (95% CI)[2]	Unstratified analysis p-Value[3]	Interaction p-Value[4]
Age (Years)							0.8841
< 65	74/ 139 (53.2)	4.2 (2.6, NE)	49/ 127 (38.6)	NE (4.2, NE)	1.32 (0.92, 1.89)	0.1343	
>= 65	30/ 80 (37.5)	NE (3.9, NE)	26/ 95 (27.4)	NE (8.4, NE)	1.39 (0.82, 2.36)	0.2146	
Sex							0.1799
Male	49/ 114 (43.0)	NE (3.1, NE)	41/ 108 (38.0)	NE (4.5, NE)	1.15 (0.76, 1.75)	0.4935	
Female	55/ 105 (52.4)	4.7 (2.8, NE)	34/ 114 (29.8)	NE (7.4, NE)	1.68 (1.09, 2.58)	0.0170	
Region							0.3973
Europe	54/ 104 (51.9)	4.2 (2.8, NE)	30/ 100 (30.0)	NE (8.2, NE)	1.67 (1.07, 2.61)	0.0231	
USA/Canada	3/ 8 (37.5)	NE (1.6, NE)	2/ 14 (14.3)	NE (NE , NE)	2.09 (0.35, 12.51)	0.4092	
Rest of World	47/ 107 (43.9)	10.3 (2.9, NE)	43/ 108 (39.8)	NE (4.5, NE)	1.11 (0.73, 1.68)	0.6356	
ECOG-PS at Randomization							0.2498
0	54/ 123 (43.9)	NE (3.5, NE)	44/ 124 (35.5)	NE (4.5, NE)	1.18 (0.79, 1.77)	0.4054	
1	50/ 96 (52.1)	3.9 (2.2, NE)	31/ 98 (31.6)	NE (7.4, NE)	1.65 (1.06, 2.59)	0.0270	
Number of Organs Involved							0.1549
<= 2	44/ 110 (40.0)	NE (8.3, NE)	40/ 115 (34.8)	NE (6.0, NE)	1.07 (0.70, 1.65)	0.7506	
>= 3	60/ 109 (55.0)	3.2 (1.7, 6.0)	35/ 107 (32.7)	NE (8.2, NE)	1.71 (1.13, 2.60)	0.0103	
Presence of Liver Metastases							0.7781
Yes	64/ 135 (47.4)	6.0 (3.1, NE)	46/ 142 (32.4)	NE (NE , NE)	1.44 (0.98, 2.10)	0.0602	
No	40/ 84 (47.6)	8.3 (2.8, NE)	29/ 80 (36.3)	NE (6.0, NE)	1.27 (0.79, 2.06)	0.3255	
Side of Tumor							0.0979
Left	45/ 83 (54.2)	3.1 (1.9, NE)	24/ 86 (27.9)	NE (NE , NE)	1.96 (1.19, 3.21)	0.0070	
Right	59/ 136 (43.4)	NE (4.0, NE)	51/ 136 (37.5)	NE (6.0, NE)	1.12 (0.77, 1.63)	0.5526	

[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio > 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.
[4] P-Value for interaction from Cox proportional hazards model using ties=exact option with treatment, subgroup and treatment*subgroup interaction as covariates.
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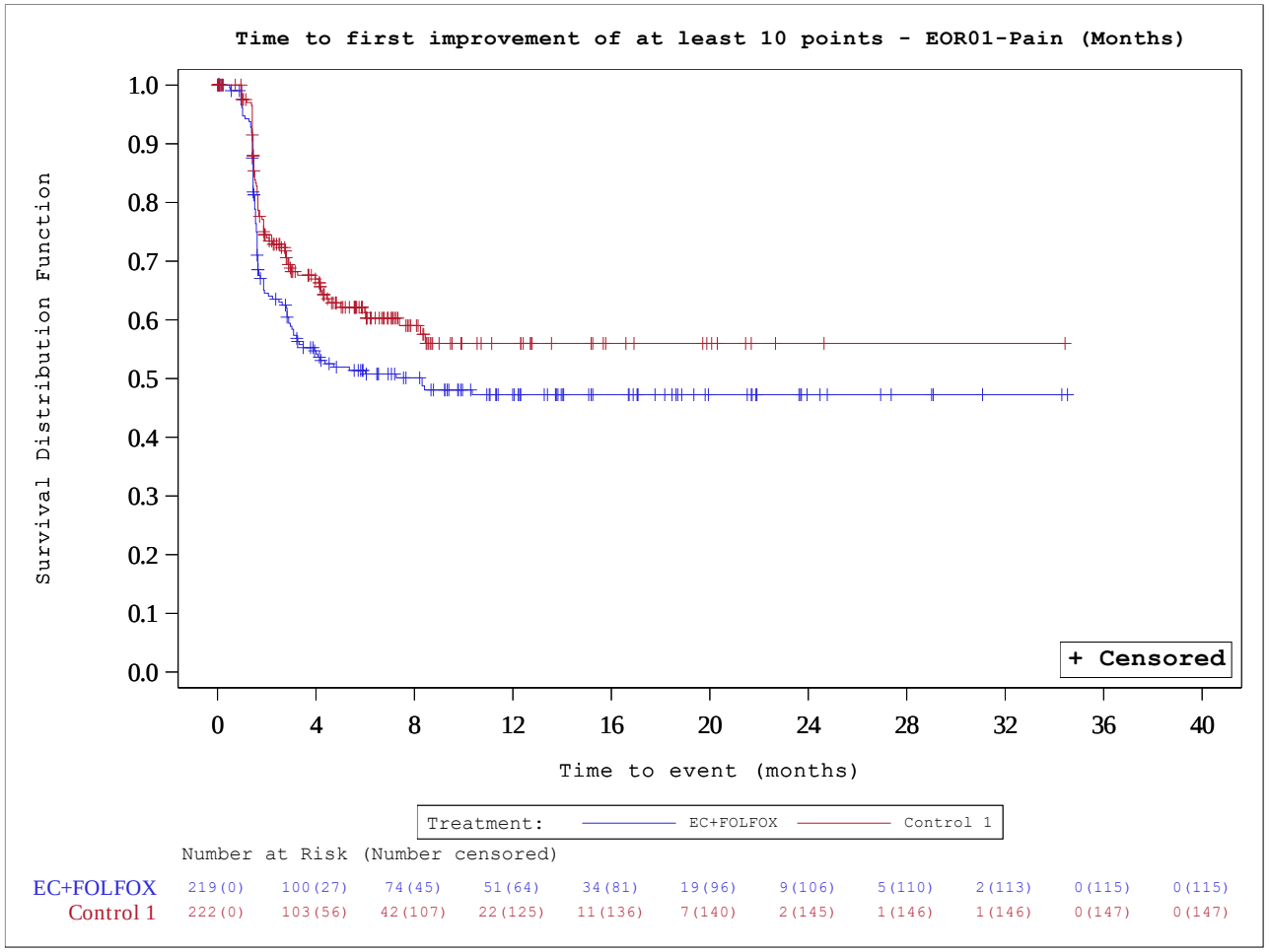

Kaplan-Meier Plots for subgroups only created if p-value for interaction < 0.05.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
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Time to first deterioration of at least 10 points - EOR01-Dyspnoea (Months)
Full Analysis Set

	EC+FOLFOX (N=219)	Control 1 (N=222)
Number of subjects with events, n (%)	103 (47.0)	67 (30.2)
Number of censored subjects, n (%)	116 (53.0)	155 (69.8)
Kaplan-Meier estimates of Time to Event (Months) [1]		
25%-ile (95% CI)	2.7 (1.9, 3.5)	2.9 (2.7, 5.6)
Median (95% CI)	12.2 (7.0, 19.8)	NE (11.2, NE)
75%-ile (95% CI)	29.8 (NE, NE)	NE (NE, NE)
Stratified analysis [2]		
Hazard Ratio (95% CI) [3]	1.27 (0.93, 1.73)	
p-value [4]	0.1394	

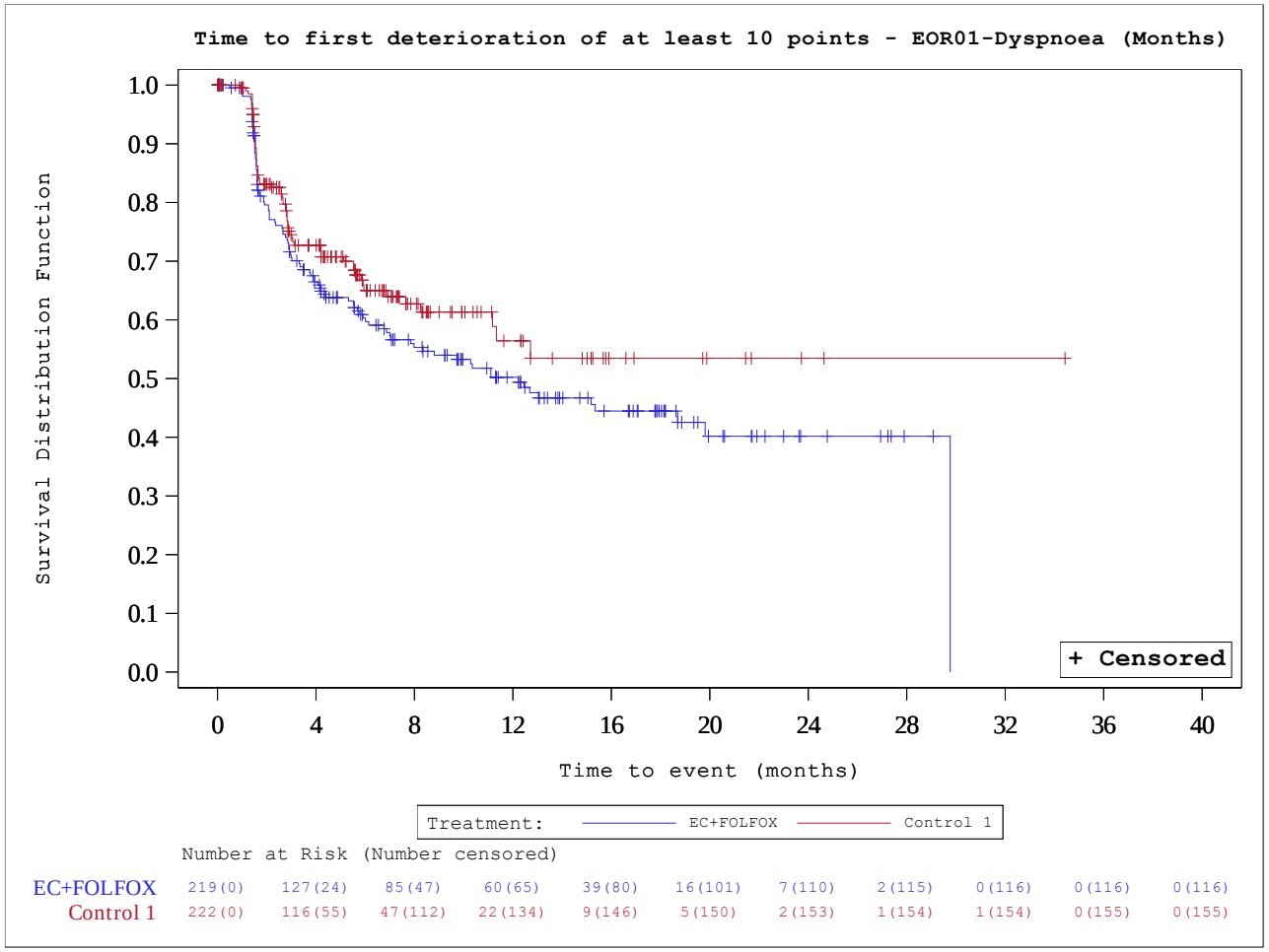
[1] Based on the Brookmeyer and Crowley method.
[2] Stratified by ECOG PS by Randomization and Geographic Region by Randomization.
[3] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[4] P-value from 2-sided log-rank test.
Including only patients from the full analysis set who completed a baseline (last PRO assessment prior to or on the first dose of study treatment) and at least 1 post-baseline PRO assessment.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Time to first deterioration of at least 10 points - EOR01-Dyspnoea (Months) - Subgroup analysis
Full Analysis Set

Subgroup Level	EC+FOLFOX (N=219) n/ N (%)	EC+FOLFOX (N=219) Median (95% CI)[1]	Control 1 (N=222) n/ N (%)	Control 1 (N=222) Median (95% CI)[1]	Unstratified analysis Hazard Ratio (95% CI)[2]	Unstratified analysis p-Value[3]	Interaction p-Value[4]
Age (Years)							0.2927
< 65	67/ 139 (48.2)	12.2 (6.9, 19.8)	42/ 127 (33.1)	NE (11.3, NE)	1.10 (0.74, 1.62)	0.6393	
>= 65	36/ 80 (45.0)	11.1 (3.9, NE)	25/ 95 (26.3)	NE (11.2, NE)	1.56 (0.93, 2.60)	0.0893	
Sex							0.2684
Male	55/ 114 (48.2)	12.2 (5.6, 29.8)	31/ 108 (28.7)	NE (NE , NE)	1.56 (1.00, 2.44)	0.0463	
Female	48/ 105 (45.7)	11.1 (7.0, NE)	36/ 114 (31.6)	12.7 (8.2, NE)	1.07 (0.69, 1.65)	0.7572	
Region							0.5130
Europe	52/ 104 (50.0)	12.5 (7.9, 19.8)	24/ 100 (24.0)	NE (11.2, NE)	1.45 (0.89, 2.37)	0.1363	
USA/Canada	4/ 8 (50.0)	12.2 (2.8, NE)	3/ 14 (21.4)	NE (2.6, NE)	1.45 (0.32, 6.52)	0.6286	
Rest of World	47/ 107 (43.9)	11.1 (5.3, NE)	40/ 108 (37.0)	NE (5.8, NE)	1.14 (0.74, 1.73)	0.5524	
ECOG-PS at Randomization							0.6327
0	63/ 123 (51.2)	8.3 (5.6, 19.8)	39/ 124 (31.5)	NE (6.9, NE)	1.39 (0.93, 2.08)	0.1029	
1	40/ 96 (41.7)	15.2 (8.8, NE)	28/ 98 (28.6)	12.7 (11.2, NE)	1.14 (0.70, 1.85)	0.6139	
Number of Organs Involved							0.1592
<= 2	51/ 110 (46.4)	15.3 (6.8, 29.8)	40/ 115 (34.8)	NE (5.8, NE)	1.12 (0.74, 1.70)	0.5938	
>= 3	52/ 109 (47.7)	10.3 (5.9, 18.7)	27/ 107 (25.2)	NE (11.2, NE)	1.58 (0.99, 2.52)	0.0520	
Presence of Liver Metastases							0.2742
Yes	63/ 135 (46.7)	11.1 (5.9, 29.8)	39/ 142 (27.5)	NE (12.7, NE)	1.48 (0.99, 2.21)	0.0538	
No	40/ 84 (47.6)	12.7 (6.1, NE)	28/ 80 (35.0)	11.3 (5.5, NE)	1.01 (0.62, 1.65)	0.9691	
Side of Tumor							0.2001
Left	44/ 83 (53.0)	9.7 (5.8, 18.7)	21/ 86 (24.4)	NE (11.3, NE)	1.58 (0.93, 2.68)	0.0864	
Right	59/ 136 (43.4)	15.2 (6.1, NE)	46/ 136 (33.8)	NE (6.9, NE)	1.12 (0.76, 1.65)	0.5574	

[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.
[4] P-Value for interaction from Cox proportional hazards model using ties=exact option with treatment, subgroup and treatment*subgroup interaction as covariates.
Including only patients from the full analysis set who completed a baseline (last PRO assessment prior to or on the first dose of study treatment) and at least 1 post-baseline PRO assessment.
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Kaplan Meier Plot of Time to first deterioration of at least 10 points - EOR01-Dyspnoea (Months)
Full Analysis Set



Kaplan-Meier Plots for subgroups only created if p-value for interaction < 0.05.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Time to first improvement of at least 10 points - EOR01-Dyspnoea (Months)
Full Analysis Set

	EC+FOLFOX (N=219)	Control 1 (N=222)
Number of subjects with events, n (%)	47 (21.5)	38 (17.1)
Number of censored subjects, n (%)	172 (78.5)	184 (82.9)
Kaplan-Meier estimates of Time to Event (Months) [1]		
25%-ile (95% CI)	NE (4.9, NE)	13.4 (5.6, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
Stratified analysis [2]		
Hazard Ratio (95% CI) [3]	1.02 (0.66, 1.57)	
p-value [4]	0.9298	

[1] Based on the Brookmeyer and Crowley method.
[2] Stratified by ECOG PS by Randomization and Geographic Region by Randomization.
[3] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio > 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[4] P-value from 2-sided log-rank test.
Including only patients from the full analysis set who completed a baseline (last PRO assessment prior to or on the first dose of study treatment) and at least 1 post-baseline PRO assessment.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Time to first improvement of at least 10 points - EOR01-Dyspnoea (Months) - Subgroup analysis
Full Analysis Set

Subgroup Level	EC+FOLFOX (N=219) n/ N (%)	EC+FOLFOX (N=219) Median (95% CI)[1]	Control 1 (N=222) n/ N (%)	Control 1 (N=222) Median (95% CI)[1]	Unstratified analysis Hazard Ratio (95% CI)[2]	Unstratified analysis p-Value[3]	Interaction p-Value[4]
Age (Years)							0.1220
< 65	33/ 139 (23.7)	NE (NE , NE)	18/ 127 (14.2)	NE (NE , NE)	1.39 (0.78, 2.48)	0.2549	
>= 65	14/ 80 (17.5)	NE (NE , NE)	20/ 95 (21.1)	NE (NE , NE)	0.65 (0.33, 1.30)	0.2236	
Sex							0.4787
Male	16/ 114 (14.0)	NE (NE , NE)	15/ 108 (13.9)	NE (NE , NE)	0.83 (0.41, 1.68)	0.6043	
Female	31/ 105 (29.5)	NE (NE , NE)	23/ 114 (20.2)	NE (NE , NE)	1.19 (0.69, 2.04)	0.5401	
Region							0.7418
Europe	24/ 104 (23.1)	NE (NE , NE)	14/ 100 (14.0)	NE (NE , NE)	1.17 (0.60, 2.28)	0.6373	
USA/Canada	1/ 8 (12.5)	NE (NE , NE)	1/ 14 (7.1)	NE (NE , NE)	1.06 (0.07, 16.98)	0.9668	
Rest of World	22/ 107 (20.6)	NE (NE , NE)	23/ 108 (21.3)	NE (NE , NE)	0.90 (0.50, 1.61)	0.7209	
ECOG-PS at Randomization							0.1005
0	18/ 123 (14.6)	NE (NE , NE)	21/ 124 (16.9)	NE (NE , NE)	0.69 (0.37, 1.30)	0.2491	
1	29/ 96 (30.2)	NE (NE , NE)	17/ 98 (17.3)	NE (NE , NE)	1.43 (0.78, 2.61)	0.2400	
Number of Organs Involved							0.2494
<= 2	19/ 110 (17.3)	NE (NE , NE)	21/ 115 (18.3)	NE (NE , NE)	0.80 (0.43, 1.49)	0.4741	
>= 3	28/ 109 (25.7)	NE (NE , NE)	17/ 107 (15.9)	NE (NE , NE)	1.28 (0.70, 2.34)	0.4267	
Presence of Liver Metastases							0.4849
Yes	30/ 135 (22.2)	NE (NE , NE)	27/ 142 (19.0)	NE (NE , NE)	0.93 (0.55, 1.57)	0.7932	
No	17/ 84 (20.2)	NE (NE , NE)	11/ 80 (13.8)	NE (13.4, NE)	1.23 (0.57, 2.64)	0.5913	
Side of Tumor							0.8248
Left	17/ 83 (20.5)	NE (NE , NE)	12/ 86 (14.0)	NE (NE , NE)	1.09 (0.52, 2.29)	0.8200	
Right	30/ 136 (22.1)	NE (NE , NE)	26/ 136 (19.1)	NE (NE , NE)	0.99 (0.59, 1.68)	0.9808	

[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio > 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.
[4] P-Value for interaction from Cox proportional hazards model using ties=exact option with treatment, subgroup and treatment*subgroup interaction as covariates.
Including only patients from the full analysis set who completed a baseline (last PRO assessment prior to or on the first dose of study treatment) and at least 1 post-baseline PRO assessment.
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
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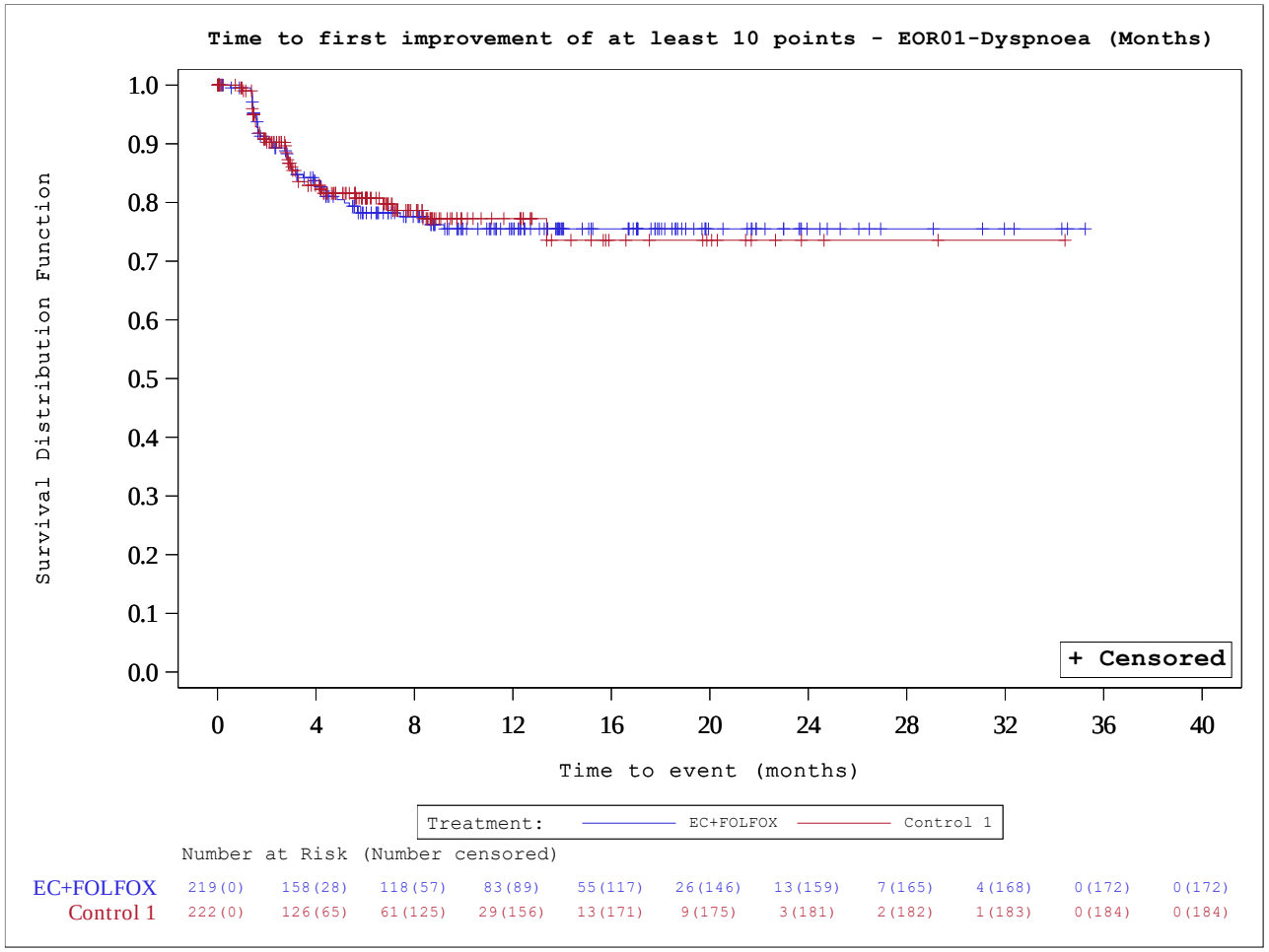
Datacut: 06JAN2025
Kaplan Meier Plot of Time to first improvement of at least 10 points - EOR01-Dyspnoea (Months)
Full Analysis Set



Kaplan-Meier Plots for subgroups only created if p-value for interaction < 0.05.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Time to first deterioration of at least 10 points - EOR01-Insomnia (Months)
Full Analysis Set

	EC+FOLFOX (N=219)	Control 1 (N=222)
Number of subjects with events, n (%)	97 (44.3)	78 (35.1)
Number of censored subjects, n (%)	122 (55.7)	144 (64.9)
Kaplan-Meier estimates of Time to Event (Months) [1]		
25%-ile (95% CI)	3.3 (2.8, 5.5)	3.1 (2.9, 4.9)
Median (95% CI)	17.1 (8.3, NE)	11.1 (7.2, NE)
75%-ile (95% CI)	29.8 (29.8, NE)	NE (NE, NE)
Stratified analysis [2]		
Hazard Ratio (95% CI) [3]	0.93 (0.69, 1.27)	
p-value [4]	0.6535	

[1] Based on the Brookmeyer and Crowley method.
[2] Stratified by ECOG PS by Randomization and Geographic Region by Randomization.
[3] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[4] P-value from 2-sided log-rank test.
Including only patients from the full analysis set who completed a baseline (last PRO assessment prior to or on the first dose of study treatment) and at least 1 post-baseline PRO assessment.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Time to first deterioration of at least 10 points - EOR01-Insomnia (Months) - Subgroup analysis
Full Analysis Set

Subgroup Level	EC+FOLFOX (N=219) n/ N (%)	EC+FOLFOX (N=219) Median (95% CI)[1]	Control 1 (N=222) n/ N (%)	Control 1 (N=222) Median (95% CI)[1]	Unstratified analysis Hazard Ratio (95% CI)[2]	Unstratified analysis p-Value[3]	Interaction p-Value[4]
Age (Years)							0.0892
< 65	55/ 139 (39.6)	29.8 (9.8, NE)	45/ 127 (35.4)	11.1 (7.0, NE)	0.75 (0.51, 1.13)	0.1640	
>= 65	42/ 80 (52.5)	7.2 (4.2, 19.0)	33/ 95 (34.7)	12.5 (5.6, NE)	1.31 (0.83, 2.08)	0.2432	
Sex							0.1535
Male	56/ 114 (49.1)	7.5 (5.8, 29.8)	40/ 108 (37.0)	11.1 (7.2, NE)	1.15 (0.76, 1.73)	0.5048	
Female	41/ 105 (39.0)	19.0 (11.4, NE)	38/ 114 (33.3)	11.3 (5.5, NE)	0.76 (0.49, 1.19)	0.2342	
Region							0.7150
Europe	46/ 104 (44.2)	17.1 (8.3, NE)	29/ 100 (29.0)	12.5 (7.0, NE)	0.98 (0.61, 1.57)	0.9235	
USA/Canada	4/ 8 (50.0)	NE (1.6, NE)	3/ 14 (21.4)	NE (6.0, NE)	1.85 (0.41, 8.27)	0.4153	
Rest of World	47/ 107 (43.9)	9.8 (6.9, NE)	46/ 108 (42.6)	8.7 (5.6, NE)	0.88 (0.58, 1.32)	0.5251	
ECOG-PS at Randomization							0.6825
0	56/ 123 (45.5)	17.1 (8.3, NE)	46/ 124 (37.1)	11.1 (6.1, NE)	0.87 (0.58, 1.29)	0.4807	
1	41/ 96 (42.7)	NE (5.7, NE)	32/ 98 (32.7)	8.7 (7.2, NE)	1.05 (0.66, 1.67)	0.8504	
Number of Organs Involved							0.1630
<= 2	63/ 110 (57.3)	7.1 (5.6, 17.1)	45/ 115 (39.1)	8.5 (5.7, NE)	1.13 (0.76, 1.66)	0.5514	
>= 3	34/ 109 (31.2)	NE (14.8, NE)	33/ 107 (30.8)	11.3 (7.2, NE)	0.74 (0.46, 1.21)	0.2259	
Presence of Liver Metastases							0.6769
Yes	60/ 135 (44.4)	14.8 (7.0, 29.8)	47/ 142 (33.1)	NE (6.9, NE)	1.01 (0.69, 1.48)	0.9684	
No	37/ 84 (44.0)	18.2 (7.1, NE)	31/ 80 (38.8)	8.7 (5.7, NE)	0.88 (0.54, 1.43)	0.6165	
Side of Tumor							0.3437
Left	36/ 83 (43.4)	17.1 (7.1, NE)	32/ 86 (37.2)	8.1 (5.7, NE)	0.77 (0.47, 1.25)	0.2853	
Right	61/ 136 (44.9)	14.8 (7.0, NE)	46/ 136 (33.8)	12.5 (7.0, NE)	1.06 (0.72, 1.56)	0.7631	

[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.
[4] P-Value for interaction from Cox proportional hazards model using ties=exact option with treatment, subgroup and treatment*subgroup interaction as covariates.
Including only patients from the full analysis set who completed a baseline (last PRO assessment prior to or on the first dose of study treatment) and at least 1 post-baseline PRO assessment.
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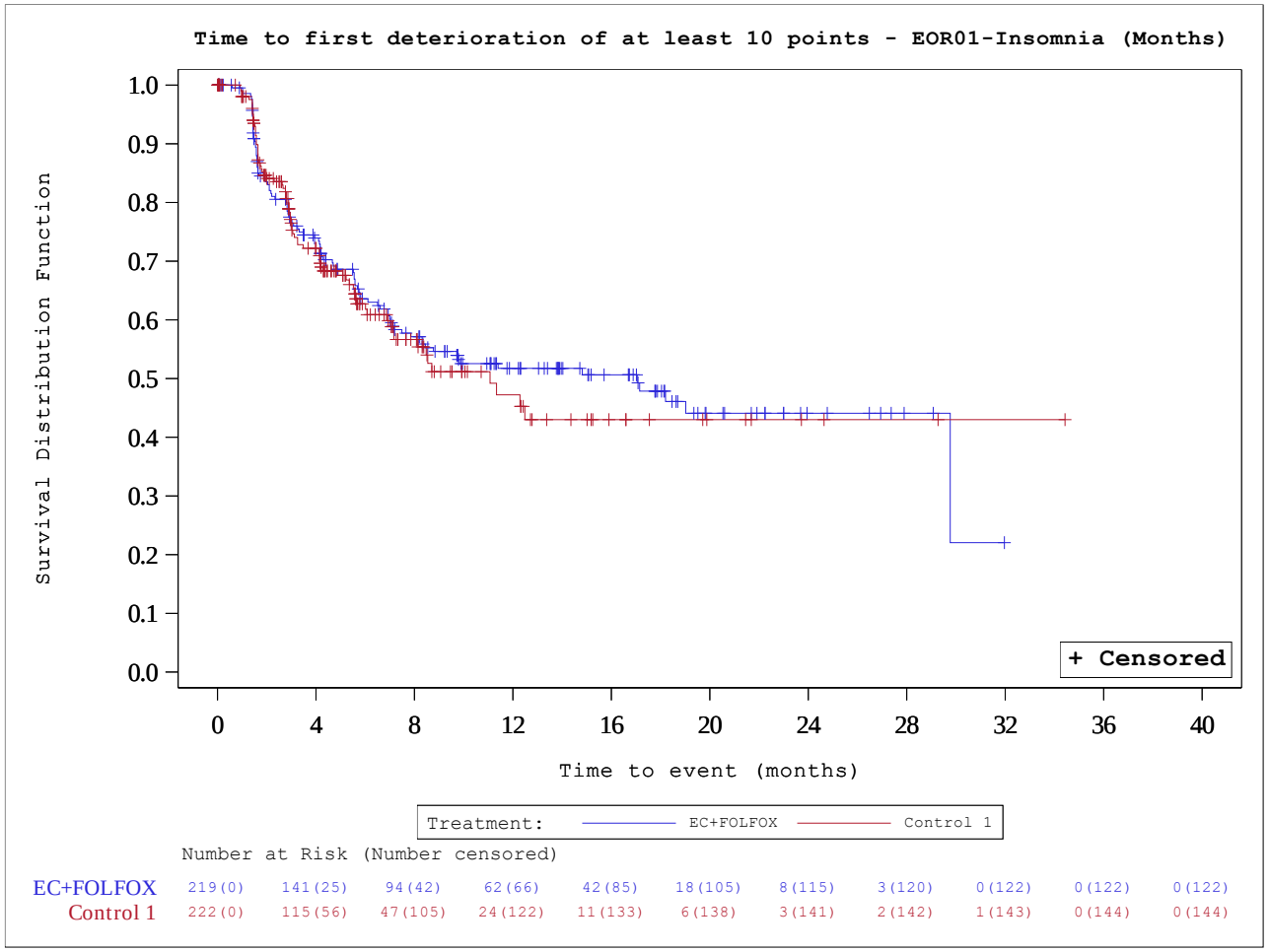
Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Kaplan Meier Plot of Time to first deterioration of at least 10 points - EOR01-Insomnia (Months)
Full Analysis Set



Kaplan-Meier Plots for subgroups only created if p-value for interaction < 0.05.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Time to first improvement of at least 10 points - EOR01-Insomnia (Months)
Full Analysis Set

	EC+FOLFOX (N=219)	Control 1 (N=222)
Number of subjects with events, n (%)	97 (44.3)	60 (27.0)
Number of censored subjects, n (%)	122 (55.7)	162 (73.0)
Kaplan-Meier estimates of Time to Event (Months) [1]		
25%-ile (95% CI)	2.1 (1.6, 3.1)	3.1 (1.9, 7.1)
Median (95% CI)	16.9 (7.1, NE)	NE (13.0, NE)
75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
Stratified analysis [2]		
Hazard Ratio (95% CI) [3]	1.45 (1.04, 2.01)	
p-value [4]	0.0255	

[1] Based on the Brookmeyer and Crowley method.
[2] Stratified by ECOG PS by Randomization and Geographic Region by Randomization.
[3] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio > 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[4] P-value from 2-sided log-rank test.
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Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Time to first improvement of at least 10 points - EOR01-Insomnia (Months) - Subgroup analysis
Full Analysis Set

Subgroup Level	EC+FOLFOX (N=219) n/ N (%)	EC+FOLFOX (N=219) Median (95% CI)[1]	Control 1 (N=222) n/ N (%)	Control 1 (N=222) Median (95% CI)[1]	Unstratified analysis Hazard Ratio (95% CI)[2]	Unstratified analysis p-Value[3]	Interaction p-Value[4]
Age (Years)							0.1396
< 65	71/ 139 (51.1)	7.1 (4.2, NE)	35/ 127 (27.6)	NE (12.9, NE)	1.67 (1.11, 2.50)	0.0128	
>= 65	26/ 80 (32.5)	NE (18.4, NE)	25/ 95 (26.3)	NE (NE , NE)	1.02 (0.58, 1.77)	0.9571	
Sex							0.1015
Male	42/ 114 (36.8)	NE (8.1, NE)	32/ 108 (29.6)	NE (NE , NE)	1.15 (0.72, 1.82)	0.5463	
Female	55/ 105 (52.4)	8.6 (4.2, 18.2)	28/ 114 (24.6)	NE (12.9, NE)	1.81 (1.14, 2.86)	0.0103	
Region							0.1243
Europe	50/ 104 (48.1)	10.4 (4.2, NE)	24/ 100 (24.0)	NE (NE , NE)	1.74 (1.07, 2.84)	0.0246	
USA/Canada	5/ 8 (62.5)	4.3 (3.0, NE)	1/ 14 (7.1)	NE (NE , NE)	8.95 (1.03, 77.47)	0.0166	
Rest of World	42/ 107 (39.3)	NE (8.1, NE)	35/ 108 (32.4)	13.0 (12.9, NE)	1.07 (0.68, 1.68)	0.7597	
ECOG-PS at Randomization							0.5716
0	51/ 123 (41.5)	NE (7.0, NE)	34/ 124 (27.4)	NE (12.9, NE)	1.33 (0.86, 2.06)	0.1993	
1	46/ 96 (47.9)	10.4 (4.2, NE)	26/ 98 (26.5)	NE (NE , NE)	1.54 (0.95, 2.50)	0.0780	
Number of Organs Involved							0.0305
<= 2	38/ 110 (34.5)	NE (NE , NE)	33/ 115 (28.7)	NE (12.9, NE)	0.99 (0.62, 1.59)	0.9787	
>= 3	59/ 109 (54.1)	5.4 (3.0, 10.9)	27/ 107 (25.2)	NE (NE , NE)	2.01 (1.27, 3.17)	0.0022	
Presence of Liver Metastases							0.6579
Yes	55/ 135 (40.7)	NE (7.1, NE)	38/ 142 (26.8)	NE (12.9, NE)	1.37 (0.90, 2.07)	0.1386	
No	42/ 84 (50.0)	10.9 (4.3, NE)	22/ 80 (27.5)	NE (13.0, NE)	1.52 (0.90, 2.57)	0.1104	
Side of Tumor							0.0916
Left	42/ 83 (50.6)	7.0 (3.7, NE)	19/ 86 (22.1)	NE (NE , NE)	2.11 (1.23, 3.64)	0.0060	
Right	55/ 136 (40.4)	18.2 (8.6, NE)	41/ 136 (30.1)	NE (12.9, NE)	1.14 (0.76, 1.71)	0.5339	

[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio > 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.
[4] P-Value for interaction from Cox proportional hazards model using ties=exact option with treatment, subgroup and treatment*subgroup interaction as covariates.
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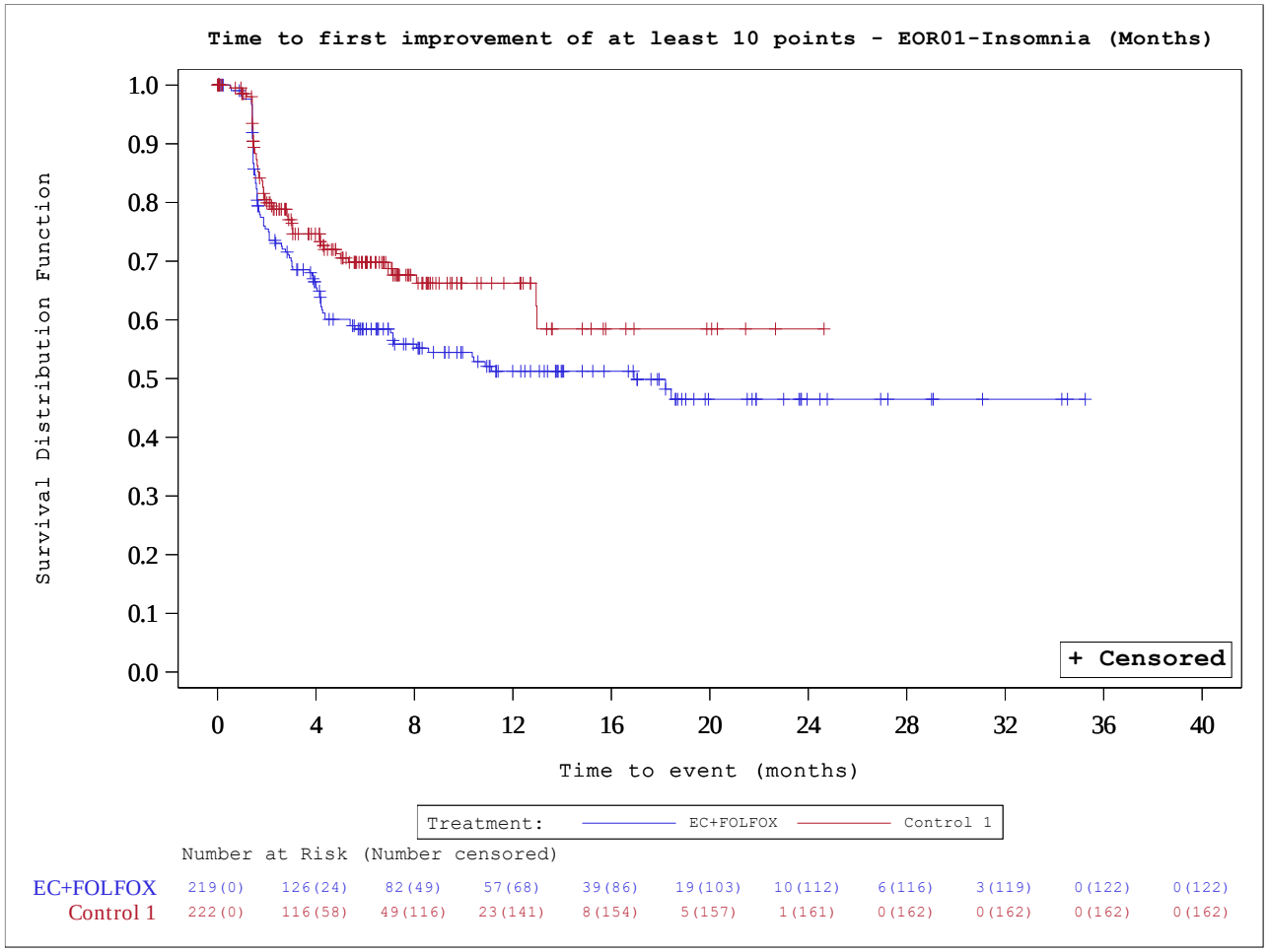

Kaplan-Meier Plots for subgroups only created if p-value for interaction < 0.05.

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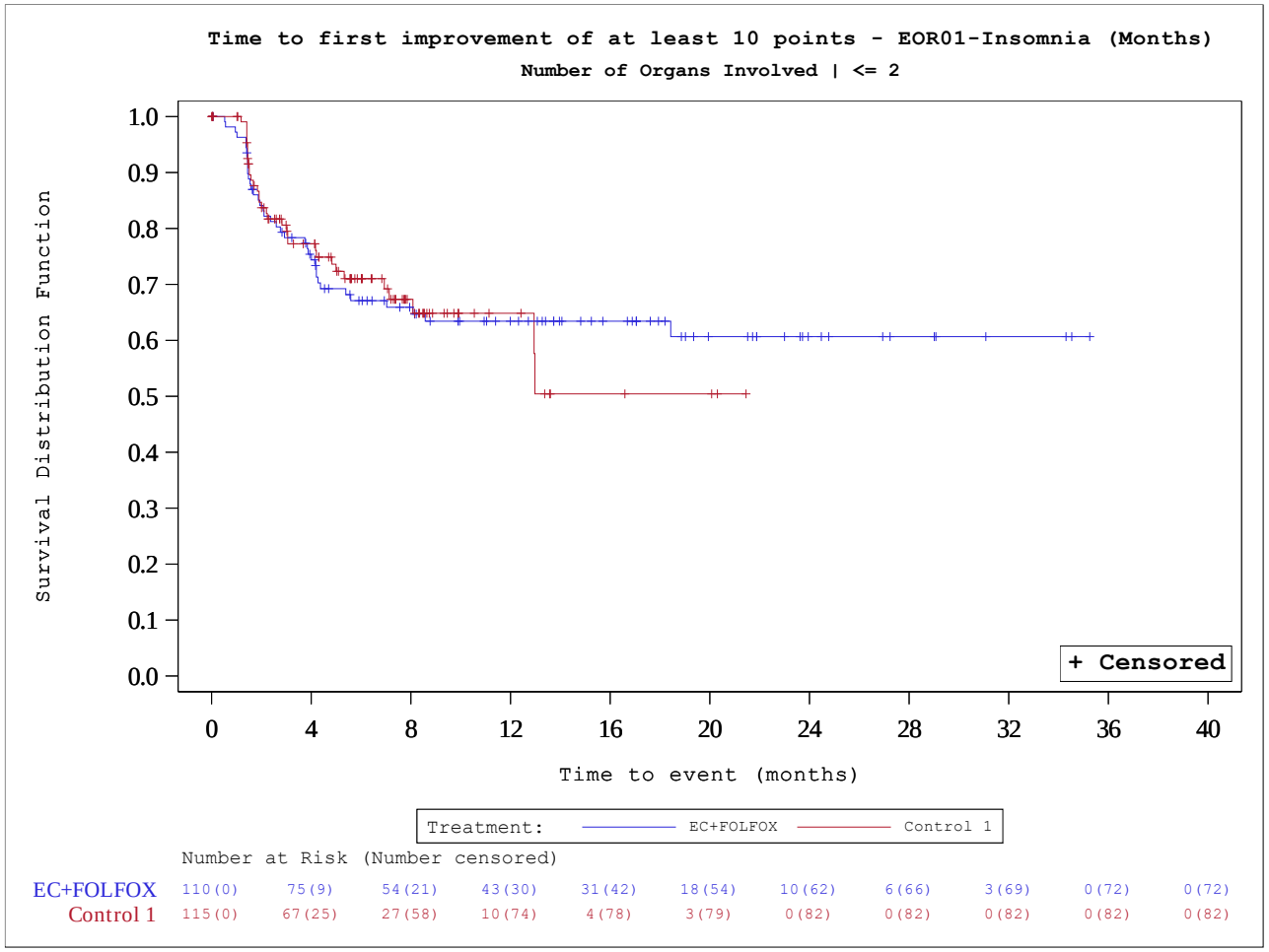
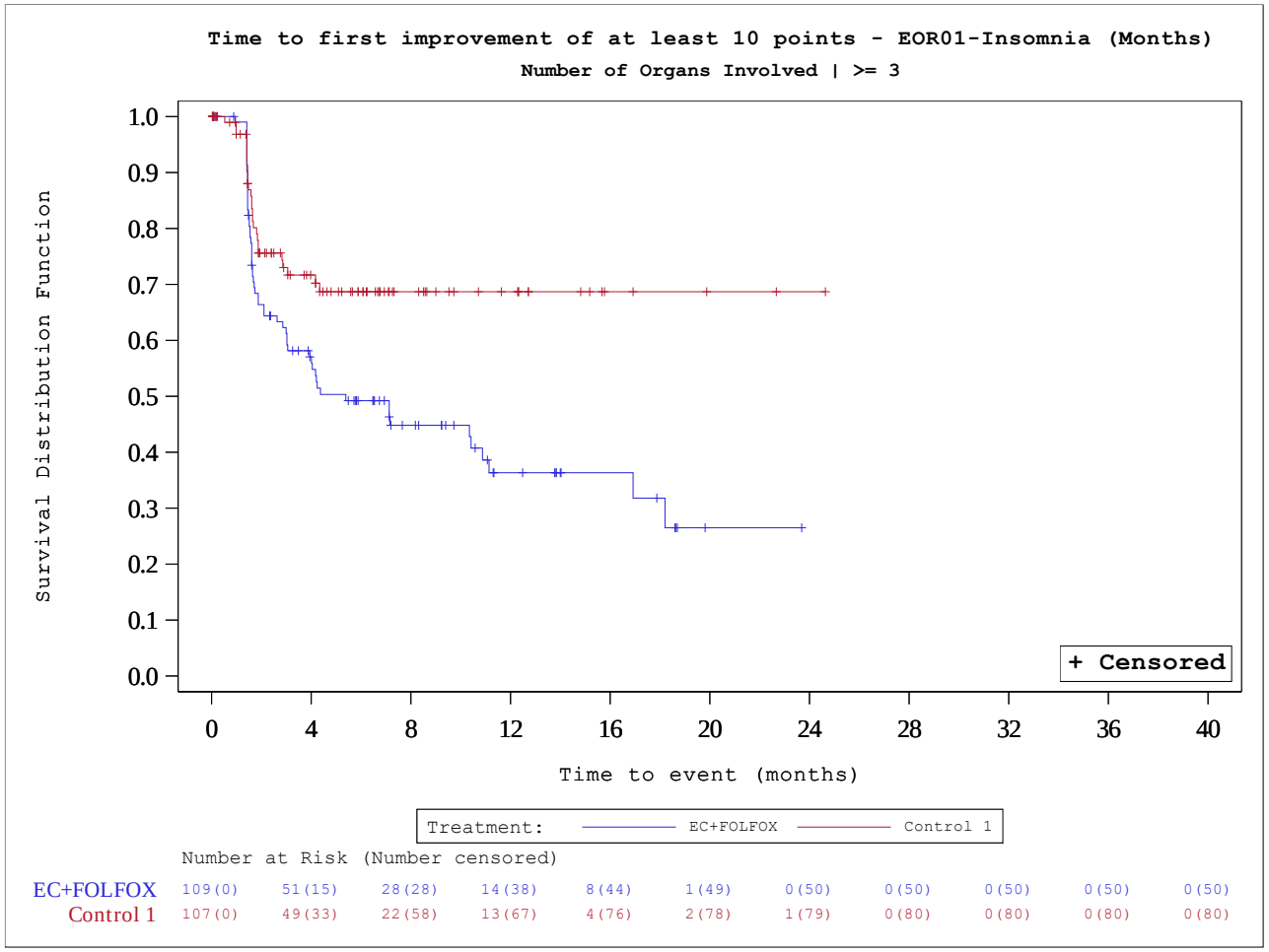
Population: arm B vs. arm C
Datacut: 06JAN2025
Kaplan Meier Plot of Time to first improvement of at least 10 points - EOR01-Insomnia (Months)
Full Analysis Set



Kaplan-Meier Plots for subgroups only created if p-value for interaction < 0.05.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Kaplan Meier Plot of Time to first improvement of at least 10 points - EOR01-Insomnia (Months)
Full Analysis Set



Kaplan-Meier Plots for subgroups only created if p-value for interaction < 0.05.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Time to first deterioration of at least 10 points - EOR01-Appetite Loss (Months)
Full Analysis Set

	EC+FOLFOX (N=219)	Control 1 (N=222)
Number of subjects with events, n (%)	128 (58.4)	101 (45.5)
Number of censored subjects, n (%)	91 (41.6)	121 (54.5)
Kaplan-Meier estimates of Time to Event (Months) [1]		
25%-ile (95% CI)	1.6 (1.5, 2.0)	1.7 (1.6, 2.8)
Median (95% CI)	4.4 (3.2, 6.9)	6.1 (5.1, 13.9)
75%-ile (95% CI)	NE (18.1, NE)	NE (15.2, NE)
Stratified analysis [2]		
Hazard Ratio (95% CI) [3]	1.13 (0.87, 1.48)	
p-value [4]	0.3457	

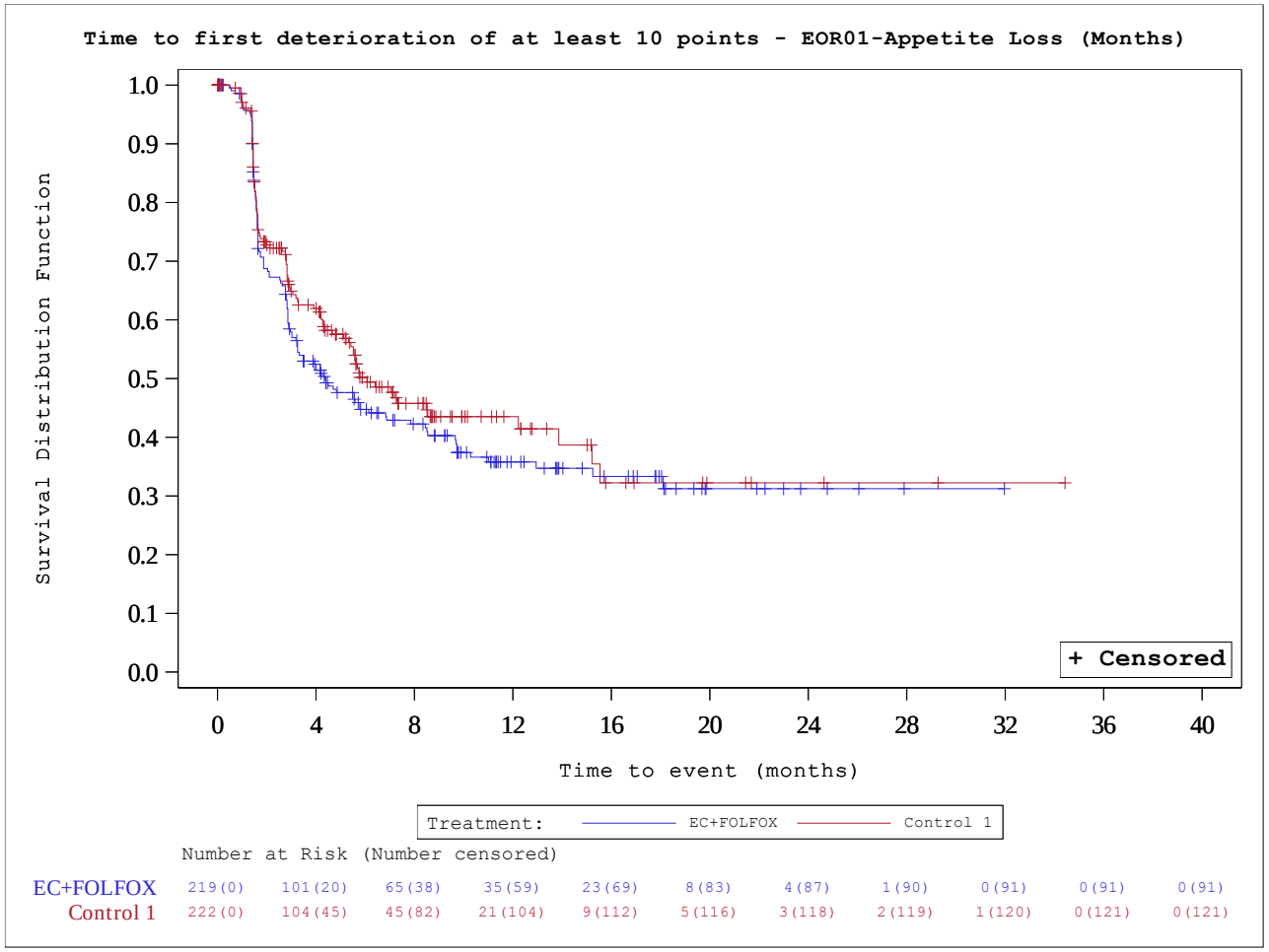
[1] Based on the Brookmeyer and Crowley method.
[2] Stratified by ECOG PS by Randomization and Geographic Region by Randomization.
[3] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[4] P-value from 2-sided log-rank test.
Including only patients from the full analysis set who completed a baseline (last PRO assessment prior to or on the first dose of study treatment) and at least 1 post-baseline PRO assessment.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Time to first deterioration of at least 10 points - EOR01-Appetite Loss (Months) - Subgroup analysis
Full Analysis Set

Subgroup Level	EC+FOLFOX (N=219) n/ N (%)	EC+FOLFOX (N=219) Median (95% CI)[1]	Control 1 (N=222) n/ N (%)	Control 1 (N=222) Median (95% CI)[1]	Unstratified analysis Hazard Ratio (95% CI)[2]	Unstratified analysis p-Value[3]	Interaction p-Value[4]
Age (Years)							0.1931
< 65	81/ 139 (58.3)	4.4 (2.9, 9.7)	52/ 127 (40.9)	8.5 (5.3, NE)	1.36 (0.96, 1.93)	0.0829	
>= 65	47/ 80 (58.8)	4.0 (2.9, 8.4)	49/ 95 (51.6)	5.6 (2.9, 8.5)	0.95 (0.63, 1.41)	0.7817	
Sex							0.8808
Male	65/ 114 (57.0)	4.4 (2.9, 9.7)	51/ 108 (47.2)	6.1 (5.1, NE)	1.19 (0.82, 1.71)	0.3642	
Female	63/ 105 (60.0)	4.4 (2.9, 8.5)	50/ 114 (43.9)	7.2 (3.3, 15.5)	1.14 (0.78, 1.65)	0.4982	
Region							0.1191
Europe	62/ 104 (59.6)	4.7 (3.0, 9.7)	38/ 100 (38.0)	8.5 (5.7, 15.5)	1.36 (0.91, 2.04)	0.1348	
USA/Canada	5/ 8 (62.5)	3.8 (1.6, NE)	2/ 14 (14.3)	NE (NE , NE)	3.82 (0.74, 19.76)	0.0853	
Rest of World	61/ 107 (57.0)	4.0 (2.9, 9.7)	61/ 108 (56.5)	4.7 (3.0, 6.4)	0.94 (0.66, 1.34)	0.7437	
ECOG-PS at Randomization							0.2212
0	72/ 123 (58.5)	4.0 (2.8, 9.7)	53/ 124 (42.7)	8.5 (5.5, NE)	1.34 (0.94, 1.91)	0.1056	
1	56/ 96 (58.3)	4.5 (3.3, 9.7)	48/ 98 (49.0)	5.3 (3.3, 12.2)	0.94 (0.64, 1.39)	0.7688	
Number of Organs Involved							0.3505
<= 2	71/ 110 (64.5)	3.3 (2.9, 5.8)	63/ 115 (54.8)	5.5 (3.1, 7.0)	1.06 (0.75, 1.49)	0.7437	
>= 3	57/ 109 (52.3)	6.8 (3.3, 11.0)	38/ 107 (35.5)	13.9 (5.8, NE)	1.34 (0.89, 2.03)	0.1556	
Presence of Liver Metastases							0.5258
Yes	73/ 135 (54.1)	5.6 (2.9, 12.9)	64/ 142 (45.1)	6.1 (4.2, 15.2)	1.09 (0.78, 1.52)	0.6222	
No	55/ 84 (65.5)	4.0 (2.9, 6.1)	37/ 80 (46.3)	5.8 (5.1, NE)	1.29 (0.85, 1.96)	0.2276	
Side of Tumor							0.8622
Left	45/ 83 (54.2)	4.7 (2.9, NE)	34/ 86 (39.5)	7.2 (5.5, NE)	1.21 (0.77, 1.89)	0.4044	
Right	83/ 136 (61.0)	4.2 (2.9, 6.8)	67/ 136 (49.3)	5.5 (3.3, 13.9)	1.14 (0.83, 1.58)	0.4236	

[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.
[4] P-Value for interaction from Cox proportional hazards model using ties=exact option with treatment, subgroup and treatment*subgroup interaction as covariates.
Including only patients from the full analysis set who completed a baseline (last PRO assessment prior to or on the first dose of study treatment) and at least 1 post-baseline PRO assessment.
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Kaplan Meier Plot of Time to first deterioration of at least 10 points - EOR01-Appetite Loss (Months)
Full Analysis Set



Kaplan-Meier Plots for subgroups only created if p-value for interaction < 0.05.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Time to first improvement of at least 10 points - EOR01-Appetite Loss (Months)
Full Analysis Set

	EC+FOLFOX (N=219)	Control 1 (N=222)
Number of subjects with events, n (%)	71 (32.4)	49 (22.1)
Number of censored subjects, n (%)	148 (67.6)	173 (77.9)
Kaplan-Meier estimates of Time to Event (Months) [1]		
25%-ile (95% CI)	4.4 (3.0, 8.3)	6.8 (3.2, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
Stratified analysis [2]		
Hazard Ratio (95% CI) [3]	1.16 (0.80, 1.68)	
p-value [4]	0.4222	

[1] Based on the Brookmeyer and Crowley method.
[2] Stratified by ECOG PS by Randomization and Geographic Region by Randomization.
[3] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio > 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[4] P-value from 2-sided log-rank test.
Including only patients from the full analysis set who completed a baseline (last PRO assessment prior to or on the first dose of study treatment) and at least 1 post-baseline PRO assessment.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Time to first improvement of at least 10 points - EOR01-Appetite Loss (Months) - Subgroup analysis
Full Analysis Set

Subgroup Level	EC+FOLFOX (N=219) n/ N (%)	EC+FOLFOX (N=219) Median (95% CI)[1]	Control 1 (N=222) n/ N (%)	Control 1 (N=222) Median (95% CI)[1]	Unstratified analysis Hazard Ratio (95% CI)[2]	Unstratified analysis p-Value[3]	Interaction p-Value[4]
Age (Years)							0.4030
< 65	49/ 139 (35.3)	NE (NE , NE)	34/ 127 (26.8)	NE (NE , NE)	1.07 (0.69, 1.65)	0.7760	
>= 65	22/ 80 (27.5)	NE (NE , NE)	15/ 95 (15.8)	NE (NE , NE)	1.31 (0.68, 2.55)	0.4211	
Sex							0.4500
Male	30/ 114 (26.3)	NE (NE , NE)	23/ 108 (21.3)	NE (NE , NE)	1.09 (0.63, 1.89)	0.7450	
Female	41/ 105 (39.0)	NE (8.5, NE)	26/ 114 (22.8)	NE (10.0, NE)	1.29 (0.78, 2.11)	0.3207	
Region							0.3695
Europe	33/ 104 (31.7)	NE (NE , NE)	15/ 100 (15.0)	NE (NE , NE)	1.54 (0.83, 2.84)	0.1655	
USA/Canada	3/ 8 (37.5)	NE (4.2, NE)	0/ 14 (0.0)	NE (NE , NE)	NE		
Rest of World	35/ 107 (32.7)	NE (11.2, NE)	34/ 108 (31.5)	NE (7.2, NE)	0.90 (0.56, 1.45)	0.6622	
ECOG-PS at Randomization							0.3043
0	34/ 123 (27.6)	NE (NE , NE)	28/ 124 (22.6)	NE (NE , NE)	1.01 (0.61, 1.67)	0.9725	
1	37/ 96 (38.5)	NE (8.5, NE)	21/ 98 (21.4)	NE (10.0, NE)	1.38 (0.80, 2.37)	0.2417	
Number of Organs Involved							0.8923
<= 2	29/ 110 (26.4)	NE (NE , NE)	22/ 115 (19.1)	NE (NE , NE)	1.11 (0.64, 1.95)	0.7064	
>= 3	42/ 109 (38.5)	NE (8.4, NE)	27/ 107 (25.2)	NE (NE , NE)	1.18 (0.73, 1.92)	0.4974	
Presence of Liver Metastases							0.7507
Yes	50/ 135 (37.0)	NE (9.8, NE)	34/ 142 (23.9)	NE (NE , NE)	1.22 (0.78, 1.89)	0.3809	
No	21/ 84 (25.0)	NE (NE , NE)	15/ 80 (18.8)	NE (NE , NE)	1.11 (0.57, 2.16)	0.7585	
Side of Tumor							0.8767
Left	30/ 83 (36.1)	NE (9.8, NE)	20/ 86 (23.3)	NE (NE , NE)	1.16 (0.65, 2.05)	0.6142	
Right	41/ 136 (30.1)	NE (NE , NE)	29/ 136 (21.3)	NE (NE , NE)	1.16 (0.72, 1.88)	0.5345	

[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio > 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.
[4] P-Value for interaction from Cox proportional hazards model using ties=exact option with treatment, subgroup and treatment*subgroup interaction as covariates.
Including only patients from the full analysis set who completed a baseline (last PRO assessment prior to or on the first dose of study treatment) and at least 1 post-baseline PRO assessment.
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Pierre Fabre Pharma GmbH: Final
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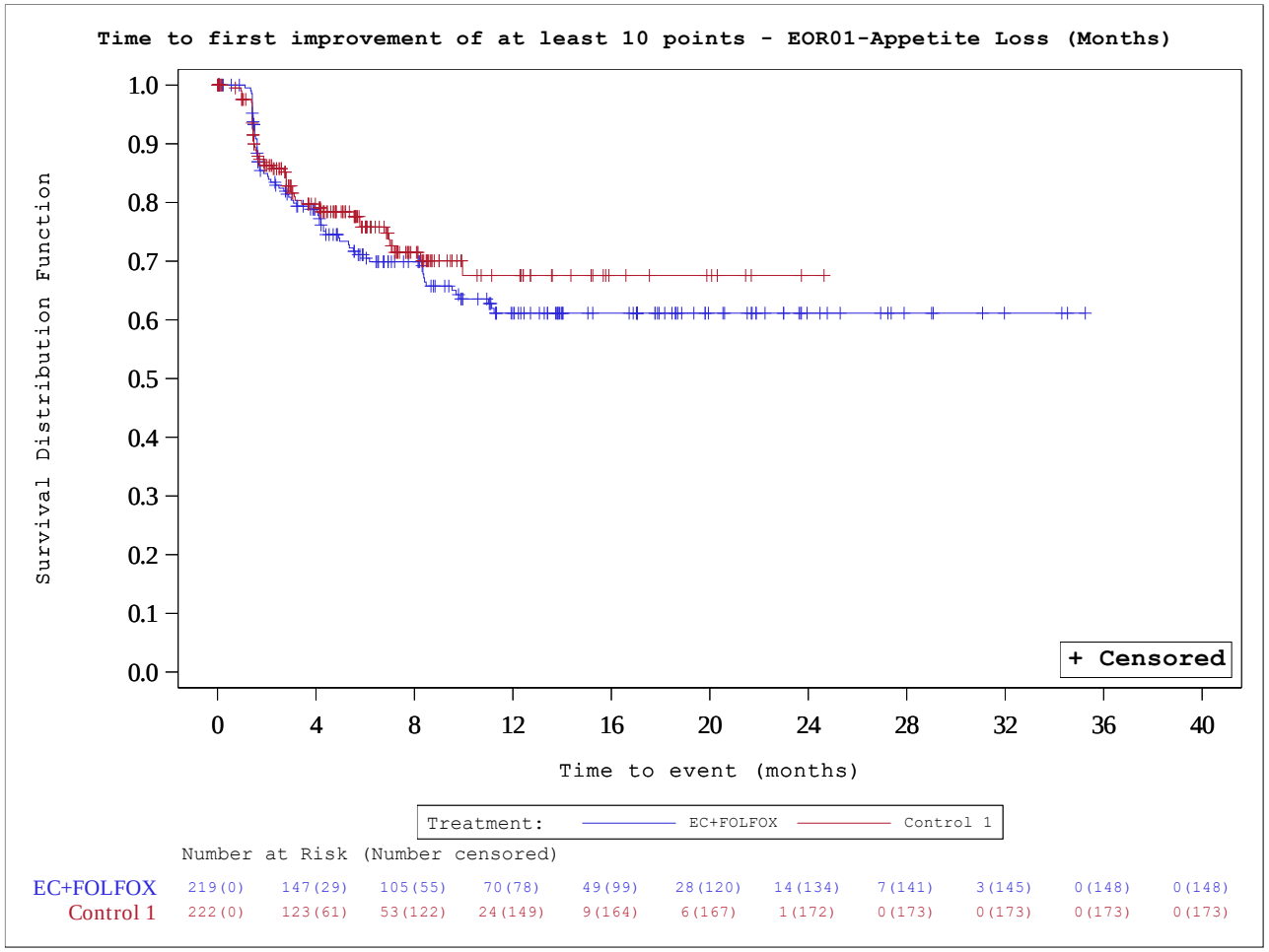
Full Analysis Set



Kaplan-Meier Plots for subgroups only created if p-value for interaction < 0.05.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Time to first deterioration of at least 10 points - EOR01-Constipation (Months)
Full Analysis Set

	EC+FOLFOX (N=219)	Control 1 (N=222)
Number of subjects with events, n (%)	96 (43.8)	71 (32.0)
Number of censored subjects, n (%)	123 (56.2)	151 (68.0)
Kaplan-Meier estimates of Time to Event (Months) [1]		
25%-ile (95% CI)	3.0 (2.2, 4.4)	4.2 (2.8, 5.6)
Median (95% CI)	16.7 (8.6, NE)	11.1 (7.2, NE)
75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
Stratified analysis [2]		
Hazard Ratio (95% CI) [3]	1.05 (0.77, 1.44)	
p-value [4]	0.7492	

[1] Based on the Brookmeyer and Crowley method.
[2] Stratified by ECOG PS by Randomization and Geographic Region by Randomization.
[3] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[4] P-value from 2-sided log-rank test.
Including only patients from the full analysis set who completed a baseline (last PRO assessment prior to or on the first dose of study treatment) and at least 1 post-baseline PRO assessment.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Time to first deterioration of at least 10 points - EOR01-Constipation (Months) - Subgroup analysis
Full Analysis Set

Subgroup Level	EC+FOLFOX (N=219) n/ N (%)	EC+FOLFOX (N=219) Median (95% CI)[1]	Control 1 (N=222) n/ N (%)	Control 1 (N=222) Median (95% CI)[1]	Unstratified analysis Hazard Ratio (95% CI)[2]	Unstratified analysis p-Value[3]	Interaction p-Value[4]
Age (Years)							0.8080
< 65	61/ 139 (43.9)	16.7 (9.2, NE)	38/ 127 (29.9)	NE (7.2, NE)	1.08 (0.72, 1.63)	0.7109	
>= 65	35/ 80 (43.8)	16.7 (5.6, NE)	33/ 95 (34.7)	9.3 (7.0, NE)	1.02 (0.63, 1.64)	0.9417	
Sex							0.3098
Male	49/ 114 (43.0)	16.7 (7.7, NE)	32/ 108 (29.6)	NE (9.3, NE)	1.22 (0.78, 1.91)	0.3920	
Female	47/ 105 (44.8)	16.7 (7.1, NE)	39/ 114 (34.2)	8.5 (5.8, NE)	0.89 (0.58, 1.37)	0.5910	
Region							0.5486
Europe	46/ 104 (44.2)	21.0 (7.7, NE)	25/ 100 (25.0)	NE (9.3, NE)	1.30 (0.79, 2.12)	0.2943	
USA/Canada	2/ 8 (25.0)	NE (5.6, NE)	2/ 14 (14.3)	NE (8.5, NE)	1.07 (0.15, 7.61)	0.9458	
Rest of World	48/ 107 (44.9)	16.7 (7.1, 20.5)	44/ 108 (40.7)	7.1 (5.6, NE)	0.87 (0.57, 1.32)	0.4978	
ECOG-PS at Randomization							0.4597
0	55/ 123 (44.7)	16.7 (8.5, NE)	38/ 124 (30.6)	NE (7.1, NE)	1.16 (0.76, 1.76)	0.5013	
1	41/ 96 (42.7)	12.7 (7.2, NE)	33/ 98 (33.7)	9.6 (6.9, NE)	0.90 (0.57, 1.44)	0.6666	
Number of Organs Involved							0.3697
<= 2	55/ 110 (50.0)	16.7 (5.6, NE)	46/ 115 (40.0)	7.2 (5.8, NE)	0.97 (0.65, 1.44)	0.8654	
>= 3	41/ 109 (37.6)	NE (9.2, NE)	25/ 107 (23.4)	NE (9.6, NE)	1.19 (0.72, 1.97)	0.4925	
Presence of Liver Metastases							0.8392
Yes	57/ 135 (42.2)	16.7 (8.5, NE)	44/ 142 (31.0)	NE (11.1, NE)	1.09 (0.73, 1.62)	0.6645	
No	39/ 84 (46.4)	16.7 (6.9, NE)	27/ 80 (33.8)	8.5 (7.0, NE)	0.97 (0.59, 1.61)	0.9231	
Side of Tumor							0.7959
Left	34/ 83 (41.0)	16.7 (7.7, NE)	24/ 86 (27.9)	NE (6.9, NE)	1.02 (0.60, 1.74)	0.9445	
Right	62/ 136 (45.6)	16.7 (7.2, 21.0)	47/ 136 (34.6)	11.1 (7.0, NE)	1.07 (0.73, 1.57)	0.7232	

[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.
[4] P-Value for interaction from Cox proportional hazards model using ties=exact option with treatment, subgroup and treatment*subgroup interaction as covariates.
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Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
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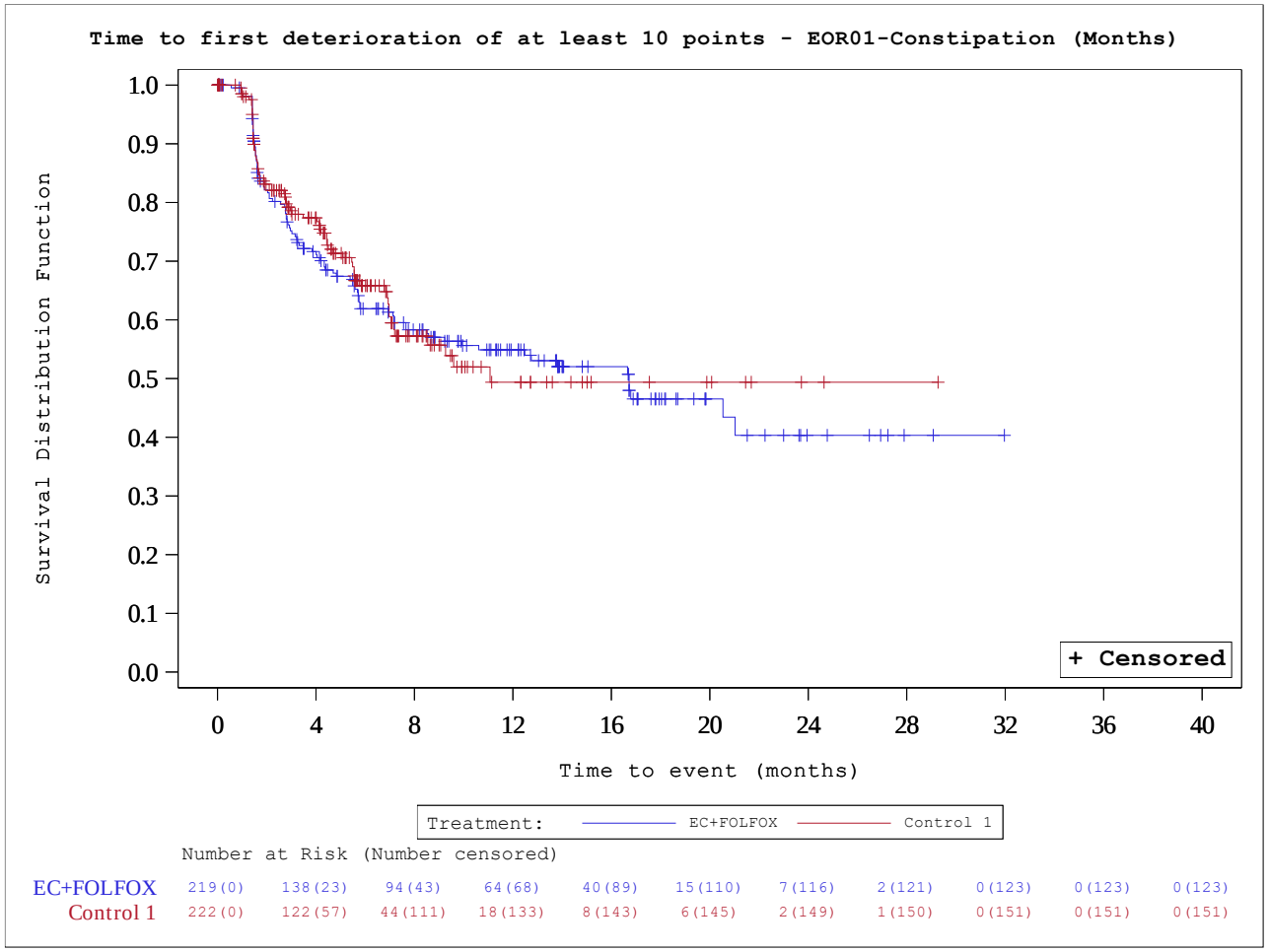
Kaplan Meier Plot of Time to first deterioration of at least 10 points - EOR01-Constipation (Months)
Full Analysis Set



Kaplan-Meier Plots for subgroups only created if p-value for interaction < 0.05.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Time to first improvement of at least 10 points - EOR01-Constipation (Months)
Full Analysis Set

	EC+FOLFOX (N=219)	Control 1 (N=222)
Number of subjects with events, n (%)	52 (23.7)	40 (18.0)
Number of censored subjects, n (%)	167 (76.3)	182 (82.0)
Kaplan-Meier estimates of Time to Event (Months) [1]		
25%-ile (95% CI)	8.9 (2.8, NE)	NE (4.2, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
Stratified analysis [2]		
Hazard Ratio (95% CI) [3]	1.14 (0.75, 1.73)	
p-value [4]	0.5323	

[1] Based on the Brookmeyer and Crowley method.
[2] Stratified by ECOG PS by Randomization and Geographic Region by Randomization.
[3] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio > 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[4] P-value from 2-sided log-rank test.
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Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
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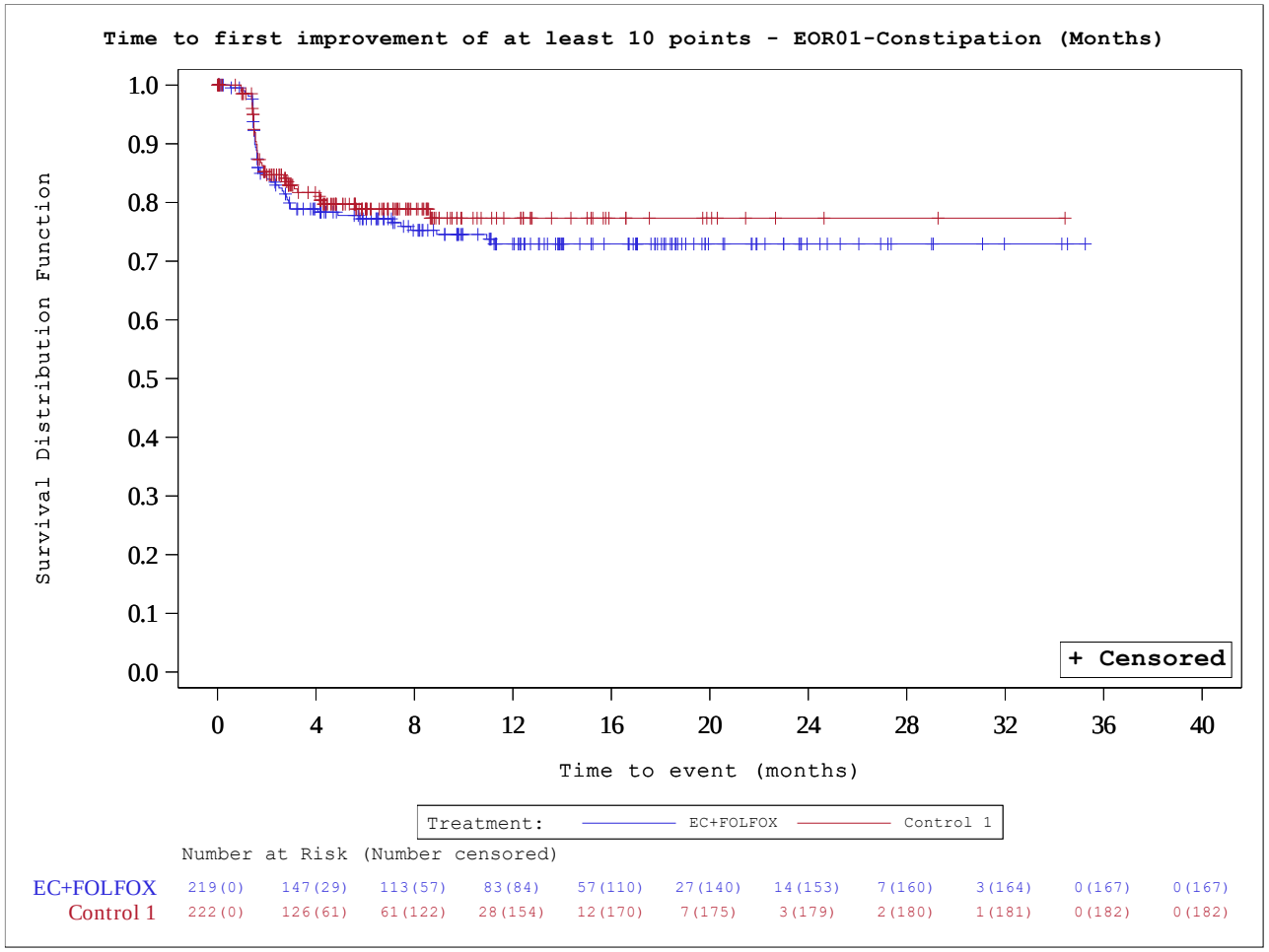
Time to first improvement of at least 10 points - EOR01-Constipation (Months) - Subgroup analysis
Full Analysis Set

Subgroup Level	EC+FOLFOX (N=219) n/ N (%)	EC+FOLFOX (N=219) Median (95% CI)[1]	Control 1 (N=222) n/ N (%)	Control 1 (N=222) Median (95% CI)[1]	Unstratified analysis Hazard Ratio (95% CI)[2]	Unstratified analysis p-Value[3]	Interaction p-Value[4]
Age (Years)							0.5883
< 65	37/ 139 (26.6)	NE (NE , NE)	24/ 127 (18.9)	NE (NE , NE)	1.21 (0.72, 2.04)	0.4626	
>= 65	15/ 80 (18.8)	NE (NE , NE)	16/ 95 (16.8)	NE (NE , NE)	1.01 (0.50, 2.05)	0.9679	
Sex							0.7061
Male	27/ 114 (23.7)	NE (NE , NE)	22/ 108 (20.4)	NE (NE , NE)	1.09 (0.62, 1.92)	0.7627	
Female	25/ 105 (23.8)	NE (NE , NE)	18/ 114 (15.8)	NE (NE , NE)	1.23 (0.67, 2.26)	0.5159	
Region							0.6132
Europe	24/ 104 (23.1)	NE (NE , NE)	14/ 100 (14.0)	NE (NE , NE)	1.33 (0.68, 2.57)	0.4009	
USA/Canada	3/ 8 (37.5)	NE (1.6, NE)	2/ 14 (14.3)	NE (NE , NE)	2.14 (0.36, 12.84)	0.3924	
Rest of World	25/ 107 (23.4)	NE (NE , NE)	24/ 108 (22.2)	NE (NE , NE)	0.98 (0.56, 1.73)	0.9502	
ECOG-PS at Randomization							0.1852
0	22/ 123 (17.9)	NE (NE , NE)	22/ 124 (17.7)	NE (NE , NE)	0.87 (0.48, 1.57)	0.6353	
1	30/ 96 (31.3)	NE (NE , NE)	18/ 98 (18.4)	NE (NE , NE)	1.52 (0.85, 2.74)	0.1549	
Number of Organs Involved							0.8021
<= 2	22/ 110 (20.0)	NE (NE , NE)	19/ 115 (16.5)	NE (NE , NE)	1.07 (0.58, 1.99)	0.8314	
>= 3	30/ 109 (27.5)	NE (NE , NE)	21/ 107 (19.6)	NE (NE , NE)	1.19 (0.68, 2.09)	0.5337	
Presence of Liver Metastases							0.3492
Yes	37/ 135 (27.4)	NE (NE , NE)	26/ 142 (18.3)	NE (NE , NE)	1.31 (0.79, 2.18)	0.2847	
No	15/ 84 (17.9)	NE (NE , NE)	14/ 80 (17.5)	NE (NE , NE)	0.88 (0.42, 1.84)	0.7401	
Side of Tumor							0.4760
Left	28/ 83 (33.7)	NE (10.9, NE)	18/ 86 (20.9)	NE (NE , NE)	1.29 (0.71, 2.34)	0.4005	
Right	24/ 136 (17.6)	NE (NE , NE)	22/ 136 (16.2)	NE (NE , NE)	1.03 (0.58, 1.85)	0.9096	

[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio > 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.
[4] P-Value for interaction from Cox proportional hazards model using ties=exact option with treatment, subgroup and treatment*subgroup interaction as covariates.
Including only patients from the full analysis set who completed a baseline (last PRO assessment prior to or on the first dose of study treatment) and at least 1 post-baseline PRO assessment.
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Kaplan Meier Plot of Time to first improvement of at least 10 points - EOR01-Constipation (Months)
Full Analysis Set



Kaplan-Meier Plots for subgroups only created if p-value for interaction < 0.05.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Time to first deterioration of at least 10 points - EOR01-Diarrhea (Months)
Full Analysis Set

	EC+FOLFOX (N=219)	Control 1 (N=222)
Number of subjects with events, n (%)	88 (40.2)	97 (43.7)
Number of censored subjects, n (%)	131 (59.8)	125 (56.3)
Kaplan-Meier estimates of Time to Event (Months) [1]		
25%-ile (95% CI)	4.2 (2.8, 6.9)	1.7 (1.6, 2.8)
Median (95% CI)	22.2 (12.5, NE)	6.9 (4.2, 12.4)
75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
Stratified analysis [2]		
Hazard Ratio (95% CI) [3]	0.60 (0.44, 0.80)	
p-value [4]	0.0006	

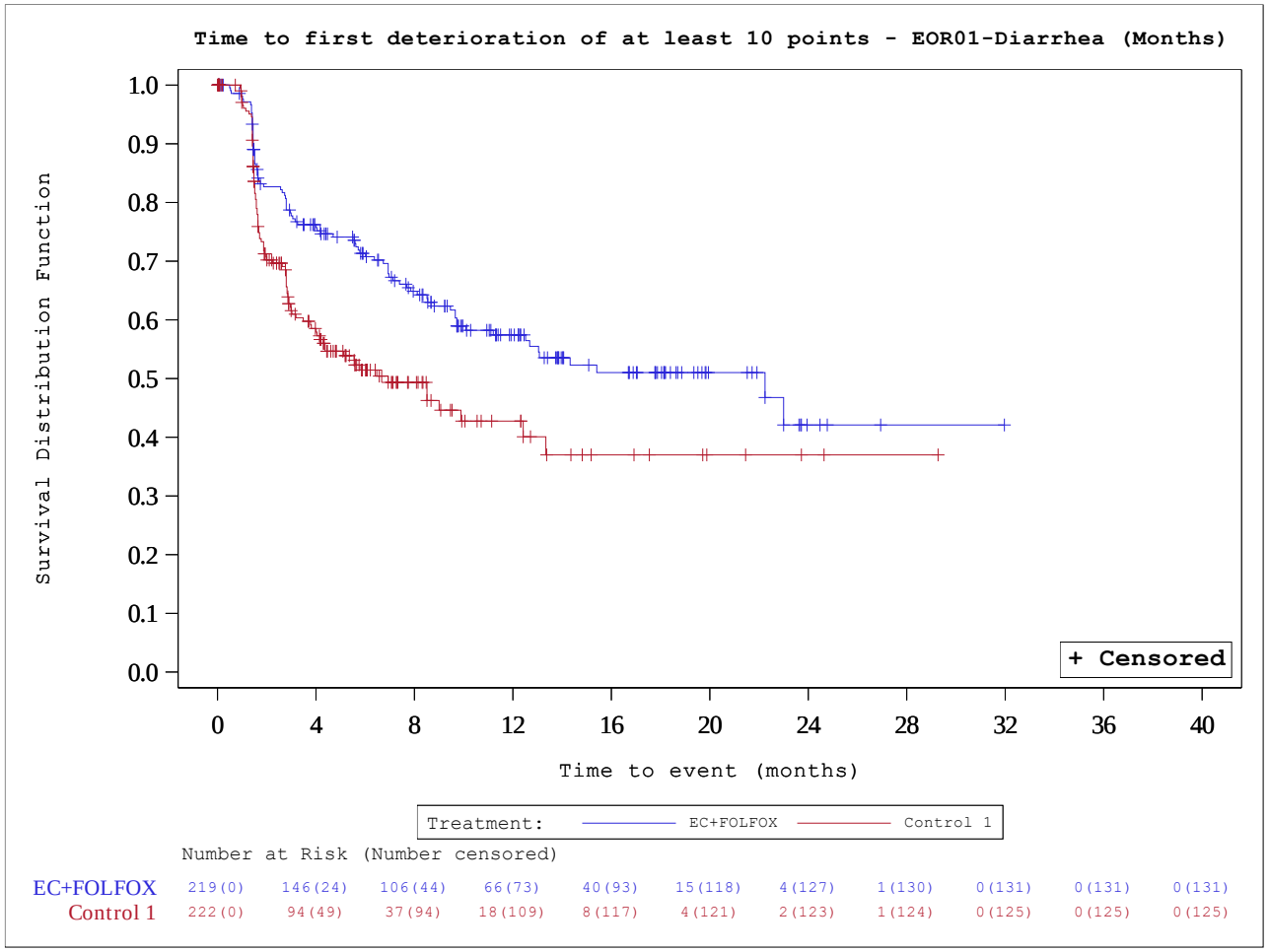
[1] Based on the Brookmeyer and Crowley method.
[2] Stratified by ECOG PS by Randomization and Geographic Region by Randomization.
[3] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[4] P-value from 2-sided log-rank test.
Including only patients from the full analysis set who completed a baseline (last PRO assessment prior to or on the first dose of study treatment) and at least 1 post-baseline PRO assessment.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Time to first deterioration of at least 10 points - EOR01-Diarrhea (Months) - Subgroup analysis
Full Analysis Set

Subgroup Level	EC+FOLFOX (N=219) n/ N (%)	EC+FOLFOX (N=219) Median (95% CI)[1]	Control 1 (N=222) n/ N (%)	Control 1 (N=222) Median (95% CI)[1]	Unstratified analysis Hazard Ratio (95% CI)[2]	Unstratified analysis p-Value[3]	Interaction p-Value[4]
Age (Years)							0.8579
< 65	55/ 139 (39.6)	22.2 (10.1, NE)	55/ 127 (43.3)	6.9 (3.2, NE)	0.60 (0.41, 0.88)	0.0083	
>= 65	33/ 80 (41.3)	13.1 (9.7, NE)	42/ 95 (44.2)	6.5 (4.3, 13.3)	0.61 (0.38, 0.97)	0.0346	
Sex							0.1722
Male	37/ 114 (32.5)	NE (13.1, NE)	49/ 108 (45.4)	5.6 (3.8, NE)	0.51 (0.33, 0.80)	0.0025	
Female	51/ 105 (48.6)	12.5 (7.7, 23.0)	48/ 114 (42.1)	8.5 (2.9, 13.3)	0.71 (0.47, 1.06)	0.0886	
Region							0.3673
Europe	43/ 104 (41.3)	22.2 (9.7, NE)	41/ 100 (41.0)	6.5 (3.0, NE)	0.59 (0.38, 0.91)	0.0169	
USA/Canada	3/ 8 (37.5)	NE (4.2, NE)	1/ 14 (7.1)	NE (NE , NE)	2.71 (0.24, 30.03)	0.3973	
Rest of World	42/ 107 (39.3)	15.4 (8.8, NE)	55/ 108 (50.9)	5.6 (3.0, 12.4)	0.56 (0.37, 0.84)	0.0049	
ECOG-PS at Randomization							0.1911
0	48/ 123 (39.0)	22.2 (12.5, NE)	60/ 124 (48.4)	5.6 (2.9, 12.4)	0.52 (0.35, 0.77)	0.0008	
1	40/ 96 (41.7)	13.1 (8.1, NE)	37/ 98 (37.8)	9.0 (4.3, NE)	0.74 (0.47, 1.16)	0.1867	
Number of Organs Involved							0.9300
<= 2	53/ 110 (48.2)	13.1 (9.7, NE)	58/ 115 (50.4)	5.6 (2.9, 9.9)	0.57 (0.39, 0.84)	0.0037	
>= 3	35/ 109 (32.1)	NE (12.5, NE)	39/ 107 (36.4)	8.5 (4.0, NE)	0.63 (0.40, 1.00)	0.0453	
Presence of Liver Metastases							0.7332
Yes	49/ 135 (36.3)	NE (12.5, NE)	61/ 142 (43.0)	8.5 (4.0, NE)	0.59 (0.40, 0.87)	0.0062	
No	39/ 84 (46.4)	14.3 (8.5, NE)	36/ 80 (45.0)	6.5 (3.0, NE)	0.61 (0.38, 0.97)	0.0350	
Side of Tumor							0.1185
Left	26/ 83 (31.3)	NE (NE , NE)	36/ 86 (41.9)	5.6 (2.8, NE)	0.49 (0.29, 0.81)	0.0047	
Right	62/ 136 (45.6)	13.0 (9.7, 23.0)	61/ 136 (44.9)	8.5 (4.3, 13.3)	0.68 (0.47, 0.97)	0.0331	

[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.
[4] P-Value for interaction from Cox proportional hazards model using ties=exact option with treatment, subgroup and treatment*subgroup interaction as covariates.
Including only patients from the full analysis set who completed a baseline (last PRO assessment prior to or on the first dose of study treatment) and at least 1 post-baseline PRO assessment.
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Kaplan Meier Plot of Time to first deterioration of at least 10 points - EOR01-Diarrhea (Months)
Full Analysis Set



Kaplan-Meier Plots for subgroups only created if p-value for interaction < 0.05.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Time to first improvement of at least 10 points - EOR01-Diarrhea (Months)
Full Analysis Set

	EC+FOLFOX (N=219)	Control 1 (N=222)
Number of subjects with events, n (%)	54 (24.7)	29 (13.1)
Number of censored subjects, n (%)	165 (75.3)	193 (86.9)
Kaplan-Meier estimates of Time to Event (Months) [1]		
25%-ile (95% CI)	7.2 (3.0, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
Stratified analysis [2]		
Hazard Ratio (95% CI) [3]	1.72 (1.10, 2.72)	
p-value [4]	0.0170	

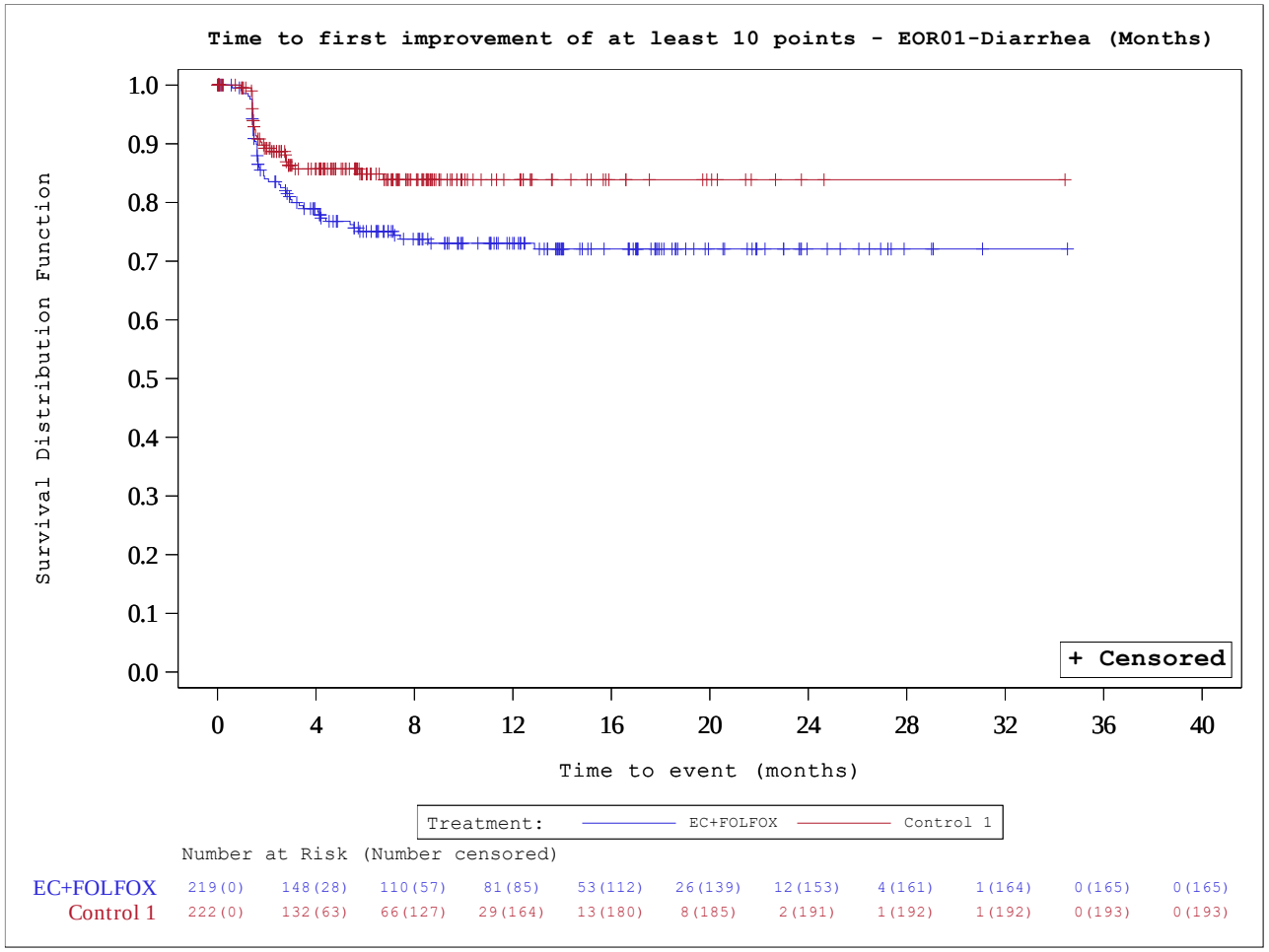
[1] Based on the Brookmeyer and Crowley method.
[2] Stratified by ECOG PS by Randomization and Geographic Region by Randomization.
[3] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio > 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[4] P-value from 2-sided log-rank test.
Including only patients from the full analysis set who completed a baseline (last PRO assessment prior to or on the first dose of study treatment) and at least 1 post-baseline PRO assessment.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Time to first improvement of at least 10 points - EOR01-Diarrhea (Months) - Subgroup analysis
Full Analysis Set

Subgroup Level	EC+FOLFOX (N=219) n/ N (%)	EC+FOLFOX (N=219) Median (95% CI)[1]	Control 1 (N=222) n/ N (%)	Control 1 (N=222) Median (95% CI)[1]	Unstratified analysis Hazard Ratio (95% CI)[2]	Unstratified analysis p-Value[3]	Interaction p-Value[4]
Age (Years)							0.4494
< 65	32/ 139 (23.0)	NE (NE , NE)	17/ 127 (13.4)	NE (NE , NE)	1.50 (0.83, 2.70)	0.1730	
>= 65	22/ 80 (27.5)	NE (NE , NE)	12/ 95 (12.6)	NE (NE , NE)	2.07 (1.02, 4.18)	0.0398	
Sex							0.0577
Male	32/ 114 (28.1)	NE (NE , NE)	11/ 108 (10.2)	NE (NE , NE)	2.71 (1.36, 5.38)	0.0029	
Female	22/ 105 (21.0)	NE (NE , NE)	18/ 114 (15.8)	NE (NE , NE)	1.10 (0.59, 2.05)	0.7704	
Region							0.5979
Europe	26/ 104 (25.0)	NE (NE , NE)	10/ 100 (10.0)	NE (NE , NE)	2.04 (0.98, 4.24)	0.0500	
USA/Canada	4/ 8 (50.0)	NE (1.6, NE)	2/ 14 (14.3)	NE (NE , NE)	2.85 (0.52, 15.60)	0.2104	
Rest of World	24/ 107 (22.4)	NE (NE , NE)	17/ 108 (15.7)	NE (NE , NE)	1.42 (0.76, 2.64)	0.2694	
ECOG-PS at Randomization							0.8125
0	28/ 123 (22.8)	NE (NE , NE)	14/ 124 (11.3)	NE (NE , NE)	1.79 (0.94, 3.41)	0.0712	
1	26/ 96 (27.1)	NE (NE , NE)	15/ 98 (15.3)	NE (NE , NE)	1.63 (0.86, 3.08)	0.1281	
Number of Organs Involved							0.3687
<= 2	22/ 110 (20.0)	NE (NE , NE)	15/ 115 (13.0)	NE (NE , NE)	1.30 (0.67, 2.51)	0.4327	
>= 3	32/ 109 (29.4)	NE (NE , NE)	14/ 107 (13.1)	NE (NE , NE)	2.12 (1.13, 3.97)	0.0163	
Presence of Liver Metastases							0.0557
Yes	40/ 135 (29.6)	NE (NE , NE)	17/ 142 (12.0)	NE (NE , NE)	2.43 (1.37, 4.28)	0.0015	
No	14/ 84 (16.7)	NE (NE , NE)	12/ 80 (15.0)	NE (NE , NE)	0.85 (0.39, 1.85)	0.6872	
Side of Tumor							0.7040
Left	25/ 83 (30.1)	NE (NE , NE)	12/ 86 (14.0)	NE (NE , NE)	1.92 (0.96, 3.81)	0.0591	
Right	29/ 136 (21.3)	NE (NE , NE)	17/ 136 (12.5)	NE (NE , NE)	1.55 (0.85, 2.82)	0.1524	

[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio > 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.
[4] P-Value for interaction from Cox proportional hazards model using ties=exact option with treatment, subgroup and treatment*subgroup interaction as covariates.
Including only patients from the full analysis set who completed a baseline (last PRO assessment prior to or on the first dose of study treatment) and at least 1 post-baseline PRO assessment.
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Kaplan Meier Plot of Time to first improvement of at least 10 points - EOR01-Diarrhea (Months)
Full Analysis Set



Kaplan-Meier Plots for subgroups only created if p-value for interaction < 0.05.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Time to first deterioration of at least 10 points - EOR01-Financial Difficulties (Months)
Full Analysis Set

	EC+FOLFOX (N=219)	Control 1 (N=222)
Number of subjects with events, n (%)	102 (46.6)	67 (30.2)
Number of censored subjects, n (%)	117 (53.4)	155 (69.8)
Kaplan-Meier estimates of Time to Event (Months) [1]		
25%-ile (95% CI)	3.5 (2.8, 4.7)	4.2 (2.9, 7.4)
Median (95% CI)	12.4 (8.3, 21.7)	13.9 (9.5, NE)
75%-ile (95% CI)	NE (29.8, NE)	NE (NE, NE)
Stratified analysis [2]		
Hazard Ratio (95% CI) [3]	1.16 (0.85, 1.59)	
p-value [4]	0.3581	

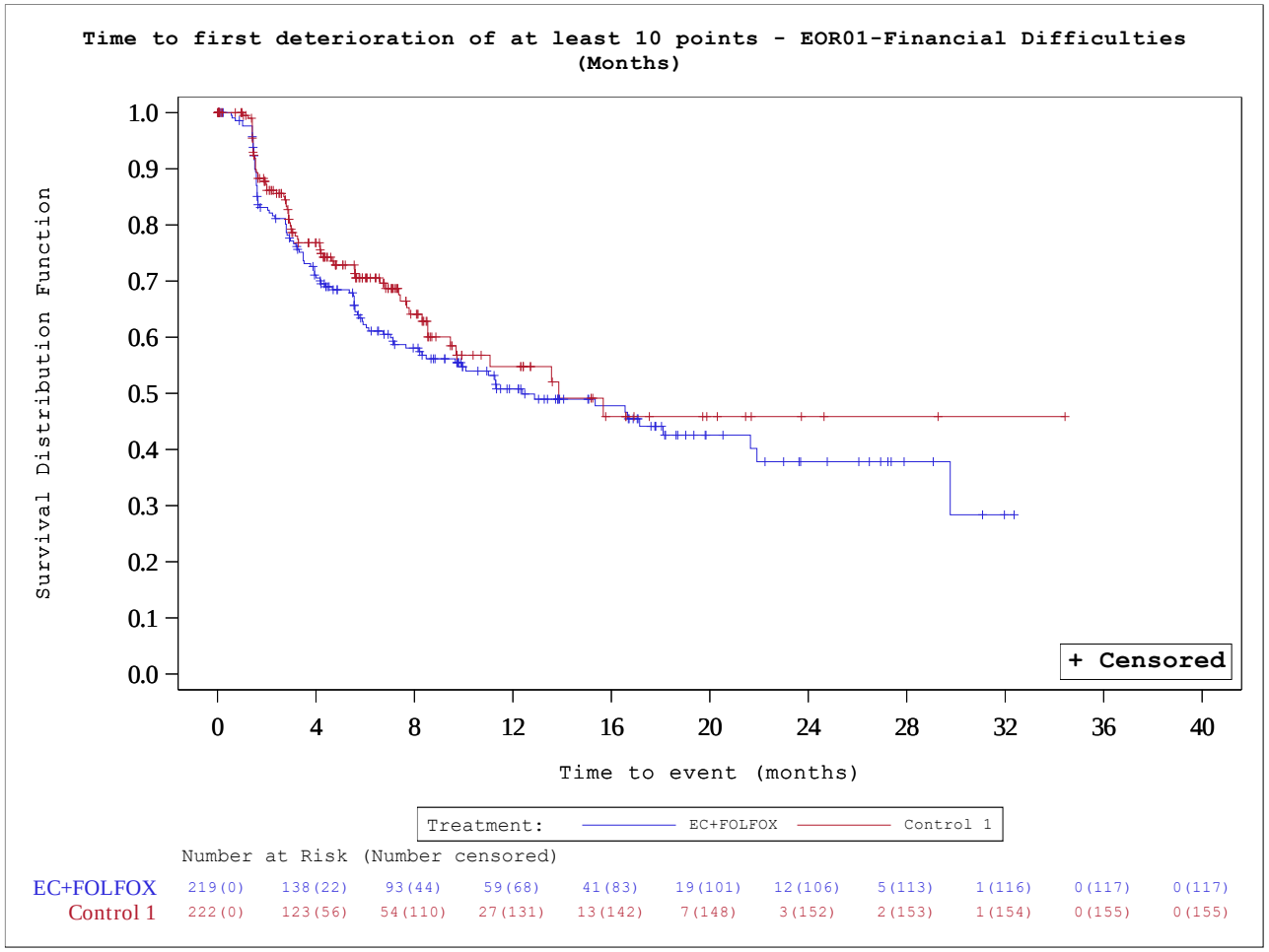
[1] Based on the Brookmeyer and Crowley method.
[2] Stratified by ECOG PS by Randomization and Geographic Region by Randomization.
[3] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[4] P-value from 2-sided log-rank test.
Including only patients from the full analysis set who completed a baseline (last PRO assessment prior to or on the first dose of study treatment) and at least 1 post-baseline PRO assessment.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Time to first deterioration of at least 10 points - EOR01-Financial Difficulties (Months) - Subgroup analysis
Full Analysis Set

Subgroup Level	EC+FOLFOX (N=219) n/ N (%)	EC+FOLFOX (N=219) Median (95% CI)[1]	Control 1 (N=222) n/ N (%)	Control 1 (N=222) Median (95% CI)[1]	Unstratified analysis Hazard Ratio (95% CI)[2]	Unstratified analysis p-Value[3]	Interaction p-Value[4]
Age (Years)							0.7430
< 65	67/ 139 (48.2)	12.9 (7.7, 21.9)	38/ 127 (29.9)	13.9 (8.5, NE)	1.20 (0.80, 1.80)	0.3685	
>= 65	35/ 80 (43.8)	12.4 (6.0, NE)	29/ 95 (30.5)	NE (7.7, NE)	1.17 (0.71, 1.92)	0.5374	
Sex							0.9110
Male	52/ 114 (45.6)	12.4 (7.0, NE)	34/ 108 (31.5)	15.7 (8.5, NE)	1.19 (0.77, 1.84)	0.4280	
Female	50/ 105 (47.6)	16.6 (7.1, 21.9)	33/ 114 (28.9)	13.9 (7.7, NE)	1.18 (0.75, 1.85)	0.4688	
Region							0.0941
Europe	52/ 104 (50.0)	11.0 (7.2, 21.7)	20/ 100 (20.0)	NE (NE , NE)	1.73 (1.03, 2.91)	0.0368	
USA/Canada	3/ 8 (37.5)	NE (3.3, NE)	0/ 14 (0.0)	NE (NE , NE)	NE		
Rest of World	47/ 107 (43.9)	16.6 (7.0, NE)	47/ 108 (43.5)	9.5 (7.4, 15.7)	0.85 (0.56, 1.28)	0.4329	
ECOG-PS at Randomization							0.5065
0	56/ 123 (45.5)	16.7 (8.2, NE)	41/ 124 (33.1)	13.6 (8.5, NE)	1.10 (0.73, 1.65)	0.6648	
1	46/ 96 (47.9)	11.3 (7.0, 18.1)	26/ 98 (26.5)	NE (8.5, NE)	1.33 (0.82, 2.16)	0.2488	
Number of Organs Involved							0.5949
<= 2	56/ 110 (50.9)	12.4 (5.9, 29.8)	35/ 115 (30.4)	NE (8.5, NE)	1.31 (0.86, 2.01)	0.2137	
>= 3	46/ 109 (42.2)	11.3 (7.7, NE)	32/ 107 (29.9)	13.9 (8.5, NE)	1.08 (0.69, 1.71)	0.7272	
Presence of Liver Metastases							0.6658
Yes	66/ 135 (48.9)	11.3 (6.7, 18.1)	44/ 142 (31.0)	13.9 (9.7, NE)	1.25 (0.85, 1.84)	0.2551	
No	36/ 84 (42.9)	15.3 (8.5, NE)	23/ 80 (28.8)	NE (8.5, NE)	1.15 (0.68, 1.95)	0.6087	
Side of Tumor							0.2918
Left	39/ 83 (47.0)	15.3 (8.5, 29.8)	28/ 86 (32.6)	15.7 (7.7, NE)	0.96 (0.58, 1.57)	0.8551	
Right	63/ 136 (46.3)	11.3 (7.1, 21.9)	39/ 136 (28.7)	13.9 (9.7, NE)	1.35 (0.90, 2.01)	0.1446	

[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.
[4] P-Value for interaction from Cox proportional hazards model using ties=exact option with treatment, subgroup and treatment*subgroup interaction as covariates.
Including only patients from the full analysis set who completed a baseline (last PRO assessment prior to or on the first dose of study treatment) and at least 1 post-baseline PRO assessment.
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Kaplan Meier Plot of Time to first deterioration of at least 10 points - EOR01-Financial Difficulties (Months)
Full Analysis Set



Kaplan-Meier Plots for subgroups only created if p-value for interaction < 0.05.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Time to first improvement of at least 10 points - EOR01-Financial Difficulties (Months)
Full Analysis Set

	EC+FOLFOX (N=219)	Control 1 (N=222)
Number of subjects with events, n (%)	52 (23.7)	44 (19.8)
Number of censored subjects, n (%)	167 (76.3)	178 (80.2)
Kaplan-Meier estimates of Time to Event (Months) [1]		
25%-ile (95% CI)	9.7 (4.8, NE)	7.4 (4.3, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
Stratified analysis [2]		
Hazard Ratio (95% CI) [3]	1.00 (0.66, 1.50)	
p-value [4]	0.9942	

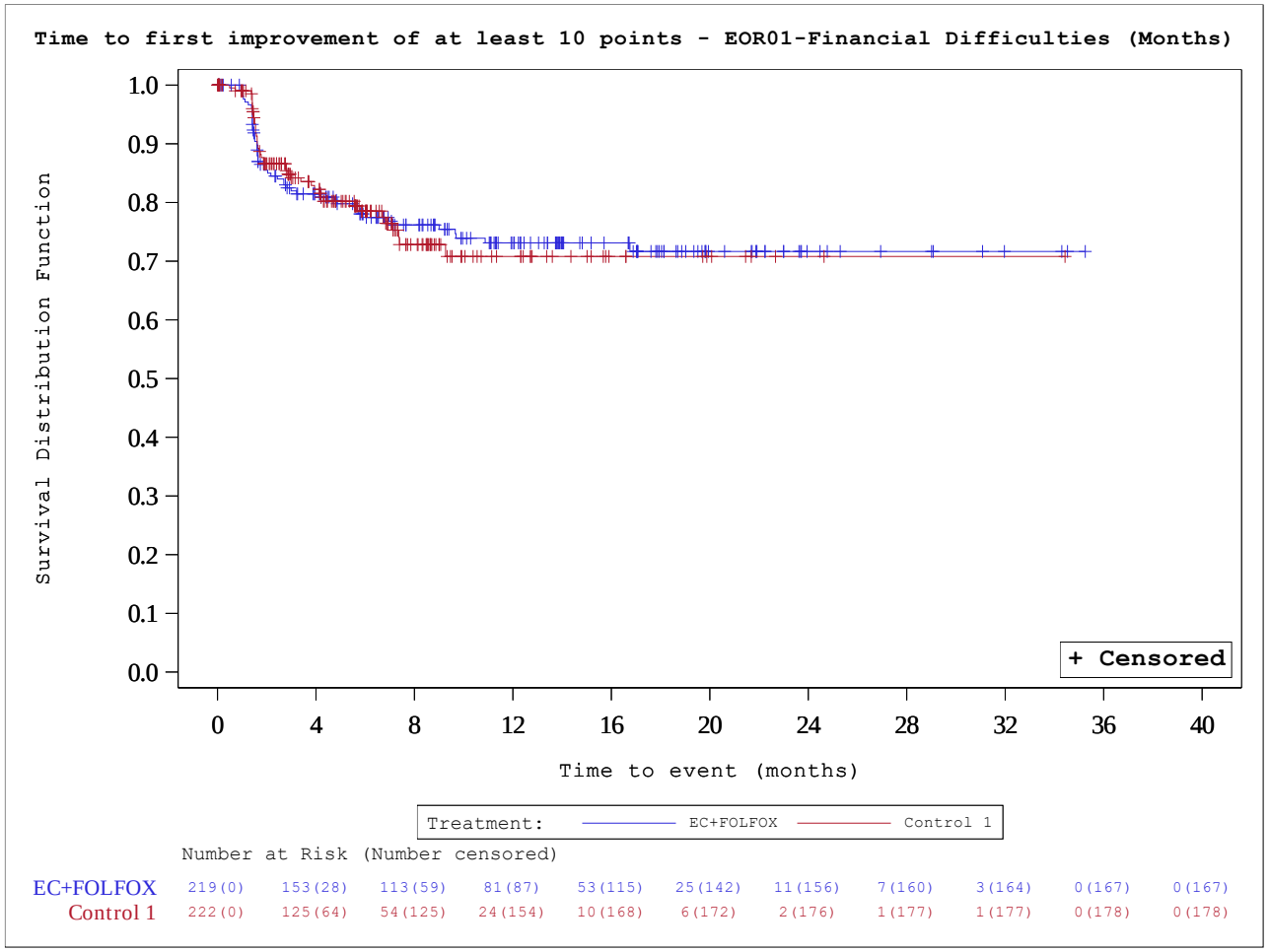
[1] Based on the Brookmeyer and Crowley method.
[2] Stratified by ECOG PS by Randomization and Geographic Region by Randomization.
[3] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio > 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[4] P-value from 2-sided log-rank test.
Including only patients from the full analysis set who completed a baseline (last PRO assessment prior to or on the first dose of study treatment) and at least 1 post-baseline PRO assessment.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Time to first improvement of at least 10 points - EOR01-Financial Difficulties (Months) - Subgroup analysis
Full Analysis Set

Subgroup Level	EC+FOLFOX (N=219) n/ N (%)	EC+FOLFOX (N=219) Median (95% CI)[1]	Control 1 (N=222) n/ N (%)	Control 1 (N=222) Median (95% CI)[1]	Unstratified analysis Hazard Ratio (95% CI)[2]	Unstratified analysis p-Value[3]	Interaction p-Value[4]
Age (Years)							0.7524
< 65	34/ 139 (24.5)	NE (NE , NE)	26/ 127 (20.5)	NE (NE , NE)	0.91 (0.54, 1.52)	0.7152	
>= 65	18/ 80 (22.5)	NE (NE , NE)	18/ 95 (18.9)	NE (NE , NE)	1.09 (0.56, 2.10)	0.8084	
Sex							0.3411
Male	27/ 114 (23.7)	NE (NE , NE)	26/ 108 (24.1)	NE (NE , NE)	0.81 (0.47, 1.39)	0.4432	
Female	25/ 105 (23.8)	NE (NE , NE)	18/ 114 (15.8)	NE (NE , NE)	1.22 (0.66, 2.24)	0.5350	
Region							0.6391
Europe	19/ 104 (18.3)	NE (NE , NE)	10/ 100 (10.0)	NE (NE , NE)	1.41 (0.65, 3.05)	0.3778	
USA/Canada	1/ 8 (12.5)	NE (NE , NE)	1/ 14 (7.1)	NE (NE , NE)	1.27 (0.08, 20.27)	0.8665	
Rest of World	32/ 107 (29.9)	NE (16.8, NE)	33/ 108 (30.6)	NE (7.4, NE)	0.86 (0.53, 1.41)	0.5434	
ECOG-PS at Randomization							0.2503
0	22/ 123 (17.9)	NE (NE , NE)	23/ 124 (18.5)	NE (NE , NE)	0.77 (0.42, 1.38)	0.3739	
1	30/ 96 (31.3)	NE (NE , NE)	21/ 98 (21.4)	NE (NE , NE)	1.21 (0.69, 2.12)	0.5080	
Number of Organs Involved							0.6782
<= 2	25/ 110 (22.7)	NE (NE , NE)	24/ 115 (20.9)	NE (NE , NE)	0.89 (0.50, 1.57)	0.6822	
>= 3	27/ 109 (24.8)	NE (NE , NE)	20/ 107 (18.7)	NE (NE , NE)	1.07 (0.60, 1.92)	0.8119	
Presence of Liver Metastases							0.7328
Yes	31/ 135 (23.0)	NE (NE , NE)	26/ 142 (18.3)	NE (NE , NE)	1.04 (0.61, 1.75)	0.8966	
No	21/ 84 (25.0)	NE (NE , NE)	18/ 80 (22.5)	NE (NE , NE)	0.90 (0.47, 1.69)	0.7332	
Side of Tumor							0.4152
Left	21/ 83 (25.3)	NE (NE , NE)	14/ 86 (16.3)	NE (NE , NE)	1.16 (0.59, 2.31)	0.6669	
Right	31/ 136 (22.8)	NE (NE , NE)	30/ 136 (22.1)	NE (NE , NE)	0.88 (0.53, 1.46)	0.6261	

[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio > 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.
[4] P-Value for interaction from Cox proportional hazards model using ties=exact option with treatment, subgroup and treatment*subgroup interaction as covariates.
Including only patients from the full analysis set who completed a baseline (last PRO assessment prior to or on the first dose of study treatment) and at least 1 post-baseline PRO assessment.
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Kaplan Meier Plot of Time to first improvement of at least 10 points - EOR01-Financial Difficulties (Months)
Full Analysis Set



Kaplan-Meier Plots for subgroups only created if p-value for interaction < 0.05.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Time to first deterioration of at least 15 percent - EQ5D02-EQ-VAS Score (Months)
Full Analysis Set

	EC+FOLFOX (N=215)	Control 1 (N=217)
Number of subjects with events, n (%)	91 (42.3)	73 (33.6)
Number of censored subjects, n (%)	124 (57.7)	144 (66.4)
Kaplan-Meier estimates of Time to Event (Months) [1]		
25%-ile (95% CI)	4.1 (3.1, 5.5)	4.2 (2.9, 5.8)
Median (95% CI)	16.7 (10.2, NE)	12.4 (8.5, NE)
75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
Stratified analysis [2]		
Hazard Ratio (95% CI) [3]	0.92 (0.68, 1.27)	
p-value [4]	0.6232	

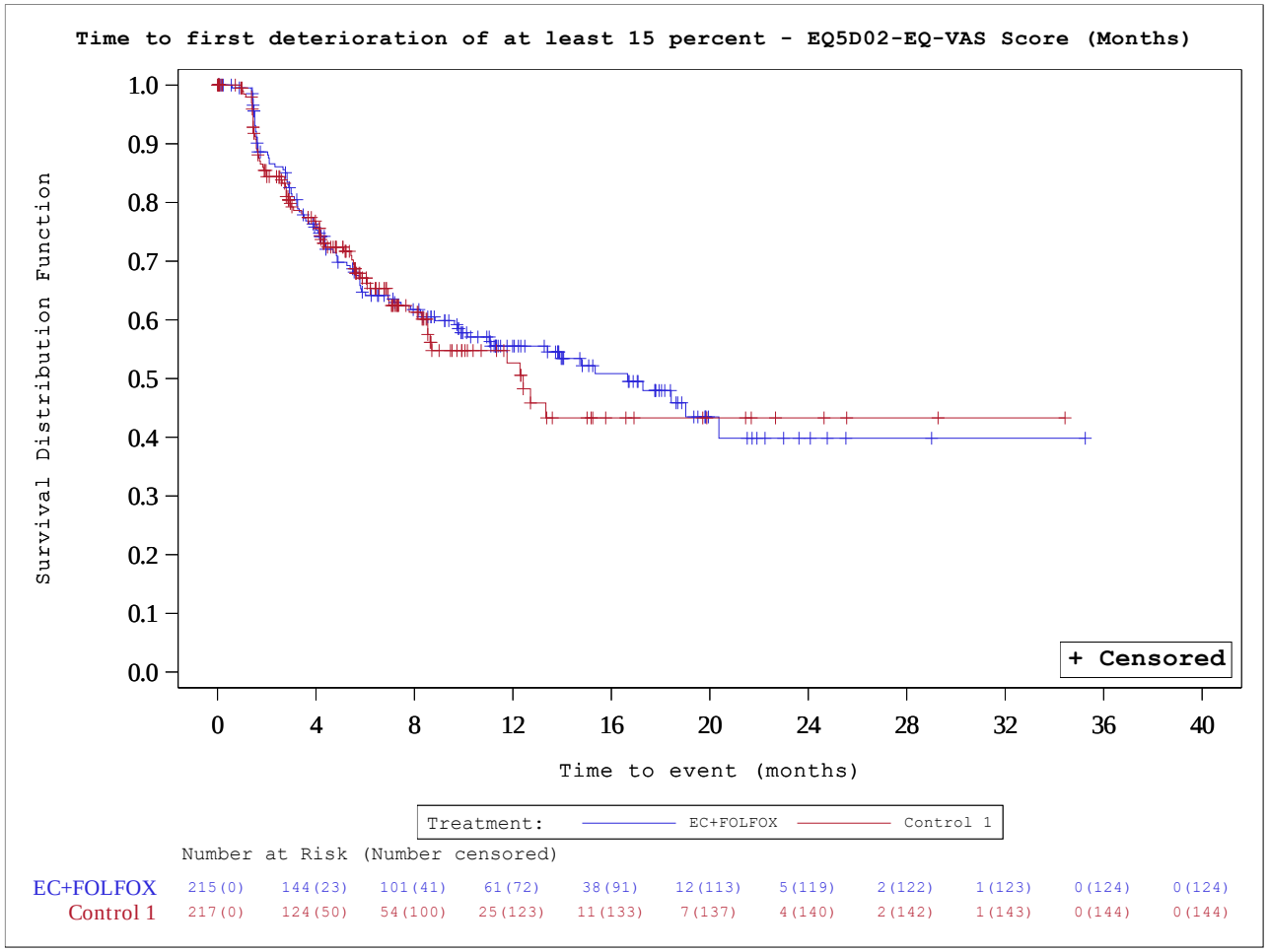
[1] Based on the Brookmeyer and Crowley method.
[2] Stratified by ECOG PS by Randomization and Geographic Region by Randomization.
[3] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[4] P-value from 2-sided log-rank test.
Including only patients from the full analysis set who completed a baseline (last PRO assessment prior to or on the first dose of study treatment) and at least 1 post-baseline PRO assessment.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Time to first deterioration of at least 15 percent - EQ5D02-EQ-VAS Score (Months) - Subgroup analysis
Full Analysis Set

Subgroup Level	EC+FOLFOX (N=215) n/ N (%)	EC+FOLFOX (N=215) Median (95% CI)[1]	Control 1 (N=217) n/ N (%)	Control 1 (N=217) Median (95% CI)[1]	Unstratified analysis Hazard Ratio (95% CI)[2]	Unstratified analysis p-Value[3]	Interaction p-Value[4]
Age (Years)							0.9051
< 65	57/ 136 (41.9)	16.7 (11.1, NE)	41/ 124 (33.1)	12.3 (8.5, NE)	0.91 (0.61, 1.37)	0.6516	
>= 65	34/ 79 (43.0)	14.8 (7.2, NE)	32/ 93 (34.4)	12.4 (7.8, NE)	0.99 (0.61, 1.60)	0.9614	
Sex							0.1255
Male	46/ 112 (41.1)	16.7 (8.8, NE)	31/ 108 (28.7)	NE (8.5, NE)	1.19 (0.75, 1.88)	0.4691	
Female	45/ 103 (43.7)	18.4 (10.2, NE)	42/ 109 (38.5)	11.8 (6.2, NE)	0.75 (0.49, 1.15)	0.1878	
Region							0.3723
Europe	43/ 100 (43.0)	17.3 (9.6, NE)	29/ 96 (30.2)	12.7 (8.3, NE)	0.96 (0.60, 1.54)	0.8597	
USA/Canada	4/ 8 (50.0)	NE (1.6, NE)	2/ 14 (14.3)	NE (NE , NE)	3.03 (0.55, 16.59)	0.1785	
Rest of World	44/ 107 (41.1)	15.3 (8.8, NE)	42/ 107 (39.3)	11.8 (6.9, NE)	0.83 (0.54, 1.28)	0.3990	
ECOG-PS at Randomization							0.3591
0	48/ 121 (39.7)	19.0 (9.6, NE)	45/ 122 (36.9)	12.3 (7.0, NE)	0.85 (0.57, 1.29)	0.4505	
1	43/ 94 (45.7)	13.9 (8.3, 20.4)	28/ 95 (29.5)	12.4 (8.6, NE)	1.05 (0.65, 1.70)	0.8407	
Number of Organs Involved							0.6748
<= 2	54/ 108 (50.0)	13.4 (5.7, NE)	42/ 112 (37.5)	8.7 (7.8, NE)	1.04 (0.69, 1.56)	0.8693	
>= 3	37/ 107 (34.6)	20.4 (13.9, NE)	31/ 105 (29.5)	12.4 (8.5, NE)	0.84 (0.52, 1.36)	0.4719	
Presence of Liver Metastases							0.0783
Yes	49/ 132 (37.1)	19.0 (13.4, NE)	50/ 140 (35.7)	11.8 (6.9, NE)	0.75 (0.50, 1.11)	0.1487	
No	42/ 83 (50.6)	11.1 (5.4, 18.4)	23/ 77 (29.9)	12.4 (8.7, NE)	1.33 (0.79, 2.22)	0.2772	
Side of Tumor							0.2149
Left	33/ 82 (40.2)	18.4 (8.8, NE)	31/ 85 (36.5)	8.7 (7.8, NE)	0.70 (0.42, 1.14)	0.1513	
Right	58/ 133 (43.6)	16.7 (8.3, NE)	42/ 132 (31.8)	13.3 (8.3, NE)	1.14 (0.77, 1.71)	0.5153	

[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.
[4] P-Value for interaction from Cox proportional hazards model using ties=exact option with treatment, subgroup and treatment*subgroup interaction as covariates.
Including only patients from the full analysis set who completed a baseline (last PRO assessment prior to or on the first dose of study treatment) and at least 1 post-baseline PRO assessment.
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Kaplan Meier Plot of Time to first deterioration of at least 15 percent - EQ5D02-EQ-VAS Score (Months)
Full Analysis Set



Kaplan-Meier Plots for subgroups only created if p-value for interaction < 0.05.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Time to first improvement of at least 15 percent - EQ5D02-EQ-VAS Score (Months)
Full Analysis Set

	EC+FOLFOX (N=215)	Control 1 (N=217)
Number of subjects with events, n (%)	65 (30.2)	37 (17.1)
Number of censored subjects, n (%)	150 (69.8)	180 (82.9)
Kaplan-Meier estimates of Time to Event (Months) [1]		
25%-ile (95% CI)	6.0 (3.0, 11.3)	11.2 (5.8, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
Stratified analysis [2]		
Hazard Ratio (95% CI) [3]	1.37 (0.91, 2.07)	
p-value [4]	0.1339	

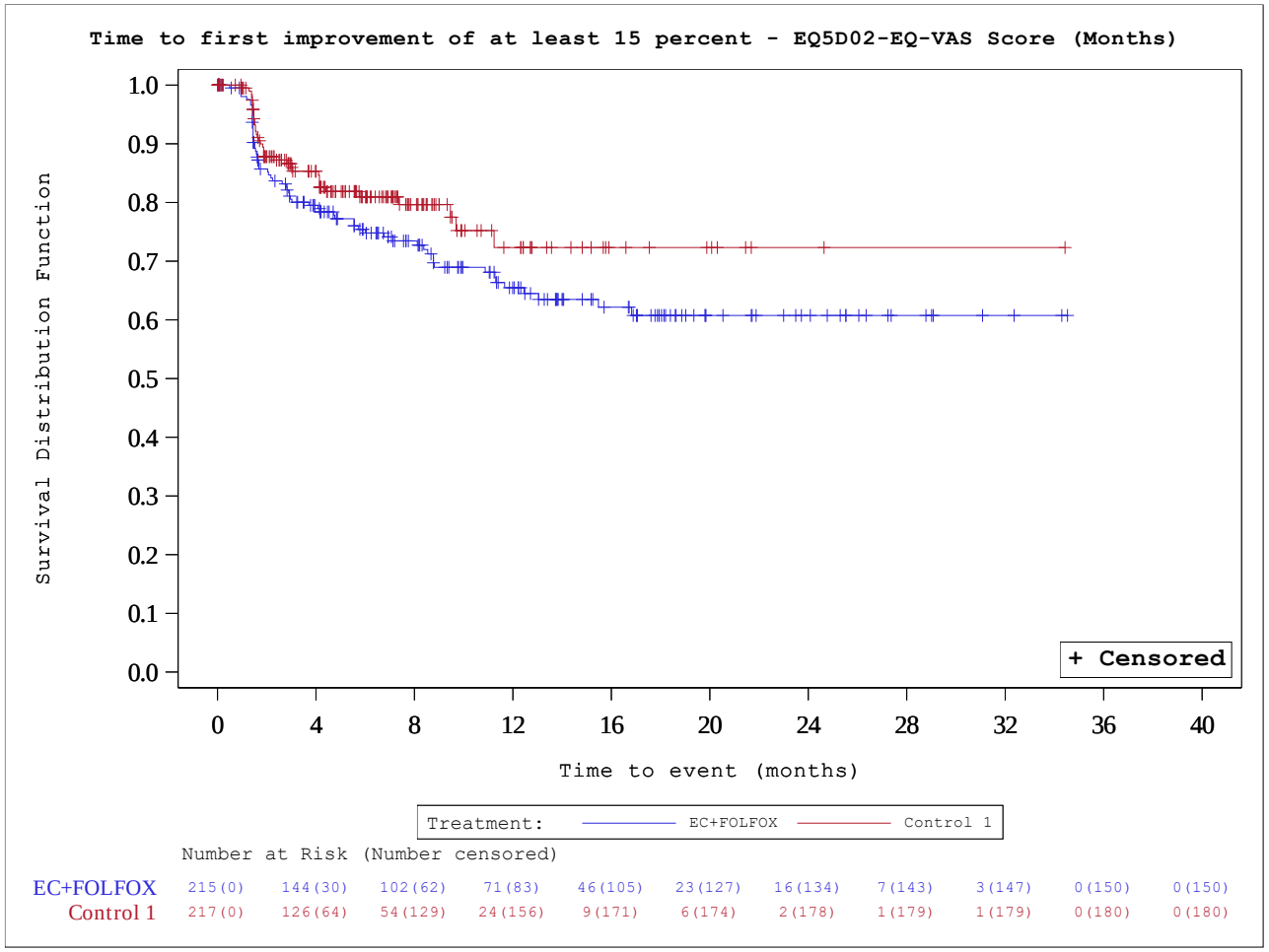
[1] Based on the Brookmeyer and Crowley method.
[2] Stratified by ECOG PS by Randomization and Geographic Region by Randomization.
[3] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio > 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[4] P-value from 2-sided log-rank test.
Including only patients from the full analysis set who completed a baseline (last PRO assessment prior to or on the first dose of study treatment) and at least 1 post-baseline PRO assessment.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Time to first improvement of at least 15 percent - EQ5D02-EQ-VAS Score (Months) - Subgroup analysis
Full Analysis Set

Subgroup Level	EC+FOLFOX (N=215) n/ N (%)	EC+FOLFOX (N=215) Median (95% CI)[1]	Control 1 (N=217) n/ N (%)	Control 1 (N=217) Median (95% CI)[1]	Unstratified analysis Hazard Ratio (95% CI)[2]	Unstratified analysis p-Value[3]	Interaction p-Value[4]
Age (Years)							0.8423
< 65	43/ 136 (31.6)	NE (NE , NE)	23/ 124 (18.5)	NE (NE , NE)	1.37 (0.82, 2.29)	0.2248	
>= 65	22/ 79 (27.8)	NE (15.5, NE)	14/ 93 (15.1)	NE (NE , NE)	1.43 (0.72, 2.81)	0.3051	
Sex							0.4400
Male	29/ 112 (25.9)	NE (NE , NE)	19/ 108 (17.6)	NE (NE , NE)	1.17 (0.65, 2.12)	0.5934	
Female	36/ 103 (35.0)	NE (13.0, NE)	18/ 109 (16.5)	NE (NE , NE)	1.68 (0.95, 2.97)	0.0731	
Region							0.1230
Europe	37/ 100 (37.0)	NE (11.7, NE)	12/ 96 (12.5)	NE (NE , NE)	2.24 (1.16, 4.32)	0.0139	
USA/Canada	1/ 8 (12.5)	NE (NE , NE)	2/ 14 (14.3)	NE (NE , NE)	0.61 (0.06, 6.75)	0.6857	
Rest of World	27/ 107 (25.2)	NE (NE , NE)	23/ 107 (21.5)	NE (NE , NE)	0.98 (0.56, 1.73)	0.9511	
ECOG-PS at Randomization							0.8512
0	33/ 121 (27.3)	NE (NE , NE)	18/ 122 (14.8)	NE (NE , NE)	1.36 (0.76, 2.44)	0.3008	
1	32/ 94 (34.0)	NE (10.9, NE)	19/ 95 (20.0)	NE (NE , NE)	1.44 (0.81, 2.55)	0.2112	
Number of Organs Involved							0.1087
<= 2	25/ 108 (23.1)	NE (NE , NE)	20/ 112 (17.9)	NE (NE , NE)	0.99 (0.55, 1.80)	0.9777	
>= 3	40/ 107 (37.4)	16.8 (8.8, NE)	17/ 105 (16.2)	NE (NE , NE)	1.90 (1.07, 3.37)	0.0254	
Presence of Liver Metastases							0.0887
Yes	45/ 132 (34.1)	NE (11.7, NE)	22/ 140 (15.7)	NE (NE , NE)	1.89 (1.13, 3.15)	0.0136	
No	20/ 83 (24.1)	NE (NE , NE)	15/ 77 (19.5)	NE (11.2, NE)	0.77 (0.38, 1.57)	0.4774	
Side of Tumor							0.1596
Left	32/ 82 (39.0)	NE (10.9, NE)	13/ 85 (15.3)	NE (11.2, NE)	1.87 (0.97, 3.60)	0.0587	
Right	33/ 133 (24.8)	NE (NE , NE)	24/ 132 (18.2)	NE (NE , NE)	1.14 (0.67, 1.93)	0.6342	

[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio > 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.
[4] P-Value for interaction from Cox proportional hazards model using ties=exact option with treatment, subgroup and treatment*subgroup interaction as covariates.
Including only patients from the full analysis set who completed a baseline (last PRO assessment prior to or on the first dose of study treatment) and at least 1 post-baseline PRO assessment.
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Kaplan Meier Plot of Time to first improvement of at least 15 percent - EQ5D02-EQ-VAS Score (Months)
Full Analysis Set



Kaplan-Meier Plots for subgroups only created if p-value for interaction < 0.05.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Time to first deterioration of at least 15 percent - PGIS01 - Colorectal Cancer (Months)
Full Analysis Set

	EC+FOLFOX (N=219)	Control 1 (N=222)
Number of subjects with events, n (%)	85 (38.8)	72 (32.4)
Number of censored subjects, n (%)	134 (61.2)	150 (67.6)
Kaplan-Meier estimates of Time to Event (Months) [1]		
25%-ile (95% CI)	4.1 (2.9, 5.7)	2.9 (2.2, 5.5)
Median (95% CI)	23.4 (8.3, NE)	16.6 (8.4, NE)
75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
Stratified analysis [2]		
Hazard Ratio (95% CI) [3]	0.91 (0.66, 1.25)	
p-value [4]	0.5547	

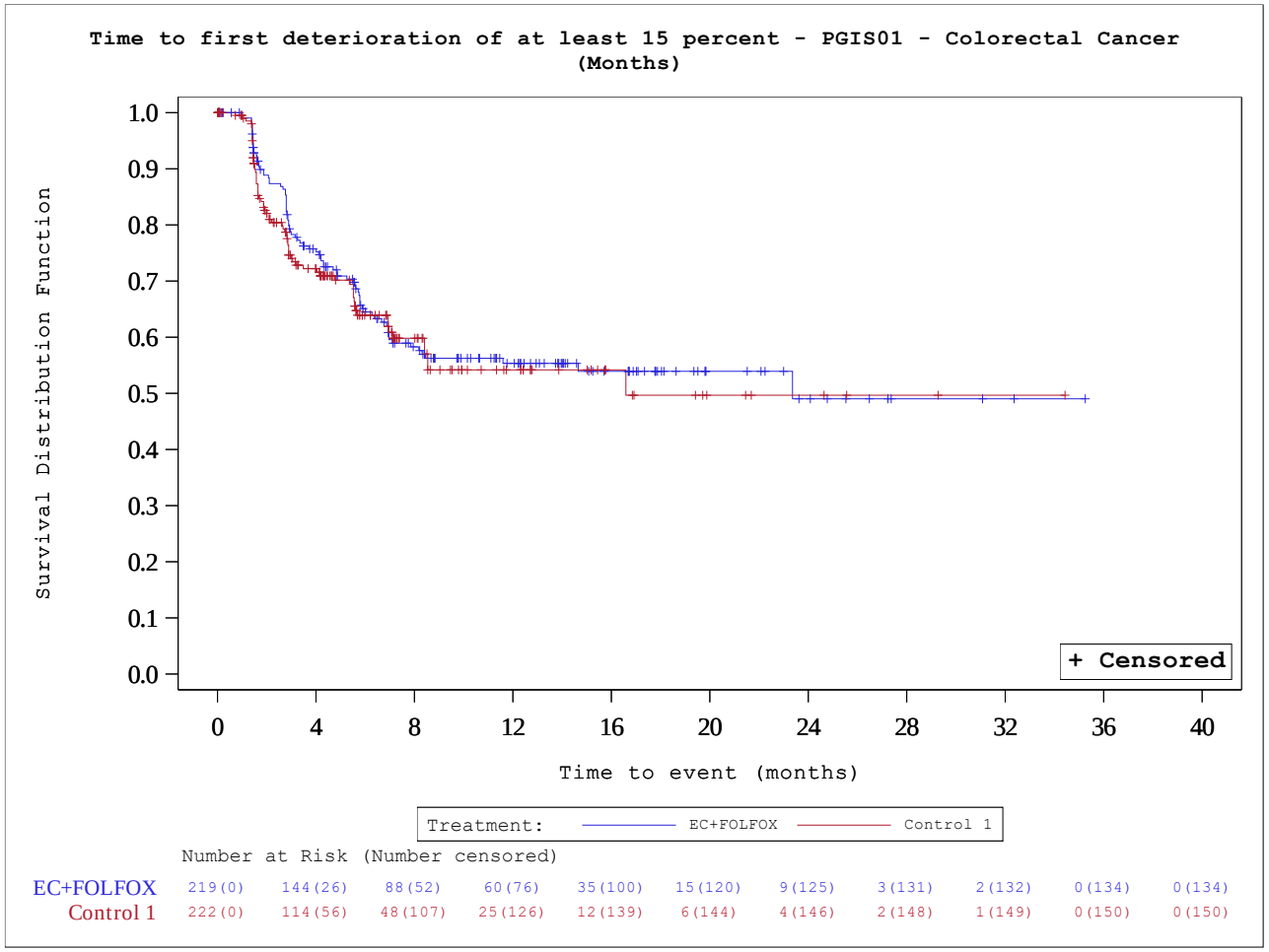
[1] Based on the Brookmeyer and Crowley method.
[2] Stratified by ECOG PS by Randomization and Geographic Region by Randomization.
[3] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[4] P-value from 2-sided log-rank test.
Including only patients from the full analysis set who completed a baseline (last PRO assessment prior to or on the first dose of study treatment) and at least 1 post-baseline PRO assessment.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Time to first deterioration of at least 15 percent - PGIS01 - Colorectal Cancer (Months) - Subgroup analysis
Full Analysis Set

Subgroup Level	EC+FOLFOX (N=219) n/ N (%)	EC+FOLFOX (N=219) Median (95% CI)[1]	Control 1 (N=222) n/ N (%)	Control 1 (N=222) Median (95% CI)[1]	Unstratified analysis Hazard Ratio (95% CI)[2]	Unstratified analysis p-Value[3]	Interaction p-Value[4]
Age (Years)							0.1784
< 65	57/ 139 (41.0)	23.4 (7.0, NE)	38/ 127 (29.9)	NE (8.4, NE)	1.09 (0.72, 1.65)	0.6789	
>= 65	28/ 80 (35.0)	NE (7.1, NE)	34/ 95 (35.8)	16.6 (5.6, NE)	0.73 (0.44, 1.21)	0.2225	
Sex							0.2721
Male	49/ 114 (43.0)	11.6 (6.7, NE)	36/ 108 (33.3)	NE (6.9, NE)	1.07 (0.69, 1.64)	0.7661	
Female	36/ 105 (34.3)	NE (23.4, NE)	36/ 114 (31.6)	16.6 (8.4, NE)	0.77 (0.48, 1.23)	0.2760	
Region							0.1375
Europe	41/ 104 (39.4)	NE (7.9, NE)	31/ 100 (31.0)	16.6 (6.9, NE)	0.87 (0.54, 1.39)	0.5549	
USA/Canada	5/ 8 (62.5)	7.9 (1.6, NE)	1/ 14 (7.1)	NE (NE , NE)	6.44 (0.75, 55.60)	0.0524	
Rest of World	39/ 107 (36.4)	23.4 (7.0, NE)	40/ 108 (37.0)	NE (5.7, NE)	0.84 (0.54, 1.30)	0.4272	
ECOG-PS at Randomization							0.6576
0	50/ 123 (40.7)	NE (6.9, NE)	42/ 124 (33.9)	16.6 (6.9, NE)	0.98 (0.65, 1.47)	0.9095	
1	35/ 96 (36.5)	23.4 (7.0, NE)	30/ 98 (30.6)	NE (8.4, NE)	0.86 (0.52, 1.40)	0.5402	
Number of Organs Involved							0.9090
<= 2	48/ 110 (43.6)	14.7 (6.9, NE)	44/ 115 (38.3)	8.5 (6.9, NE)	0.92 (0.61, 1.39)	0.6937	
>= 3	37/ 109 (33.9)	23.4 (8.3, NE)	28/ 107 (26.2)	NE (8.5, NE)	0.96 (0.59, 1.57)	0.8706	
Presence of Liver Metastases							0.7393
Yes	47/ 135 (34.8)	23.4 (23.4, NE)	44/ 142 (31.0)	16.6 (8.4, NE)	0.88 (0.58, 1.32)	0.5316	
No	38/ 84 (45.2)	11.6 (5.8, NE)	28/ 80 (35.0)	NE (5.5, NE)	0.97 (0.59, 1.59)	0.9090	
Side of Tumor							0.1982
Left	28/ 83 (33.7)	NE (8.3, NE)	29/ 86 (33.7)	8.5 (6.9, NE)	0.71 (0.42, 1.19)	0.1946	
Right	57/ 136 (41.9)	14.7 (6.7, NE)	43/ 136 (31.6)	NE (8.4, NE)	1.09 (0.73, 1.62)	0.6783	

[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.
[4] P-Value for interaction from Cox proportional hazards model using ties=exact option with treatment, subgroup and treatment*subgroup interaction as covariates.
Including only patients from the full analysis set who completed a baseline (last PRO assessment prior to or on the first dose of study treatment) and at least 1 post-baseline PRO assessment.
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Kaplan Meier Plot of Time to first deterioration of at least 15 percent - PGIS01 - Colorectal Cancer (Months)
Full Analysis Set



Kaplan-Meier Plots for subgroups only created if p-value for interaction < 0.05.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Time to first improvement of at least 15 percent - PGIS01 - Colorectal Cancer (Months)
Full Analysis Set

	EC+FOLFOX (N=219)	Control 1 (N=222)
Number of subjects with events, n (%)	116 (53.0)	88 (39.6)
Number of censored subjects, n (%)	103 (47.0)	134 (60.4)
Kaplan-Meier estimates of Time to Event (Months) [1]		
25%-ile (95% CI)	1.6 (1.5, 2.1)	1.7 (1.6, 2.8)
Median (95% CI)	6.0 (3.9, 8.5)	9.8 (5.1, NE)
75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
Stratified analysis [2]		
Hazard Ratio (95% CI) [3]	1.15 (0.87, 1.52)	
p-value [4]	0.3274	

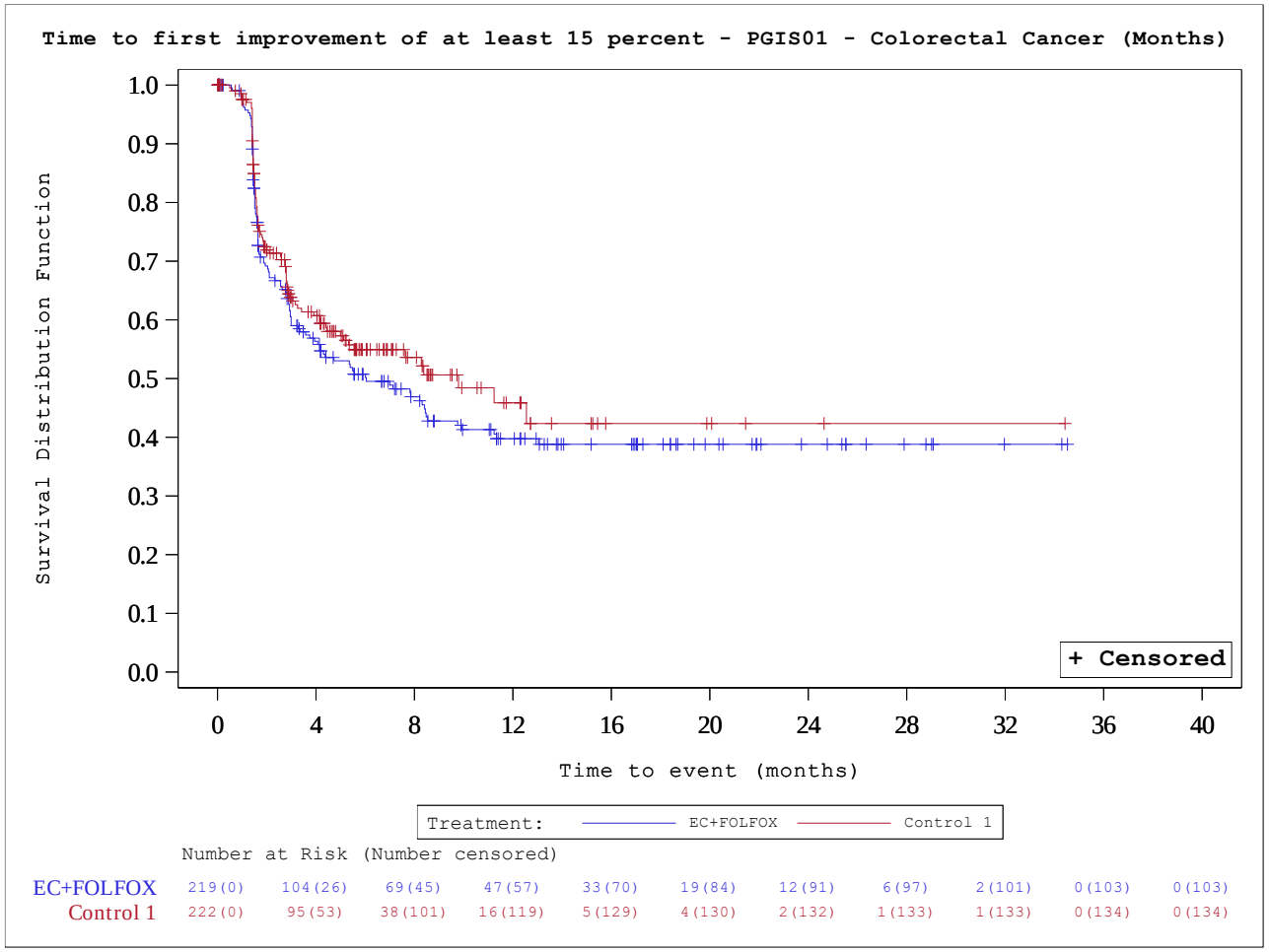
[1] Based on the Brookmeyer and Crowley method.
[2] Stratified by ECOG PS by Randomization and Geographic Region by Randomization.
[3] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio > 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[4] P-value from 2-sided log-rank test.
Including only patients from the full analysis set who completed a baseline (last PRO assessment prior to or on the first dose of study treatment) and at least 1 post-baseline PRO assessment.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Time to first improvement of at least 15 percent - PGIS01 - Colorectal Cancer (Months) - Subgroup analysis
Full Analysis Set

Subgroup Level	EC+FOLFOX (N=219) n/ N (%)	EC+FOLFOX (N=219) Median (95% CI)[1]	Control 1 (N=222) n/ N (%)	Control 1 (N=222) Median (95% CI)[1]	Unstratified analysis Hazard Ratio (95% CI)[2]	Unstratified analysis p-Value[3]	Interaction p-Value[4]
Age (Years)							0.4872
< 65	79/ 139 (56.8)	5.6 (3.4, 9.8)	48/ 127 (37.8)	12.6 (4.2, NE)	1.24 (0.87, 1.78)	0.2360	
>= 65	37/ 80 (46.3)	7.9 (3.0, NE)	40/ 95 (42.1)	7.6 (4.2, NE)	1.04 (0.66, 1.62)	0.8809	
Sex							0.9880
Male	56/ 114 (49.1)	5.6 (3.0, NE)	43/ 108 (39.8)	11.2 (4.4, NE)	1.19 (0.80, 1.78)	0.3771	
Female	60/ 105 (57.1)	7.0 (3.3, 8.5)	45/ 114 (39.5)	8.3 (3.4, NE)	1.12 (0.76, 1.66)	0.5719	
Region							0.1959
Europe	55/ 104 (52.9)	7.9 (3.0, NE)	33/ 100 (33.0)	9.8 (5.0, NE)	1.33 (0.86, 2.06)	0.1972	
USA/Canada	4/ 8 (50.0)	7.8 (3.0, NE)	1/ 14 (7.1)	NE (NE , NE)	4.74 (0.53, 42.46)	0.1253	
Rest of World	57/ 107 (53.3)	5.5 (3.0, 9.8)	54/ 108 (50.0)	5.3 (2.8, NE)	0.96 (0.66, 1.40)	0.8595	
ECOG-PS at Randomization							0.3911
0	57/ 123 (46.3)	8.5 (5.4, NE)	47/ 124 (37.9)	12.6 (4.4, NE)	1.05 (0.71, 1.56)	0.7877	
1	59/ 96 (61.5)	3.9 (2.6, 7.9)	41/ 98 (41.8)	7.6 (3.9, NE)	1.29 (0.87, 1.93)	0.2027	
Number of Organs Involved							0.0230
<= 2	53/ 110 (48.2)	8.4 (5.6, NE)	53/ 115 (46.1)	7.6 (3.3, NE)	0.84 (0.57, 1.24)	0.3800	
>= 3	63/ 109 (57.8)	4.2 (2.6, 7.9)	35/ 107 (32.7)	NE (8.4, NE)	1.64 (1.08, 2.48)	0.0175	
Presence of Liver Metastases							0.2046
Yes	71/ 135 (52.6)	5.4 (3.0, 11.2)	62/ 142 (43.7)	5.0 (3.1, NE)	1.03 (0.73, 1.45)	0.8681	
No	45/ 84 (53.6)	7.8 (3.6, 13.0)	26/ 80 (32.5)	11.2 (7.6, NE)	1.42 (0.87, 2.32)	0.1531	
Side of Tumor							0.8581
Left	44/ 83 (53.0)	6.0 (2.8, NE)	33/ 86 (38.4)	11.2 (2.9, NE)	1.23 (0.79, 1.94)	0.3605	
Right	72/ 136 (52.9)	7.8 (3.6, 11.3)	55/ 136 (40.4)	8.4 (5.1, NE)	1.12 (0.78, 1.59)	0.5351	

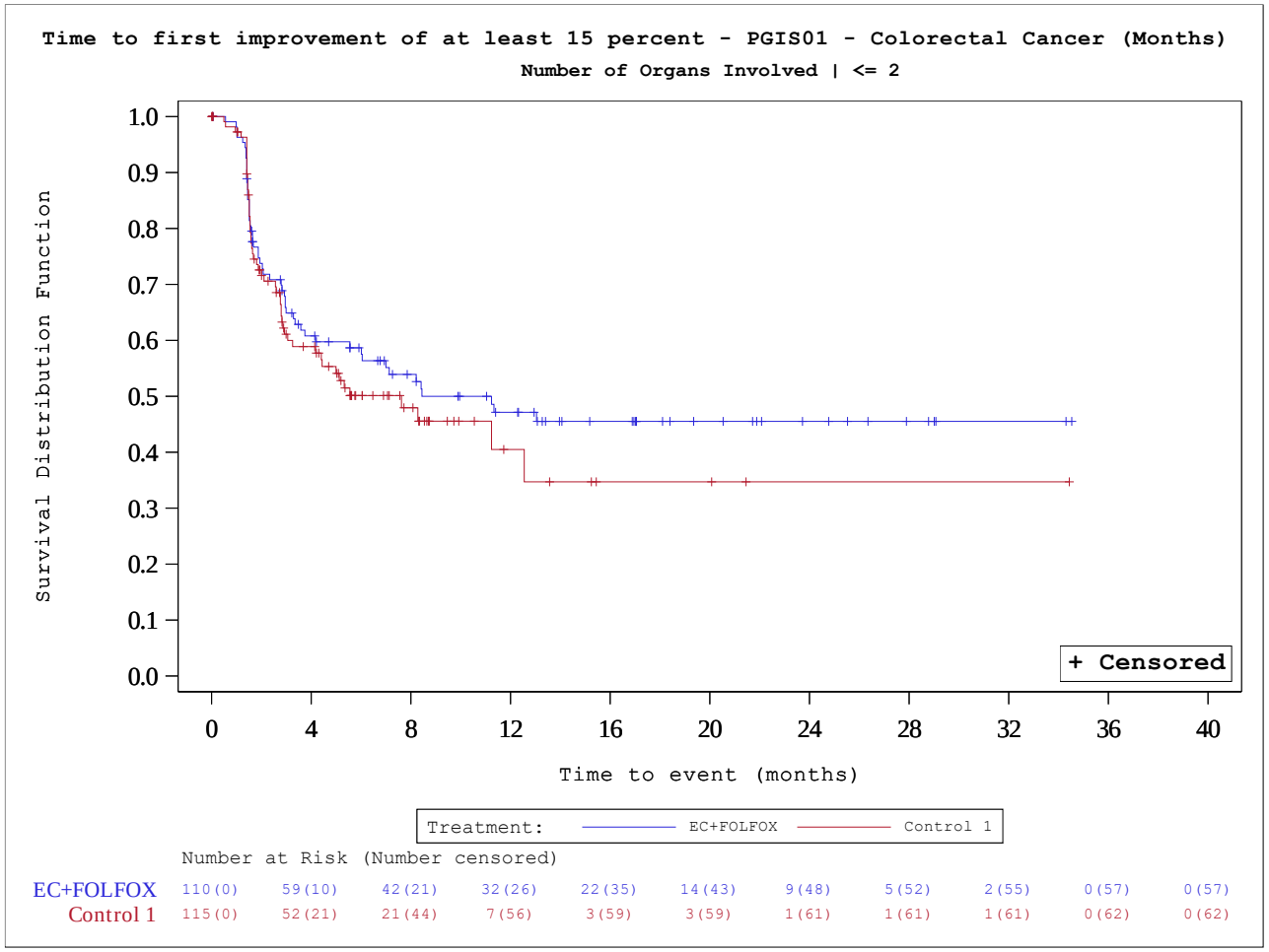
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio > 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.
[4] P-Value for interaction from Cox proportional hazards model using ties=exact option with treatment, subgroup and treatment*subgroup interaction as covariates.
Including only patients from the full analysis set who completed a baseline (last PRO assessment prior to or on the first dose of study treatment) and at least 1 post-baseline PRO assessment.
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Kaplan Meier Plot of Time to first improvement of at least 15 percent - PGIS01 - Colorectal Cancer (Months)
Full Analysis Set



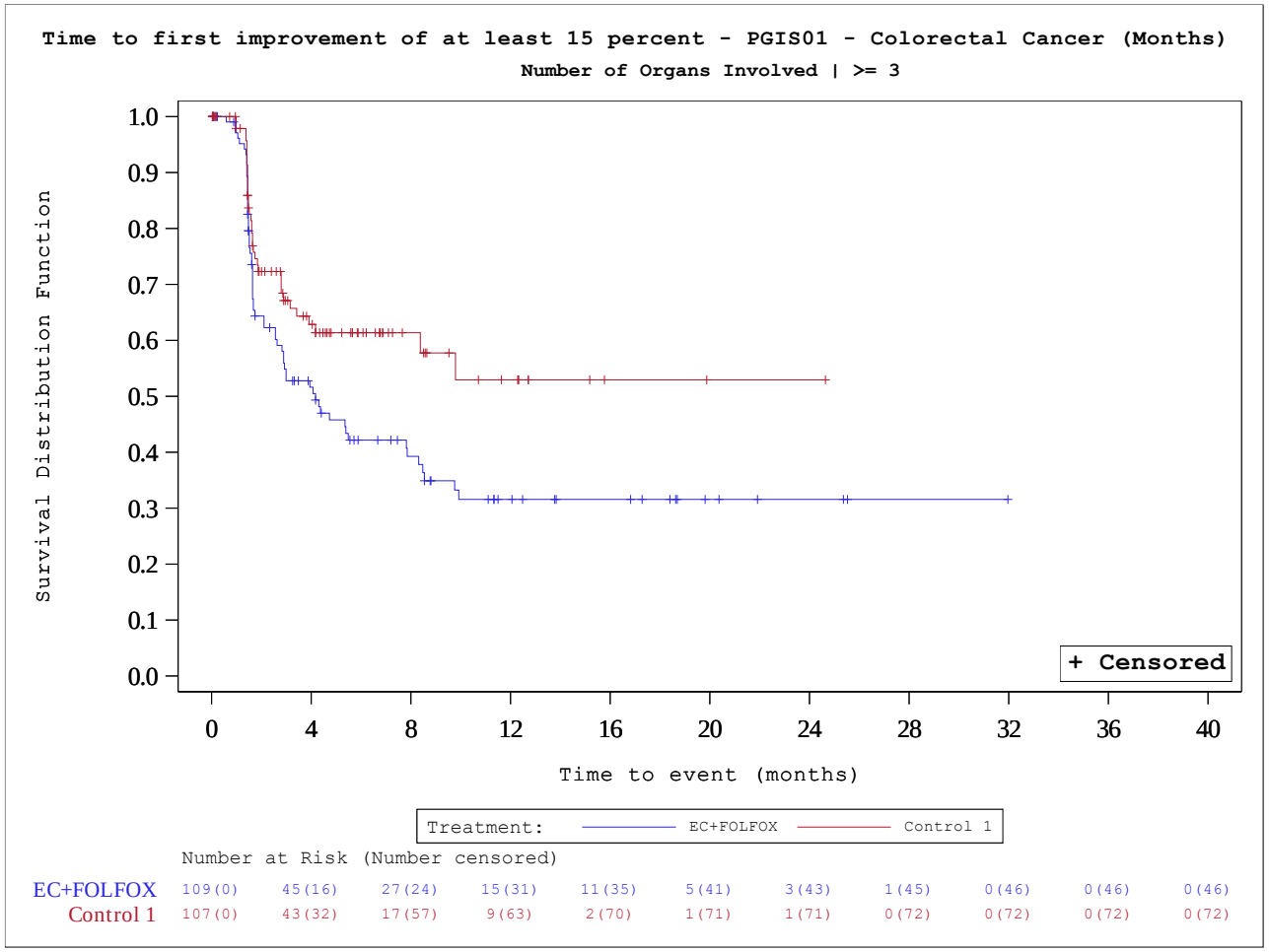
Kaplan-Meier Plots for subgroups only created if p-value for interaction < 0.05.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Kaplan Meier Plot of Time to first improvement of at least 15 percent - PGIS01 - Colorectal Cancer (Months)
Full Analysis Set



Kaplan-Meier Plots for subgroups only created if p-value for interaction < 0.05.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Kaplan Meier Plot of Time to first improvement of at least 15 percent - PGIS01 - Colorectal Cancer (Months)
Full Analysis Set



Kaplan-Meier Plots for subgroups only created if p-value for interaction < 0.05.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Time to first deterioration of at least 15 percent - PGI01-Change (Months)
Full Analysis Set

	EC+FOLFOX (N=212)	Control 1 (N=202)
Number of subjects with events, n (%)	136 (64.2)	120 (59.4)
Number of censored subjects, n (%)	76 (35.8)	82 (40.6)
Kaplan-Meier estimates of Time to Event (Months) [1]		
25%-ile (95% CI)	1.6 (1.5, 2.3)	1.5 (1.5, 1.6)
Median (95% CI)	6.4 (4.7, 7.7)	4.3 (2.8, 7.2)
75%-ile (95% CI)	22.1 (12.9, NE)	NE (10.4, NE)
Stratified analysis [2]		
Hazard Ratio (95% CI) [3]	0.91 (0.71, 1.17)	
p-value [4]	0.4823	

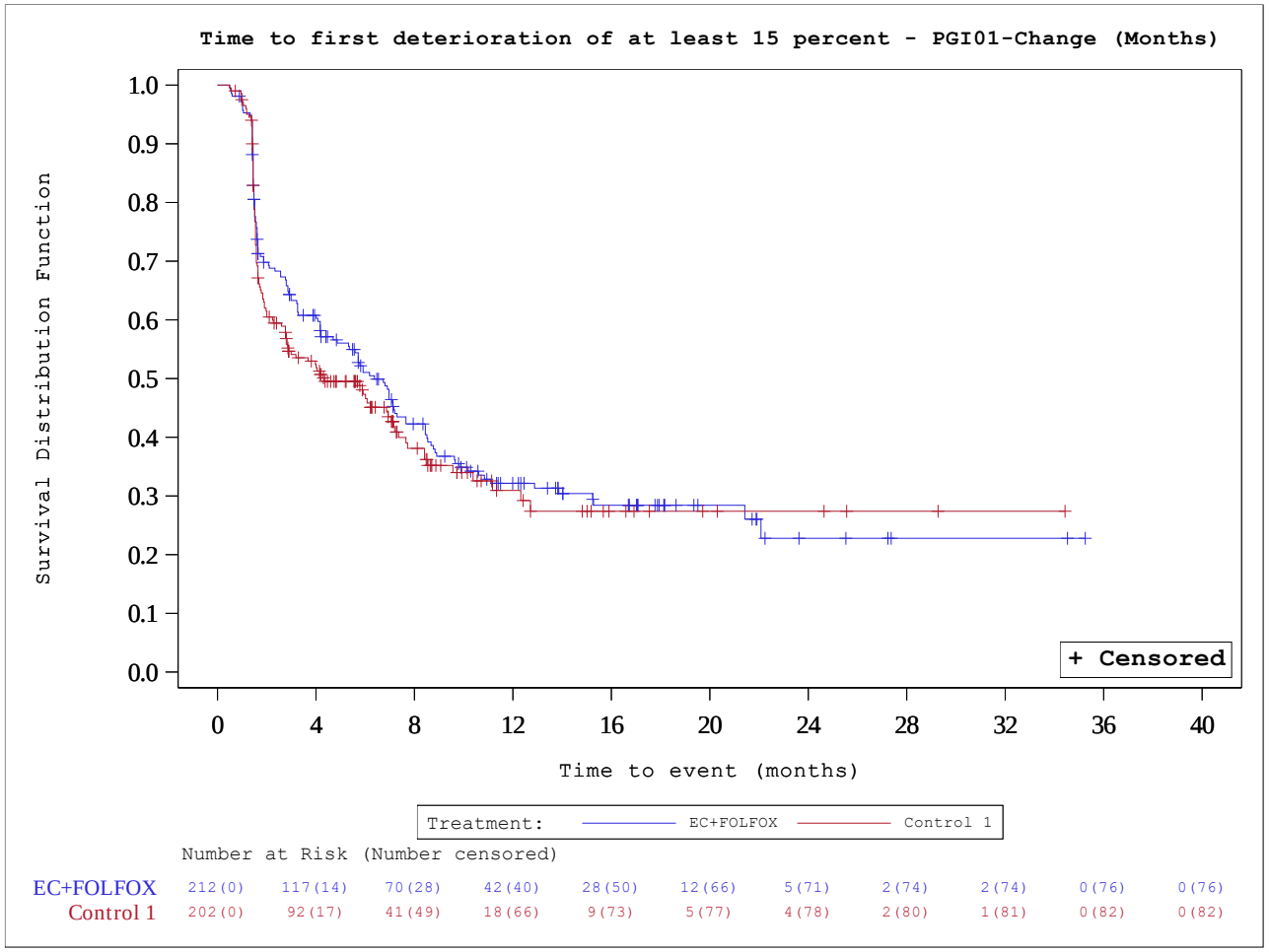
[1] Based on the Brookmeyer and Crowley method.
[2] Stratified by ECOG PS by Randomization and Geographic Region by Randomization.
[3] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[4] P-value from 2-sided log-rank test.
Including only patients from the full analysis set who completed at least 1 post-baseline PRO assessment.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Time to first deterioration of at least 15 percent - PGI01-Change (Months) - Subgroup analysis
Full Analysis Set

Subgroup Level	EC+FOLFOX (N=212) n/ N (%)	EC+FOLFOX (N=212) Median (95% CI)[1]	Control 1 (N=202) n/ N (%)	Control 1 (N=202) Median (95% CI)[1]	Unstratified analysis Hazard Ratio (95% CI)[2]	Unstratified analysis p-Value[3]	Interaction p-Value[4]
Age (Years)							0.3064
< 65	84/ 135 (62.2)	7.0 (5.7, 8.7)	61/ 116 (52.6)	6.9 (4.0, 11.2)	1.02 (0.73, 1.43)	0.8945	
>= 65	52/ 77 (67.5)	5.3 (2.9, 7.7)	59/ 86 (68.6)	2.8 (1.6, 6.0)	0.79 (0.54, 1.16)	0.2279	
Sex							0.1230
Male	70/ 109 (64.2)	5.8 (4.1, 7.1)	57/ 103 (55.3)	5.7 (2.8, 8.5)	1.10 (0.77, 1.56)	0.5961	
Female	66/ 103 (64.1)	7.2 (4.9, 9.6)	63/ 99 (63.6)	4.0 (1.7, 7.7)	0.72 (0.51, 1.02)	0.0685	
Region							0.4487
Europe	69/ 103 (67.0)	5.6 (2.9, 7.3)	59/ 87 (67.8)	3.2 (1.9, 6.9)	0.81 (0.57, 1.15)	0.2320	
USA/Canada	7/ 8 (87.5)	4.2 (1.6, 7.0)	6/ 11 (54.5)	7.7 (1.5, 12.3)	2.14 (0.67, 6.85)	0.1840	
Rest of World	60/ 101 (59.4)	7.7 (5.7, 10.2)	55/ 104 (52.9)	5.9 (2.8, NE)	0.94 (0.65, 1.36)	0.7378	
ECOG-PS at Randomization							0.8002
0	75/ 119 (63.0)	5.9 (3.3, 9.6)	68/ 115 (59.1)	3.2 (2.0, 7.2)	0.90 (0.65, 1.26)	0.5354	
1	61/ 93 (65.6)	6.8 (4.2, 7.7)	52/ 87 (59.8)	6.0 (2.8, 8.4)	0.91 (0.63, 1.32)	0.6103	
Number of Organs Involved							0.2229
<= 2	72/ 108 (66.7)	5.3 (3.2, 8.9)	70/ 108 (64.8)	2.6 (1.6, 5.7)	0.82 (0.59, 1.15)	0.2494	
>= 3	64/ 104 (61.5)	7.0 (5.7, 8.4)	50/ 94 (53.2)	7.2 (4.3, 9.6)	1.03 (0.71, 1.50)	0.8643	
Presence of Liver Metastases							0.1979
Yes	80/ 131 (61.1)	7.0 (4.2, 8.4)	81/ 130 (62.3)	3.7 (2.0, 6.9)	0.80 (0.58, 1.09)	0.1498	
No	56/ 81 (69.1)	5.9 (4.0, 8.5)	39/ 72 (54.2)	5.9 (2.8, 10.4)	1.12 (0.74, 1.69)	0.5800	
Side of Tumor							0.4366
Left	51/ 80 (63.8)	7.0 (4.9, 8.4)	41/ 76 (53.9)	6.1 (2.8, 11.2)	1.03 (0.68, 1.56)	0.8947	
Right	85/ 132 (64.4)	5.8 (4.1, 8.5)	79/ 126 (62.7)	3.7 (2.0, 7.2)	0.84 (0.62, 1.15)	0.2762	

[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.
[4] P-Value for interaction from Cox proportional hazards model using ties=exact option with treatment, subgroup and treatment*subgroup interaction as covariates.
Including only patients from the full analysis set who completed at least 1 post-baseline PRO assessment.
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Kaplan Meier Plot of Time to first deterioration of at least 15 percent - PGI01-Change (Months)
Full Analysis Set



Kaplan-Meier Plots for subgroups only created if p-value for interaction < 0.05.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Time to first improvement of at least 15 percent - PGI01-Change (Months)
Full Analysis Set

	EC+FOLFOX (N=212)	Control 1 (N=202)
Number of subjects with events, n (%)	150 (70.8)	106 (52.5)
Number of censored subjects, n (%)	62 (29.2)	96 (47.5)
Kaplan-Meier estimates of Time to Event (Months) [1]		
25%-ile (95% CI)	2.6 (1.7, 2.8)	2.8 (1.9, 3.1)
Median (95% CI)	4.3 (3.4, 5.6)	5.7 (4.4, 7.2)
75%-ile (95% CI)	11.7 (9.0, 17.1)	12.6 (9.0, NE)
Stratified analysis [2]		
Hazard Ratio (95% CI) [3]	1.17 (0.90, 1.50)	
p-value [4]	0.2475	

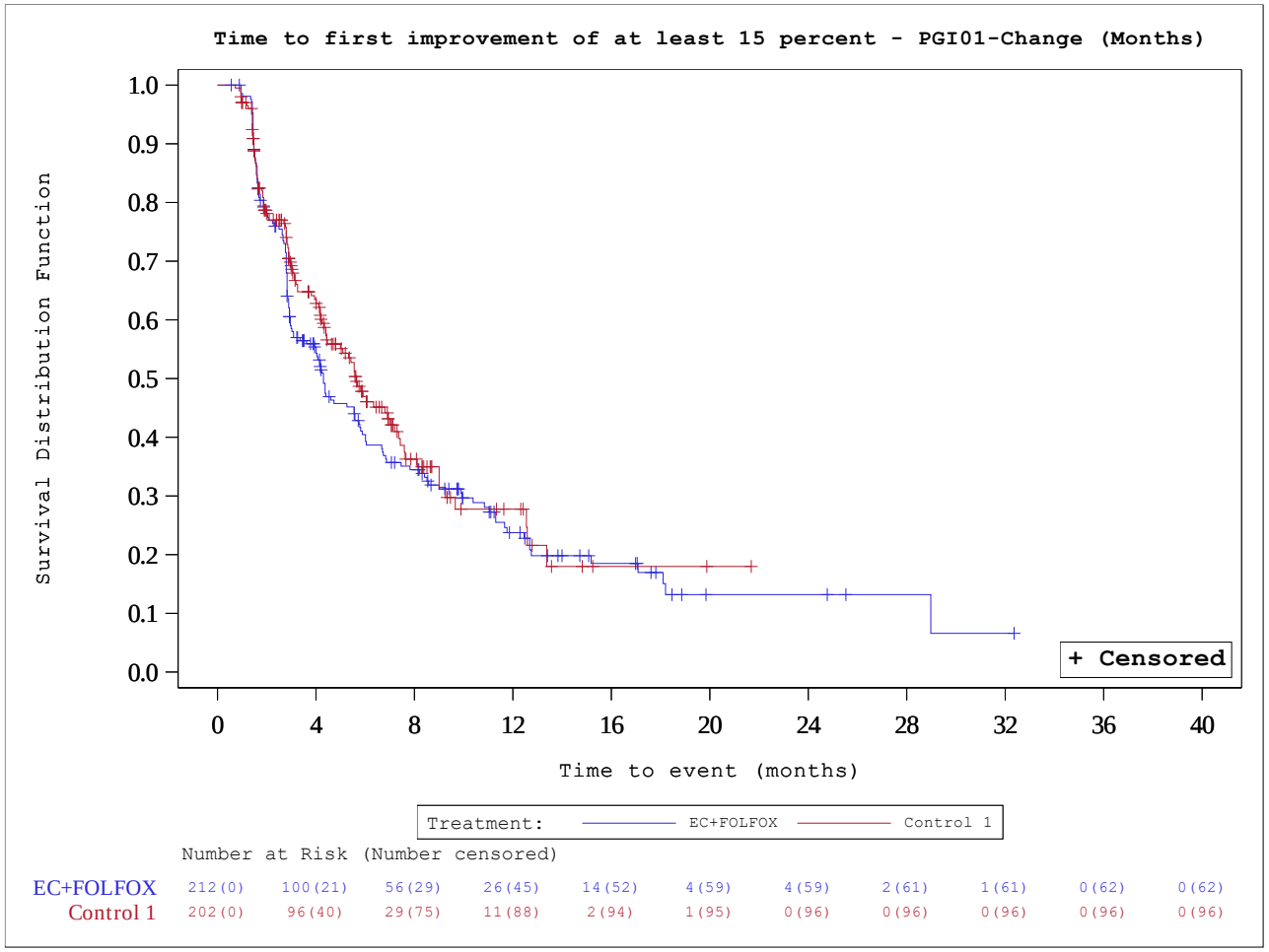
[1] Based on the Brookmeyer and Crowley method.
[2] Stratified by ECOG PS by Randomization and Geographic Region by Randomization.
[3] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio > 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[4] P-value from 2-sided log-rank test.
Including only patients from the full analysis set who completed at least 1 post-baseline PRO assessment.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Time to first improvement of at least 15 percent - PGI01-Change (Months) - Subgroup analysis
Full Analysis Set

Subgroup Level	EC+FOLFOX (N=212) n/ N (%)	EC+FOLFOX (N=212) Median (95% CI)[1]	Control 1 (N=202) n/ N (%)	Control 1 (N=202) Median (95% CI)[1]	Unstratified analysis Hazard Ratio (95% CI)[2]	Unstratified analysis p-Value[3]	Interaction p-Value[4]
Age (Years)							0.3081
< 65	92/ 135 (68.1)	4.4 (3.0, 6.0)	61/ 116 (52.6)	5.6 (4.3, 7.4)	1.04 (0.75, 1.45)	0.8217	
>= 65	58/ 77 (75.3)	4.2 (2.9, 5.9)	45/ 86 (52.3)	5.7 (4.0, 9.0)	1.33 (0.90, 1.96)	0.1570	
Sex							0.3471
Male	76/ 109 (69.7)	5.6 (3.4, 6.9)	54/ 103 (52.4)	5.7 (4.2, 7.6)	0.99 (0.70, 1.42)	0.9662	
Female	74/ 103 (71.8)	4.2 (2.9, 5.3)	52/ 99 (52.5)	5.6 (4.1, 7.6)	1.31 (0.92, 1.87)	0.1412	
Region							0.3757
Europe	68/ 103 (66.0)	5.3 (4.2, 6.8)	43/ 87 (49.4)	5.6 (4.4, 7.6)	0.96 (0.65, 1.41)	0.8349	
USA/Canada	6/ 8 (75.0)	4.4 (1.6, 7.5)	8/ 11 (72.7)	4.1 (2.8, 6.8)	0.71 (0.24, 2.09)	0.5323	
Rest of World	76/ 101 (75.2)	2.9 (2.8, 4.4)	55/ 104 (52.9)	5.7 (4.2, 7.6)	1.36 (0.96, 1.94)	0.0855	
ECOG-PS at Randomization							0.3910
0	88/ 119 (73.9)	4.3 (2.9, 6.7)	59/ 115 (51.3)	5.9 (4.4, 7.4)	1.22 (0.88, 1.71)	0.2369	
1	62/ 93 (66.7)	4.4 (4.0, 5.8)	47/ 87 (54.0)	5.6 (4.0, 7.6)	1.05 (0.71, 1.54)	0.8217	
Number of Organs Involved							0.0954
<= 2	83/ 108 (76.9)	4.3 (2.9, 6.0)	56/ 108 (51.9)	6.0 (5.0, 9.0)	1.34 (0.95, 1.89)	0.0974	
>= 3	67/ 104 (64.4)	4.4 (3.6, 6.0)	50/ 94 (53.2)	4.5 (3.1, 6.9)	0.95 (0.66, 1.37)	0.7794	
Presence of Liver Metastases							0.3120
Yes	94/ 131 (71.8)	4.2 (3.0, 5.7)	65/ 130 (50.0)	5.6 (4.2, 7.4)	1.29 (0.93, 1.77)	0.1217	
No	56/ 81 (69.1)	5.3 (2.9, 8.6)	41/ 72 (56.9)	5.7 (4.2, 8.1)	0.93 (0.62, 1.41)	0.7361	
Side of Tumor							0.6967
Left	53/ 80 (66.3)	4.6 (3.0, 9.9)	35/ 76 (46.1)	6.9 (4.4, NE)	1.11 (0.71, 1.73)	0.6448	
Right	97/ 132 (73.5)	4.2 (2.9, 5.6)	71/ 126 (56.3)	5.4 (4.2, 7.2)	1.19 (0.88, 1.62)	0.2699	

[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio > 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.
[4] P-Value for interaction from Cox proportional hazards model using ties=exact option with treatment, subgroup and treatment*subgroup interaction as covariates.
Including only patients from the full analysis set who completed at least 1 post-baseline PRO assessment.
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Kaplan Meier Plot of Time to first improvement of at least 15 percent - PGI01-Change (Months)
Full Analysis Set



Kaplan-Meier Plots for subgroups only created if p-value for interaction < 0.05.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Responder Analysis of Objective Response Rate based on BICR Assessment
Full Analysis Set

	EC+FOLFOX (N=236)	Control 1 (N=243)
Number of subjects with events, n (%)	155 (65.7)	91 (37.4)
Number of censored subjects, n (%)	81 (34.3)	152 (62.6)
Stratified analysis [1]		
Relative Risk (95% CI) [2]	1.70 (1.41, 2.05)	
p-value	<.0001	
Odds Ratio (95% CI) [2]	3.17 (2.17, 4.62)	
p-value	<.0001	
Risk Difference (95% CI) [2]	28.00 (19.40, 36.61)	
p-value	<.0001	

[1] Stratified by ECOG PS by Randomization and Geographic Region by Randomization.
[2] Calculated using normal approximation (Wald).
Risk ratio > 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Responder Analysis of Objective Response Rate based on BICR Assessment - Subgroup analysis
Full Analysis Set

Subgroup Level	EC+FOLFOX (N=236) n/ N (%)	Control 1 (N=243) n/ N (%)	Unstratified analysis Relative Risk (95% CI) [1]	p-Value [1]	Interaction p-Value [2]
Age (Years)					0.4914
< 65	100/ 150 (66.7)	50/ 139 (36.0)	1.85 (1.44, 2.38)	<.0001	
>= 65	55/ 86 (64.0)	41/ 104 (39.4)	1.62 (1.22, 2.16)	0.0009	
Sex					0.4506
Male	82/ 123 (66.7)	42/ 119 (35.3)	1.89 (1.44, 2.48)	<.0001	
Female	73/ 113 (64.6)	49/ 124 (39.5)	1.63 (1.26, 2.11)	0.0002	
Region					0.2238
Europe	76/ 109 (69.7)	37/ 111 (33.3)	2.09 (1.56, 2.80)	<.0001	
USA/Canada	8/ 15 (53.3)	8/ 19 (42.1)	1.27 (0.62, 2.57)	0.5132	
Rest of World	71/ 112 (63.4)	46/ 113 (40.7)	1.56 (1.20, 2.03)	0.0010	
ECOG-PS at Randomization					0.8772
0	89/ 131 (67.9)	52/ 136 (38.2)	1.78 (1.39, 2.27)	<.0001	
1	66/ 105 (62.9)	39/ 107 (36.4)	1.72 (1.29, 2.31)	0.0002	
Number of Organs Involved					0.8388
<= 2	77/ 119 (64.7)	46/ 127 (36.2)	1.79 (1.37, 2.33)	<.0001	
>= 3	78/ 117 (66.7)	45/ 116 (38.8)	1.72 (1.32, 2.23)	<.0001	
Presence of Liver Metastases					0.9711
Yes	100/ 147 (68.0)	62/ 160 (38.8)	1.76 (1.40, 2.20)	<.0001	
No	55/ 89 (61.8)	29/ 83 (34.9)	1.77 (1.26, 2.47)	0.0009	
Side of Tumor					0.7729
Left	60/ 90 (66.7)	36/ 98 (36.7)	1.81 (1.35, 2.45)	<.0001	
Right	95/ 146 (65.1)	55/ 145 (37.9)	1.72 (1.35, 2.18)	<.0001	

[1] Calculated using normal approximation (Wald).
[2] p-Value for interaction based on Cochran´s Q Test.
Risk ratio > 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Completion Rates of EORTC QLQ-C30
Full Analysis Set

	EC+FOLFOX (N=236)		Control 1 (N=243)	
Visit	Number of patients [1]	Completed (%)	Number of patients [1]	Completed (%)
BASELINE	201	201 (100.0)	181	181 (100.0)
WEEK6	194	190 (97.9)	188	182 (96.8)
WEEK12	187	182 (97.3)	167	164 (98.2)
WEEK18	180	179 (99.4)	137	134 (97.8)
WEEK24	163	161 (98.8)	122	121 (99.2)
WEEK30	144	140 (97.2)	91	89 (97.8)
WEEK36	140	139 (99.3)	66	65 (98.5)
WEEK42	123	123 (100.0)	47	47 (100.0)
WEEK48	112	106 (94.6)	38	37 (97.4)
WEEK54	98	93 (94.9)	30	28 (93.3)
WEEK60	82	79 (96.3)	27	27 (100.0)
WEEK66	71	67 (94.4)	19	19 (100.0)
WEEK72	63	59 (93.7)	10	10 (100.0)
WEEK78	50	49 (98.0)	6	6 (100.0)
WEEK86	37	35 (94.6)	5	5 (100.0)
WEEK94	34	33 (97.1)	6	6 (100.0)
WEEK102	22	21 (95.5)	4	4 (100.0)
WEEK110	0		0	
WEEK118	13	12 (92.3)	2	2 (100.0)
WEEK126	8	8 (100.0)	1	1 (100.0)
WEEK134	8	7 (87.5)	0	
WEEK142	4	4 (100.0)	1	1 (100.0)
WEEK150	2	2 (100.0)	0	
WEEK158	1	1 (100.0)	0	
WEEK166	0		0	
WEEK174	0		0	
WEEK182	0		0	
WEEK190	0		0	
WEEK198	0		0	
WEEK206	0		0	
WEEK214	0		0	
END OF TRT	79	77 (97.5)	96	95 (99.0)
FOLLOW UP	50	48 (96.0)	56	56 (100.0)

Baseline is the last non-missing measurement prior to first dose of study intervention.
[1] Defined as the number of patients who are eligible to complete the questionnaire at the respective visit.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Completion Rates of EQ-5D-5L
Full Analysis Set

	EC+FOLFOX (N=236)		Control 1 (N=243)	
Visit	Number of patients [1]	Completed (%)	Number of patients [1]	Completed (%)
BASELINE	197	197 (100.0)	176	176 (100.0)
WEEK6	192	188 (97.9)	183	177 (96.7)
WEEK12	185	180 (97.3)	163	160 (98.2)
WEEK18	177	175 (98.9)	134	131 (97.8)
WEEK24	161	159 (98.8)	120	119 (99.2)
WEEK30	136	136 (100.0)	88	88 (100.0)
WEEK36	136	136 (100.0)	64	64 (100.0)
WEEK42	121	121 (100.0)	47	47 (100.0)
WEEK48	110	104 (94.5)	38	37 (97.4)
WEEK54	96	91 (94.8)	30	27 (90.0)
WEEK60	81	78 (96.3)	27	27 (100.0)
WEEK66	70	66 (94.3)	19	19 (100.0)
WEEK72	62	58 (93.5)	10	10 (100.0)
WEEK78	49	48 (98.0)	6	6 (100.0)
WEEK86	36	34 (94.4)	5	5 (100.0)
WEEK94	33	32 (97.0)	6	6 (100.0)
WEEK102	22	20 (90.9)	4	4 (100.0)
WEEK110	19	19 (100.0)	3	3 (100.0)
WEEK118	12	11 (91.7)	2	2 (100.0)
WEEK126	8	8 (100.0)	1	1 (100.0)
WEEK134	7	6 (85.7)	0	
WEEK142	4	4 (100.0)	1	1 (100.0)
WEEK150	2	2 (100.0)	0	
WEEK158	1	1 (100.0)	0	
WEEK166	0		0	
WEEK174	0		0	
WEEK182	0		0	
WEEK190	0		0	
WEEK198	0		0	
WEEK206	4	0 (0.0)	2	0 (0.0)
WEEK214	2	0 (0.0)	0	
END OF TRT	75	75 (100.0)	92	92 (100.0)
FOLLOW UP	51	47 (92.2)	56	54 (96.4)

Baseline is the last non-missing measurement prior to first dose of study intervention.
[1] Defined as the number of patients who are eligible to complete the questionnaire at the respective visit.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Completion Rates of PGIS
Full Analysis Set

	EC+FOLFOX (N=236)		Control 1 (N=243)	
Visit	Number of patients [1]	Completed (%)	Number of patients [1]	Completed (%)
BASELINE	201	201 (100.0)	182	182 (100.0)
WEEK6	195	191 (97.9)	188	182 (96.8)
WEEK12	187	182 (97.3)	167	164 (98.2)
WEEK18	181	180 (99.4)	137	134 (97.8)
WEEK24	163	161 (98.8)	122	121 (99.2)
WEEK30	144	140 (97.2)	91	89 (97.8)
WEEK36	140	139 (99.3)	66	65 (98.5)
WEEK42	123	123 (100.0)	47	47 (100.0)
WEEK48	112	106 (94.6)	38	37 (97.4)
WEEK54	98	93 (94.9)	30	28 (93.3)
WEEK60	82	79 (96.3)	27	27 (100.0)
WEEK66	71	67 (94.4)	19	19 (100.0)
WEEK72	63	59 (93.7)	10	10 (100.0)
WEEK78	50	49 (98.0)	6	6 (100.0)
WEEK86	37	35 (94.6)	5	5 (100.0)
WEEK94	34	33 (97.1)	6	6 (100.0)
WEEK102	22	21 (95.5)	4	4 (100.0)
WEEK110	20	20 (100.0)	3	3 (100.0)
WEEK118	13	12 (92.3)	2	2 (100.0)
WEEK126	8	8 (100.0)	1	1 (100.0)
WEEK134	8	7 (87.5)	0	
WEEK142	4	4 (100.0)	1	1 (100.0)
WEEK150	2	2 (100.0)	0	
WEEK158	1	1 (100.0)	0	
WEEK166	0		0	
WEEK174	0		0	
WEEK182	0		0	
WEEK190	0		0	
WEEK198	0		0	
WEEK206	0		0	
WEEK214	0		0	
END OF TRT	79	77 (97.5)	96	95 (99.0)
FOLLOW UP	2	0 (0.0)	0	

Baseline is the last non-missing measurement prior to first dose of study intervention.
[1] Defined as the number of patients who are eligible to complete the questionnaire at the respective visit.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Completion Rates of PGIC
Full Analysis Set

	EC+FOLFOX (N=236)		Control 1 (N=243)	
Visit	Number of patients [1]	Completed (%)	Number of patients [1]	Completed (%)
WEEK6	195	190 (97.4)	188	180 (95.7)
WEEK12	187	181 (96.8)	167	162 (97.0)
WEEK18	181	180 (99.4)	137	131 (95.6)
WEEK24	163	156 (95.7)	122	119 (97.5)
WEEK30	144	140 (97.2)	91	89 (97.8)
WEEK36	140	138 (98.6)	66	64 (97.0)
WEEK42	123	123 (100.0)	47	47 (100.0)
WEEK48	112	105 (93.8)	38	37 (97.4)
WEEK54	98	91 (92.9)	30	28 (93.3)
WEEK60	82	79 (96.3)	27	27 (100.0)
WEEK66	71	67 (94.4)	19	19 (100.0)
WEEK72	63	59 (93.7)	10	10 (100.0)
WEEK78	50	49 (98.0)	6	6 (100.0)
WEEK86	37	35 (94.6)	5	5 (100.0)
WEEK94	34	32 (94.1)	6	6 (100.0)
WEEK102	22	21 (95.5)	4	4 (100.0)
WEEK110	20	20 (100.0)	3	3 (100.0)
WEEK118	13	12 (92.3)	2	2 (100.0)
WEEK126	8	8 (100.0)	1	1 (100.0)
WEEK134	8	7 (87.5)	0	
WEEK142	4	4 (100.0)	1	1 (100.0)
WEEK150	2	2 (100.0)	0	
WEEK158	1	1 (100.0)	0	
WEEK166	0		0	
WEEK174	0		0	
WEEK182	0		0	
WEEK190	0		0	
WEEK198	0		0	
WEEK206	0		0	
WEEK214	0		0	
END OF TRT	79	75 (94.9)	96	88 (91.7)
FOLLOW UP	50	48 (96.0)	56	54 (96.4)

[1] Defined as the number of patients who are eligible to complete the questionnaire at the respective visit.

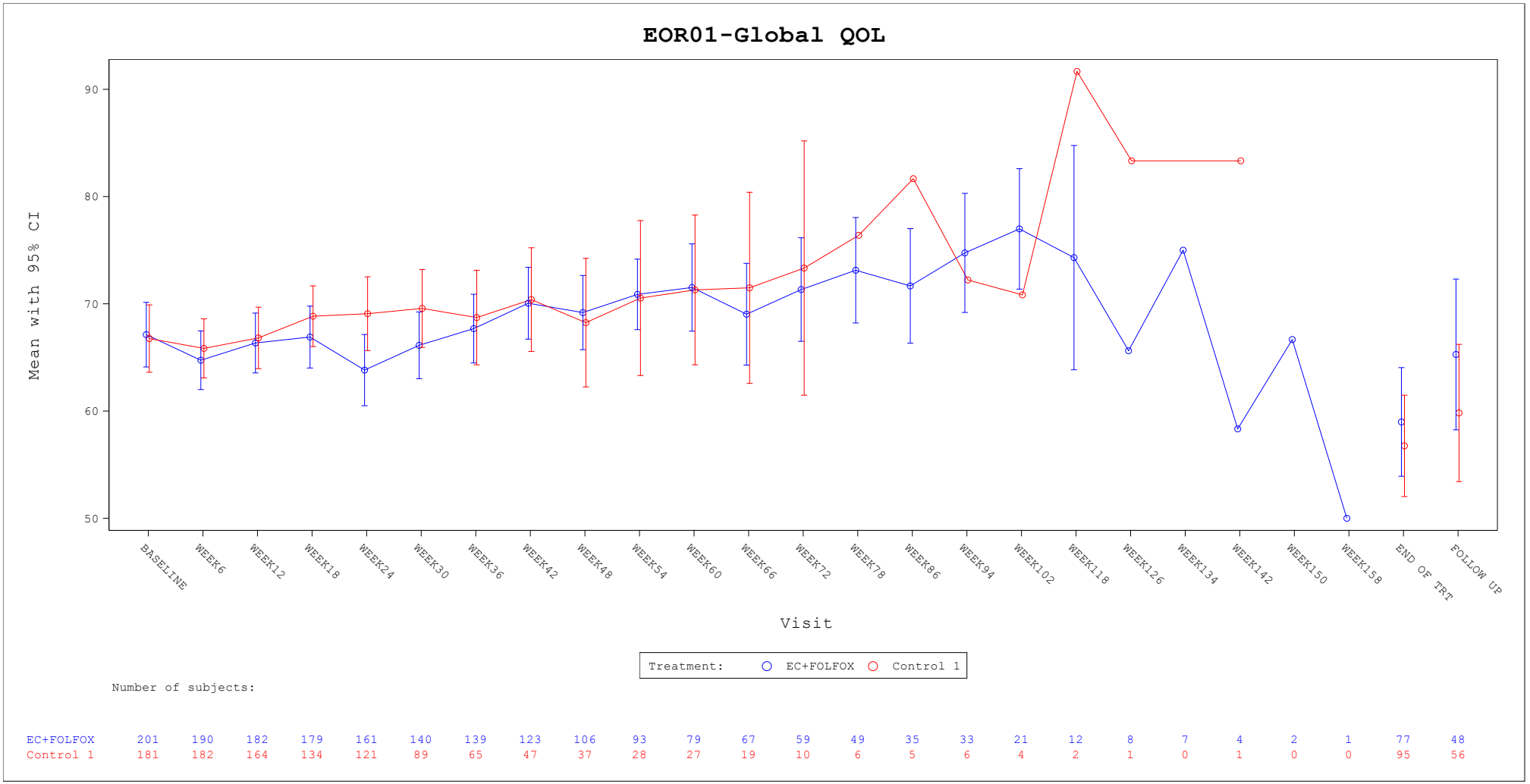
		___EC+FOLFOX (N=236)___	___Control 1 (N=243)___
EOR01-Global QOL	n (missing)	201 (35)	181 (62)
	Mean (SD)	67.12 (21.654)	66.76 (21.427)
	Median	66.67	66.67
	Q1, Q3	50.00, 83.33	50.00, 83.33
	Min, Max	0.0, 100.0	0.0, 100.0
EOR01-Physical Functioning	n (missing)	201 (35)	181 (62)
	Mean (SD)	82.92 (16.650)	81.33 (17.532)
	Median	86.67	86.67
	Q1, Q3	73.33, 93.33	73.33, 93.33
	Min, Max	13.3, 100.0	13.3, 100.0
EOR01-Role Functioning	n (missing)	201 (35)	181 (62)
	Mean (SD)	76.12 (24.982)	76.61 (26.222)
	Median	83.33	83.33
	Q1, Q3	66.67, 100.00	66.67, 100.00
	Min, Max	0.0, 100.0	0.0, 100.0
EOR01-Emotional Functioning	n (missing)	201 (35)	181 (62)
	Mean (SD)	73.71 (20.533)	76.10 (19.233)
	Median	75.00	83.33
	Q1, Q3	66.67, 83.33	66.67, 91.67
	Min, Max	0.0, 100.0	0.0, 100.0
EOR01-Cognitive Functioning	n (missing)	201 (35)	181 (62)
	Mean (SD)	87.73 (16.626)	89.23 (14.770)
	Median	100.00	100.00
	Q1, Q3	83.33, 100.00	83.33, 100.00
	Min, Max	16.7, 100.0	33.3, 100.0
EOR01-Social Functioning	n (missing)	201 (35)	181 (62)
	Mean (SD)	75.46 (24.384)	75.23 (24.127)
	Median	83.33	83.33
	Q1, Q3	66.67, 100.00	66.67, 100.00
	Min, Max	0.0, 100.0	0.0, 100.0
EOR01-Fatigue	n (missing)	201 (35)	181 (62)
	Mean (SD)	28.08 (21.944)	28.79 (21.624)
	Median	33.33	33.33
	Q1, Q3	11.11, 33.33	11.11, 33.33
	Min, Max	0.0, 88.9	0.0, 100.0
EOR01-Nausea and Vomiting	n (missing)	201 (35)	181 (62)
	Mean (SD)	4.81 (10.492)	7.09 (15.125)
	Median	0.00	0.00
	Q1, Q3	0.00, 0.00	0.00, 16.67
	Min, Max	0.0, 66.7	0.0, 100.0
EOR01-Pain	n (missing)	201 (35)	181 (62)
	Mean (SD)	25.54 (25.112)	22.01 (26.276)
	Median	16.67	16.67
	Q1, Q3	0.00, 33.33	0.00, 33.33
	Min, Max	0.0, 100.0	0.0, 100.0
EOR01-Dyspnoea	n (missing)	201 (35)	181 (62)
	Mean (SD)	13.60 (21.415)	13.44 (21.017)
	Median	0.00	0.00
	Q1, Q3	0.00, 33.33	0.00, 33.33
	Min, Max	0.0, 100.0	0.0, 100.0

		EC+FOLFOX (N=236)	Control 1 (N=243)
EOR01-Insomnia	n (missing)	201 (35)	181 (62)
	Mean (SD)	30.35 (28.905)	26.34 (27.891)
	Median	33.33	33.33
	Q1, Q3	0.00, 33.33	0.00, 33.33
	Min, Max	0.0, 100.0	0.0, 100.0
EOR01-Appetite Loss	n (missing)	201 (35)	181 (62)
	Mean (SD)	20.90 (26.354)	18.78 (27.275)
	Median	0.00	0.00
	Q1, Q3	0.00, 33.33	0.00, 33.33
	Min, Max	0.0, 100.0	0.0, 100.0
EOR01-Constipation	n (missing)	201 (35)	181 (62)
	Mean (SD)	14.10 (22.737)	13.81 (23.030)
	Median	0.00	0.00
	Q1, Q3	0.00, 33.33	0.00, 33.33
	Min, Max	0.0, 100.0	0.0, 100.0
EOR01-Diarrhea	n (missing)	201 (35)	181 (62)
	Mean (SD)	13.43 (23.376)	10.68 (20.399)
	Median	0.00	0.00
	Q1, Q3	0.00, 33.33	0.00, 33.33
	Min, Max	0.0, 100.0	0.0, 100.0
EOR01-Financial Difficulties	n (missing)	201 (35)	181 (62)
	Mean (SD)	17.41 (26.682)	18.78 (25.400)
	Median	0.00	0.00
	Q1, Q3	0.00, 33.33	0.00, 33.33
	Min, Max	0.0, 100.0	0.0, 100.0
EQ5D02-EQ-VAS Score	n (missing)	197 (39)	176 (67)
	Mean (SD)	70.85 (17.672)	73.38 (18.276)
	Median	70.00	79.50
	Q1, Q3	60.00, 83.00	66.00, 86.50
	Min, Max	16.0, 100.0	5.0, 100.0
PGIS01 - Colorectal Cancer	n (missing)	201 (35)	182 (61)
	Mean (SD)	1.31 (0.997)	1.25 (0.986)
	Median	1.00	1.00
	Q1, Q3	1.00, 2.00	0.00, 2.00
	Min, Max	0.0, 3.0	0.0, 3.0

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Summary over time - EOR01-Global QOL
Full Analysis Set

	EC+FOLFOX (N=236)				Control 1 (N=243)			
Visit	n	Median (Range)	Mean (SD)	95% CI [1]	n	Median (Range)	Mean (SD)	95% CI [1]
BASELINE	201	66.67 (0.0, 100.0)	67.12 (21.654)	[64.11, 70.13]	181	66.67 (0.0, 100.0)	66.76 (21.427)	[63.62, 69.90]
WEEK6	190	66.67 (0.0, 100.0)	64.74 (19.109)	[62.00, 67.47]	182	66.67 (0.0, 100.0)	65.84 (18.831)	[63.09, 68.60]
WEEK12	182	66.67 (0.0, 100.0)	66.35 (19.079)	[63.56, 69.14]	164	66.67 (16.7, 100.0)	66.82 (18.565)	[63.96, 69.68]
WEEK18	179	66.67 (0.0, 100.0)	66.90 (19.562)	[64.01, 69.78]	134	66.67 (0.0, 100.0)	68.84 (16.570)	[66.01, 71.67]
WEEK24	161	66.67 (0.0, 100.0)	63.82 (21.330)	[60.50, 67.14]	121	75.00 (0.0, 100.0)	69.08 (19.107)	[65.64, 72.52]
WEEK30	140	66.67 (0.0, 100.0)	66.13 (18.626)	[63.02, 69.24]	89	66.67 (16.7, 100.0)	69.57 (17.230)	[65.94, 73.20]
WEEK36	139	66.67 (0.0, 100.0)	67.69 (19.100)	[64.48, 70.89]	65	66.67 (16.7, 100.0)	68.72 (17.802)	[64.31, 73.13]
WEEK42	123	66.67 (0.0, 100.0)	70.05 (18.751)	[66.71, 73.40]	47	66.67 (33.3, 100.0)	70.39 (16.467)	[65.56, 75.22]
WEEK48	106	66.67 (0.0, 100.0)	69.18 (17.972)	[65.72, 72.64]	37	66.67 (33.3, 100.0)	68.24 (17.985)	[62.25, 74.24]
WEEK54	93	75.00 (16.7, 100.0)	70.88 (15.955)	[67.59, 74.16]	28	79.17 (33.3, 100.0)	70.54 (18.631)	[63.31, 77.76]
WEEK60	79	75.00 (16.7, 100.0)	71.52 (18.180)	[67.45, 75.59]	27	66.67 (33.3, 100.0)	71.30 (17.652)	[64.31, 78.28]
WEEK66	67	75.00 (0.0, 100.0)	69.03 (19.452)	[64.29, 73.77]	19	66.67 (41.7, 100.0)	71.49 (18.492)	[62.58, 80.40]
WEEK72	59	83.33 (25.0, 100.0)	71.33 (18.522)	[66.50, 76.15]	10	70.83 (50.0, 100.0)	73.33 (16.574)	[61.48, 85.19]
WEEK78	49	75.00 (33.3, 100.0)	73.13 (17.118)	[68.21, 78.05]	6	79.17 (50.0, 100.0)	76.39 (17.010)	[58.54, 94.24]
WEEK86	35	75.00 (33.3, 100.0)	71.67 (15.551)	[66.32, 77.01]	5	83.33 (66.7, 100.0)	81.67 (14.907)	[63.16, 100.18]
WEEK94	33	83.33 (33.3, 100.0)	74.75 (15.658)	[69.20, 80.30]	6	75.00 (50.0, 100.0)	72.22 (20.184)	[51.04, 93.40]
WEEK102	21	83.33 (50.0, 100.0)	76.98 (12.334)	[71.37, 82.60]	4	75.00 (33.3, 100.0)	70.83 (28.464)	[25.54, 116.13]
WEEK118	12	83.33 (41.7, 100.0)	74.31 (16.460)	[63.85, 84.76]	2	91.67 (83.3, 100.0)	91.67 (11.785)	[-14.22, 197.55]
WEEK126	8	66.67 (33.3, 91.7)	65.62 (18.059)	[50.53, 80.72]	1	83.33 (83.3, 83.3)	83.33 (NE)	[NE, NE]
WEEK134	7	75.00 (41.7, 100.0)	75.00 (19.245)	[57.20, 92.80]	0	NE (NE, NE)	NE (NE)	[NE, NE]
WEEK142	4	58.33 (33.3, 83.3)	58.33 (21.517)	[24.10, 92.57]	1	83.33 (83.3, 83.3)	83.33 (NE)	[NE, NE]
WEEK150	2	66.67 (66.7, 66.7)	66.67 (0.000)	[NE, NE]	0	NE (NE, NE)	NE (NE)	[NE, NE]
WEEK158	1	50.00 (50.0, 50.0)	50.00 (NE)	[NE, NE]	0	NE (NE, NE)	NE (NE)	[NE, NE]
END OF TRT	77	58.33 (16.7, 100.0)	58.98 (22.327)	[53.92, 64.05]	95	58.33 (0.0, 100.0)	56.75 (23.200)	[52.03, 61.48]
FOLLOW UP	48	66.67 (0.0, 100.0)	65.28 (24.209)	[58.25, 72.31]	56	66.67 (16.7, 100.0)	59.82 (23.895)	[53.42, 66.22]

Baseline is the last non-missing measurement prior to first dose of study intervention.
[1] Confidence interval based on the normal distribution.
For functional scales, higher scores represent a better level of functioning. For symptom-oriented scales, a higher score represents more severe symptoms.



Number of subjects:

EC+FOLFOX	201	190	182	179	161	140	139	123	106	93	79	67	59	49	35	33	21	12	8	7	4	2	1	77	48
Control 1	181	182	164	134	121	89	65	47	37	28	27	19	10	6	5	6	4	2	1	0	1	0	0	95	56

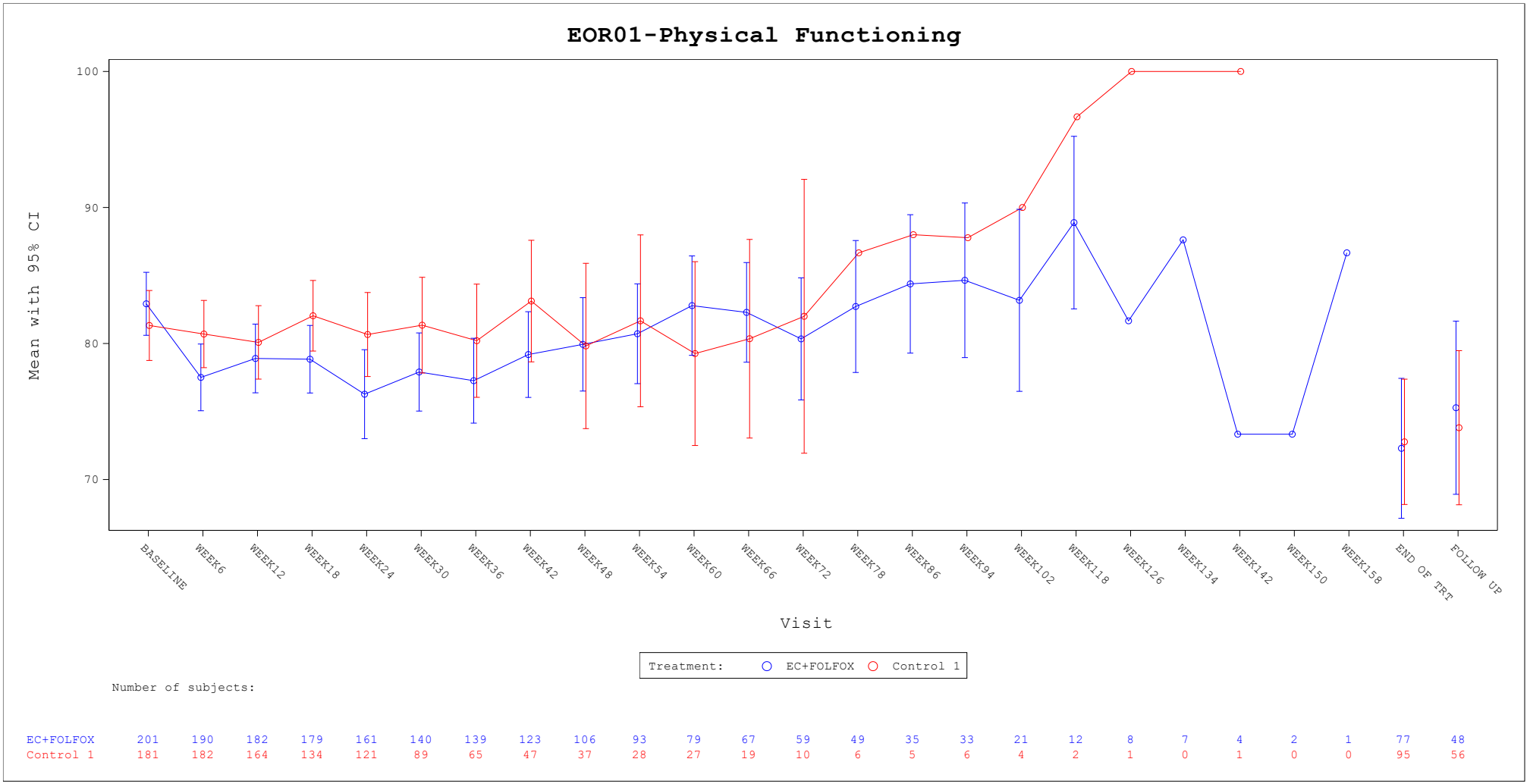
Baseline is the last non-missing measurement prior to first dose of study intervention.
No confidence intervalls are drawn, when there are less than 10 patients in treatment arm.
For functional scales, higher scores represent a better level of functioning. For symptom-oriented scales, a higher score represents more severe symptoms.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Summary over time - EOR01-Physical Functioning
Full Analysis Set

	EC+FOLFOX (N=236)				Control 1 (N=243)			
Visit	n	Median (Range)	Mean (SD)	95% CI [1]	n	Median (Range)	Mean (SD)	95% CI [1]
BASELINE	201	86.67 (13.3, 100.0)	82.92 (16.650)	[80.60, 85.23]	181	86.67 (13.3, 100.0)	81.33 (17.532)	[78.75, 83.90]
WEEK6	190	80.00 (20.0, 100.0)	77.51 (17.134)	[75.06, 79.96]	182	86.67 (13.3, 100.0)	80.70 (16.899)	[78.22, 83.17]
WEEK12	182	80.00 (26.7, 100.0)	78.90 (17.273)	[76.37, 81.43]	164	86.67 (20.0, 100.0)	80.08 (17.506)	[77.38, 82.78]
WEEK18	179	80.00 (26.7, 100.0)	78.85 (16.839)	[76.36, 81.33]	134	86.67 (20.0, 100.0)	82.04 (15.190)	[79.44, 84.64]
WEEK24	161	80.00 (0.0, 100.0)	76.27 (21.014)	[73.00, 79.54]	121	80.00 (20.0, 100.0)	80.66 (17.157)	[77.57, 83.75]
WEEK30	140	80.00 (6.7, 100.0)	77.90 (17.190)	[75.03, 80.78]	89	86.67 (20.0, 100.0)	81.35 (16.702)	[77.83, 84.87]
WEEK36	139	80.00 (0.0, 100.0)	77.27 (18.595)	[74.15, 80.38]	65	80.00 (20.0, 100.0)	80.21 (16.790)	[76.04, 84.37]
WEEK42	123	80.00 (13.3, 100.0)	79.19 (17.650)	[76.04, 82.34]	47	86.67 (40.0, 100.0)	83.12 (15.218)	[78.65, 87.59]
WEEK48	106	80.00 (0.0, 100.0)	79.94 (17.829)	[76.50, 83.37]	37	80.00 (26.7, 100.0)	79.82 (18.223)	[73.74, 85.90]
WEEK54	93	86.67 (20.0, 100.0)	80.72 (17.814)	[77.05, 84.39]	28	83.33 (40.0, 100.0)	81.67 (16.292)	[75.35, 87.98]
WEEK60	79	86.67 (20.0, 100.0)	82.78 (16.316)	[79.13, 86.44]	27	80.00 (33.3, 100.0)	79.26 (17.080)	[72.50, 86.02]
WEEK66	67	80.00 (33.3, 100.0)	82.29 (15.022)	[78.62, 85.95]	19	80.00 (40.0, 100.0)	80.35 (15.149)	[73.05, 87.65]
WEEK72	59	80.00 (26.7, 100.0)	80.34 (17.217)	[75.85, 84.83]	10	80.00 (53.3, 100.0)	82.00 (14.072)	[71.93, 92.07]
WEEK78	49	86.67 (26.7, 100.0)	82.72 (16.883)	[77.87, 87.57]	6	86.67 (66.7, 100.0)	86.67 (13.333)	[72.67, 100.66]
WEEK86	35	86.67 (46.7, 100.0)	84.38 (14.814)	[79.29, 89.47]	5	93.33 (73.3, 100.0)	88.00 (13.663)	[71.04, 104.96]
WEEK94	33	86.67 (40.0, 100.0)	84.65 (16.028)	[78.96, 90.33]	6	93.33 (66.7, 100.0)	87.78 (14.857)	[72.19, 103.37]
WEEK102	21	86.67 (40.0, 100.0)	83.17 (14.700)	[76.48, 89.87]	4	96.67 (66.7, 100.0)	90.00 (15.870)	[64.75, 115.25]
WEEK118	12	90.00 (73.3, 100.0)	88.89 (9.983)	[82.55, 95.23]	2	96.67 (93.3, 100.0)	96.67 (4.714)	[54.31, 139.02]
WEEK126	8	80.00 (60.0, 100.0)	81.67 (15.430)	[68.77, 94.57]	1	100.00 (100.0, 100.0)	100.00 (NE)	[NE, NE]
WEEK134	7	93.33 (66.7, 100.0)	87.62 (14.105)	[74.57, 100.66]	0	NE (NE, NE)	NE (NE)	[NE, NE]
WEEK142	4	70.00 (60.0, 93.3)	73.33 (14.402)	[50.42, 96.25]	1	100.00 (100.0, 100.0)	100.00 (NE)	[NE, NE]
WEEK150	2	73.33 (73.3, 73.3)	73.33 (0.000)	[NE, NE]	0	NE (NE, NE)	NE (NE)	[NE, NE]
WEEK158	1	86.67 (86.7, 86.7)	86.67 (NE)	[NE, NE]	0	NE (NE, NE)	NE (NE)	[NE, NE]
END OF TRT	77	80.00 (0.0, 100.0)	72.29 (22.661)	[67.15, 77.44]	95	80.00 (0.0, 100.0)	72.77 (22.611)	[68.17, 77.38]
FOLLOW UP	48	80.00 (6.7, 100.0)	75.28 (21.916)	[68.91, 81.64]	56	80.00 (20.0, 100.0)	73.81 (21.153)	[68.14, 79.47]

Baseline is the last non-missing measurement prior to first dose of study intervention.
[1] Confidence interval based on the normal distribution.
For functional scales, higher scores represent a better level of functioning. For symptom-oriented scales, a higher score represents more severe symptoms.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Plot over time - EOR01-Physical Functioning
Full Analysis Set



Number of subjects:

EC+FOLFOX	201	190	182	179	161	140	139	123	106	93	79	67	59	49	35	33	21	12	8	7	4	2	1	77	48
Control 1	181	182	164	134	121	89	65	47	37	28	27	19	10	6	5	6	4	2	1	0	1	0	0	95	56

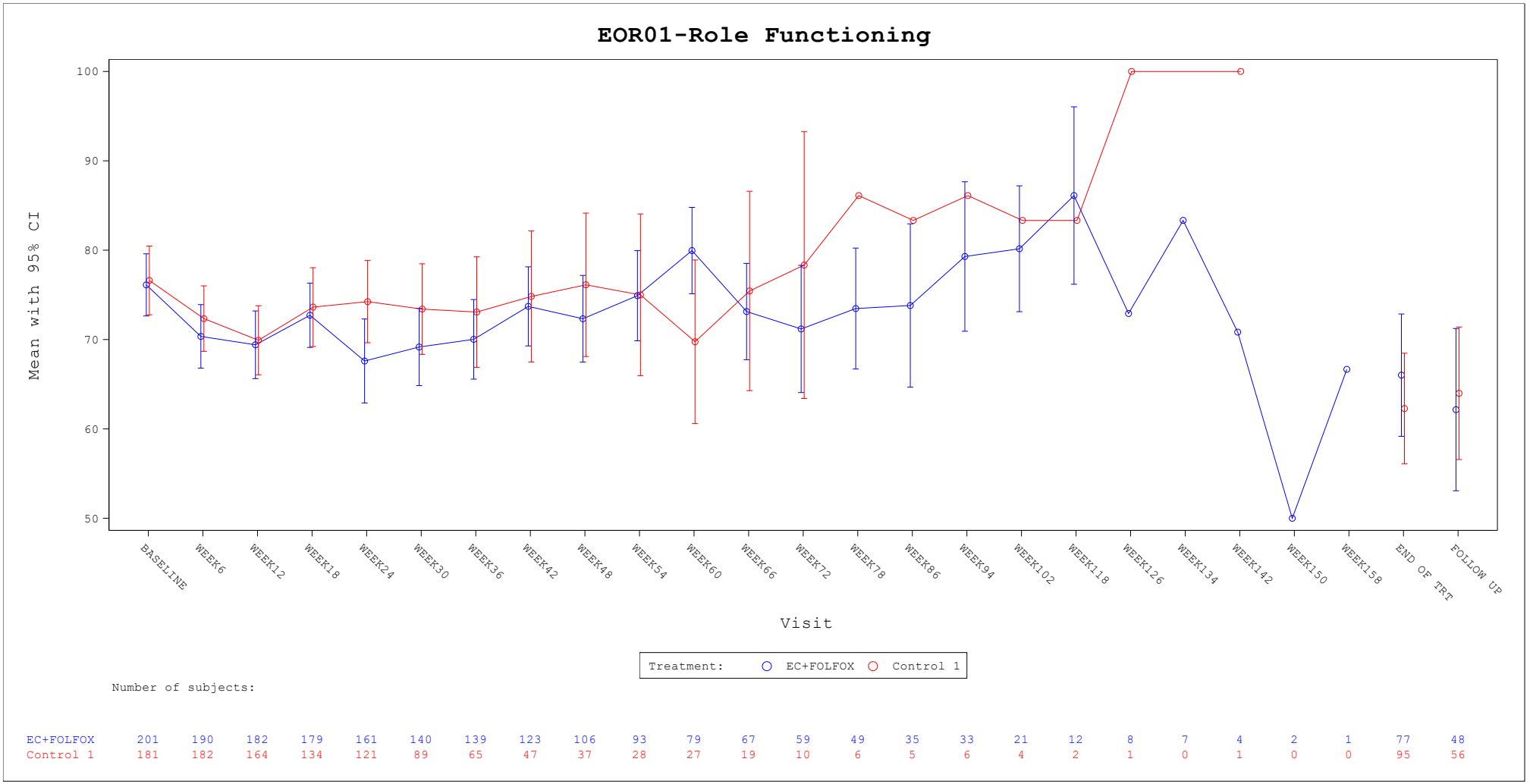
Baseline is the last non-missing measurement prior to first dose of study intervention.
No confidence intervalls are drawn, when there are less than 10 patients in treatment arm.
For functional scales, higher scores represent a better level of functioning. For symptom-oriented scales, a higher score represents more severe symptoms.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Summary over time - EOR01-Role Functioning
Full Analysis Set

	EC+FOLFOX (N=236)				Control 1 (N=243)			
Visit	n	Median (Range)	Mean (SD)	95% CI [1]	n	Median (Range)	Mean (SD)	95% CI [1]
BASELINE	201	83.33 (0.0, 100.0)	76.12 (24.982)	[72.64, 79.59]	181	83.33 (0.0, 100.0)	76.61 (26.222)	[72.77, 80.46]
WEEK6	190	66.67 (0.0, 100.0)	70.35 (24.866)	[66.79, 73.91]	182	66.67 (0.0, 100.0)	72.34 (25.050)	[68.68, 76.01]
WEEK12	182	66.67 (0.0, 100.0)	69.41 (25.899)	[65.63, 73.20]	164	66.67 (0.0, 100.0)	69.92 (25.034)	[66.06, 73.78]
WEEK18	179	66.67 (0.0, 100.0)	72.72 (24.396)	[69.12, 76.32]	134	75.00 (0.0, 100.0)	73.63 (25.795)	[69.22, 78.04]
WEEK24	161	66.67 (0.0, 100.0)	67.60 (30.233)	[62.89, 72.30]	121	83.33 (0.0, 100.0)	74.24 (25.550)	[69.64, 78.84]
WEEK30	140	66.67 (0.0, 100.0)	69.17 (25.830)	[64.85, 73.48]	89	66.67 (0.0, 100.0)	73.41 (24.063)	[68.34, 78.48]
WEEK36	139	66.67 (0.0, 100.0)	70.02 (26.556)	[65.57, 74.48]	65	66.67 (0.0, 100.0)	73.08 (24.947)	[66.90, 79.26]
WEEK42	123	66.67 (0.0, 100.0)	73.71 (24.795)	[69.29, 78.14]	47	66.67 (0.0, 100.0)	74.82 (25.030)	[67.47, 82.17]
WEEK48	106	66.67 (0.0, 100.0)	72.33 (25.186)	[67.48, 77.18]	37	83.33 (0.0, 100.0)	76.13 (24.069)	[68.10, 84.15]
WEEK54	93	66.67 (0.0, 100.0)	74.91 (24.527)	[69.86, 79.96]	28	83.33 (33.3, 100.0)	75.00 (23.351)	[65.95, 84.05]
WEEK60	79	83.33 (16.7, 100.0)	79.96 (21.579)	[75.12, 84.79]	27	66.67 (33.3, 100.0)	69.75 (23.130)	[60.60, 78.90]
WEEK66	67	66.67 (0.0, 100.0)	73.13 (22.087)	[67.75, 78.52]	19	66.67 (33.3, 100.0)	75.44 (23.153)	[64.28, 86.60]
WEEK72	59	66.67 (0.0, 100.0)	71.19 (27.304)	[64.07, 78.30]	10	83.33 (33.3, 100.0)	78.33 (20.861)	[63.41, 93.26]
WEEK78	49	66.67 (0.0, 100.0)	73.47 (23.550)	[66.70, 80.23]	6	91.67 (66.7, 100.0)	86.11 (16.387)	[68.91, 103.31]
WEEK86	35	66.67 (0.0, 100.0)	73.81 (26.595)	[64.67, 82.95]	5	83.33 (66.7, 100.0)	83.33 (16.667)	[62.64, 104.03]
WEEK94	33	83.33 (0.0, 100.0)	79.29 (23.581)	[70.93, 87.65]	6	91.67 (66.7, 100.0)	86.11 (16.387)	[68.91, 103.31]
WEEK102	21	83.33 (50.0, 100.0)	80.16 (15.473)	[73.12, 87.20]	4	83.33 (66.7, 100.0)	83.33 (19.245)	[52.71, 113.96]
WEEK118	12	91.67 (66.7, 100.0)	86.11 (15.624)	[76.18, 96.04]	2	83.33 (66.7, 100.0)	83.33 (23.570)	[-128.44, 295.10]
WEEK126	8	66.67 (33.3, 100.0)	72.92 (25.099)	[51.93, 93.90]	1	100.00 (100.0, 100.0)	100.00 (NE)	[NE, NE]
WEEK134	7	83.33 (50.0, 100.0)	83.33 (19.245)	[65.53, 101.13]	0	NE (NE, NE)	NE (NE)	[NE, NE]
WEEK142	4	66.67 (50.0, 100.0)	70.83 (20.972)	[37.46, 104.20]	1	100.00 (100.0, 100.0)	100.00 (NE)	[NE, NE]
WEEK150	2	50.00 (33.3, 66.7)	50.00 (23.570)	[-161.77, 261.77]	0	NE (NE, NE)	NE (NE)	[NE, NE]
WEEK158	1	66.67 (66.7, 66.7)	66.67 (NE)	[NE, NE]	0	NE (NE, NE)	NE (NE)	[NE, NE]
END OF TRT	77	66.67 (0.0, 100.0)	66.02 (30.161)	[59.17, 72.86]	95	66.67 (0.0, 100.0)	62.28 (30.385)	[56.09, 68.47]
FOLLOW UP	48	66.67 (0.0, 100.0)	62.15 (31.273)	[53.07, 71.23]	56	66.67 (0.0, 100.0)	63.99 (27.666)	[56.58, 71.40]

Baseline is the last non-missing measurement prior to first dose of study intervention.
[1] Confidence interval based on the normal distribution.
For functional scales, higher scores represent a better level of functioning. For symptom-oriented scales, a higher score represents more severe symptoms.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Plot over time - EOR01-Role Functioning
Full Analysis Set



Number of subjects:

EC+FOLFOX	201	190	182	179	161	140	139	123	106	93	79	67	59	49	35	33	21	12	8	7	4	2	1	77	48
Control 1	181	182	164	134	121	89	65	47	37	28	27	19	10	6	5	6	4	2	1	0	1	0	0	95	56

Baseline is the last non-missing measurement prior to first dose of study intervention.
No confidence intervalls are drawn, when there are less than 10 patients in treatment arm.
For functional scales, higher scores represent a better level of functioning. For symptom-oriented scales, a higher score represents more severe symptoms.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Summary over time - EOR01-Emotional Functioning
Full Analysis Set

	EC+FOLFOX (N=236)				Control 1 (N=243)			
Visit	n	Median (Range)	Mean (SD)	95% CI [1]	n	Median (Range)	Mean (SD)	95% CI [1]
BASELINE	201	75.00 (0.0, 100.0)	73.71 (20.533)	[70.86, 76.57]	181	83.33 (0.0, 100.0)	76.10 (19.233)	[73.28, 78.93]
WEEK6	190	83.33 (0.0, 100.0)	80.70 (18.555)	[78.05, 83.36]	182	83.33 (0.0, 100.0)	81.23 (18.042)	[78.59, 83.87]
WEEK12	182	83.33 (0.0, 100.0)	82.14 (18.104)	[79.49, 84.79]	164	83.33 (33.3, 100.0)	81.71 (16.432)	[79.17, 84.24]
WEEK18	179	83.33 (8.3, 100.0)	79.93 (20.194)	[76.96, 82.91]	134	91.67 (25.0, 100.0)	84.02 (16.574)	[81.19, 86.85]
WEEK24	161	83.33 (0.0, 100.0)	77.23 (22.836)	[73.67, 80.78]	121	83.33 (41.7, 100.0)	82.09 (16.125)	[79.19, 85.00]
WEEK30	140	83.33 (0.0, 100.0)	79.94 (20.039)	[76.59, 83.29]	89	83.33 (33.3, 100.0)	83.43 (16.925)	[79.86, 86.99]
WEEK36	139	83.33 (0.0, 100.0)	80.40 (20.111)	[77.02, 83.77]	65	83.33 (33.3, 100.0)	80.38 (16.564)	[76.28, 84.49]
WEEK42	123	83.33 (25.0, 100.0)	82.79 (17.973)	[79.58, 86.00]	47	91.67 (41.7, 100.0)	83.51 (15.877)	[78.85, 88.17]
WEEK48	106	91.67 (8.3, 100.0)	83.18 (19.787)	[79.37, 86.99]	37	83.33 (33.3, 100.0)	81.31 (17.056)	[75.62, 86.99]
WEEK54	93	91.67 (8.3, 100.0)	84.86 (17.590)	[81.23, 88.48]	28	83.33 (50.0, 100.0)	82.74 (14.860)	[76.98, 88.50]
WEEK60	79	91.67 (16.7, 100.0)	85.76 (16.940)	[81.97, 89.55]	27	83.33 (41.7, 100.0)	80.56 (19.199)	[72.96, 88.15]
WEEK66	67	83.33 (33.3, 100.0)	83.46 (16.823)	[79.35, 87.56]	19	91.67 (58.3, 100.0)	86.40 (14.754)	[79.29, 93.51]
WEEK72	59	91.67 (16.7, 100.0)	83.05 (19.326)	[78.01, 88.09]	10	100.00 (50.0, 100.0)	90.83 (15.933)	[79.44, 102.23]
WEEK78	49	91.67 (33.3, 100.0)	86.73 (15.675)	[82.23, 91.24]	6	100.00 (91.7, 100.0)	98.61 (3.402)	[95.04, 102.18]
WEEK86	35	91.67 (25.0, 100.0)	82.38 (20.884)	[75.21, 89.55]	5	100.00 (91.7, 100.0)	96.67 (4.564)	[91.00, 102.33]
WEEK94	33	91.67 (41.7, 100.0)	86.62 (16.789)	[80.66, 92.57]	6	95.83 (83.3, 100.0)	93.06 (8.193)	[84.46, 101.65]
WEEK102	21	83.33 (66.7, 100.0)	86.11 (12.454)	[80.44, 91.78]	4	100.00 (75.0, 100.0)	93.75 (12.500)	[73.86, 113.64]
WEEK118	12	87.50 (58.3, 100.0)	86.11 (14.794)	[76.71, 95.51]	2	95.83 (91.7, 100.0)	95.83 (5.893)	[42.89, 148.78]
WEEK126	8	75.00 (66.7, 100.0)	80.21 (14.731)	[67.89, 92.52]	1	100.00 (100.0, 100.0)	100.00 (NE)	[NE, NE]
WEEK134	7	91.67 (41.7, 100.0)	83.33 (20.412)	[64.45, 102.21]	0	NE (NE, NE)	NE (NE)	[NE, NE]
WEEK142	4	79.17 (50.0, 91.7)	75.00 (18.002)	[46.35, 103.65]	1	100.00 (100.0, 100.0)	100.00 (NE)	[NE, NE]
WEEK150	2	87.50 (75.0, 100.0)	87.50 (17.678)	[-71.33, 246.33]	0	NE (NE, NE)	NE (NE)	[NE, NE]
WEEK158	1	91.67 (91.7, 91.7)	91.67 (NE)	[NE, NE]	0	NE (NE, NE)	NE (NE)	[NE, NE]
END OF TRT	77	75.00 (0.0, 100.0)	68.07 (25.592)	[62.26, 73.88]	95	75.00 (0.0, 100.0)	73.51 (21.845)	[69.06, 77.96]
FOLLOW UP	48	75.00 (0.0, 100.0)	71.01 (25.147)	[63.71, 78.31]	56	75.00 (0.0, 100.0)	73.07 (23.246)	[66.84, 79.29]

Baseline is the last non-missing measurement prior to first dose of study intervention.
[1] Confidence interval based on the normal distribution.
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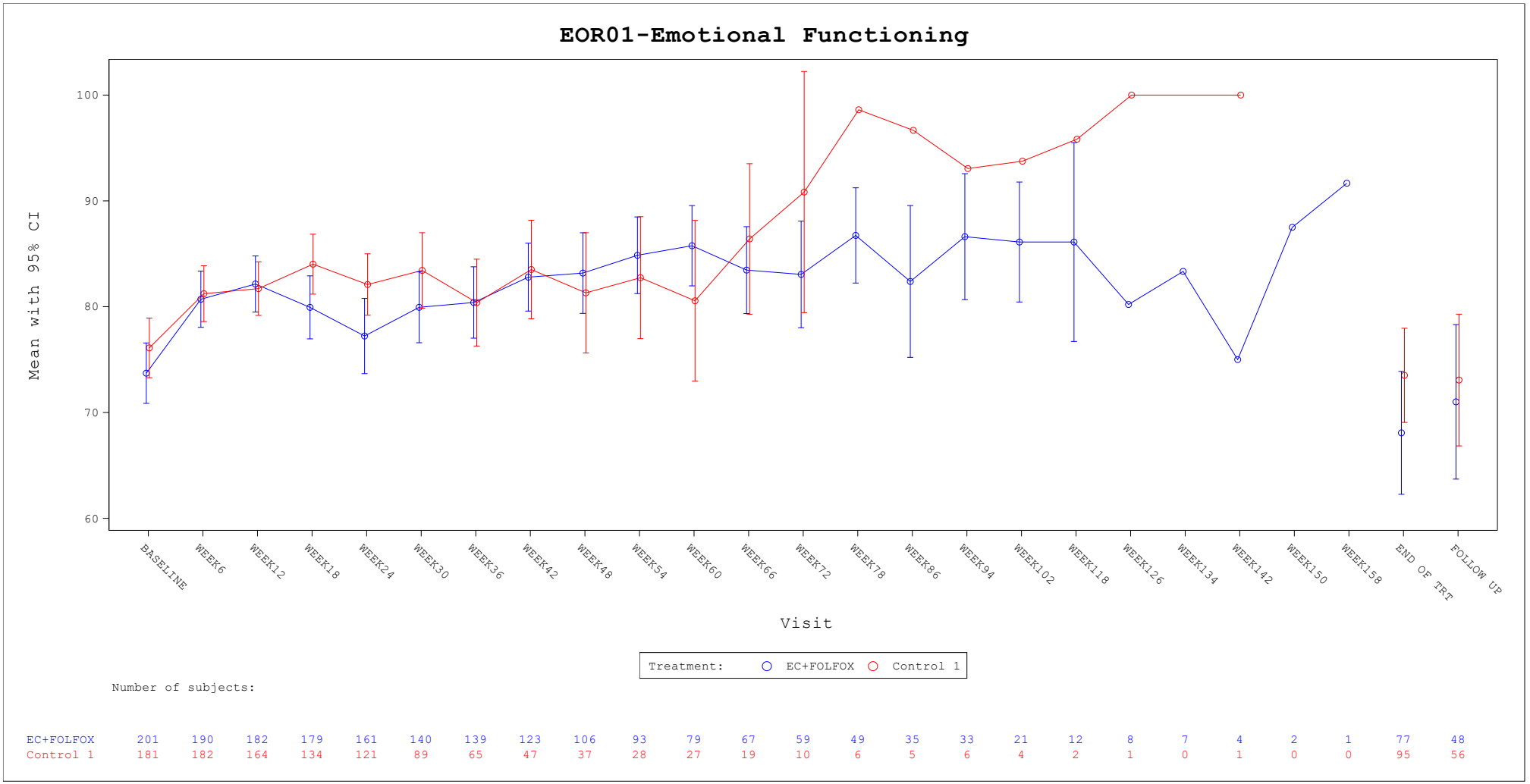
Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Plot over time - EOR01-Emotional Functioning
Full Analysis Set



Number of subjects:

EC+FOLFOX	201	190	182	179	161	140	139	123	106	93	79	67	59	49	35	33	21	12	8	7	4	2	1	77	48
Control 1	181	182	164	134	121	89	65	47	37	28	27	19	10	6	5	6	4	2	1	0	1	0	0	95	56

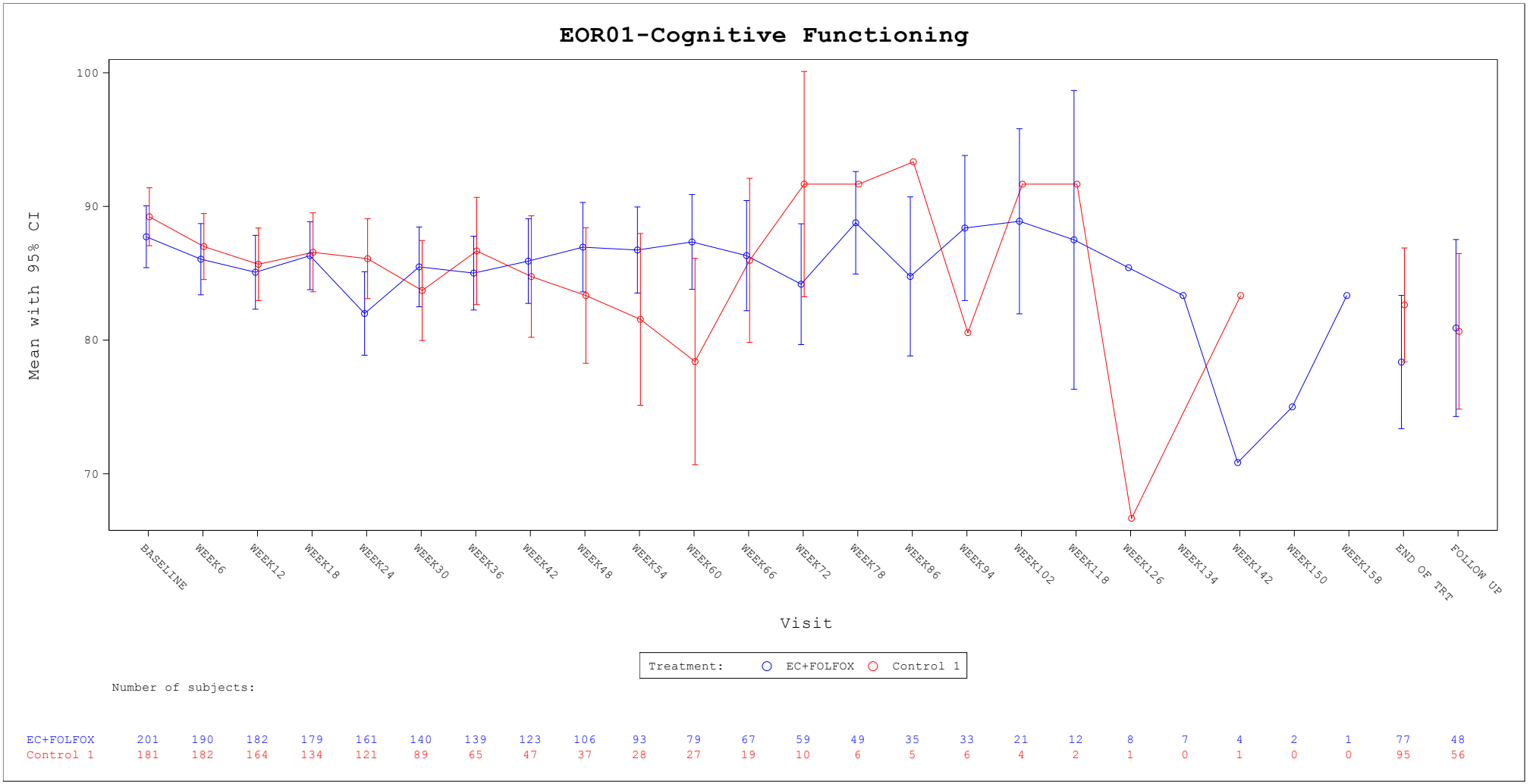
Baseline is the last non-missing measurement prior to first dose of study intervention.
No confidence intervalls are drawn, when there are less than 10 patients in treatment arm.
For functional scales, higher scores represent a better level of functioning. For symptom-oriented scales, a higher score represents more severe symptoms.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Summary over time - EOR01-Cognitive Functioning
Full Analysis Set

	EC+FOLFOX (N=236)				Control 1 (N=243)			
Visit	n	Median (Range)	Mean (SD)	95% CI [1]	n	Median (Range)	Mean (SD)	95% CI [1]
BASELINE	201	100.00 (16.7, 100.0)	87.73 (16.626)	[85.42, 90.04]	181	100.00 (33.3, 100.0)	89.23 (14.770)	[87.06, 91.39]
WEEK6	190	100.00 (0.0, 100.0)	86.05 (18.622)	[83.39, 88.72]	182	100.00 (16.7, 100.0)	87.00 (16.859)	[84.53, 89.46]
WEEK12	182	83.33 (0.0, 100.0)	85.07 (18.910)	[82.31, 87.84]	164	91.67 (16.7, 100.0)	85.67 (17.600)	[82.96, 88.38]
WEEK18	179	100.00 (33.3, 100.0)	86.31 (17.232)	[83.77, 88.85]	134	100.00 (16.7, 100.0)	86.57 (17.279)	[83.61, 89.52]
WEEK24	161	83.33 (0.0, 100.0)	81.99 (20.067)	[78.86, 85.11]	121	83.33 (33.3, 100.0)	86.09 (16.576)	[83.10, 89.07]
WEEK30	140	83.33 (0.0, 100.0)	85.48 (17.864)	[82.49, 88.46]	89	83.33 (33.3, 100.0)	83.71 (17.763)	[79.97, 87.45]
WEEK36	139	83.33 (16.7, 100.0)	85.01 (16.459)	[82.25, 87.77]	65	100.00 (33.3, 100.0)	86.67 (16.191)	[82.65, 90.68]
WEEK42	123	83.33 (16.7, 100.0)	85.91 (17.730)	[82.74, 89.07]	47	83.33 (33.3, 100.0)	84.75 (15.475)	[80.21, 89.30]
WEEK48	106	100.00 (0.0, 100.0)	86.95 (17.367)	[83.61, 90.29]	37	83.33 (50.0, 100.0)	83.33 (15.215)	[78.26, 88.41]
WEEK54	93	83.33 (33.3, 100.0)	86.74 (15.650)	[83.52, 89.96]	28	83.33 (50.0, 100.0)	81.55 (16.567)	[75.12, 87.97]
WEEK60	79	100.00 (33.3, 100.0)	87.34 (15.837)	[83.79, 90.89]	27	83.33 (33.3, 100.0)	78.40 (19.510)	[70.68, 86.11]
WEEK66	67	83.33 (33.3, 100.0)	86.32 (16.899)	[82.20, 90.44]	19	83.33 (66.7, 100.0)	85.96 (12.745)	[79.82, 92.11]
WEEK72	59	83.33 (33.3, 100.0)	84.18 (17.349)	[79.66, 88.70]	10	100.00 (66.7, 100.0)	91.67 (11.785)	[83.24, 100.10]
WEEK78	49	100.00 (50.0, 100.0)	88.78 (13.345)	[84.94, 92.61]	6	91.67 (83.3, 100.0)	91.67 (9.129)	[82.09, 101.25]
WEEK86	35	83.33 (50.0, 100.0)	84.76 (17.326)	[78.81, 90.71]	5	100.00 (83.3, 100.0)	93.33 (9.129)	[82.00, 104.67]
WEEK94	33	100.00 (50.0, 100.0)	88.38 (15.301)	[82.96, 93.81]	6	91.67 (33.3, 100.0)	80.56 (26.701)	[52.53, 108.58]
WEEK102	21	100.00 (50.0, 100.0)	88.89 (15.215)	[81.96, 95.81]	4	100.00 (66.7, 100.0)	91.67 (16.667)	[65.15, 118.19]
WEEK118	12	100.00 (50.0, 100.0)	87.50 (17.588)	[76.33, 98.67]	2	91.67 (83.3, 100.0)	91.67 (11.785)	[-14.22, 197.55]
WEEK126	8	100.00 (50.0, 100.0)	85.42 (22.603)	[66.52, 104.31]	1	66.67 (66.7, 66.7)	66.67 (NE)	[NE, NE]
WEEK134	7	83.33 (33.3, 100.0)	83.33 (23.570)	[61.53, 105.13]	0	NE (NE, NE)	NE (NE)	[NE, NE]
WEEK142	4	75.00 (33.3, 100.0)	70.83 (28.464)	[25.54, 116.13]	1	83.33 (83.3, 83.3)	83.33 (NE)	[NE, NE]
WEEK150	2	75.00 (66.7, 83.3)	75.00 (11.785)	[-30.89, 180.89]	0	NE (NE, NE)	NE (NE)	[NE, NE]
WEEK158	1	83.33 (83.3, 83.3)	83.33 (NE)	[NE, NE]	0	NE (NE, NE)	NE (NE)	[NE, NE]
END OF TRT	77	83.33 (0.0, 100.0)	78.35 (21.976)	[73.37, 83.34]	95	83.33 (0.0, 100.0)	82.63 (20.901)	[78.37, 86.89]
FOLLOW UP	48	83.33 (0.0, 100.0)	80.90 (22.803)	[74.28, 87.52]	56	83.33 (16.7, 100.0)	80.65 (21.737)	[74.83, 86.48]

Baseline is the last non-missing measurement prior to first dose of study intervention.
[1] Confidence interval based on the normal distribution.
For functional scales, higher scores represent a better level of functioning. For symptom-oriented scales, a higher score represents more severe symptoms.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Plot over time - EOR01-Cognitive Functioning
Full Analysis Set



Number of subjects:

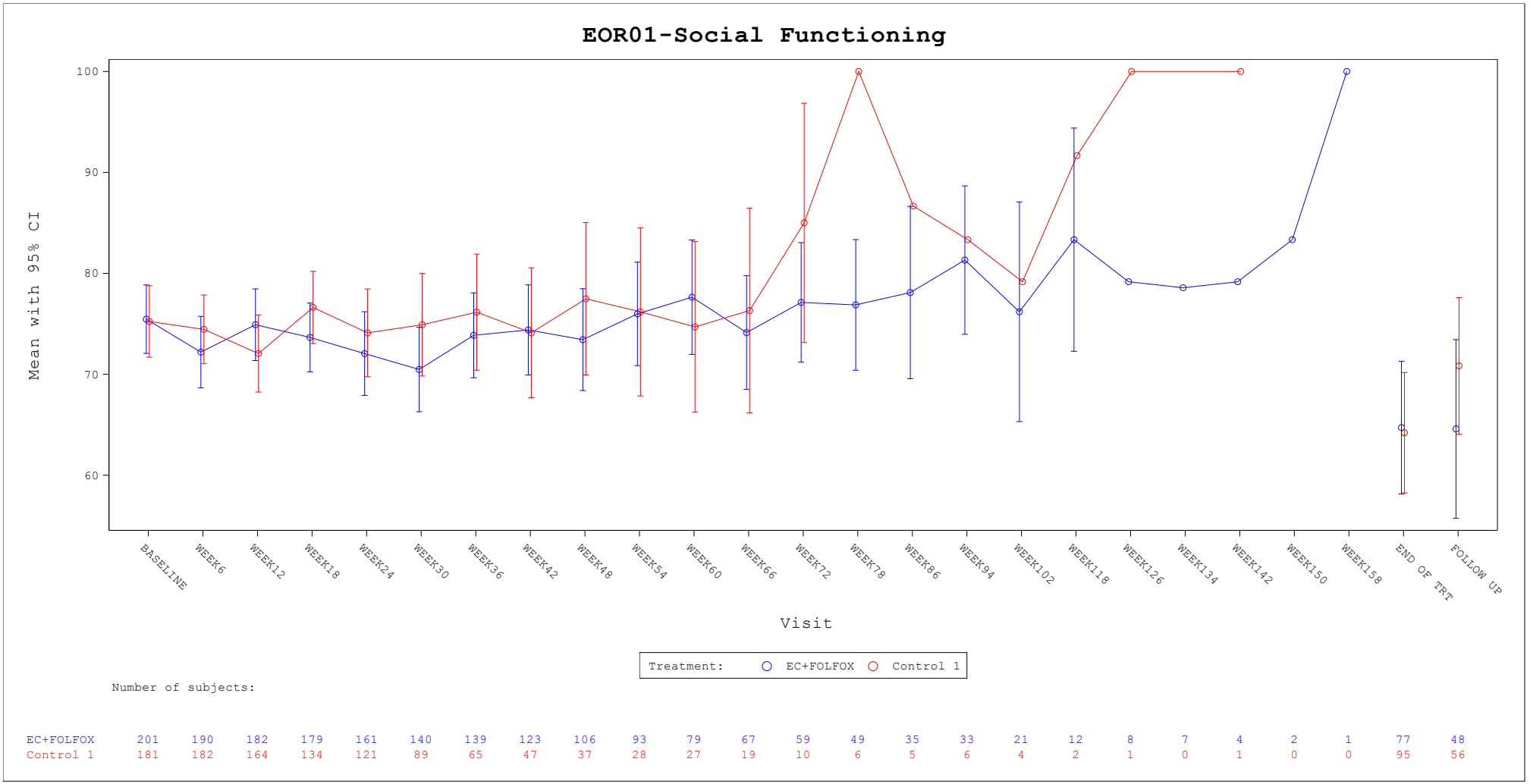
EC+FOLFOX	201	190	182	179	161	140	139	123	106	93	79	67	59	49	35	33	21	12	8	7	4	2	1	77	48
Control 1	181	182	164	134	121	89	65	47	37	28	27	19	10	6	5	6	4	2	1	0	1	0	0	95	56

Baseline is the last non-missing measurement prior to first dose of study intervention.
No confidence intervalls are drawn, when there are less than 10 patients in treatment arm.
For functional scales, higher scores represent a better level of functioning. For symptom-oriented scales, a higher score represents more severe symptoms.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Summary over time - EOR01-Social Functioning
Full Analysis Set

	EC+FOLFOX (N=236)				Control 1 (N=243)			
Visit	n	Median (Range)	Mean (SD)	95% CI [1]	n	Median (Range)	Mean (SD)	95% CI [1]
BASELINE	201	83.33 (0.0, 100.0)	75.46 (24.384)	[72.06, 78.85]	181	83.33 (0.0, 100.0)	75.23 (24.127)	[71.69, 78.77]
WEEK6	190	66.67 (0.0, 100.0)	72.19 (24.789)	[68.65, 75.74]	182	75.00 (16.7, 100.0)	74.45 (23.285)	[71.04, 77.86]
WEEK12	182	66.67 (0.0, 100.0)	74.91 (24.260)	[71.36, 78.46]	164	66.67 (0.0, 100.0)	72.05 (24.764)	[68.23, 75.87]
WEEK18	179	66.67 (0.0, 100.0)	73.65 (23.088)	[70.24, 77.06]	134	66.67 (0.0, 100.0)	76.62 (20.955)	[73.04, 80.20]
WEEK24	161	66.67 (0.0, 100.0)	72.05 (26.654)	[67.90, 76.20]	121	66.67 (0.0, 100.0)	74.10 (24.148)	[69.76, 78.45]
WEEK30	140	66.67 (0.0, 100.0)	70.48 (25.077)	[66.29, 74.67]	89	66.67 (0.0, 100.0)	74.91 (24.116)	[69.83, 79.99]
WEEK36	139	66.67 (0.0, 100.0)	73.86 (25.064)	[69.66, 78.06]	65	83.33 (16.7, 100.0)	76.15 (23.193)	[70.41, 81.90]
WEEK42	123	66.67 (0.0, 100.0)	74.39 (25.004)	[69.93, 78.85]	47	66.67 (16.7, 100.0)	74.11 (21.927)	[67.68, 80.55]
WEEK48	106	66.67 (0.0, 100.0)	73.43 (26.204)	[68.38, 78.47]	37	83.33 (33.3, 100.0)	77.48 (22.641)	[69.93, 85.03]
WEEK54	93	83.33 (0.0, 100.0)	75.99 (24.874)	[70.86, 81.11]	28	66.67 (33.3, 100.0)	76.19 (21.482)	[67.86, 84.52]
WEEK60	79	83.33 (0.0, 100.0)	77.64 (25.302)	[71.97, 83.30]	27	66.67 (33.3, 100.0)	74.69 (21.369)	[66.24, 83.14]
WEEK66	67	66.67 (0.0, 100.0)	74.13 (23.080)	[68.50, 79.76]	19	66.67 (33.3, 100.0)	76.32 (21.020)	[66.18, 86.45]
WEEK72	59	83.33 (0.0, 100.0)	77.12 (22.722)	[71.20, 83.04]	10	91.67 (66.7, 100.0)	85.00 (16.574)	[73.14, 96.86]
WEEK78	49	66.67 (0.0, 100.0)	76.87 (22.520)	[70.40, 83.34]	6	100.00 (100.0, 100.0)	100.00 (0.000)	[NE, NE]
WEEK86	35	83.33 (0.0, 100.0)	78.10 (24.843)	[69.56, 86.63]	5	83.33 (66.7, 100.0)	86.67 (13.944)	[69.35, 103.98]
WEEK94	33	83.33 (0.0, 100.0)	81.31 (20.732)	[73.96, 88.66]	6	83.33 (50.0, 100.0)	83.33 (18.257)	[64.17, 102.49]
WEEK102	21	66.67 (0.0, 100.0)	76.19 (23.905)	[65.31, 87.07]	4	91.67 (33.3, 100.0)	79.17 (31.549)	[28.96, 129.37]
WEEK118	12	83.33 (50.0, 100.0)	83.33 (17.408)	[72.27, 94.39]	2	91.67 (83.3, 100.0)	91.67 (11.785)	[-14.22, 197.55]
WEEK126	8	75.00 (66.7, 100.0)	79.17 (14.773)	[66.82, 91.52]	1	100.00 (100.0, 100.0)	100.00 (NE)	[NE, NE]
WEEK134	7	66.67 (50.0, 100.0)	78.57 (20.893)	[59.25, 97.89]	0	NE (NE, NE)	NE (NE)	[NE, NE]
WEEK142	4	83.33 (50.0, 100.0)	79.17 (25.000)	[39.39, 118.95]	1	100.00 (100.0, 100.0)	100.00 (NE)	[NE, NE]
WEEK150	2	83.33 (66.7, 100.0)	83.33 (23.570)	[-128.44, 295.10]	0	NE (NE, NE)	NE (NE)	[NE, NE]
WEEK158	1	100.00 (100.0, 100.0)	100.00 (NE)	[NE, NE]	0	NE (NE, NE)	NE (NE)	[NE, NE]
END OF TRT	77	66.67 (0.0, 100.0)	64.72 (28.991)	[58.14, 71.30]	95	66.67 (0.0, 100.0)	64.21 (29.271)	[58.25, 70.17]
FOLLOW UP	48	66.67 (0.0, 100.0)	64.58 (30.486)	[55.73, 73.44]	56	66.67 (0.0, 100.0)	70.83 (25.276)	[64.06, 77.60]

Baseline is the last non-missing measurement prior to first dose of study intervention.
[1] Confidence interval based on the normal distribution.
For functional scales, higher scores represent a better level of functioning. For symptom-oriented scales, a higher score represents more severe symptoms.



Number of subjects:

EC+FOLFOX	201	190	182	179	161	140	139	123	106	93	79	67	59	49	35	33	21	12	8	7	4	2	1	77	48
Control 1	181	182	164	134	121	89	65	47	37	28	27	19	10	6	5	6	4	2	1	0	1	0	0	95	56

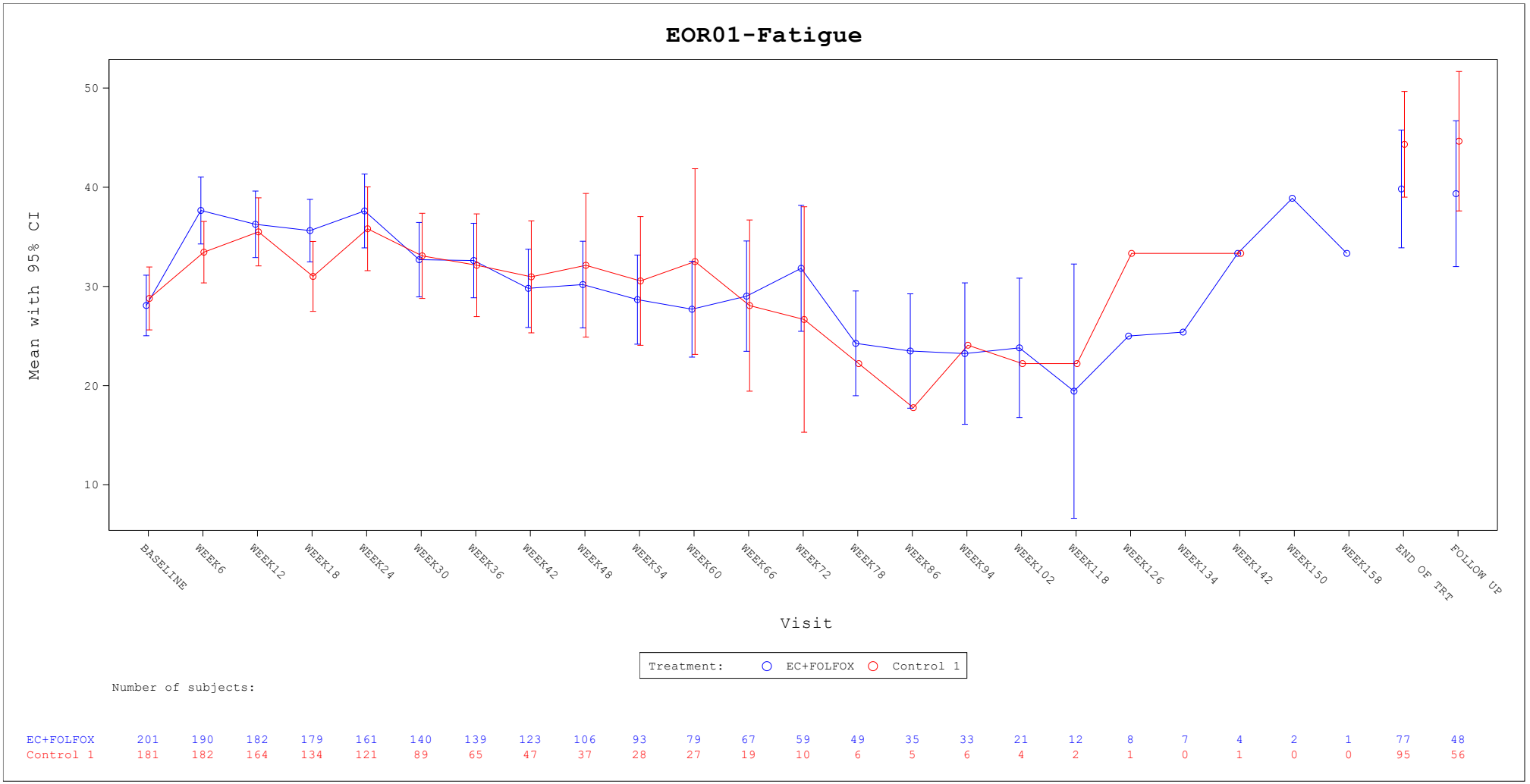
Baseline is the last non-missing measurement prior to first dose of study intervention.
No confidence intervalls are drawn, when there are less than 10 patients in treatment arm.
For functional scales, higher scores represent a better level of functioning. For symptom-oriented scales, a higher score represents more severe symptoms.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Summary over time - EOR01-Fatigue
Full Analysis Set

	EC+FOLFOX (N=236)				Control 1 (N=243)			
Visit	n	Median (Range)	Mean (SD)	95% CI [1]	n	Median (Range)	Mean (SD)	95% CI [1]
BASELINE	201	33.33 (0.0, 88.9)	28.08 (21.944)	[25.03, 31.13]	181	33.33 (0.0, 100.0)	28.79 (21.624)	[25.62, 31.96]
WEEK6	190	33.33 (0.0, 100.0)	37.66 (23.607)	[34.28, 41.04]	182	33.33 (0.0, 100.0)	33.46 (21.185)	[30.36, 36.55]
WEEK12	182	33.33 (0.0, 100.0)	36.26 (22.907)	[32.91, 39.61]	164	33.33 (0.0, 100.0)	35.50 (22.252)	[32.07, 38.93]
WEEK18	179	33.33 (0.0, 88.9)	35.63 (21.352)	[32.48, 38.78]	134	33.33 (0.0, 100.0)	31.01 (20.622)	[27.49, 34.54]
WEEK24	161	33.33 (0.0, 100.0)	37.61 (23.930)	[33.89, 41.34]	121	33.33 (0.0, 100.0)	35.81 (23.460)	[31.59, 40.04]
WEEK30	140	33.33 (0.0, 100.0)	32.70 (22.452)	[28.95, 36.45]	89	33.33 (0.0, 100.0)	33.08 (20.376)	[28.79, 37.38]
WEEK36	139	33.33 (0.0, 100.0)	32.61 (22.391)	[28.86, 36.37]	65	33.33 (0.0, 88.9)	32.14 (20.891)	[26.96, 37.31]
WEEK42	123	33.33 (0.0, 100.0)	29.81 (22.100)	[25.87, 33.75]	47	33.33 (0.0, 88.9)	30.97 (19.236)	[25.32, 36.62]
WEEK48	106	33.33 (0.0, 100.0)	30.19 (22.681)	[25.82, 34.56]	37	33.33 (0.0, 88.9)	32.13 (21.720)	[24.89, 39.37]
WEEK54	93	33.33 (0.0, 88.9)	28.67 (21.815)	[24.18, 33.17]	28	33.33 (0.0, 66.7)	30.56 (16.735)	[24.07, 37.04]
WEEK60	79	33.33 (0.0, 77.8)	27.71 (21.562)	[22.88, 32.54]	27	33.33 (0.0, 77.8)	32.51 (23.656)	[23.15, 41.87]
WEEK66	67	33.33 (0.0, 100.0)	29.02 (22.800)	[23.46, 34.58]	19	33.33 (0.0, 55.6)	28.07 (17.904)	[19.44, 36.70]
WEEK72	59	33.33 (0.0, 100.0)	31.83 (24.366)	[25.48, 38.18]	10	33.33 (0.0, 55.6)	26.67 (15.887)	[15.30, 38.03]
WEEK78	49	33.33 (0.0, 66.7)	24.26 (18.380)	[18.98, 29.54]	6	27.78 (0.0, 33.3)	22.22 (14.055)	[7.47, 36.97]
WEEK86	35	33.33 (0.0, 55.6)	23.49 (16.780)	[17.73, 29.26]	5	11.11 (0.0, 33.3)	17.78 (14.907)	[-0.73, 36.29]
WEEK94	33	33.33 (0.0, 66.7)	23.23 (20.101)	[16.10, 30.36]	6	27.78 (0.0, 44.4)	24.07 (16.355)	[6.91, 41.24]
WEEK102	21	33.33 (0.0, 44.4)	23.81 (15.430)	[16.79, 30.83]	4	27.78 (0.0, 33.3)	22.22 (15.713)	[-2.78, 47.23]
WEEK118	12	16.67 (0.0, 55.6)	19.44 (20.170)	[6.63, 32.26]	2	22.22 (11.1, 33.3)	22.22 (15.713)	[-118.96, 163.40]
WEEK126	8	27.78 (0.0, 66.7)	25.00 (22.023)	[6.59, 43.41]	1	33.33 (33.3, 33.3)	33.33 (NE)	[NE, NE]
WEEK134	7	33.33 (0.0, 66.7)	25.40 (26.227)	[1.14, 49.65]	0	NE (NE, NE)	NE (NE)	[NE, NE]
WEEK142	4	33.33 (0.0, 66.7)	33.33 (27.217)	[-9.97, 76.64]	1	33.33 (33.3, 33.3)	33.33 (NE)	[NE, NE]
WEEK150	2	38.89 (33.3, 44.4)	38.89 (7.857)	[-31.70, 109.48]	0	NE (NE, NE)	NE (NE)	[NE, NE]
WEEK158	1	33.33 (33.3, 33.3)	33.33 (NE)	[NE, NE]	0	NE (NE, NE)	NE (NE)	[NE, NE]
END OF TRT	77	33.33 (0.0, 100.0)	39.83 (26.142)	[33.89, 45.76]	95	33.33 (0.0, 100.0)	44.33 (26.158)	[39.00, 49.66]
FOLLOW UP	48	33.33 (0.0, 100.0)	39.35 (25.312)	[32.00, 46.70]	56	33.33 (0.0, 100.0)	44.64 (26.250)	[37.61, 51.67]

Baseline is the last non-missing measurement prior to first dose of study intervention.
[1] Confidence interval based on the normal distribution.
For functional scales, higher scores represent a better level of functioning. For symptom-oriented scales, a higher score represents more severe symptoms.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Plot over time - EOR01-Fatigue
Full Analysis Set



Number of subjects:

EC+FOLFOX	201	190	182	179	161	140	139	123	106	93	79	67	59	49	35	33	21	12	8	7	4	2	1	77	48
Control 1	181	182	164	134	121	89	65	47	37	28	27	19	10	6	5	6	4	2	1	0	1	0	0	95	56

Baseline is the last non-missing measurement prior to first dose of study intervention.
No confidence intervalls are drawn, when there are less than 10 patients in treatment arm.
For functional scales, higher scores represent a better level of functioning. For symptom-oriented scales, a higher score represents more severe symptoms.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Summary over time - EOR01-Nausea and Vomiting
Full Analysis Set

	EC+FOLFOX (N=236)				Control 1 (N=243)			
Visit	n	Median (Range)	Mean (SD)	95% CI [1]	n	Median (Range)	Mean (SD)	95% CI [1]
BASELINE	201	0.00 (0.0, 66.7)	4.81 (10.492)	[3.35, 6.27]	181	0.00 (0.0, 100.0)	7.09 (15.125)	[4.87, 9.31]
WEEK6	190	0.00 (0.0, 100.0)	13.16 (20.772)	[10.19, 16.13]	182	0.00 (0.0, 83.3)	12.09 (16.447)	[9.68, 14.49]
WEEK12	182	0.00 (0.0, 100.0)	11.54 (17.900)	[8.92, 14.16]	164	0.00 (0.0, 83.3)	11.99 (17.175)	[9.34, 14.64]
WEEK18	179	0.00 (0.0, 100.0)	10.34 (18.536)	[7.60, 13.07]	134	0.00 (0.0, 83.3)	10.20 (14.583)	[7.71, 12.69]
WEEK24	161	0.00 (0.0, 100.0)	7.66 (16.351)	[5.12, 10.21]	121	0.00 (0.0, 50.0)	10.06 (12.996)	[7.72, 12.39]
WEEK30	140	0.00 (0.0, 50.0)	5.95 (11.669)	[4.00, 7.90]	89	0.00 (0.0, 33.3)	6.55 (10.841)	[4.27, 8.84]
WEEK36	139	0.00 (0.0, 50.0)	6.12 (11.895)	[4.12, 8.11]	65	0.00 (0.0, 33.3)	7.44 (11.796)	[4.51, 10.36]
WEEK42	123	0.00 (0.0, 50.0)	4.88 (10.825)	[2.95, 6.81]	47	0.00 (0.0, 50.0)	6.03 (10.669)	[2.90, 9.16]
WEEK48	106	0.00 (0.0, 66.7)	5.82 (11.511)	[3.60, 8.03]	37	0.00 (0.0, 33.3)	3.60 (7.988)	[0.94, 6.27]
WEEK54	93	0.00 (0.0, 66.7)	6.27 (12.983)	[3.60, 8.95]	28	0.00 (0.0, 33.3)	5.95 (10.358)	[1.94, 9.97]
WEEK60	79	0.00 (0.0, 50.0)	4.85 (11.053)	[2.38, 7.33]	27	0.00 (0.0, 66.7)	11.11 (17.903)	[4.03, 18.19]
WEEK66	67	0.00 (0.0, 33.3)	5.97 (11.124)	[3.26, 8.68]	19	0.00 (0.0, 33.3)	5.26 (9.707)	[0.58, 9.94]
WEEK72	59	0.00 (0.0, 66.7)	4.52 (11.919)	[1.41, 7.63]	10	0.00 (0.0, 16.7)	5.00 (8.051)	[-0.76, 10.76]
WEEK78	49	0.00 (0.0, 33.3)	3.74 (8.516)	[1.30, 6.19]	6	0.00 (0.0, 0.0)	0.00 (0.000)	[NE, NE]
WEEK86	35	0.00 (0.0, 33.3)	3.81 (9.116)	[0.68, 6.94]	5	0.00 (0.0, 0.0)	0.00 (0.000)	[NE, NE]
WEEK94	33	0.00 (0.0, 50.0)	4.04 (10.232)	[0.41, 7.67]	6	0.00 (0.0, 16.7)	2.78 (6.804)	[-4.36, 9.92]
WEEK102	21	0.00 (0.0, 33.3)	4.76 (9.344)	[0.51, 9.02]	4	0.00 (0.0, 16.7)	4.17 (8.333)	[-9.09, 17.43]
WEEK118	12	0.00 (0.0, 16.7)	1.39 (4.811)	[-1.67, 4.45]	2	0.00 (0.0, 0.0)	0.00 (0.000)	[NE, NE]
WEEK126	8	0.00 (0.0, 0.0)	0.00 (0.000)	[NE, NE]	1	0.00 (0.0, 0.0)	0.00 (NE)	[NE, NE]
WEEK134	7	0.00 (0.0, 16.7)	2.38 (6.299)	[-3.45, 8.21]	0	NE (NE, NE)	NE (NE)	[NE, NE]
WEEK142	4	0.00 (0.0, 0.0)	0.00 (0.000)	[NE, NE]	1	0.00 (0.0, 0.0)	0.00 (NE)	[NE, NE]
WEEK150	2	0.00 (0.0, 0.0)	0.00 (0.000)	[NE, NE]	0	NE (NE, NE)	NE (NE)	[NE, NE]
WEEK158	1	0.00 (0.0, 0.0)	0.00 (NE)	[NE, NE]	0	NE (NE, NE)	NE (NE)	[NE, NE]
END OF TRT	77	0.00 (0.0, 100.0)	10.17 (18.168)	[6.05, 14.30]	95	0.00 (0.0, 100.0)	11.58 (22.944)	[6.90, 16.25]
FOLLOW UP	48	0.00 (0.0, 66.7)	5.90 (12.150)	[2.37, 9.43]	56	0.00 (0.0, 100.0)	11.61 (19.311)	[6.44, 16.78]

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[1] Confidence interval based on the normal distribution.
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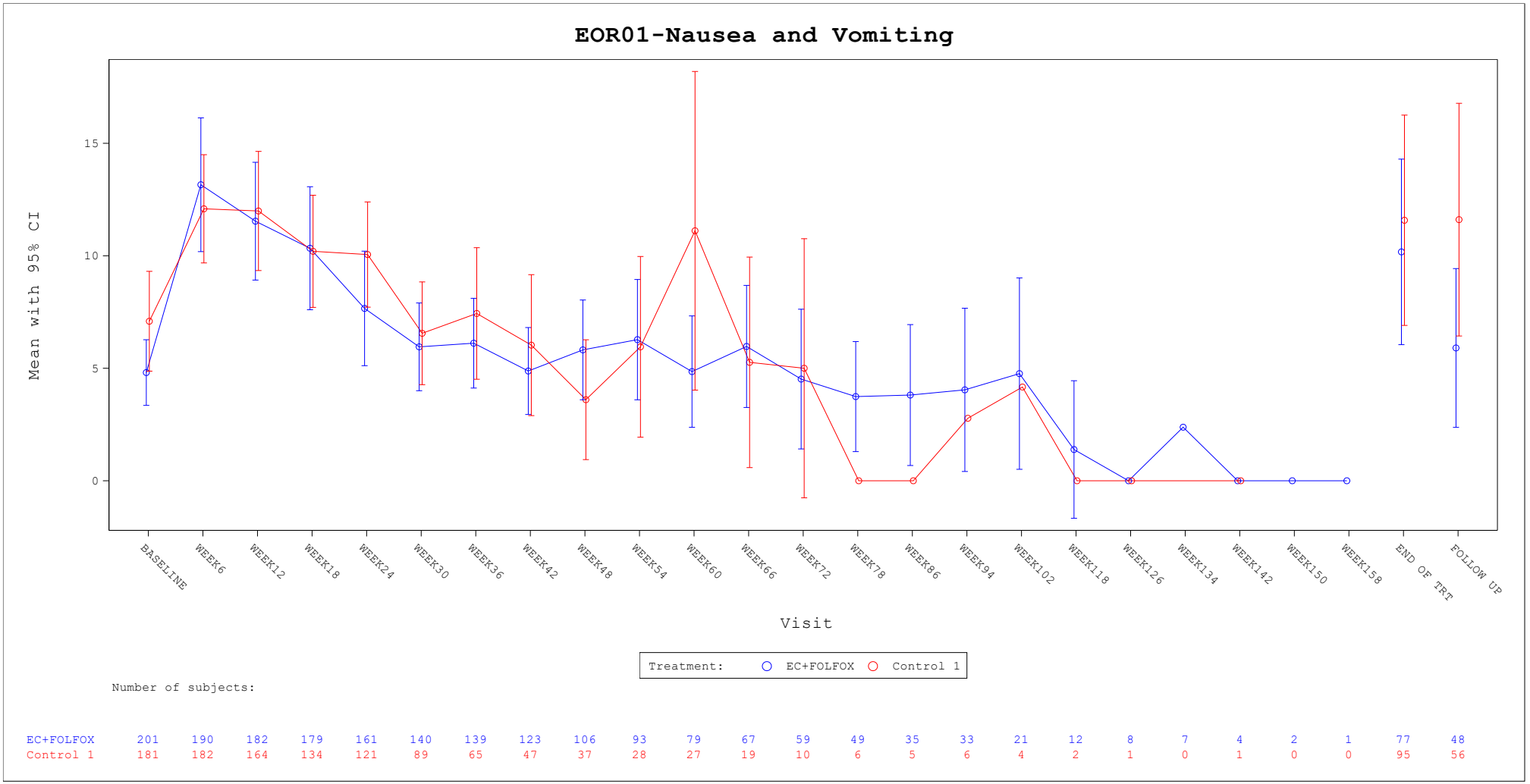
Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Plot over time - EOR01-Nausea and Vomiting
Full Analysis Set



Number of subjects:

EC+FOLFOX	201	190	182	179	161	140	139	123	106	93	79	67	59	49	35	33	21	12	8	7	4	2	1	77	48
Control 1	181	182	164	134	121	89	65	47	37	28	27	19	10	6	5	6	4	2	1	0	1	0	0	95	56

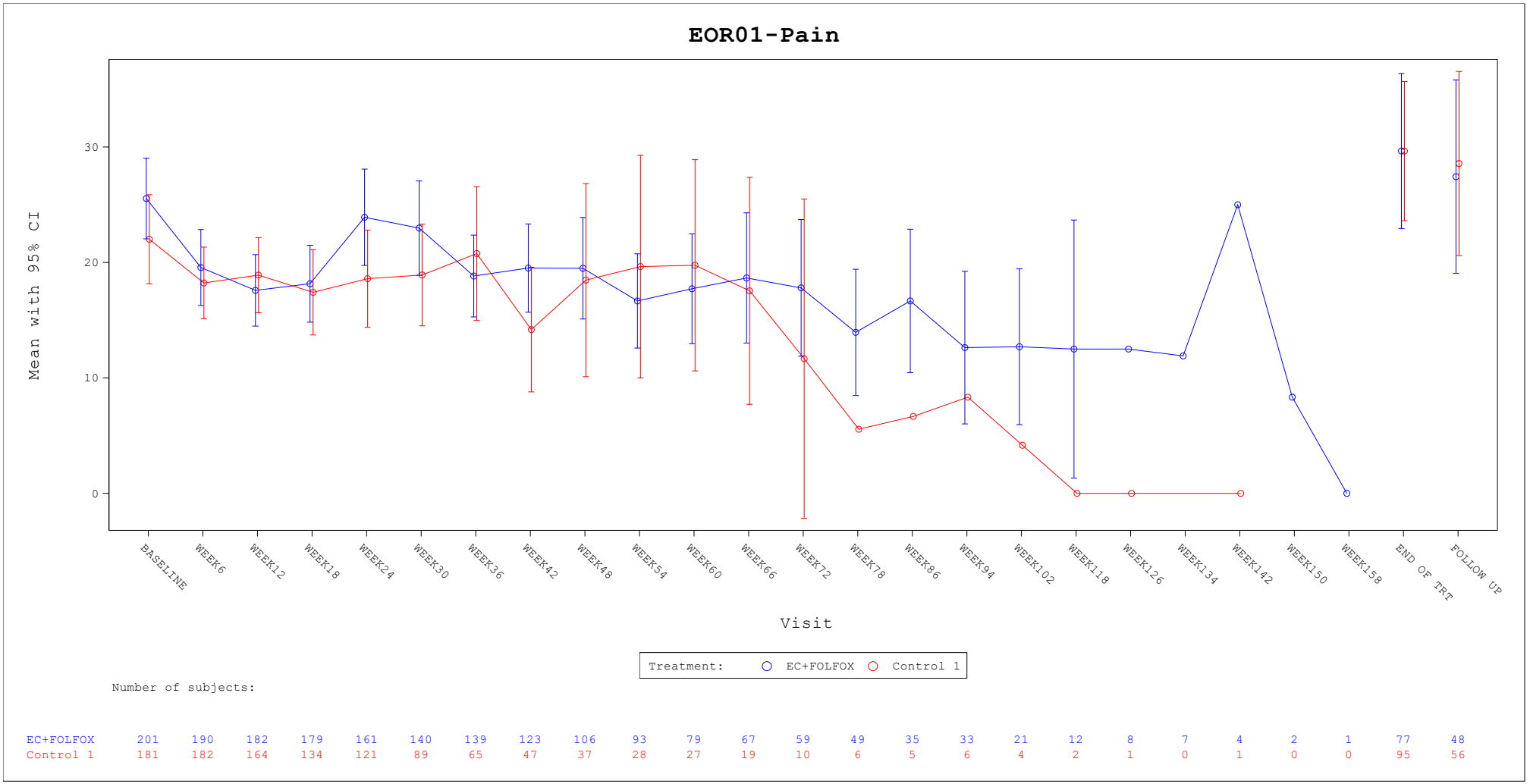
Baseline is the last non-missing measurement prior to first dose of study intervention.
No confidence intervalls are drawn, when there are less than 10 patients in treatment arm.
For functional scales, higher scores represent a better level of functioning. For symptom-oriented scales, a higher score represents more severe symptoms.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Summary over time - EOR01-Pain
Full Analysis Set

	EC+FOLFOX (N=236)				Control 1 (N=243)			
Visit	n	Median (Range)	Mean (SD)	95% CI [1]	n	Median (Range)	Mean (SD)	95% CI [1]
BASELINE	201	16.67 (0.0, 100.0)	25.54 (25.112)	[22.05, 29.03]	181	16.67 (0.0, 100.0)	22.01 (26.276)	[18.15, 25.86]
WEEK6	190	16.67 (0.0, 100.0)	19.56 (22.979)	[16.27, 22.85]	182	16.67 (0.0, 83.3)	18.22 (21.220)	[15.12, 21.33]
WEEK12	182	16.67 (0.0, 100.0)	17.58 (21.149)	[14.49, 20.68]	164	16.67 (0.0, 100.0)	18.90 (21.092)	[15.65, 22.15]
WEEK18	179	16.67 (0.0, 100.0)	18.16 (22.575)	[14.83, 21.49]	134	16.67 (0.0, 100.0)	17.41 (21.617)	[13.72, 21.11]
WEEK24	161	16.67 (0.0, 100.0)	23.91 (26.795)	[19.74, 28.08]	121	16.67 (0.0, 100.0)	18.60 (23.392)	[14.38, 22.81]
WEEK30	140	16.67 (0.0, 100.0)	22.98 (24.442)	[18.89, 27.06]	89	16.67 (0.0, 100.0)	18.91 (20.900)	[14.51, 23.32]
WEEK36	139	16.67 (0.0, 100.0)	18.82 (21.123)	[15.28, 22.37]	65	16.67 (0.0, 83.3)	20.77 (23.391)	[14.97, 26.57]
WEEK42	123	16.67 (0.0, 83.3)	19.51 (21.415)	[15.69, 23.33]	47	0.00 (0.0, 66.7)	14.18 (18.382)	[8.79, 19.58]
WEEK48	106	16.67 (0.0, 100.0)	19.50 (22.826)	[15.10, 23.89]	37	16.67 (0.0, 100.0)	18.47 (25.087)	[10.10, 26.83]
WEEK54	93	16.67 (0.0, 100.0)	16.67 (19.812)	[12.59, 20.75]	28	8.33 (0.0, 100.0)	19.64 (24.867)	[10.00, 29.29]
WEEK60	79	16.67 (0.0, 100.0)	17.72 (21.240)	[12.96, 22.48]	27	16.67 (0.0, 83.3)	19.75 (23.130)	[10.60, 28.90]
WEEK66	67	16.67 (0.0, 100.0)	18.66 (23.124)	[13.02, 24.30]	19	0.00 (0.0, 50.0)	17.54 (20.393)	[7.71, 27.37]
WEEK72	59	0.00 (0.0, 83.3)	17.80 (22.714)	[11.88, 23.72]	10	0.00 (0.0, 50.0)	11.67 (19.325)	[-2.16, 25.49]
WEEK78	49	0.00 (0.0, 83.3)	13.95 (19.048)	[8.47, 19.42]	6	0.00 (0.0, 33.3)	5.56 (13.608)	[-8.73, 19.84]
WEEK86	35	16.67 (0.0, 66.7)	16.67 (18.078)	[10.46, 22.88]	5	0.00 (0.0, 33.3)	6.67 (14.907)	[-11.84, 25.18]
WEEK94	33	0.00 (0.0, 66.7)	12.63 (18.648)	[6.01, 19.24]	6	0.00 (0.0, 33.3)	8.33 (13.944)	[-6.30, 22.97]
WEEK102	21	0.00 (0.0, 33.3)	12.70 (14.818)	[5.95, 19.44]	4	0.00 (0.0, 16.7)	4.17 (8.333)	[-9.09, 17.43]
WEEK118	12	0.00 (0.0, 50.0)	12.50 (17.588)	[1.33, 23.67]	2	0.00 (0.0, 0.0)	0.00 (0.000)	[NE, NE]
WEEK126	8	0.00 (0.0, 50.0)	12.50 (19.416)	[-3.73, 28.73]	1	0.00 (0.0, 0.0)	0.00 (NE)	[NE, NE]
WEEK134	7	0.00 (0.0, 66.7)	11.90 (24.934)	[-11.16, 34.96]	0	NE (NE, NE)	NE (NE)	[NE, NE]
WEEK142	4	16.67 (0.0, 66.7)	25.00 (31.914)	[-25.78, 75.78]	1	0.00 (0.0, 0.0)	0.00 (NE)	[NE, NE]
WEEK150	2	8.33 (0.0, 16.7)	8.33 (11.785)	[-97.55, 114.22]	0	NE (NE, NE)	NE (NE)	[NE, NE]
WEEK158	1	0.00 (0.0, 0.0)	0.00 (NE)	[NE, NE]	0	NE (NE, NE)	NE (NE)	[NE, NE]
END OF TRT	77	33.33 (0.0, 100.0)	29.65 (29.571)	[22.94, 36.37]	95	16.67 (0.0, 100.0)	29.65 (29.593)	[23.62, 35.68]
FOLLOW UP	48	33.33 (0.0, 100.0)	27.43 (28.865)	[19.05, 35.81]	56	16.67 (0.0, 100.0)	28.57 (29.766)	[20.60, 36.54]

Baseline is the last non-missing measurement prior to first dose of study intervention.
[1] Confidence interval based on the normal distribution.
For functional scales, higher scores represent a better level of functioning. For symptom-oriented scales, a higher score represents more severe symptoms.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Plot over time - EOR01-Pain
Full Analysis Set



Number of subjects:

EC+FOLFOX	201	190	182	179	161	140	139	123	106	93	79	67	59	49	35	33	21	12	8	7	4	2	1	77	48
Control 1	181	182	164	134	121	89	65	47	37	28	27	19	10	6	5	6	4	2	1	0	1	0	0	95	56

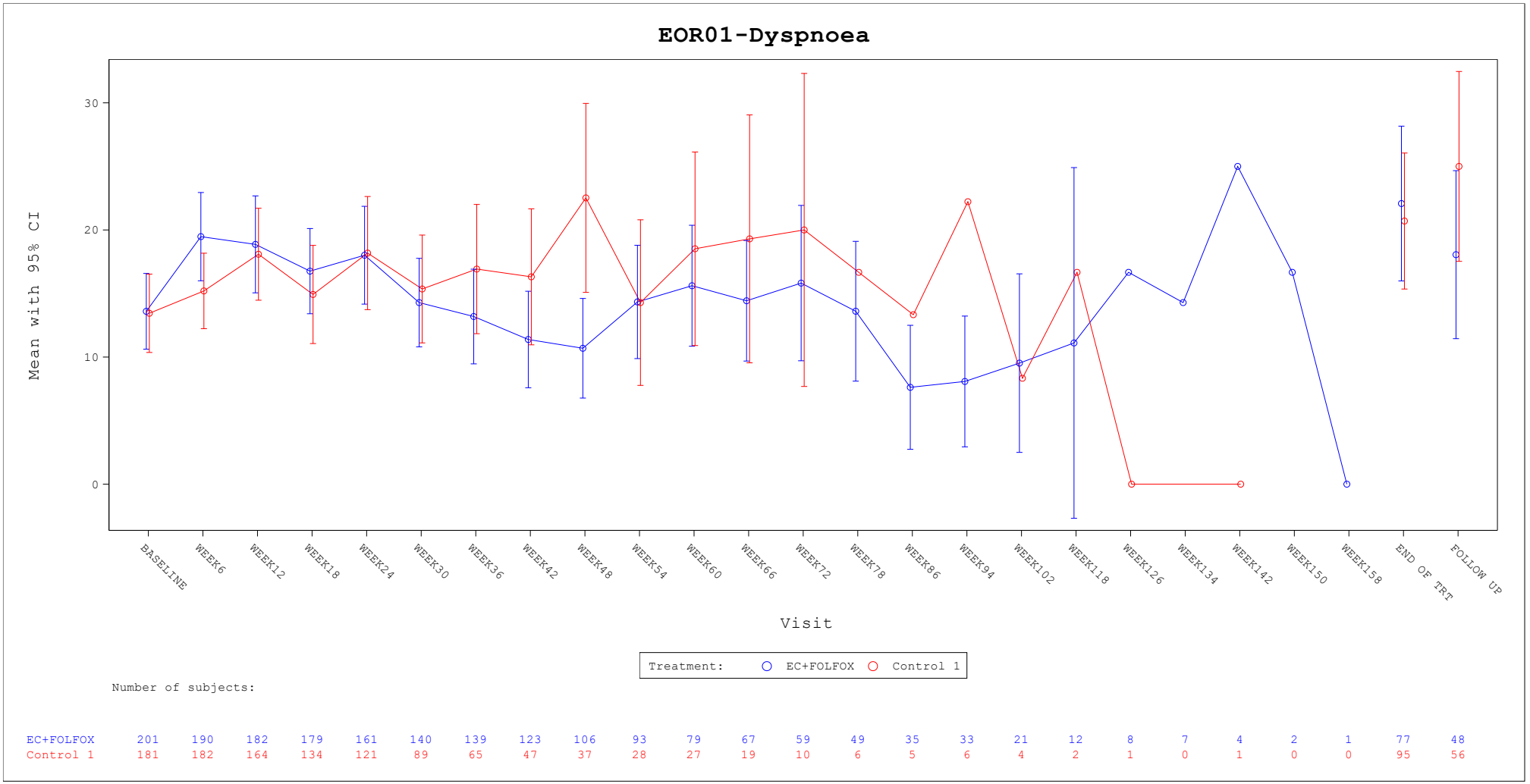
Baseline is the last non-missing measurement prior to first dose of study intervention.
No confidence intervalls are drawn, when there are less than 10 patients in treatment arm.
For functional scales, higher scores represent a better level of functioning. For symptom-oriented scales, a higher score represents more severe symptoms.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Summary over time - EOR01-Dyspnoea
Full Analysis Set

	EC+FOLFOX (N=236)				Control 1 (N=243)			
Visit	n	Median (Range)	Mean (SD)	95% CI [1]	n	Median (Range)	Mean (SD)	95% CI [1]
BASELINE	201	0.00 (0.0, 100.0)	13.60 (21.415)	[10.62, 16.58]	181	0.00 (0.0, 100.0)	13.44 (21.017)	[10.36, 16.53]
WEEK6	190	0.00 (0.0, 100.0)	19.47 (24.265)	[16.00, 22.95]	182	0.00 (0.0, 66.7)	15.20 (20.303)	[12.23, 18.17]
WEEK12	182	0.00 (0.0, 100.0)	18.86 (26.069)	[15.05, 22.68]	164	0.00 (0.0, 100.0)	18.09 (23.454)	[14.47, 21.71]
WEEK18	179	0.00 (0.0, 100.0)	16.76 (22.727)	[13.41, 20.11]	134	0.00 (0.0, 100.0)	14.93 (22.599)	[11.06, 18.79]
WEEK24	161	0.00 (0.0, 100.0)	18.01 (24.719)	[14.17, 21.86]	121	0.00 (0.0, 100.0)	18.18 (24.721)	[13.73, 22.63]
WEEK30	140	0.00 (0.0, 100.0)	14.29 (20.831)	[10.80, 17.77]	89	0.00 (0.0, 66.7)	15.36 (20.136)	[11.11, 19.60]
WEEK36	139	0.00 (0.0, 100.0)	13.19 (22.205)	[9.47, 16.91]	65	0.00 (0.0, 66.7)	16.92 (20.517)	[11.84, 22.01]
WEEK42	123	0.00 (0.0, 100.0)	11.38 (21.266)	[7.59, 15.18]	47	0.00 (0.0, 66.7)	16.31 (18.221)	[10.96, 21.66]
WEEK48	106	0.00 (0.0, 100.0)	10.69 (20.340)	[6.77, 14.61]	37	33.33 (0.0, 66.7)	22.52 (22.297)	[15.09, 29.96]
WEEK54	93	0.00 (0.0, 100.0)	14.34 (21.646)	[9.88, 18.79]	28	0.00 (0.0, 33.3)	14.29 (16.798)	[7.77, 20.80]
WEEK60	79	0.00 (0.0, 66.7)	15.61 (21.240)	[10.85, 20.37]	27	33.33 (0.0, 66.7)	18.52 (19.245)	[10.91, 26.13]
WEEK66	67	0.00 (0.0, 66.7)	14.43 (19.440)	[9.69, 19.17]	19	33.33 (0.0, 66.7)	19.30 (20.233)	[9.55, 29.05]
WEEK72	59	0.00 (0.0, 100.0)	15.82 (23.453)	[9.71, 21.93]	10	33.33 (0.0, 33.3)	20.00 (17.213)	[7.69, 32.31]
WEEK78	49	0.00 (0.0, 66.7)	13.61 (19.147)	[8.11, 19.10]	6	16.67 (0.0, 33.3)	16.67 (18.257)	[-2.49, 35.83]
WEEK86	35	0.00 (0.0, 33.3)	7.62 (14.201)	[2.74, 12.50]	5	0.00 (0.0, 33.3)	13.33 (18.257)	[-9.34, 36.00]
WEEK94	33	0.00 (0.0, 33.3)	8.08 (14.506)	[2.94, 13.22]	6	33.33 (0.0, 33.3)	22.22 (17.213)	[4.16, 40.29]
WEEK102	21	0.00 (0.0, 33.3)	9.52 (15.430)	[2.50, 16.55]	4	0.00 (0.0, 33.3)	8.33 (16.667)	[-18.19, 34.85]
WEEK118	12	0.00 (0.0, 66.7)	11.11 (21.711)	[-2.68, 24.91]	2	16.67 (0.0, 33.3)	16.67 (23.570)	[-195.10, 228.44]
WEEK126	8	0.00 (0.0, 66.7)	16.67 (25.198)	[-4.40, 37.73]	1	0.00 (0.0, 0.0)	0.00 (NE)	[NE, NE]
WEEK134	7	0.00 (0.0, 66.7)	14.29 (26.227)	[-9.97, 38.54]	0	NE (NE, NE)	NE (NE)	[NE, NE]
WEEK142	4	16.67 (0.0, 66.7)	25.00 (31.914)	[-25.78, 75.78]	1	0.00 (0.0, 0.0)	0.00 (NE)	[NE, NE]
WEEK150	2	16.67 (0.0, 33.3)	16.67 (23.570)	[-195.10, 228.44]	0	NE (NE, NE)	NE (NE)	[NE, NE]
WEEK158	1	0.00 (0.0, 0.0)	0.00 (NE)	[NE, NE]	0	NE (NE, NE)	NE (NE)	[NE, NE]
END OF TRT	77	33.33 (0.0, 100.0)	22.08 (26.825)	[15.99, 28.17]	95	0.00 (0.0, 100.0)	20.70 (26.264)	[15.35, 26.05]
FOLLOW UP	48	0.00 (0.0, 100.0)	18.06 (22.762)	[11.45, 24.67]	56	33.33 (0.0, 100.0)	25.00 (27.889)	[17.53, 32.47]

Baseline is the last non-missing measurement prior to first dose of study intervention.
[1] Confidence interval based on the normal distribution.
For functional scales, higher scores represent a better level of functioning. For symptom-oriented scales, a higher score represents more severe symptoms.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Plot over time - EOR01-Dyspnoea
Full Analysis Set



Number of subjects:

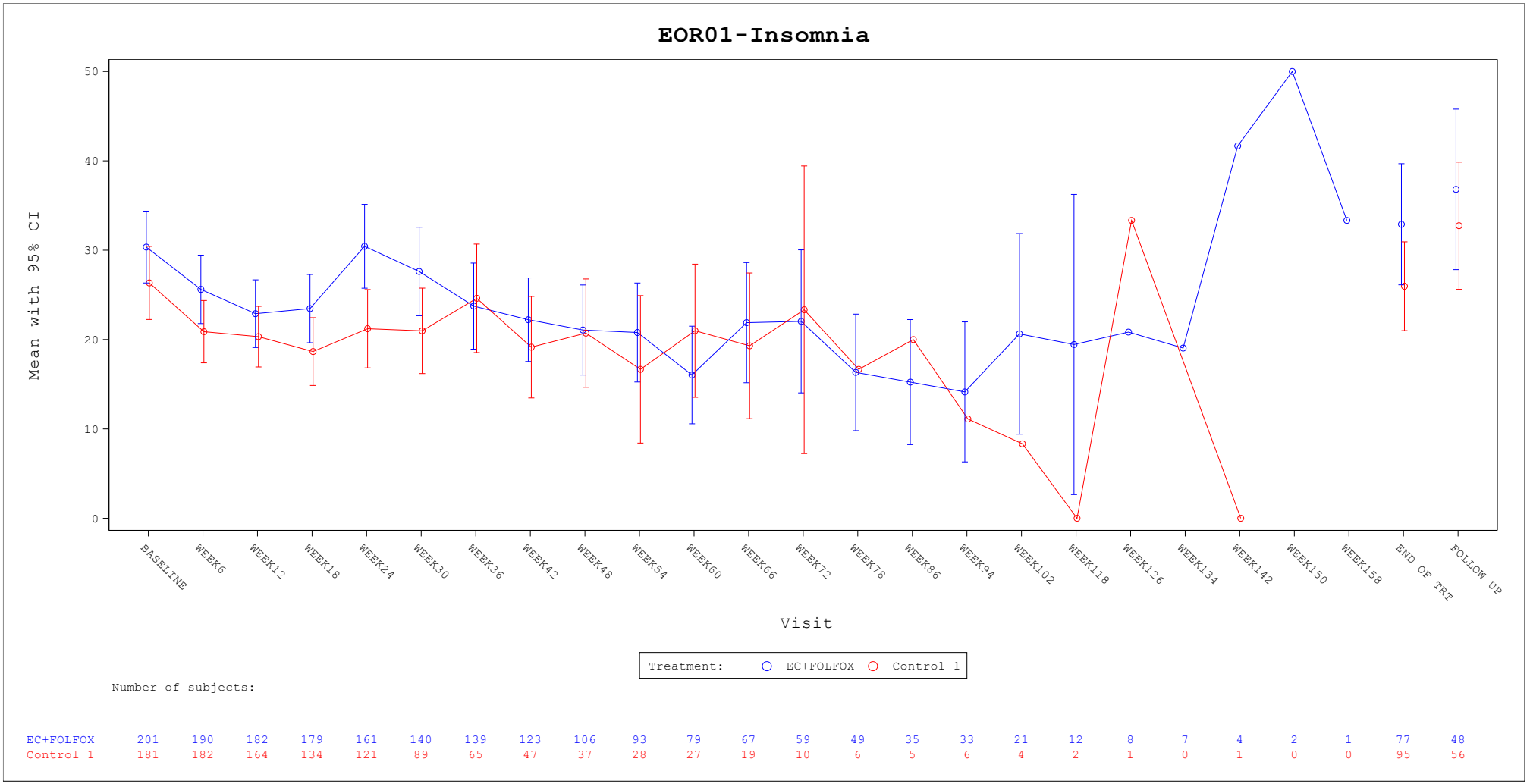
EC+FOLFOX	201	190	182	179	161	140	139	123	106	93	79	67	59	49	35	33	21	12	8	7	4	2	1	77	48
Control 1	181	182	164	134	121	89	65	47	37	28	27	19	10	6	5	6	4	2	1	0	1	0	0	95	56

Baseline is the last non-missing measurement prior to first dose of study intervention.
No confidence intervalls are drawn, when there are less than 10 patients in treatment arm.
For functional scales, higher scores represent a better level of functioning. For symptom-oriented scales, a higher score represents more severe symptoms.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Summary over time - EOR01-Insomnia
Full Analysis Set

	EC+FOLFOX (N=236)				Control 1 (N=243)			
Visit	n	Median (Range)	Mean (SD)	95% CI [1]	n	Median (Range)	Mean (SD)	95% CI [1]
BASELINE	201	33.33 (0.0, 100.0)	30.35 (28.905)	[26.33, 34.37]	181	33.33 (0.0, 100.0)	26.34 (27.891)	[22.24, 30.43]
WEEK6	190	33.33 (0.0, 100.0)	25.61 (26.760)	[21.78, 29.44]	182	16.67 (0.0, 100.0)	20.88 (23.841)	[17.39, 24.37]
WEEK12	182	33.33 (0.0, 100.0)	22.89 (25.885)	[19.11, 26.68]	164	33.33 (0.0, 100.0)	20.33 (22.003)	[16.93, 23.72]
WEEK18	179	33.33 (0.0, 100.0)	23.46 (25.881)	[19.65, 27.28]	134	0.00 (0.0, 66.7)	18.66 (22.206)	[14.86, 22.45]
WEEK24	161	33.33 (0.0, 100.0)	30.43 (30.137)	[25.74, 35.13]	121	33.33 (0.0, 100.0)	21.21 (24.343)	[16.83, 25.59]
WEEK30	140	33.33 (0.0, 100.0)	27.62 (29.638)	[22.67, 32.57]	89	33.33 (0.0, 100.0)	20.97 (22.687)	[16.19, 25.75]
WEEK36	139	0.00 (0.0, 100.0)	23.74 (28.726)	[18.92, 28.56]	65	33.33 (0.0, 100.0)	24.62 (24.493)	[18.55, 30.68]
WEEK42	123	0.00 (0.0, 100.0)	22.22 (26.193)	[17.55, 26.90]	47	33.33 (0.0, 66.7)	19.15 (19.343)	[13.47, 24.83]
WEEK48	106	0.00 (0.0, 100.0)	21.07 (26.156)	[16.03, 26.11]	37	33.33 (0.0, 66.7)	20.72 (18.175)	[14.66, 26.78]
WEEK54	93	0.00 (0.0, 100.0)	20.79 (26.880)	[15.25, 26.32]	28	0.00 (0.0, 66.7)	16.67 (21.276)	[8.42, 24.92]
WEEK60	79	0.00 (0.0, 100.0)	16.03 (24.379)	[10.57, 21.49]	27	33.33 (0.0, 66.7)	20.99 (18.829)	[13.54, 28.44]
WEEK66	67	0.00 (0.0, 100.0)	21.89 (27.556)	[15.17, 28.61]	19	33.33 (0.0, 33.3)	19.30 (16.909)	[11.15, 27.45]
WEEK72	59	0.00 (0.0, 100.0)	22.03 (30.707)	[14.03, 30.04]	10	33.33 (0.0, 66.7)	23.33 (22.498)	[7.24, 39.43]
WEEK78	49	0.00 (0.0, 100.0)	16.33 (22.692)	[9.81, 22.84]	6	16.67 (0.0, 33.3)	16.67 (18.257)	[-2.49, 35.83]
WEEK86	35	0.00 (0.0, 66.7)	15.24 (20.361)	[8.24, 22.23]	5	33.33 (0.0, 33.3)	20.00 (18.257)	[-2.67, 42.67]
WEEK94	33	0.00 (0.0, 66.7)	14.14 (22.096)	[6.31, 21.98]	6	0.00 (0.0, 33.3)	11.11 (17.213)	[-6.95, 29.18]
WEEK102	21	0.00 (0.0, 66.7)	20.63 (24.667)	[9.41, 31.86]	4	0.00 (0.0, 33.3)	8.33 (16.667)	[-18.19, 34.85]
WEEK118	12	0.00 (0.0, 66.7)	19.44 (26.432)	[2.65, 36.24]	2	0.00 (0.0, 0.0)	0.00 (0.000)	[NE, NE]
WEEK126	8	16.67 (0.0, 66.7)	20.83 (24.801)	[0.10, 41.57]	1	33.33 (33.3, 33.3)	33.33 (NE)	[NE, NE]
WEEK134	7	0.00 (0.0, 66.7)	19.05 (26.227)	[-5.21, 43.30]	0	NE (NE, NE)	NE (NE)	[NE, NE]
WEEK142	4	50.00 (0.0, 66.7)	41.67 (31.914)	[-9.12, 92.45]	1	0.00 (0.0, 0.0)	0.00 (NE)	[NE, NE]
WEEK150	2	50.00 (33.3, 66.7)	50.00 (23.570)	[-161.77, 261.77]	0	NE (NE, NE)	NE (NE)	[NE, NE]
WEEK158	1	33.33 (33.3, 33.3)	33.33 (NE)	[NE, NE]	0	NE (NE, NE)	NE (NE)	[NE, NE]
END OF TRT	77	33.33 (0.0, 100.0)	32.90 (29.860)	[26.12, 39.68]	95	33.33 (0.0, 100.0)	25.96 (24.398)	[20.99, 30.93]
FOLLOW UP	48	33.33 (0.0, 100.0)	36.81 (30.935)	[27.82, 45.79]	56	33.33 (0.0, 100.0)	32.74 (26.584)	[25.62, 39.86]

Baseline is the last non-missing measurement prior to first dose of study intervention.
[1] Confidence interval based on the normal distribution.
For functional scales, higher scores represent a better level of functioning. For symptom-oriented scales, a higher score represents more severe symptoms.



Number of subjects:

EC+FOLFOX	201	190	182	179	161	140	139	123	106	93	79	67	59	49	35	33	21	12	8	7	4	2	1	77	48
Control 1	181	182	164	134	121	89	65	47	37	28	27	19	10	6	5	6	4	2	1	0	1	0	0	95	56

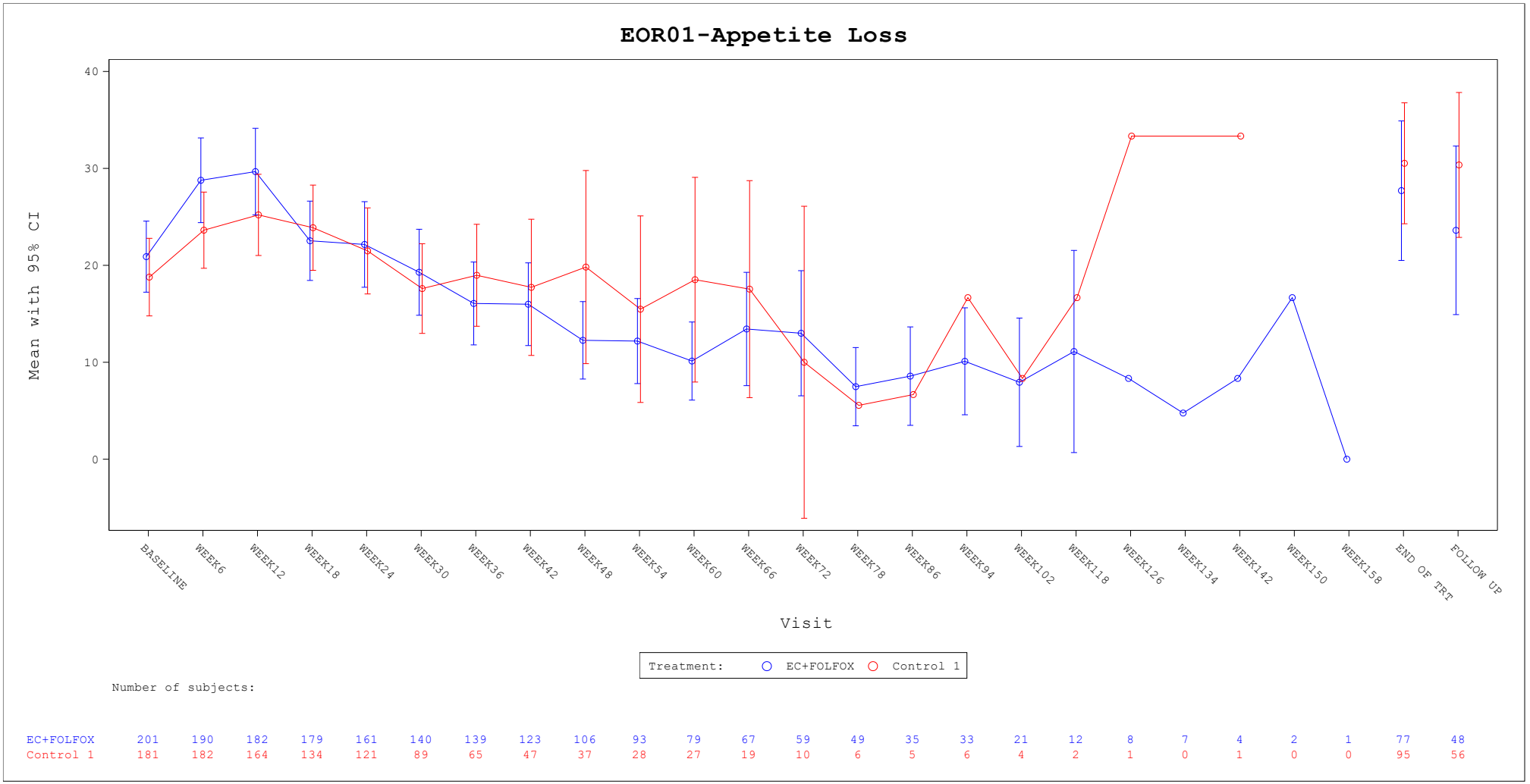
Baseline is the last non-missing measurement prior to first dose of study intervention.
No confidence intervalls are drawn, when there are less than 10 patients in treatment arm.
For functional scales, higher scores represent a better level of functioning. For symptom-oriented scales, a higher score represents more severe symptoms.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Summary over time - EOR01-Appetite Loss
Full Analysis Set

	EC+FOLFOX (N=236)				Control 1 (N=243)			
Visit	n	Median (Range)	Mean (SD)	95% CI [1]	n	Median (Range)	Mean (SD)	95% CI [1]
BASELINE	201	0.00 (0.0, 100.0)	20.90 (26.354)	[17.23, 24.56]	181	0.00 (0.0, 100.0)	18.78 (27.275)	[14.78, 22.78]
WEEK6	190	33.33 (0.0, 100.0)	28.77 (30.520)	[24.40, 33.14]	182	33.33 (0.0, 100.0)	23.63 (26.865)	[19.70, 27.56]
WEEK12	182	33.33 (0.0, 100.0)	29.67 (30.527)	[25.21, 34.14]	164	33.33 (0.0, 100.0)	25.20 (27.164)	[21.01, 29.39]
WEEK18	179	0.00 (0.0, 100.0)	22.53 (27.732)	[18.44, 26.62]	134	33.33 (0.0, 100.0)	23.88 (25.727)	[19.48, 28.28]
WEEK24	161	0.00 (0.0, 100.0)	22.15 (28.369)	[17.74, 26.57]	121	33.33 (0.0, 100.0)	21.49 (24.668)	[17.05, 25.93]
WEEK30	140	0.00 (0.0, 100.0)	19.29 (26.543)	[14.85, 23.72]	89	0.00 (0.0, 100.0)	17.60 (21.956)	[12.98, 22.23]
WEEK36	139	0.00 (0.0, 100.0)	16.07 (25.491)	[11.79, 20.34]	65	0.00 (0.0, 66.7)	18.97 (21.221)	[13.72, 24.23]
WEEK42	123	0.00 (0.0, 100.0)	15.99 (23.896)	[11.72, 20.25]	47	0.00 (0.0, 66.7)	17.73 (23.927)	[10.71, 24.76]
WEEK48	106	0.00 (0.0, 100.0)	12.26 (20.741)	[8.27, 16.26]	37	0.00 (0.0, 100.0)	19.82 (29.876)	[9.86, 29.78]
WEEK54	93	0.00 (0.0, 100.0)	12.19 (21.301)	[7.80, 16.57]	28	0.00 (0.0, 100.0)	15.48 (24.816)	[5.85, 25.10]
WEEK60	79	0.00 (0.0, 66.7)	10.13 (17.986)	[6.10, 14.16]	27	0.00 (0.0, 100.0)	18.52 (26.688)	[7.96, 29.08]
WEEK66	67	0.00 (0.0, 100.0)	13.43 (23.967)	[7.59, 19.28]	19	0.00 (0.0, 66.7)	17.54 (23.223)	[6.35, 28.74]
WEEK72	59	0.00 (0.0, 100.0)	12.99 (24.772)	[6.54, 19.45]	10	0.00 (0.0, 66.7)	10.00 (22.498)	[-6.09, 26.09]
WEEK78	49	0.00 (0.0, 33.3)	7.48 (14.052)	[3.45, 11.52]	6	0.00 (0.0, 33.3)	5.56 (13.608)	[-8.73, 19.84]
WEEK86	35	0.00 (0.0, 33.3)	8.57 (14.781)	[3.49, 13.65]	5	0.00 (0.0, 33.3)	6.67 (14.907)	[-11.84, 25.18]
WEEK94	33	0.00 (0.0, 33.3)	10.10 (15.556)	[4.58, 15.62]	6	0.00 (0.0, 66.7)	16.67 (27.889)	[-12.60, 45.93]
WEEK102	21	0.00 (0.0, 33.3)	7.94 (14.548)	[1.31, 14.56]	4	0.00 (0.0, 33.3)	8.33 (16.667)	[-18.19, 34.85]
WEEK118	12	0.00 (0.0, 33.3)	11.11 (16.412)	[0.68, 21.54]	2	16.67 (0.0, 33.3)	16.67 (23.570)	[-195.10, 228.44]
WEEK126	8	0.00 (0.0, 33.3)	8.33 (15.430)	[-4.57, 21.23]	1	33.33 (33.3, 33.3)	33.33 (NE)	[NE, NE]
WEEK134	7	0.00 (0.0, 33.3)	4.76 (12.599)	[-6.89, 16.41]	0	NE (NE, NE)	NE (NE)	[NE, NE]
WEEK142	4	0.00 (0.0, 33.3)	8.33 (16.667)	[-18.19, 34.85]	1	33.33 (33.3, 33.3)	33.33 (NE)	[NE, NE]
WEEK150	2	16.67 (0.0, 33.3)	16.67 (23.570)	[-195.10, 228.44]	0	NE (NE, NE)	NE (NE)	[NE, NE]
WEEK158	1	0.00 (0.0, 0.0)	0.00 (NE)	[NE, NE]	0	NE (NE, NE)	NE (NE)	[NE, NE]
END OF TRT	77	33.33 (0.0, 100.0)	27.71 (31.716)	[20.51, 34.90]	95	33.33 (0.0, 100.0)	30.53 (30.621)	[24.29, 36.76]
FOLLOW UP	48	0.00 (0.0, 100.0)	23.61 (29.940)	[14.92, 32.30]	56	33.33 (0.0, 100.0)	30.36 (27.908)	[22.88, 37.83]

Baseline is the last non-missing measurement prior to first dose of study intervention.
[1] Confidence interval based on the normal distribution.
For functional scales, higher scores represent a better level of functioning. For symptom-oriented scales, a higher score represents more severe symptoms.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Plot over time - EOR01-Appetite Loss
Full Analysis Set



Number of subjects:

EC+FOLFOX	201	190	182	179	161	140	139	123	106	93	79	67	59	49	35	33	21	12	8	7	4	2	1	77	48
Control 1	181	182	164	134	121	89	65	47	37	28	27	19	10	6	5	6	4	2	1	0	1	0	0	95	56

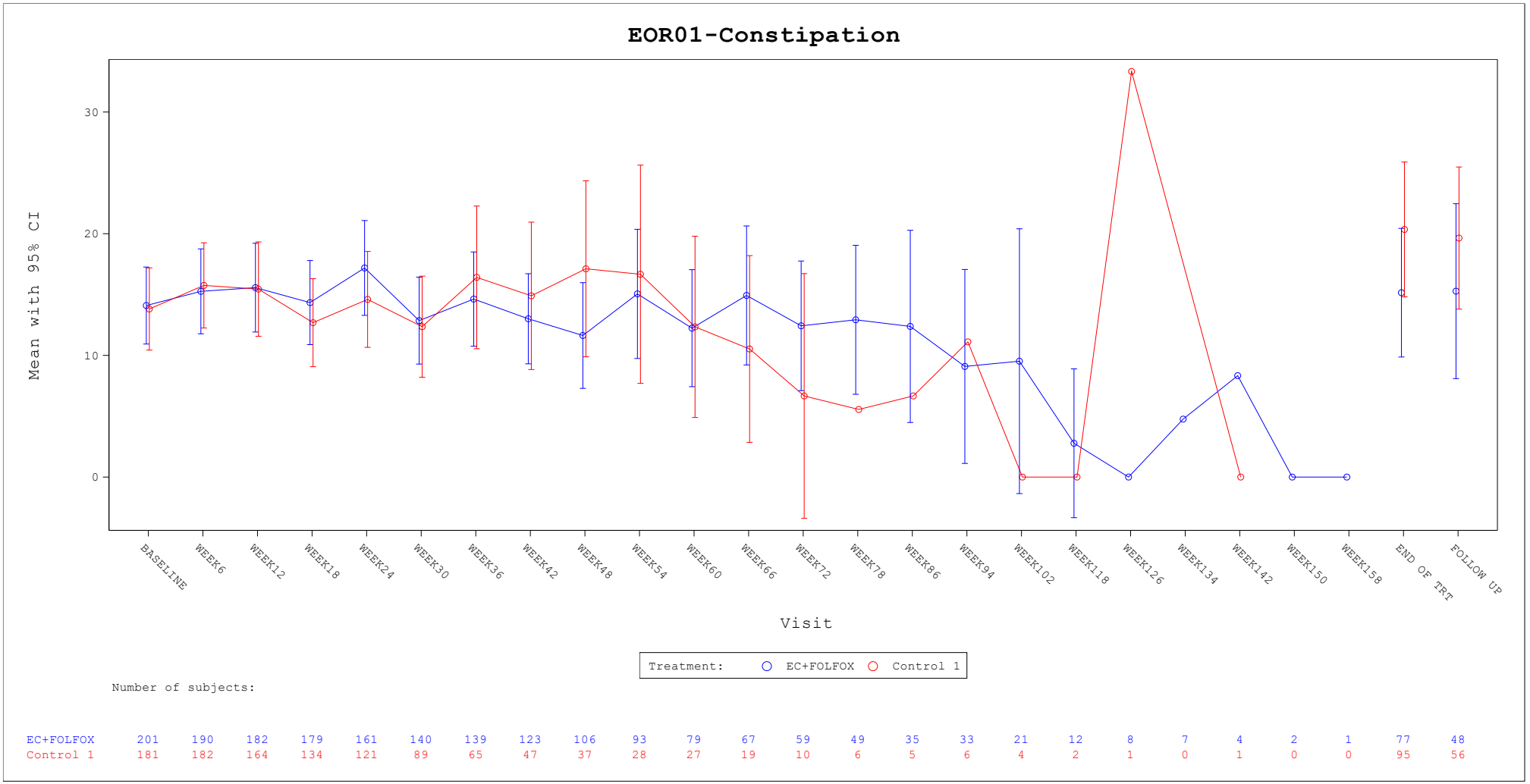
Baseline is the last non-missing measurement prior to first dose of study intervention.
No confidence intervalls are drawn, when there are less than 10 patients in treatment arm.
For functional scales, higher scores represent a better level of functioning. For symptom-oriented scales, a higher score represents more severe symptoms.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Summary over time - EOR01-Constipation
Full Analysis Set

	EC+FOLFOX (N=236)				Control 1 (N=243)			
Visit	n	Median (Range)	Mean (SD)	95% CI [1]	n	Median (Range)	Mean (SD)	95% CI [1]
BASELINE	201	0.00 (0.0, 100.0)	14.10 (22.737)	[10.93, 17.26]	181	0.00 (0.0, 100.0)	13.81 (23.030)	[10.43, 17.19]
WEEK6	190	0.00 (0.0, 100.0)	15.26 (24.387)	[11.77, 18.75]	182	0.00 (0.0, 100.0)	15.75 (23.940)	[12.25, 19.25]
WEEK12	182	0.00 (0.0, 100.0)	15.57 (24.937)	[11.92, 19.22]	164	0.00 (0.0, 100.0)	15.45 (25.149)	[11.57, 19.32]
WEEK18	179	0.00 (0.0, 100.0)	14.34 (23.421)	[10.88, 17.79]	134	0.00 (0.0, 66.7)	12.69 (21.159)	[9.07, 16.30]
WEEK24	161	0.00 (0.0, 100.0)	17.18 (25.029)	[13.29, 21.08]	121	0.00 (0.0, 100.0)	14.60 (21.897)	[10.66, 18.54]
WEEK30	140	0.00 (0.0, 100.0)	12.86 (21.378)	[9.28, 16.43]	89	0.00 (0.0, 66.7)	12.36 (19.709)	[8.21, 16.51]
WEEK36	139	0.00 (0.0, 100.0)	14.63 (23.092)	[10.76, 18.50]	65	0.00 (0.0, 100.0)	16.41 (23.661)	[10.55, 22.27]
WEEK42	123	0.00 (0.0, 100.0)	13.01 (20.748)	[9.30, 16.71]	47	0.00 (0.0, 66.7)	14.89 (20.628)	[8.84, 20.95]
WEEK48	106	0.00 (0.0, 100.0)	11.64 (22.557)	[7.29, 15.98]	37	0.00 (0.0, 66.7)	17.12 (21.690)	[9.89, 24.35]
WEEK54	93	0.00 (0.0, 100.0)	15.05 (25.781)	[9.74, 20.36]	28	0.00 (0.0, 100.0)	16.67 (23.130)	[7.70, 25.64]
WEEK60	79	0.00 (0.0, 100.0)	12.24 (21.468)	[7.43, 17.04]	27	0.00 (0.0, 66.7)	12.35 (18.829)	[4.90, 19.79]
WEEK66	67	0.00 (0.0, 100.0)	14.93 (23.415)	[9.21, 20.64]	19	0.00 (0.0, 33.3)	10.53 (15.919)	[2.85, 18.20]
WEEK72	59	0.00 (0.0, 100.0)	12.43 (20.434)	[7.10, 17.75]	10	0.00 (0.0, 33.3)	6.67 (14.055)	[-3.39, 16.72]
WEEK78	49	0.00 (0.0, 100.0)	12.93 (21.318)	[6.80, 19.05]	6	0.00 (0.0, 33.3)	5.56 (13.608)	[-8.73, 19.84]
WEEK86	35	0.00 (0.0, 100.0)	12.38 (22.989)	[4.48, 20.28]	5	0.00 (0.0, 33.3)	6.67 (14.907)	[-11.84, 25.18]
WEEK94	33	0.00 (0.0, 100.0)	9.09 (22.473)	[1.12, 17.06]	6	0.00 (0.0, 33.3)	11.11 (17.213)	[-6.95, 29.18]
WEEK102	21	0.00 (0.0, 100.0)	9.52 (23.905)	[-1.36, 20.41]	4	0.00 (0.0, 0.0)	0.00 (0.000)	[NE, NE]
WEEK118	12	0.00 (0.0, 33.3)	2.78 (9.623)	[-3.34, 8.89]	2	0.00 (0.0, 0.0)	0.00 (0.000)	[NE, NE]
WEEK126	8	0.00 (0.0, 0.0)	0.00 (0.000)	[NE, NE]	1	33.33 (33.3, 33.3)	33.33 (NE)	[NE, NE]
WEEK134	7	0.00 (0.0, 33.3)	4.76 (12.599)	[-6.89, 16.41]	0	NE (NE, NE)	NE (NE)	[NE, NE]
WEEK142	4	0.00 (0.0, 33.3)	8.33 (16.667)	[-18.19, 34.85]	1	0.00 (0.0, 0.0)	0.00 (NE)	[NE, NE]
WEEK150	2	0.00 (0.0, 0.0)	0.00 (0.000)	[NE, NE]	0	NE (NE, NE)	NE (NE)	[NE, NE]
WEEK158	1	0.00 (0.0, 0.0)	0.00 (NE)	[NE, NE]	0	NE (NE, NE)	NE (NE)	[NE, NE]
END OF TRT	77	0.00 (0.0, 100.0)	15.15 (23.287)	[9.87, 20.44]	95	0.00 (0.0, 100.0)	20.35 (27.200)	[14.81, 25.89]
FOLLOW UP	48	0.00 (0.0, 100.0)	15.28 (24.753)	[8.09, 22.47]	56	33.33 (0.0, 100.0)	19.64 (21.814)	[13.80, 25.48]

Baseline is the last non-missing measurement prior to first dose of study intervention.
[1] Confidence interval based on the normal distribution.
For functional scales, higher scores represent a better level of functioning. For symptom-oriented scales, a higher score represents more severe symptoms.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Plot over time - EOR01-Constipation
Full Analysis Set



Number of subjects:

EC+FOLFOX	201	190	182	179	161	140	139	123	106	93	79	67	59	49	35	33	21	12	8	7	4	2	1	77	48
Control 1	181	182	164	134	121	89	65	47	37	28	27	19	10	6	5	6	4	2	1	0	1	0	0	95	56

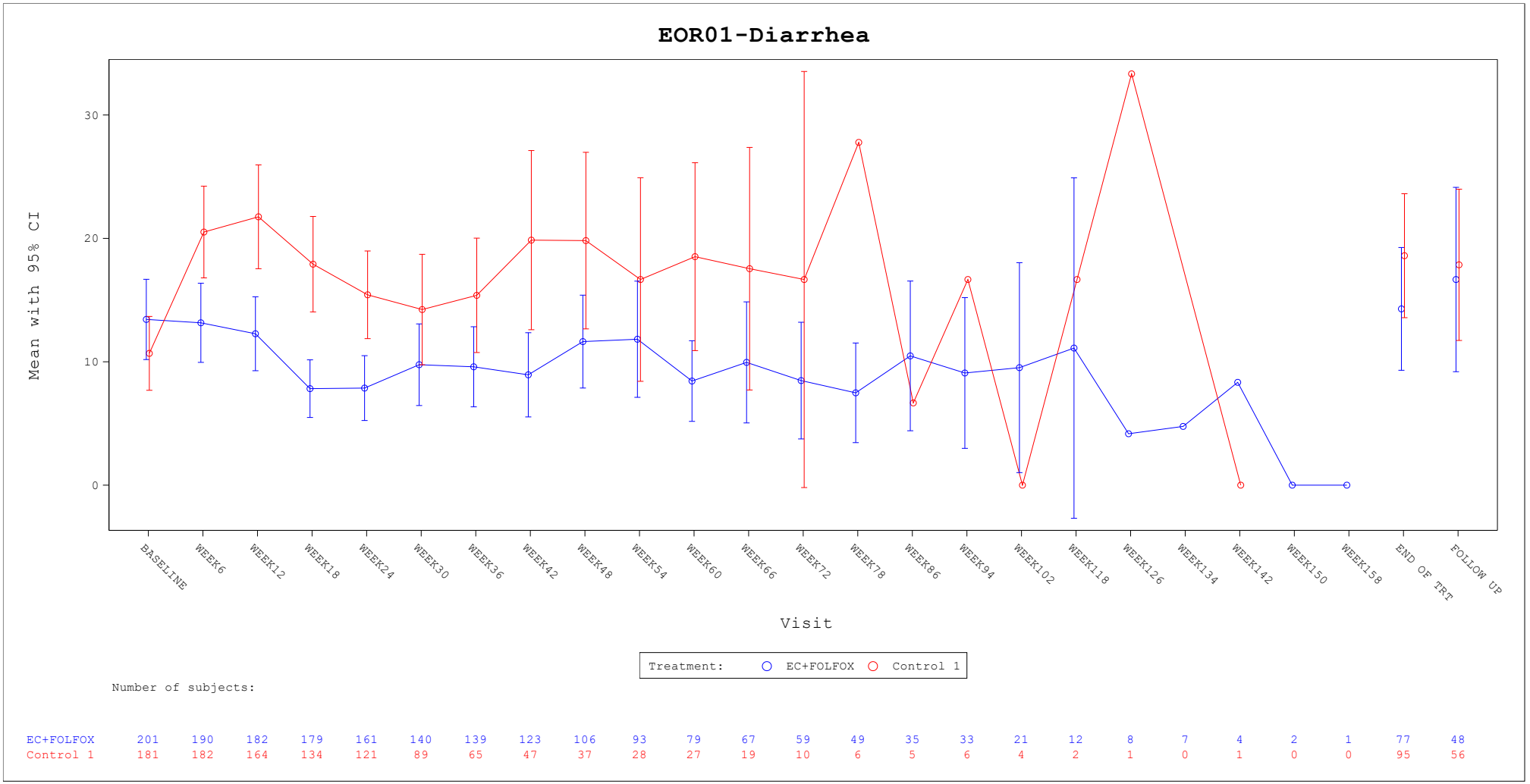
Baseline is the last non-missing measurement prior to first dose of study intervention.
No confidence intervalls are drawn, when there are less than 10 patients in treatment arm.
For functional scales, higher scores represent a better level of functioning. For symptom-oriented scales, a higher score represents more severe symptoms.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Summary over time - EOR01-Diarrhea
Full Analysis Set

	EC+FOLFOX (N=236)				Control 1 (N=243)			
Visit	n	Median (Range)	Mean (SD)	95% CI [1]	n	Median (Range)	Mean (SD)	95% CI [1]
BASELINE	201	0.00 (0.0, 100.0)	13.43 (23.376)	[10.18, 16.68]	181	0.00 (0.0, 100.0)	10.68 (20.399)	[7.69, 13.67]
WEEK6	190	0.00 (0.0, 100.0)	13.16 (22.406)	[9.95, 16.36]	182	0.00 (0.0, 100.0)	20.51 (25.398)	[16.80, 24.23]
WEEK12	182	0.00 (0.0, 100.0)	12.27 (20.481)	[9.28, 15.27]	164	0.00 (0.0, 100.0)	21.75 (27.282)	[17.54, 25.95]
WEEK18	179	0.00 (0.0, 66.7)	7.82 (15.830)	[5.49, 10.16]	134	0.00 (0.0, 100.0)	17.91 (22.632)	[14.04, 21.78]
WEEK24	161	0.00 (0.0, 100.0)	7.87 (16.880)	[5.24, 10.49]	121	0.00 (0.0, 66.7)	15.43 (19.740)	[11.87, 18.98]
WEEK30	140	0.00 (0.0, 66.7)	9.76 (19.790)	[6.46, 13.07]	89	0.00 (0.0, 100.0)	14.23 (21.253)	[9.76, 18.71]
WEEK36	139	0.00 (0.0, 100.0)	9.59 (19.347)	[6.35, 12.84]	65	0.00 (0.0, 66.7)	15.38 (18.705)	[10.75, 20.02]
WEEK42	123	0.00 (0.0, 100.0)	8.94 (19.121)	[5.53, 12.36]	47	0.00 (0.0, 100.0)	19.86 (24.730)	[12.60, 27.12]
WEEK48	106	0.00 (0.0, 100.0)	11.64 (19.541)	[7.87, 15.40]	37	33.33 (0.0, 66.7)	19.82 (21.458)	[12.67, 26.97]
WEEK54	93	0.00 (0.0, 100.0)	11.83 (22.865)	[7.12, 16.54]	28	0.00 (0.0, 66.7)	16.67 (21.276)	[8.42, 24.92]
WEEK60	79	0.00 (0.0, 33.3)	8.44 (14.587)	[5.17, 11.71]	27	33.33 (0.0, 66.7)	18.52 (19.245)	[10.91, 26.13]
WEEK66	67	0.00 (0.0, 100.0)	9.95 (20.113)	[5.04, 14.86]	19	0.00 (0.0, 66.7)	17.54 (20.393)	[7.71, 27.37]
WEEK72	59	0.00 (0.0, 66.7)	8.47 (18.145)	[3.75, 13.20]	10	0.00 (0.0, 66.7)	16.67 (23.570)	[-0.19, 33.53]
WEEK78	49	0.00 (0.0, 33.3)	7.48 (14.052)	[3.45, 11.52]	6	16.67 (0.0, 100.0)	27.78 (38.968)	[-13.12, 68.67]
WEEK86	35	0.00 (0.0, 66.7)	10.48 (17.660)	[4.41, 16.54]	5	0.00 (0.0, 33.3)	6.67 (14.907)	[-11.84, 25.18]
WEEK94	33	0.00 (0.0, 66.7)	9.09 (17.225)	[2.98, 15.20]	6	16.67 (0.0, 33.3)	16.67 (18.257)	[-2.49, 35.83]
WEEK102	21	0.00 (0.0, 66.7)	9.52 (18.687)	[1.02, 18.03]	4	0.00 (0.0, 0.0)	0.00 (0.000)	[NE, NE]
WEEK118	12	0.00 (0.0, 66.7)	11.11 (21.711)	[-2.68, 24.91]	2	16.67 (0.0, 33.3)	16.67 (23.570)	[-195.10, 228.44]
WEEK126	8	0.00 (0.0, 33.3)	4.17 (11.785)	[-5.69, 14.02]	1	33.33 (33.3, 33.3)	33.33 (NE)	[NE, NE]
WEEK134	7	0.00 (0.0, 33.3)	4.76 (12.599)	[-6.89, 16.41]	0	NE (NE, NE)	NE (NE)	[NE, NE]
WEEK142	4	0.00 (0.0, 33.3)	8.33 (16.667)	[-18.19, 34.85]	1	0.00 (0.0, 0.0)	0.00 (NE)	[NE, NE]
WEEK150	2	0.00 (0.0, 0.0)	0.00 (0.000)	[NE, NE]	0	NE (NE, NE)	NE (NE)	[NE, NE]
WEEK158	1	0.00 (0.0, 0.0)	0.00 (NE)	[NE, NE]	0	NE (NE, NE)	NE (NE)	[NE, NE]
END OF TRT	77	0.00 (0.0, 100.0)	14.29 (21.917)	[9.31, 19.26]	95	0.00 (0.0, 100.0)	18.60 (24.656)	[13.57, 23.62]
FOLLOW UP	48	0.00 (0.0, 100.0)	16.67 (25.728)	[9.20, 24.14]	56	0.00 (0.0, 100.0)	17.86 (22.887)	[11.73, 23.99]

Baseline is the last non-missing measurement prior to first dose of study intervention.
[1] Confidence interval based on the normal distribution.
For functional scales, higher scores represent a better level of functioning. For symptom-oriented scales, a higher score represents more severe symptoms.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Plot over time - EOR01-Diarrhea
Full Analysis Set



Number of subjects:

EC+FOLFOX	201	190	182	179	161	140	139	123	106	93	79	67	59	49	35	33	21	12	8	7	4	2	1	77	48
Control 1	181	182	164	134	121	89	65	47	37	28	27	19	10	6	5	6	4	2	1	0	1	0	0	95	56

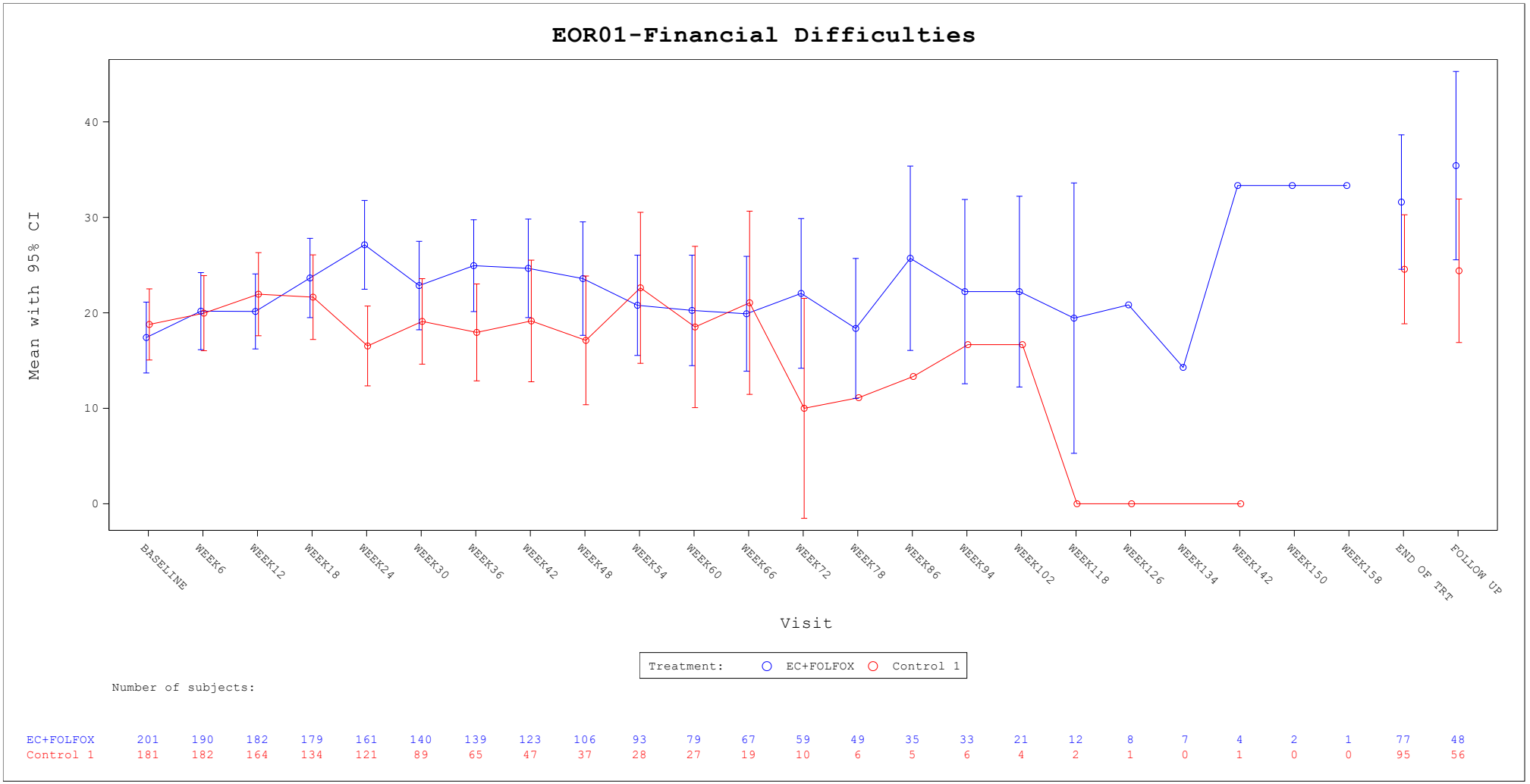
Baseline is the last non-missing measurement prior to first dose of study intervention.
No confidence intervalls are drawn, when there are less than 10 patients in treatment arm.
For functional scales, higher scores represent a better level of functioning. For symptom-oriented scales, a higher score represents more severe symptoms.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Summary over time - EOR01-Financial Difficulties
Full Analysis Set

	EC+FOLFOX (N=236)				Control 1 (N=243)			
Visit	n	Median (Range)	Mean (SD)	95% CI [1]	n	Median (Range)	Mean (SD)	95% CI [1]
BASELINE	201	0.00 (0.0, 100.0)	17.41 (26.682)	[13.70, 21.12]	181	0.00 (0.0, 100.0)	18.78 (25.400)	[15.06, 22.51]
WEEK6	190	0.00 (0.0, 100.0)	20.18 (28.213)	[16.14, 24.21]	182	0.00 (0.0, 100.0)	19.96 (26.882)	[16.03, 23.90]
WEEK12	182	0.00 (0.0, 100.0)	20.15 (26.859)	[16.22, 24.07]	164	0.00 (0.0, 100.0)	21.95 (28.226)	[17.60, 26.30]
WEEK18	179	33.33 (0.0, 100.0)	23.65 (28.144)	[19.50, 27.80]	134	16.67 (0.0, 100.0)	21.64 (25.935)	[17.21, 26.07]
WEEK24	161	33.33 (0.0, 100.0)	27.12 (29.862)	[22.47, 31.77]	121	0.00 (0.0, 100.0)	16.53 (23.224)	[12.35, 20.71]
WEEK30	140	33.33 (0.0, 100.0)	22.86 (27.726)	[18.22, 27.49]	89	0.00 (0.0, 66.7)	19.10 (21.253)	[14.62, 23.58]
WEEK36	139	33.33 (0.0, 100.0)	24.94 (28.684)	[20.13, 29.75]	65	0.00 (0.0, 66.7)	17.95 (20.478)	[12.87, 23.02]
WEEK42	123	33.33 (0.0, 100.0)	24.66 (28.895)	[19.50, 29.82]	47	0.00 (0.0, 66.7)	19.15 (21.697)	[12.78, 25.52]
WEEK48	106	0.00 (0.0, 100.0)	23.58 (30.849)	[17.64, 29.53]	37	0.00 (0.0, 66.7)	17.12 (20.217)	[10.38, 23.86]
WEEK54	93	0.00 (0.0, 100.0)	20.79 (25.497)	[15.54, 26.04]	28	33.33 (0.0, 66.7)	22.62 (20.394)	[14.71, 30.53]
WEEK60	79	0.00 (0.0, 100.0)	20.25 (25.830)	[14.47, 26.04]	27	0.00 (0.0, 66.7)	18.52 (21.350)	[10.07, 26.96]
WEEK66	67	0.00 (0.0, 100.0)	19.90 (24.659)	[13.89, 25.92]	19	33.33 (0.0, 66.7)	21.05 (19.909)	[11.46, 30.65]
WEEK72	59	0.00 (0.0, 100.0)	22.03 (30.077)	[14.20, 29.87]	10	0.00 (0.0, 33.3)	10.00 (16.102)	[-1.52, 21.52]
WEEK78	49	0.00 (0.0, 100.0)	18.37 (25.514)	[11.04, 25.70]	6	0.00 (0.0, 33.3)	11.11 (17.213)	[-6.95, 29.18]
WEEK86	35	33.33 (0.0, 100.0)	25.71 (28.105)	[16.06, 35.37]	5	0.00 (0.0, 33.3)	13.33 (18.257)	[-9.34, 36.00]
WEEK94	33	0.00 (0.0, 100.0)	22.22 (27.217)	[12.57, 31.87]	6	0.00 (0.0, 66.7)	16.67 (27.889)	[-12.60, 45.93]
WEEK102	21	33.33 (0.0, 66.7)	22.22 (21.943)	[12.23, 32.21]	4	0.00 (0.0, 66.7)	16.67 (33.333)	[-36.37, 69.71]
WEEK118	12	16.67 (0.0, 66.7)	19.44 (22.285)	[5.29, 33.60]	2	0.00 (0.0, 0.0)	0.00 (0.000)	[NE, NE]
WEEK126	8	16.67 (0.0, 66.7)	20.83 (24.801)	[0.10, 41.57]	1	0.00 (0.0, 0.0)	0.00 (NE)	[NE, NE]
WEEK134	7	0.00 (0.0, 33.3)	14.29 (17.817)	[-2.19, 30.76]	0	NE (NE, NE)	NE (NE)	[NE, NE]
WEEK142	4	33.33 (0.0, 66.7)	33.33 (27.217)	[-9.97, 76.64]	1	0.00 (0.0, 0.0)	0.00 (NE)	[NE, NE]
WEEK150	2	33.33 (0.0, 66.7)	33.33 (47.140)	[-390.21, 456.87]	0	NE (NE, NE)	NE (NE)	[NE, NE]
WEEK158	1	33.33 (33.3, 33.3)	33.33 (NE)	[NE, NE]	0	NE (NE, NE)	NE (NE)	[NE, NE]
END OF TRT	77	33.33 (0.0, 100.0)	31.60 (31.014)	[24.56, 38.64]	95	33.33 (0.0, 100.0)	24.56 (28.020)	[18.85, 30.27]
FOLLOW UP	48	33.33 (0.0, 100.0)	35.42 (33.970)	[25.55, 45.28]	56	33.33 (0.0, 100.0)	24.40 (28.063)	[16.89, 31.92]

Baseline is the last non-missing measurement prior to first dose of study intervention.
[1] Confidence interval based on the normal distribution.
For functional scales, higher scores represent a better level of functioning. For symptom-oriented scales, a higher score represents more severe symptoms.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Plot over time - EOR01-Financial Difficulties
Full Analysis Set



Number of subjects:

EC+FOLFOX	201	190	182	179	161	140	139	123	106	93	79	67	59	49	35	33	21	12	8	7	4	2	1	77	48
Control 1	181	182	164	134	121	89	65	47	37	28	27	19	10	6	5	6	4	2	1	0	1	0	0	95	56

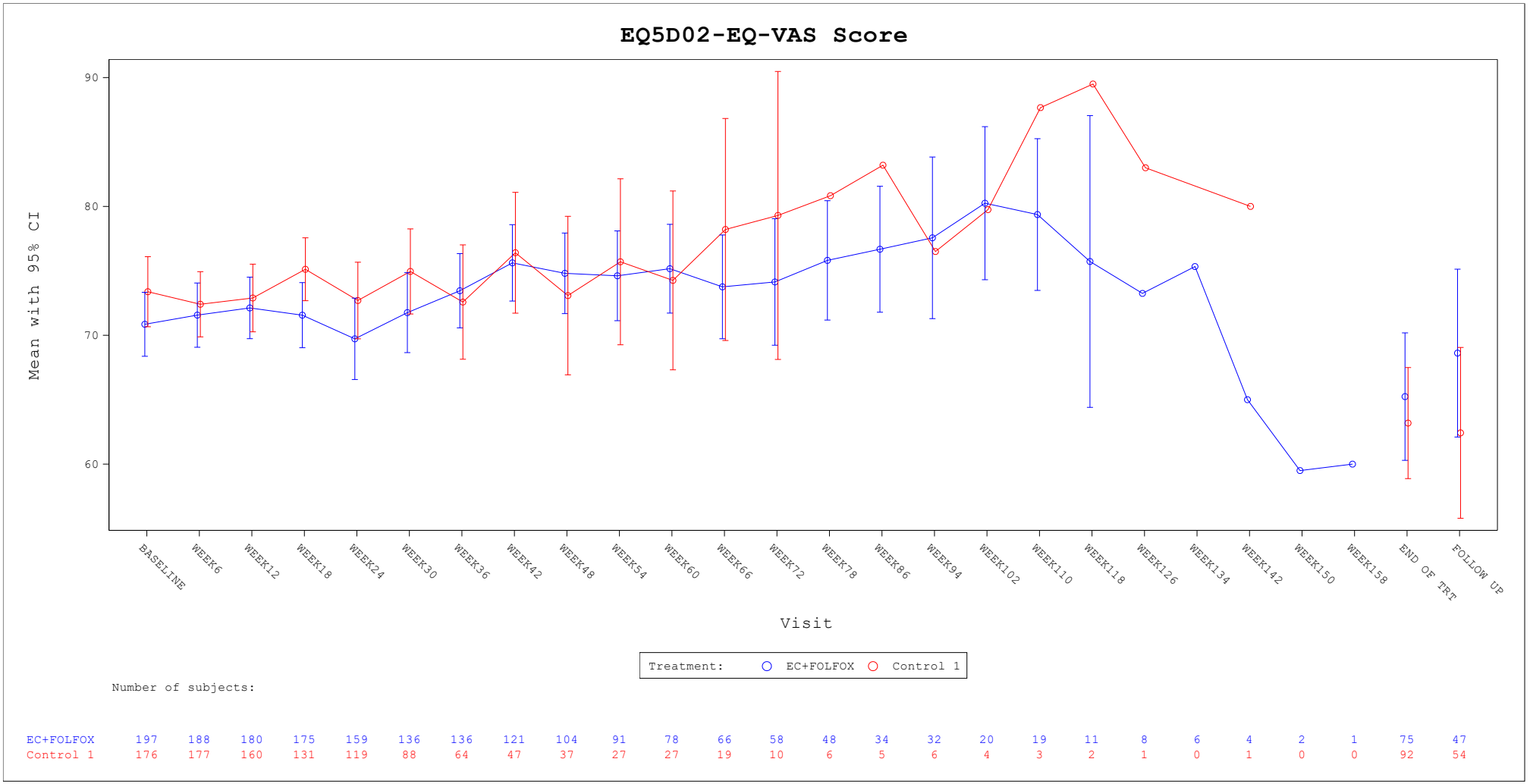
Baseline is the last non-missing measurement prior to first dose of study intervention.
No confidence intervalls are drawn, when there are less than 10 patients in treatment arm.
For functional scales, higher scores represent a better level of functioning. For symptom-oriented scales, a higher score represents more severe symptoms.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Summary over time - EQ5D02-EQ-VAS Score
Full Analysis Set

	EC+FOLFOX (N=236)				Control 1 (N=243)			
Visit	n	Median (Range)	Mean (SD)	95% CI [1]	n	Median (Range)	Mean (SD)	95% CI [1]
BASELINE	197	70.00 (16.0, 100.0)	70.85 (17.672)	[68.37, 73.34]	176	79.50 (5.0, 100.0)	73.38 (18.276)	[70.66, 76.10]
WEEK6	188	75.00 (15.0, 100.0)	71.56 (17.330)	[69.07, 74.06]	177	75.00 (8.0, 100.0)	72.41 (17.056)	[69.88, 74.94]
WEEK12	180	75.00 (20.0, 100.0)	72.12 (16.233)	[69.73, 74.51]	160	75.00 (20.0, 100.0)	72.89 (16.820)	[70.27, 75.52]
WEEK18	175	71.00 (20.0, 99.0)	71.56 (16.937)	[69.03, 74.09]	131	78.00 (20.0, 100.0)	75.12 (14.119)	[72.68, 77.56]
WEEK24	159	72.00 (0.0, 99.0)	69.72 (20.162)	[66.57, 72.88]	119	76.00 (15.0, 100.0)	72.70 (16.375)	[69.72, 75.67]
WEEK30	136	79.00 (25.0, 100.0)	71.76 (18.290)	[68.66, 74.86]	88	79.00 (30.0, 100.0)	74.95 (15.581)	[71.65, 78.26]
WEEK36	136	79.00 (14.0, 99.0)	73.46 (16.987)	[70.58, 76.34]	64	78.50 (20.0, 100.0)	72.58 (17.763)	[68.14, 77.02]
WEEK42	121	80.00 (30.0, 100.0)	75.62 (16.465)	[72.66, 78.58]	47	79.00 (39.0, 100.0)	76.40 (15.968)	[71.72, 81.09]
WEEK48	104	80.00 (30.0, 100.0)	74.81 (16.079)	[71.68, 77.93]	37	80.00 (31.0, 100.0)	73.08 (18.447)	[66.93, 79.23]
WEEK54	91	80.00 (20.0, 100.0)	74.62 (16.736)	[71.13, 78.10]	27	79.00 (35.0, 98.0)	75.70 (16.281)	[69.26, 82.14]
WEEK60	78	78.00 (40.0, 98.0)	75.17 (15.273)	[71.72, 78.61]	27	80.00 (35.0, 100.0)	74.26 (17.542)	[67.32, 81.20]
WEEK66	66	79.00 (9.0, 98.0)	73.76 (16.378)	[69.73, 77.78]	19	80.00 (40.0, 100.0)	78.21 (17.875)	[69.60, 86.83]
WEEK72	58	80.00 (20.0, 100.0)	74.14 (18.670)	[69.23, 79.05]	10	80.00 (50.0, 100.0)	79.30 (15.621)	[68.13, 90.47]
WEEK78	48	80.00 (36.0, 100.0)	75.81 (15.952)	[71.18, 80.44]	6	79.50 (70.0, 98.0)	80.83 (9.538)	[70.82, 90.84]
WEEK86	34	80.00 (39.0, 99.0)	76.68 (14.006)	[71.79, 81.56]	5	80.00 (78.0, 99.0)	83.20 (8.871)	[72.18, 94.22]
WEEK94	32	83.00 (30.0, 99.0)	77.56 (17.391)	[71.29, 83.83]	6	78.00 (60.0, 99.0)	76.50 (13.576)	[62.25, 90.75]
WEEK102	20	80.00 (55.0, 98.0)	80.25 (12.690)	[74.31, 86.19]	4	75.50 (69.0, 99.0)	79.75 (13.937)	[57.57, 101.93]
WEEK110	19	80.00 (51.0, 97.0)	79.37 (12.217)	[73.48, 85.26]	3	84.00 (80.0, 99.0)	87.67 (10.017)	[62.78, 112.55]
WEEK118	11	80.00 (45.0, 94.0)	75.73 (16.853)	[64.41, 87.05]	2	89.50 (80.0, 99.0)	89.50 (13.435)	[-31.21, 210.21]
WEEK126	8	77.50 (51.0, 90.0)	73.25 (16.799)	[59.21, 87.29]	1	83.00 (83.0, 83.0)	83.00 (NE)	[NE, NE]
WEEK134	6	77.50 (50.0, 93.0)	75.33 (14.692)	[59.91, 90.75]	0	NE (NE, NE)	NE (NE)	[NE, NE]
WEEK142	4	60.50 (50.0, 89.0)	65.00 (18.129)	[36.15, 93.85]	1	80.00 (80.0, 80.0)	80.00 (NE)	[NE, NE]
WEEK150	2	59.50 (50.0, 69.0)	59.50 (13.435)	[-61.21, 180.21]	0	NE (NE, NE)	NE (NE)	[NE, NE]
WEEK158	1	60.00 (60.0, 60.0)	60.00 (NE)	[NE, NE]	0	NE (NE, NE)	NE (NE)	[NE, NE]
END OF TRT	75	70.00 (19.0, 100.0)	65.24 (21.498)	[60.29, 70.19]	92	63.50 (6.0, 99.0)	63.18 (20.808)	[58.88, 67.49]
FOLLOW UP	47	73.00 (1.0, 100.0)	68.62 (22.183)	[62.10, 75.13]	54	67.00 (6.0, 99.0)	62.43 (24.287)	[55.80, 69.06]

Baseline is the last non-missing measurement prior to first dose of study intervention.
[1] Confidence interval based on the normal distribution.
Higher score means better health state.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Plot over time - EQ5D02-EQ-VAS Score
Full Analysis Set



Number of subjects:

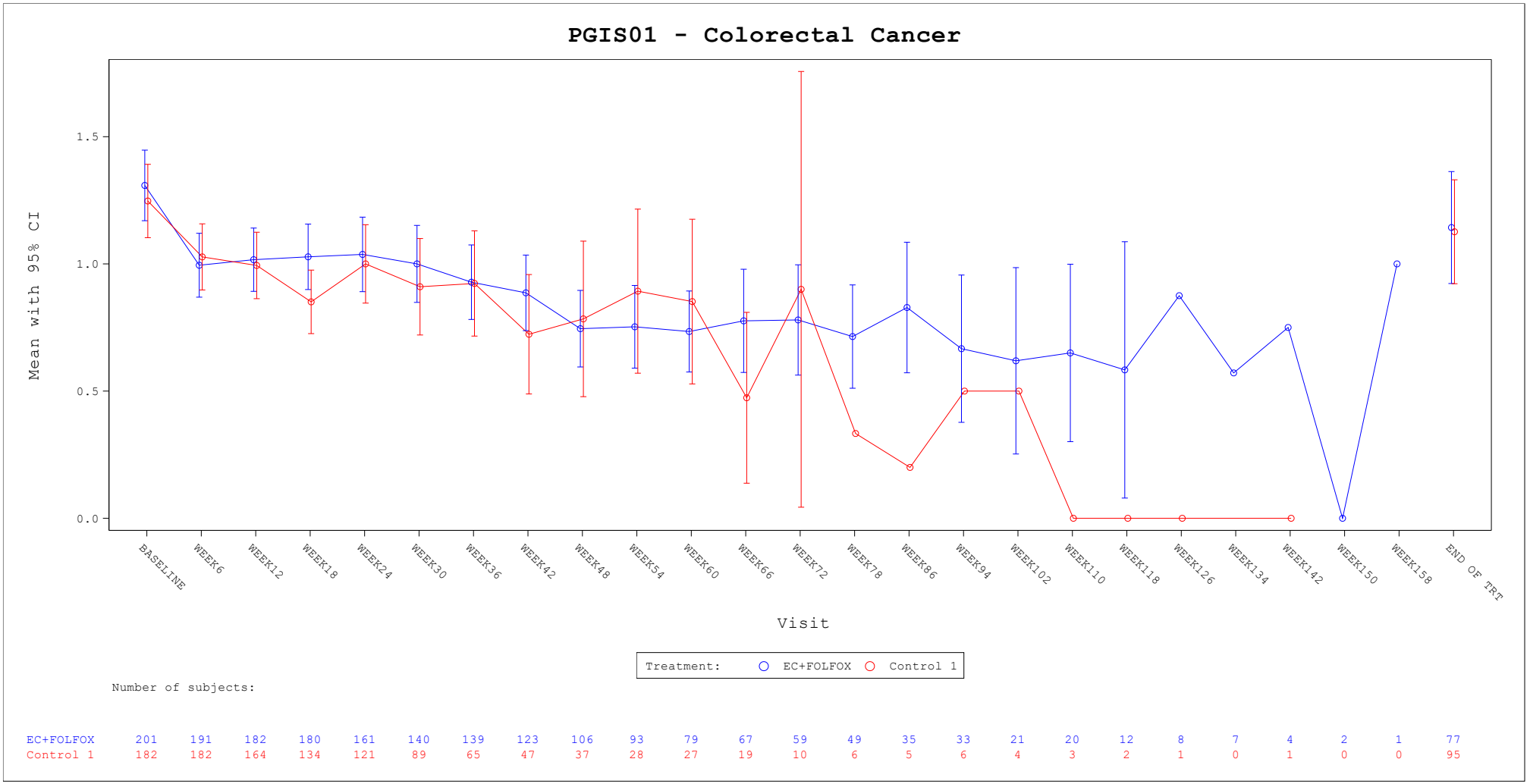
EC+FOLFOX	197	188	180	175	159	136	136	121	104	91	78	66	58	48	34	32	20	19	11	8	6	4	2	1	75	47
Control 1	176	177	160	131	119	88	64	47	37	27	27	19	10	6	5	6	4	3	2	1	0	1	0	0	92	54

Baseline is the last non-missing measurement prior to first dose of study intervention.
No confidence intervalls are drawn, when there are less than 10 patients in treatment arm.
Higher score means better health state.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Summary over time - PGIS01 - Colorectal Cancer
Full Analysis Set

	EC+FOLFOX (N=236)				Control 1 (N=243)			
Visit	n	Median (Range)	Mean (SD)	95% CI [1]	n	Median (Range)	Mean (SD)	95% CI [1]
BASELINE	201	1.00 (0.0, 3.0)	1.31 (0.997)	[1.17, 1.45]	182	1.00 (0.0, 3.0)	1.25 (0.986)	[1.10, 1.39]
WEEK6	191	1.00 (0.0, 3.0)	0.99 (0.880)	[0.87, 1.12]	182	1.00 (0.0, 3.0)	1.03 (0.888)	[0.90, 1.16]
WEEK12	182	1.00 (0.0, 3.0)	1.02 (0.851)	[0.89, 1.14]	164	1.00 (0.0, 3.0)	0.99 (0.847)	[0.86, 1.12]
WEEK18	180	1.00 (0.0, 3.0)	1.03 (0.874)	[0.90, 1.16]	134	1.00 (0.0, 3.0)	0.85 (0.731)	[0.73, 0.98]
WEEK24	161	1.00 (0.0, 3.0)	1.04 (0.941)	[0.89, 1.18]	121	1.00 (0.0, 3.0)	1.00 (0.856)	[0.85, 1.15]
WEEK30	140	1.00 (0.0, 3.0)	1.00 (0.906)	[0.85, 1.15]	89	1.00 (0.0, 3.0)	0.91 (0.900)	[0.72, 1.10]
WEEK36	139	1.00 (0.0, 3.0)	0.93 (0.873)	[0.78, 1.07]	65	1.00 (0.0, 3.0)	0.92 (0.835)	[0.72, 1.13]
WEEK42	123	1.00 (0.0, 3.0)	0.89 (0.832)	[0.74, 1.03]	47	1.00 (0.0, 3.0)	0.72 (0.800)	[0.49, 0.96]
WEEK48	106	1.00 (0.0, 3.0)	0.75 (0.781)	[0.59, 0.90]	37	1.00 (0.0, 3.0)	0.78 (0.917)	[0.48, 1.09]
WEEK54	93	1.00 (0.0, 3.0)	0.75 (0.789)	[0.59, 0.92]	28	1.00 (0.0, 2.0)	0.89 (0.832)	[0.57, 1.22]
WEEK60	79	1.00 (0.0, 3.0)	0.73 (0.711)	[0.57, 0.89]	27	1.00 (0.0, 2.0)	0.85 (0.818)	[0.53, 1.18]
WEEK66	67	1.00 (0.0, 3.0)	0.78 (0.832)	[0.57, 0.98]	19	0.00 (0.0, 2.0)	0.47 (0.697)	[0.14, 0.81]
WEEK72	59	1.00 (0.0, 3.0)	0.78 (0.832)	[0.56, 1.00]	10	0.50 (0.0, 3.0)	0.90 (1.197)	[0.04, 1.76]
WEEK78	49	1.00 (0.0, 2.0)	0.71 (0.707)	[0.51, 0.92]	6	0.00 (0.0, 1.0)	0.33 (0.516)	[-0.21, 0.88]
WEEK86	35	1.00 (0.0, 3.0)	0.83 (0.747)	[0.57, 1.09]	5	0.00 (0.0, 1.0)	0.20 (0.447)	[-0.36, 0.76]
WEEK94	33	0.00 (0.0, 3.0)	0.67 (0.816)	[0.38, 0.96]	6	0.00 (0.0, 2.0)	0.50 (0.837)	[-0.38, 1.38]
WEEK102	21	0.00 (0.0, 3.0)	0.62 (0.805)	[0.25, 0.99]	4	0.00 (0.0, 2.0)	0.50 (1.000)	[-1.09, 2.09]
WEEK110	20	0.50 (0.0, 2.0)	0.65 (0.745)	[0.30, 1.00]	3	0.00 (0.0, 0.0)	0.00 (0.000)	[NE, NE]
WEEK118	12	0.00 (0.0, 2.0)	0.58 (0.793)	[0.08, 1.09]	2	0.00 (0.0, 0.0)	0.00 (0.000)	[NE, NE]
WEEK126	8	0.00 (0.0, 3.0)	0.88 (1.246)	[-0.17, 1.92]	1	0.00 (0.0, 0.0)	0.00 (NE)	[NE, NE]
WEEK134	7	0.00 (0.0, 2.0)	0.57 (0.787)	[-0.16, 1.30]	0	NE (NE, NE)	NE (NE)	[NE, NE]
WEEK142	4	0.00 (0.0, 3.0)	0.75 (1.500)	[-1.64, 3.14]	1	0.00 (0.0, 0.0)	0.00 (NE)	[NE, NE]
WEEK150	2	0.00 (0.0, 0.0)	0.00 (0.000)	[NE, NE]	0	NE (NE, NE)	NE (NE)	[NE, NE]
WEEK158	1	1.00 (1.0, 1.0)	1.00 (NE)	[NE, NE]	0	NE (NE, NE)	NE (NE)	[NE, NE]
END OF TRT	77	1.00 (0.0, 3.0)	1.14 (0.969)	[0.92, 1.36]	95	1.00 (0.0, 3.0)	1.13 (1.003)	[0.92, 1.33]

Baseline is the last non-missing measurement prior to first dose of study intervention.
[1] Confidence interval based on the normal distribution.
Higher score means worse impression of severity.



Number of subjects:

EC+FOLFOX	201	191	182	180	161	140	139	123	106	93	79	67	59	49	35	33	21	20	12	8	7	4	2	1	77
Control 1	182	182	164	134	121	89	65	47	37	28	27	19	10	6	5	6	4	3	2	1	0	1	0	0	95

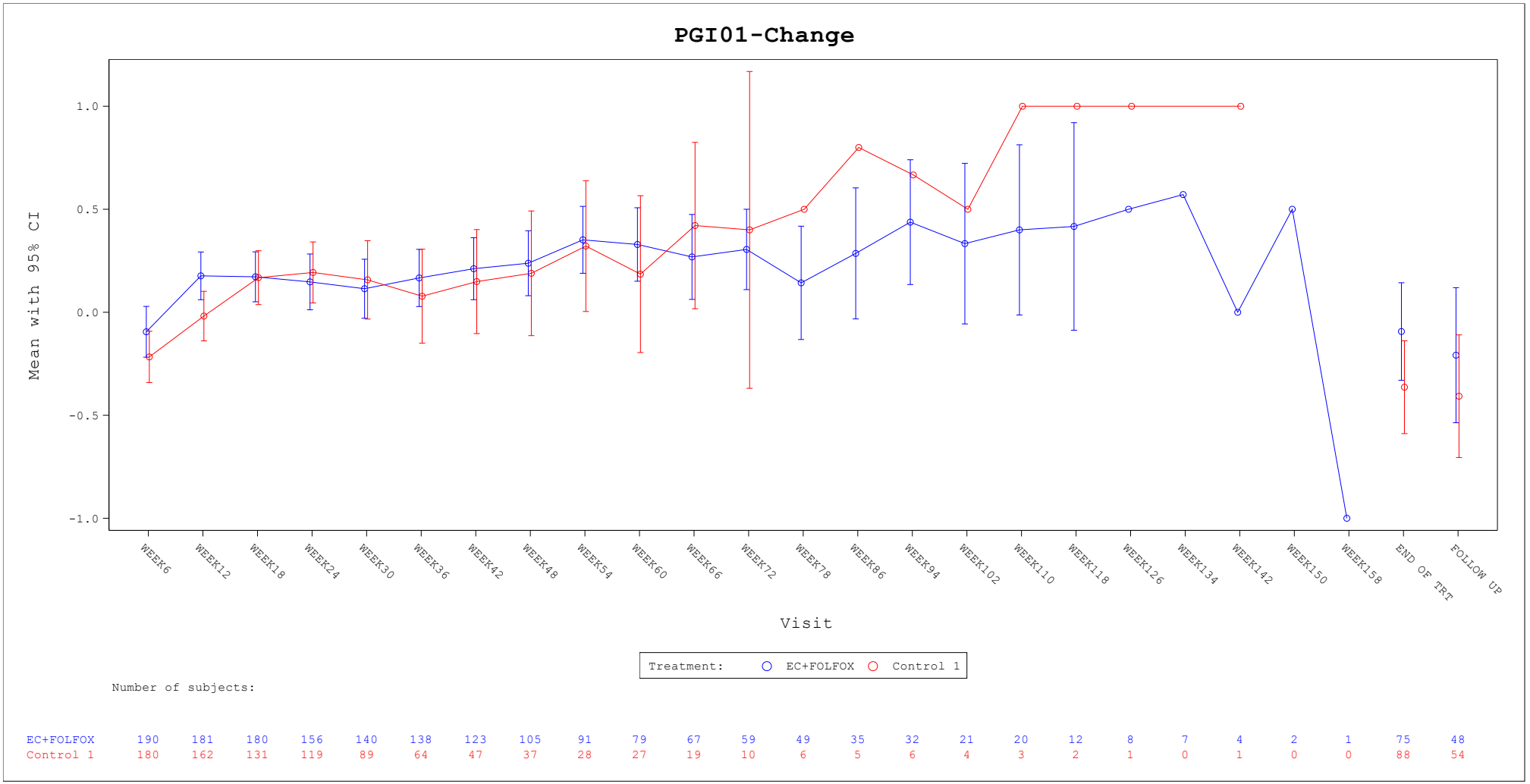
Baseline is the last non-missing measurement prior to first dose of study intervention.
No confidence intervalls are drawn, when there are less than 10 patients in treatment arm.
Higher score means worse impression of severity.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Summary over time - PGI01-Change
Full Analysis Set

	EC+FOLFOX (N=236)				Control 1 (N=243)			
Visit	n	Median (Range)	Mean (SD)	95% CI [1]	n	Median (Range)	Mean (SD)	95% CI [1]
WEEK6	190	0.00 (-2.0, 1.0)	-0.09 (0.862)	[-0.22, 0.03]	180	0.00 (-2.0, 1.0)	-0.22 (0.847)	[-0.34, -0.09]
WEEK12	181	0.00 (-2.0, 1.0)	0.18 (0.790)	[0.06, 0.29]	162	0.00 (-2.0, 1.0)	-0.02 (0.776)	[-0.14, 0.10]
WEEK18	180	0.00 (-2.0, 1.0)	0.17 (0.824)	[0.05, 0.29]	131	0.00 (-2.0, 1.0)	0.17 (0.756)	[0.04, 0.30]
WEEK24	156	0.00 (-2.0, 1.0)	0.15 (0.856)	[0.01, 0.28]	119	0.00 (-2.0, 1.0)	0.19 (0.816)	[0.05, 0.34]
WEEK30	140	0.00 (-2.0, 1.0)	0.11 (0.857)	[-0.03, 0.26]	89	0.00 (-2.0, 1.0)	0.16 (0.903)	[-0.03, 0.35]
WEEK36	138	0.00 (-2.0, 1.0)	0.17 (0.825)	[0.03, 0.31]	64	0.00 (-2.0, 1.0)	0.08 (0.914)	[-0.15, 0.31]
WEEK42	123	0.00 (-2.0, 1.0)	0.21 (0.842)	[0.06, 0.36]	47	0.00 (-2.0, 1.0)	0.15 (0.859)	[-0.10, 0.40]
WEEK48	105	0.00 (-2.0, 1.0)	0.24 (0.815)	[0.08, 0.40]	37	0.00 (-2.0, 1.0)	0.19 (0.908)	[-0.11, 0.49]
WEEK54	91	1.00 (-2.0, 1.0)	0.35 (0.780)	[0.19, 0.51]	28	1.00 (-1.0, 1.0)	0.32 (0.819)	[0.00, 0.64]
WEEK60	79	1.00 (-2.0, 1.0)	0.33 (0.796)	[0.15, 0.51]	27	0.00 (-2.0, 1.0)	0.19 (0.962)	[-0.20, 0.57]
WEEK66	67	0.00 (-2.0, 1.0)	0.27 (0.845)	[0.06, 0.47]	19	1.00 (-2.0, 1.0)	0.42 (0.838)	[0.02, 0.82]
WEEK72	59	0.00 (-1.0, 1.0)	0.31 (0.749)	[0.11, 0.50]	10	1.00 (-2.0, 1.0)	0.40 (1.075)	[-0.37, 1.17]
WEEK78	49	0.00 (-2.0, 1.0)	0.14 (0.957)	[-0.13, 0.42]	6	1.00 (-1.0, 1.0)	0.50 (0.837)	[-0.38, 1.38]
WEEK86	35	1.00 (-2.0, 1.0)	0.29 (0.926)	[-0.03, 0.60]	5	1.00 (0.0, 1.0)	0.80 (0.447)	[0.24, 1.36]
WEEK94	32	1.00 (-2.0, 1.0)	0.44 (0.840)	[0.13, 0.74]	6	1.00 (-1.0, 1.0)	0.67 (0.816)	[-0.19, 1.52]
WEEK102	21	1.00 (-2.0, 1.0)	0.33 (0.856)	[-0.06, 0.72]	4	1.00 (-1.0, 1.0)	0.50 (1.000)	[-1.09, 2.09]
WEEK110	20	1.00 (-2.0, 1.0)	0.40 (0.883)	[-0.01, 0.81]	3	1.00 (1.0, 1.0)	1.00 (0.000)	[NE, NE]
WEEK118	12	1.00 (-1.0, 1.0)	0.42 (0.793)	[-0.09, 0.92]	2	1.00 (1.0, 1.0)	1.00 (0.000)	[NE, NE]
WEEK126	8	1.00 (-1.0, 1.0)	0.50 (0.926)	[-0.27, 1.27]	1	1.00 (1.0, 1.0)	1.00 (NE)	[NE, NE]
WEEK134	7	1.00 (-1.0, 1.0)	0.57 (0.787)	[-0.16, 1.30]	0	NE (NE, NE)	NE (NE)	[NE, NE]
WEEK142	4	0.50 (-2.0, 1.0)	0.00 (1.414)	[-2.25, 2.25]	1	1.00 (1.0, 1.0)	1.00 (NE)	[NE, NE]
WEEK150	2	0.50 (0.0, 1.0)	0.50 (0.707)	[-5.85, 6.85]	0	NE (NE, NE)	NE (NE)	[NE, NE]
WEEK158	1	-1.00 (-1.0, -1.0)	-1.00 (NE)	[NE, NE]	0	NE (NE, NE)	NE (NE)	[NE, NE]
END OF TRT	75	0.00 (-2.0, 1.0)	-0.09 (1.029)	[-0.33, 0.14]	88	0.00 (-2.0, 1.0)	-0.36 (1.063)	[-0.59, -0.14]
FOLLOW UP	48	0.00 (-2.0, 1.0)	-0.21 (1.129)	[-0.54, 0.12]	54	0.00 (-2.0, 1.0)	-0.41 (1.091)	[-0.71, -0.11]

Baseline is the last non-missing measurement prior to first dose of study intervention.
[1] Confidence interval based on the normal distribution.
Categories were transformed to ordinal scale: 2=MUCH BETTER, 1=A LITTLE BETTER, 0=NO CHANGE, -1=A LITTLE WORSE, -2=MUCH WORSE.
Higher score means better impression of change.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Plot over time - PGI01-Change
Full Analysis Set



Number of subjects:

EC+FOLFOX	190	181	180	156	140	138	123	105	91	79	67	59	49	35	32	21	20	12	8	7	4	2	1	75	48
Control 1	180	162	131	119	89	64	47	37	28	27	19	10	6	5	6	4	3	2	1	0	1	0	0	88	54

Baseline is the last non-missing measurement prior to first dose of study intervention.
No confidence intervalls are drawn, when there are less than 10 patients in treatment arm.
Categories were transformed to ordinal scale: 2=MUCH BETTER, 1=A LITTLE BETTER, 0=NO CHANGE, -1=A LITTLE WORSE, -2=MUCH WORSE.
Higher score means better impression of change.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Any AE
Safety Analysis Set

	EC+FOLFOX (N=232)	Control 1 (N=229)
Number of subjects with events, n (%)	232 (100.0)	227 (99.1)
Number of censored subjects, n (%)	0 (0.0)	2 (0.9)
Kaplan-Meier estimates of Time to Event (months) [1]		
25%-ile (95% CI)	0.0 (NE, NE)	0.0 (NE, NE)
Median (95% CI)	0.1 (0.1, 0.1)	0.1 (0.1, 0.1)
75%-ile (95% CI)	0.3 (0.2, 0.5)	0.4 (0.3, 0.5)
Unstratified analysis		
Hazard Ratio (95% CI) [2]	1.15 (0.95, 1.38)	
p-value [3]	0.1453	

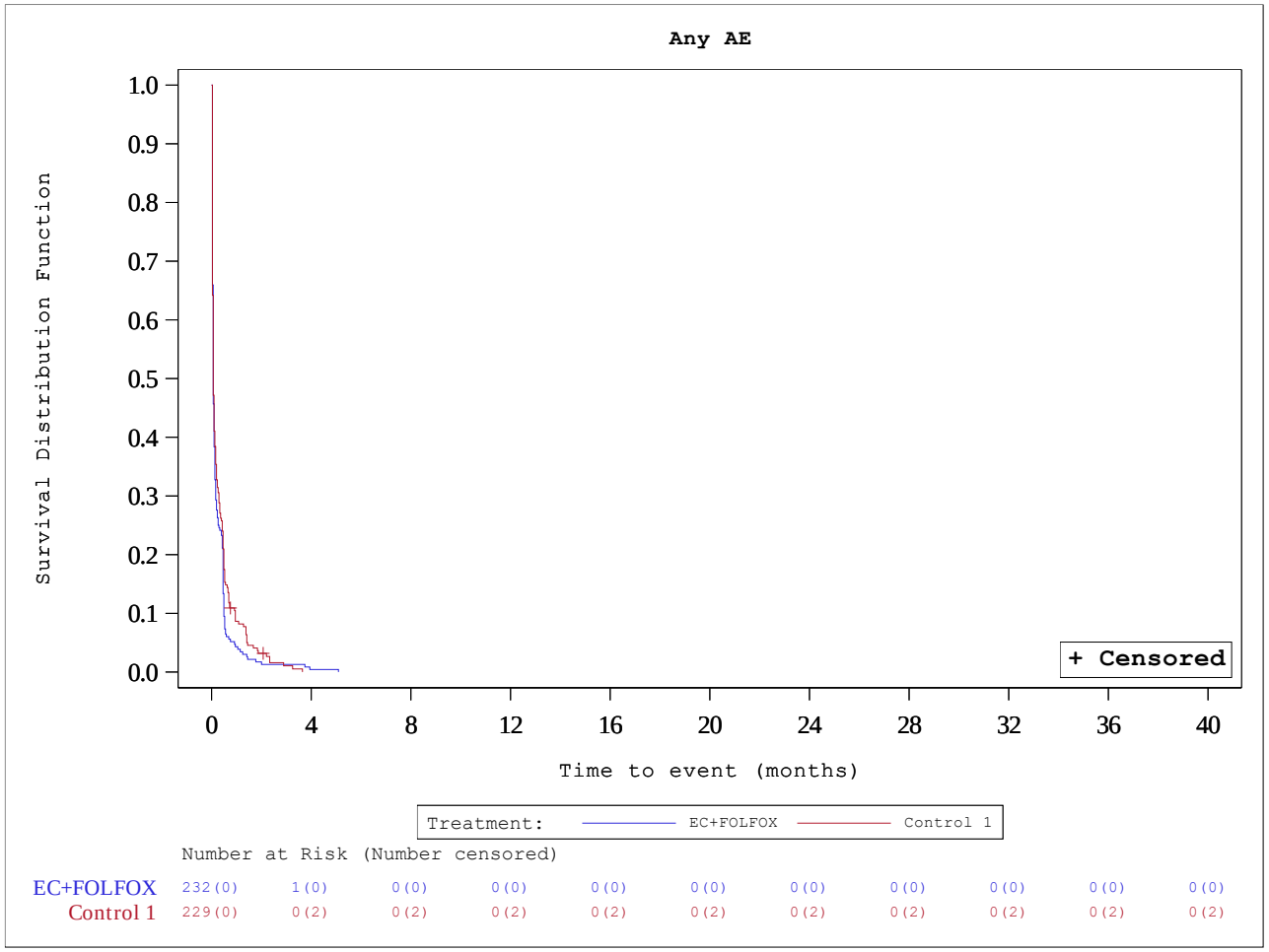
Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Any AE - Subgroup analysis
Safety Analysis Set

Subgroup Level	EC+FOLFOX (N=232) n/ N (%)	EC+FOLFOX (N=232) Median (95% CI)[1]	Control 1 (N=229) n/ N (%)	Control 1 (N=229) Median (95% CI)[1]	Unstratified analysis Hazard Ratio (95% CI)[2]	Unstratified analysis p-Value[3]	Interaction p-Value[4]
Age (Years)							0.6044
< 65	148/ 148 (100.0)	0.1 (0.1, 0.1)	129/ 131 (98.5)	0.1 (0.1, 0.1)	1.17 (0.92, 1.50)	0.1725	
>= 65	84/ 84 (100.0)	0.1 (0.1, 0.1)	98/ 98 (100.0)	0.1 (0.1, 0.2)	1.09 (0.81, 1.46)	0.5740	
Sex							0.1631
Male	121/ 121 (100.0)	0.1 (0.1, 0.1)	110/ 112 (98.2)	0.1 (0.1, 0.2)	1.31 (1.00, 1.70)	0.0465	
Female	111/ 111 (100.0)	0.1 (0.1, 0.1)	117/ 117 (100.0)	0.1 (0.0, 0.1)	0.99 (0.76, 1.29)	0.9723	
Region							0.2035
Europe	108/ 108 (100.0)	0.1 (0.1, 0.1)	102/ 103 (99.0)	0.1 (0.1, 0.2)	1.14 (0.87, 1.50)	0.3706	
USA/Canada	15/ 15 (100.0)	0.1 (0.0, 0.2)	17/ 17 (100.0)	0.0 (0.0, 0.1)	0.62 (0.29, 1.29)	0.2656	
Rest of World	109/ 109 (100.0)	0.1 (0.1, 0.1)	108/ 109 (99.1)	0.1 (0.1, 0.1)	1.25 (0.95, 1.64)	0.0978	
ECOG-PS at Randomization							0.5712
0	130/ 130 (100.0)	0.1 (0.1, 0.1)	128/ 130 (98.5)	0.1 (0.1, 0.1)	1.17 (0.91, 1.50)	0.2113	
1	102/ 102 (100.0)	0.1 (0.1, 0.1)	99/ 99 (100.0)	0.1 (0.1, 0.1)	1.13 (0.85, 1.50)	0.3743	
Number of Organs Involved							0.4965
<= 2	116/ 116 (100.0)	0.1 (0.1, 0.1)	119/ 119 (100.0)	0.1 (0.1, 0.1)	1.10 (0.85, 1.42)	0.5095	
>= 3	116/ 116 (100.0)	0.1 (0.1, 0.1)	108/ 110 (98.2)	0.1 (0.1, 0.1)	1.20 (0.92, 1.57)	0.1535	
Presence of Liver Metastases							0.6224
Yes	146/ 146 (100.0)	0.1 (0.1, 0.1)	148/ 149 (99.3)	0.1 (0.1, 0.1)	1.10 (0.87, 1.39)	0.4033	
No	86/ 86 (100.0)	0.1 (0.1, 0.1)	79/ 80 (98.8)	0.1 (0.1, 0.2)	1.24 (0.90, 1.69)	0.1758	
Side of Tumor							0.7150
Left	88/ 88 (100.0)	0.1 (0.1, 0.1)	89/ 90 (98.9)	0.1 (0.1, 0.2)	1.22 (0.91, 1.65)	0.1869	
Right	144/ 144 (100.0)	0.1 (0.1, 0.1)	138/ 139 (99.3)	0.1 (0.1, 0.1)	1.11 (0.87, 1.40)	0.4106	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.
[4] P-Value for interaction from Cox proportional hazards model using ties=exact option with treatment, subgroup and treatment*subgroup interaction as covariates.
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Kaplan Meier Plot of Any AE
Safety Analysis Set



Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
Kaplan-Meier Plots for subgroups only created if p-value for interaction < 0.05.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Any AE excluding events related to underlying disease progression
Safety Analysis Set

	EC+FOLFOX (N=232)	Control 1 (N=229)
Number of subjects with events, n (%)	231 (99.6)	220 (96.1)
Number of censored subjects, n (%)	1 (0.4)	9 (3.9)
Kaplan-Meier estimates of Time to Event (months) [1]		
25%-ile (95% CI)	0.0 (0.0, 0.1)	0.0 (0.0, 0.1)
Median (95% CI)	0.1 (0.1, 0.2)	0.2 (0.1, 0.3)
75%-ile (95% CI)	0.5 (0.5, 0.6)	0.9 (0.6, 1.3)
Unstratified analysis		
Hazard Ratio (95% CI) [2]	1.27 (1.05, 1.53)	
p-value [3]	0.0129	

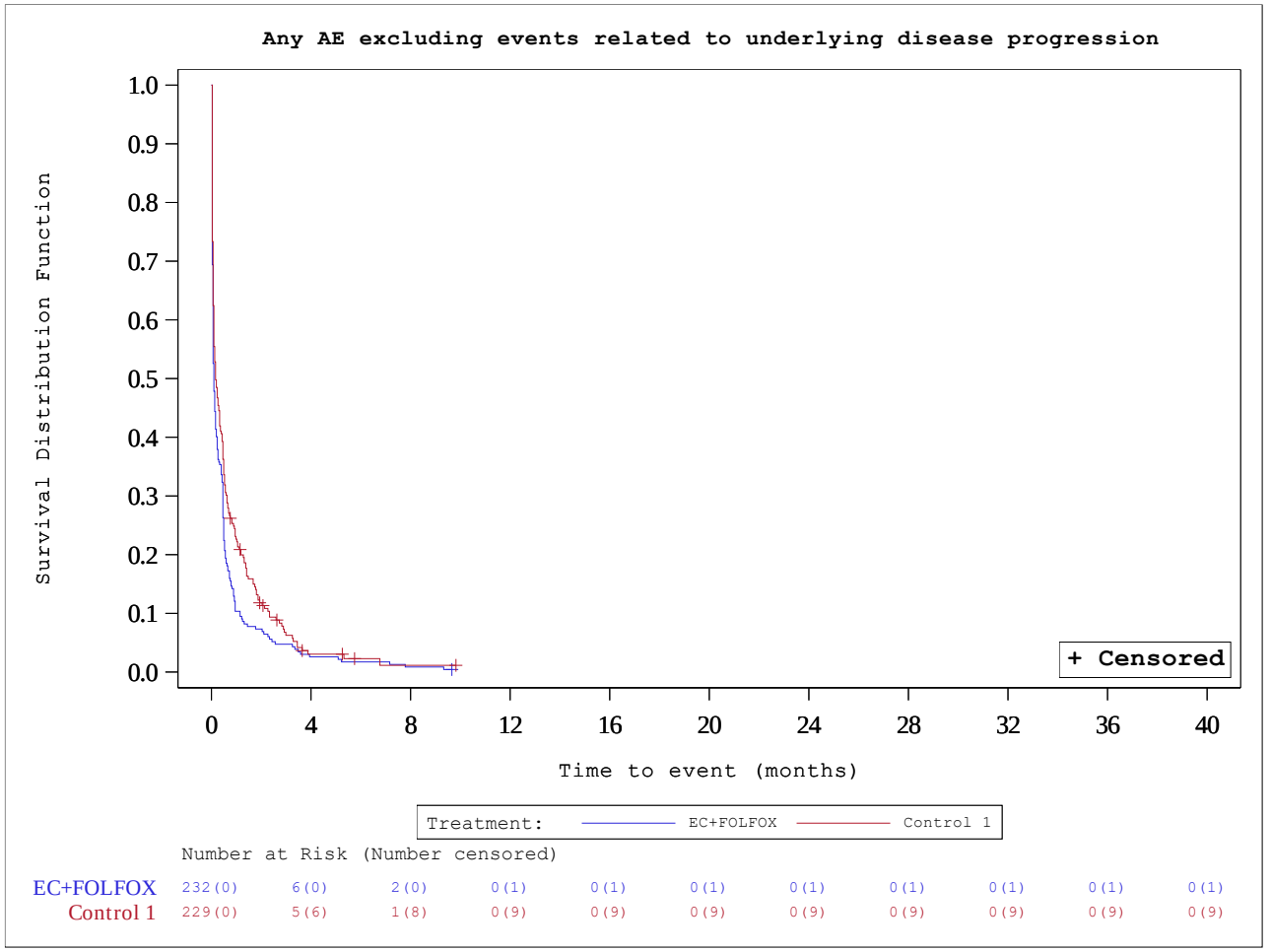
Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Any AE excluding events related to underlying disease progression - Subgroup analysis
Safety Analysis Set

Subgroup Level	EC+FOLFOX (N=232) n/ N (%)	EC+FOLFOX (N=232) Median (95% CI)[1]	Control 1 (N=229) n/ N (%)	Control 1 (N=229) Median (95% CI)[1]	Unstratified analysis Hazard Ratio (95% CI)[2]	Unstratified analysis p-Value[3]	Interaction p-Value[4]
Age (Years)							0.9600
< 65	147/ 148 (99.3)	0.1 (0.1, 0.1)	126/ 131 (96.2)	0.1 (0.1, 0.3)	1.26 (0.99, 1.60)	0.0615	
>= 65	84/ 84 (100.0)	0.1 (0.1, 0.4)	94/ 98 (95.9)	0.3 (0.1, 0.5)	1.27 (0.94, 1.70)	0.1195	
Sex							0.6453
Male	120/ 121 (99.2)	0.1 (0.1, 0.2)	106/ 112 (94.6)	0.3 (0.1, 0.5)	1.34 (1.03, 1.74)	0.0320	
Female	111/ 111 (100.0)	0.1 (0.1, 0.2)	114/ 117 (97.4)	0.1 (0.1, 0.3)	1.21 (0.93, 1.58)	0.1521	
Region							0.1676
Europe	107/ 108 (99.1)	0.2 (0.1, 0.5)	99/ 103 (96.1)	0.3 (0.1, 0.4)	1.12 (0.85, 1.48)	0.5025	
USA/Canada	15/ 15 (100.0)	0.1 (0.1, 0.2)	17/ 17 (100.0)	0.0 (0.0, 0.2)	0.89 (0.44, 1.82)	0.8739	
Rest of World	109/ 109 (100.0)	0.1 (0.1, 0.1)	104/ 109 (95.4)	0.2 (0.1, 0.5)	1.50 (1.14, 1.97)	0.0034	
ECOG-PS at Randomization							0.1209
0	130/ 130 (100.0)	0.1 (0.1, 0.2)	123/ 130 (94.6)	0.2 (0.1, 0.4)	1.43 (1.11, 1.84)	0.0055	
1	101/ 102 (99.0)	0.1 (0.1, 0.4)	97/ 99 (98.0)	0.2 (0.1, 0.4)	1.08 (0.82, 1.43)	0.6393	
Number of Organs Involved							0.3028
<= 2	116/ 116 (100.0)	0.1 (0.1, 0.2)	113/ 119 (95.0)	0.2 (0.1, 0.5)	1.40 (1.08, 1.83)	0.0115	
>= 3	115/ 116 (99.1)	0.1 (0.1, 0.2)	107/ 110 (97.3)	0.1 (0.1, 0.3)	1.14 (0.87, 1.48)	0.3526	
Presence of Liver Metastases							0.9197
Yes	145/ 146 (99.3)	0.1 (0.1, 0.2)	142/ 149 (95.3)	0.2 (0.1, 0.3)	1.26 (1.00, 1.60)	0.0493	
No	86/ 86 (100.0)	0.1 (0.1, 0.2)	78/ 80 (97.5)	0.2 (0.1, 0.5)	1.24 (0.91, 1.70)	0.1942	
Side of Tumor							0.6899
Left	88/ 88 (100.0)	0.1 (0.1, 0.2)	84/ 90 (93.3)	0.2 (0.1, 0.5)	1.33 (0.99, 1.80)	0.0604	
Right	143/ 144 (99.3)	0.1 (0.1, 0.2)	136/ 139 (97.8)	0.2 (0.1, 0.3)	1.22 (0.96, 1.55)	0.1112	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.
[4] P-Value for interaction from Cox proportional hazards model using ties=exact option with treatment, subgroup and treatment*subgroup interaction as covariates.
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Kaplan Meier Plot of Any AE excluding events related to underlying disease progression
Safety Analysis Set



Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
Kaplan-Meier Plots for subgroups only created if p-value for interaction < 0.05.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Serious AE
Safety Analysis Set

	EC+FOLFOX (N=232)	Control 1 (N=229)
Number of subjects with events, n (%)	107 (46.1)	89 (38.9)
Number of censored subjects, n (%)	125 (53.9)	140 (61.1)
Kaplan-Meier estimates of Time to Event (months) [1]		
25%-ile (95% CI)	3.1 (1.5, 5.0)	2.4 (1.7, 4.9)
Median (95% CI)	15.4 (10.7, NE)	13.2 (11.4, NE)
75%-ile (95% CI)	NE (NE, NE)	30.2 (30.2, NE)
Unstratified analysis		
Hazard Ratio (95% CI) [2]	0.95 (0.72, 1.27)	
p-value [3]	0.7391	

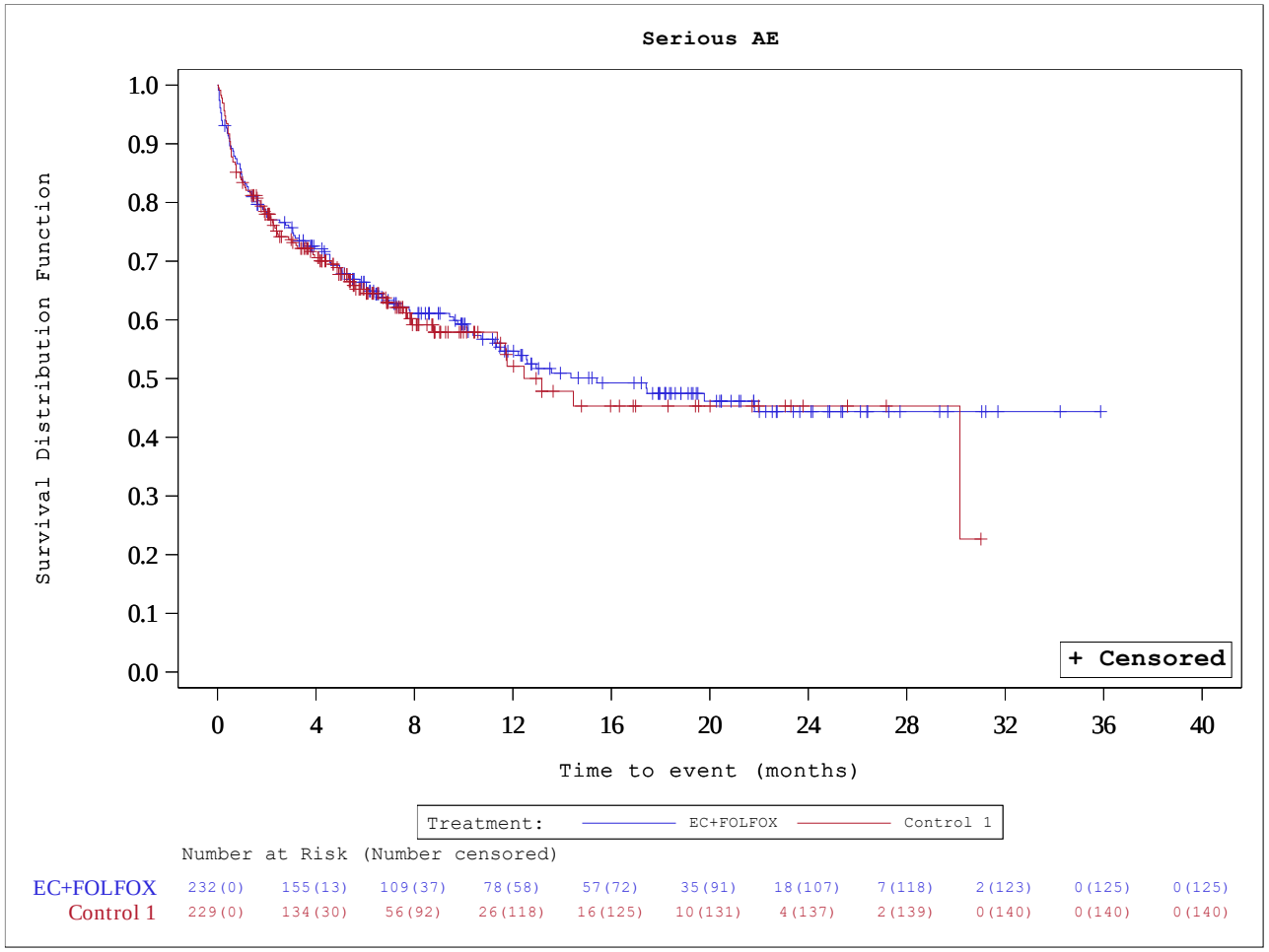
Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Serious AE - Subgroup analysis
Safety Analysis Set

Subgroup Level	EC+FOLFOX (N=232) n/ N (%)	EC+FOLFOX (N=232) Median (95% CI)[1]	Control 1 (N=229) n/ N (%)	Control 1 (N=229) Median (95% CI)[1]	Unstratified analysis Hazard Ratio (95% CI)[2]	Unstratified analysis p-Value[3]	Interaction p-Value[4]
Age (Years)							0.1816
< 65	59/ 148 (39.9)	NE (12.9, NE)	48/ 131 (36.6)	11.7 (7.7, NE)	0.84 (0.57, 1.23)	0.3646	
>= 65	48/ 84 (57.1)	10.1 (4.6, 17.4)	41/ 98 (41.8)	12.5 (8.8, 30.2)	1.20 (0.79, 1.83)	0.3927	
Sex							0.1574
Male	47/ 121 (38.8)	21.8 (13.6, NE)	43/ 112 (38.4)	11.7 (7.9, 30.2)	0.75 (0.49, 1.15)	0.1897	
Female	60/ 111 (54.1)	10.7 (6.0, 15.4)	46/ 117 (39.3)	13.2 (7.7, NE)	1.19 (0.80, 1.75)	0.3890	
Region							0.8711
Europe	50/ 108 (46.3)	17.4 (10.2, NE)	37/ 103 (35.9)	14.5 (11.7, NE)	1.03 (0.66, 1.58)	0.9112	
USA/Canada	7/ 15 (46.7)	15.4 (1.5, NE)	8/ 17 (47.1)	11.8 (1.0, NE)	0.85 (0.30, 2.39)	0.7591	
Rest of World	50/ 109 (45.9)	13.6 (7.0, NE)	44/ 109 (40.4)	12.5 (7.6, NE)	0.93 (0.62, 1.40)	0.7311	
ECOG-PS at Randomization							0.1690
0	50/ 130 (38.5)	NE (17.4, NE)	49/ 130 (37.7)	12.5 (8.8, NE)	0.77 (0.51, 1.15)	0.1984	
1	57/ 102 (55.9)	10.1 (5.0, 14.4)	40/ 99 (40.4)	14.5 (5.4, NE)	1.18 (0.78, 1.78)	0.4254	
Number of Organs Involved							0.1135
<= 2	44/ 116 (37.9)	NE (17.4, NE)	45/ 119 (37.8)	13.2 (8.8, NE)	0.72 (0.47, 1.11)	0.1338	
>= 3	63/ 116 (54.3)	10.1 (5.4, 13.6)	44/ 110 (40.0)	11.8 (7.6, NE)	1.20 (0.81, 1.76)	0.3661	
Presence of Liver Metastases							0.7058
Yes	71/ 146 (48.6)	12.6 (9.4, NE)	60/ 149 (40.3)	12.5 (7.7, 30.2)	1.00 (0.70, 1.41)	0.9885	
No	36/ 86 (41.9)	NE (11.2, NE)	29/ 80 (36.3)	13.2 (11.7, NE)	0.88 (0.54, 1.46)	0.6284	
Side of Tumor							0.5270
Left	37/ 88 (42.0)	19.8 (10.1, NE)	34/ 90 (37.8)	NE (7.6, NE)	0.82 (0.51, 1.33)	0.4252	
Right	70/ 144 (48.6)	12.9 (9.8, NE)	55/ 139 (39.6)	13.2 (11.4, NE)	1.03 (0.72, 1.48)	0.8566	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.
[4] P-Value for interaction from Cox proportional hazards model using ties=exact option with treatment, subgroup and treatment*subgroup interaction as covariates.
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Kaplan Meier Plot of Serious AE
Safety Analysis Set



Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
Kaplan-Meier Plots for subgroups only created if p-value for interaction < 0.05.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Serious AE excluding events related to underlying disease progression
Safety Analysis Set

	EC+FOLFOX (N=232)	Control 1 (N=229)
Number of subjects with events, n (%)	72 (31.0)	59 (25.8)
Number of censored subjects, n (%)	160 (69.0)	170 (74.2)
Kaplan-Meier estimates of Time to Event (months) [1]		
25%-ile (95% CI)	7.3 (5.0, 11.5)	6.7 (3.9, 14.5)
Median (95% CI)	NE (NE, NE)	30.2 (30.2, NE)
75%-ile (95% CI)	NE (NE, NE)	NE (30.2, NE)
Unstratified analysis		
Hazard Ratio (95% CI) [2]	0.94 (0.66, 1.34)	
p-value [3]	0.7386	

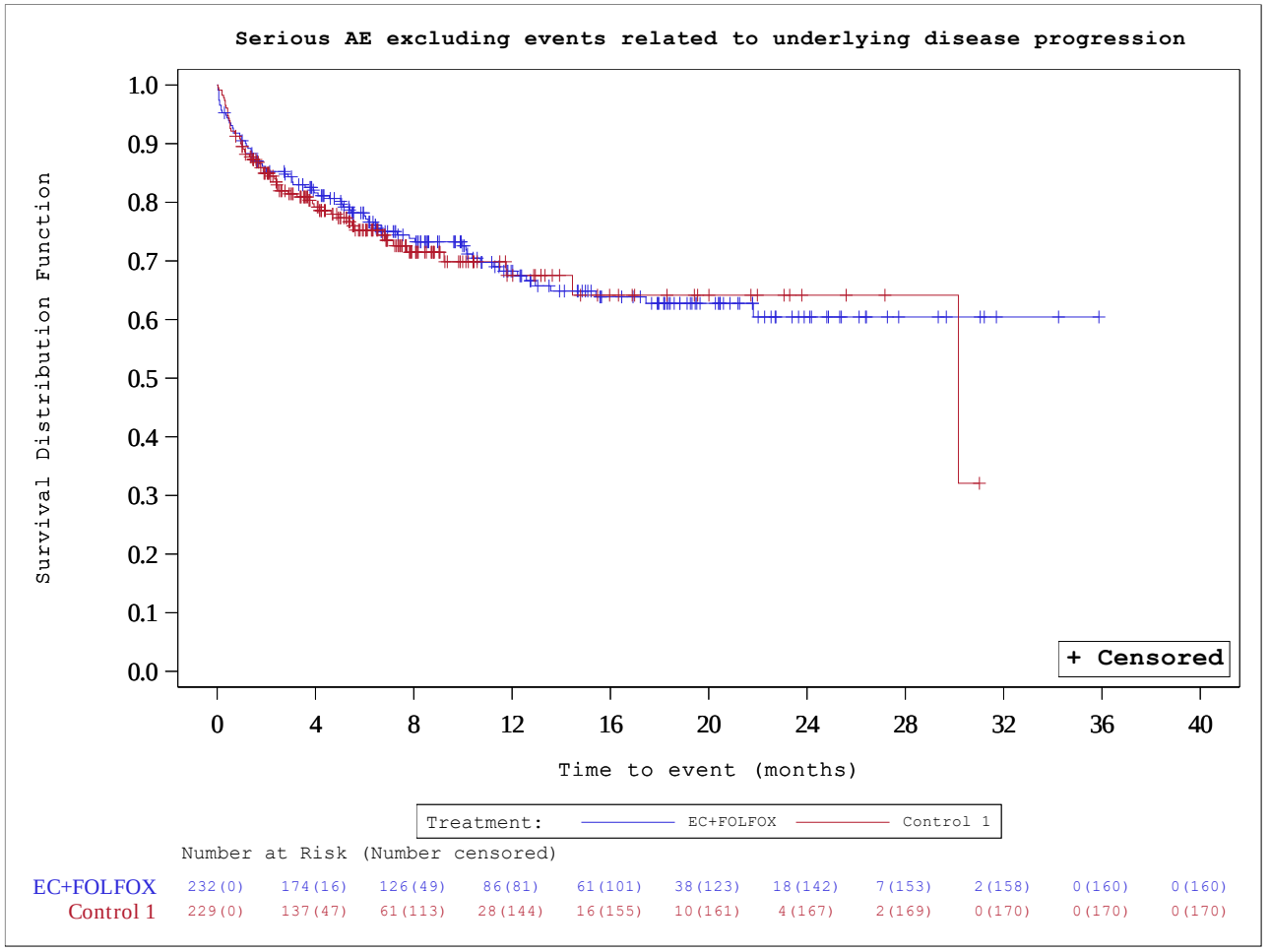
Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Serious AE excluding events related to underlying disease progression - Subgroup analysis
Safety Analysis Set

Subgroup Level	EC+FOLFOX (N=232) n/ N (%)	EC+FOLFOX (N=232) Median (95% CI)[1]	Control 1 (N=229) n/ N (%)	Control 1 (N=229) Median (95% CI)[1]	Unstratified analysis Hazard Ratio (95% CI)[2]	Unstratified analysis p-Value[3]	Interaction p-Value[4]
Age (Years)							0.6144
< 65	40/ 148 (27.0)	NE (NE , NE)	30/ 131 (22.9)	NE (NE , NE)	0.92 (0.57, 1.48)	0.7191	
>= 65	32/ 84 (38.1)	21.8 (10.7, NE)	29/ 98 (29.6)	30.2 (11.8, 30.2)	1.05 (0.63, 1.74)	0.8611	
Sex							0.9475
Male	32/ 121 (26.4)	NE (21.8, NE)	24/ 112 (21.4)	30.2 (14.5, 30.2)	0.95 (0.55, 1.63)	0.8520	
Female	40/ 111 (36.0)	NE (12.9, NE)	35/ 117 (29.9)	NE (11.8, NE)	0.95 (0.60, 1.51)	0.8319	
Region							0.8895
Europe	31/ 108 (28.7)	NE (21.8, NE)	23/ 103 (22.3)	NE (14.5, NE)	0.99 (0.57, 1.71)	0.9573	
USA/Canada	6/ 15 (40.0)	15.4 (5.5, NE)	7/ 17 (41.2)	11.8 (1.0, NE)	0.74 (0.24, 2.26)	0.5996	
Rest of World	35/ 109 (32.1)	NE (17.4, NE)	29/ 109 (26.6)	30.2 (30.2, NE)	0.99 (0.60, 1.63)	0.9642	
ECOG-PS at Randomization							0.8539
0	34/ 130 (26.2)	NE (NE , NE)	29/ 130 (22.3)	30.2 (30.2, NE)	0.90 (0.55, 1.49)	0.6878	
1	38/ 102 (37.3)	NE (12.2, NE)	30/ 99 (30.3)	NE (14.5, NE)	0.96 (0.59, 1.55)	0.8549	
Number of Organs Involved							0.1562
<= 2	27/ 116 (23.3)	NE (NE , NE)	29/ 119 (24.4)	30.2 (14.5, NE)	0.68 (0.40, 1.16)	0.1566	
>= 3	45/ 116 (38.8)	NE (11.2, NE)	30/ 110 (27.3)	NE (NE , NE)	1.20 (0.75, 1.92)	0.4382	
Presence of Liver Metastases							0.5585
Yes	50/ 146 (34.2)	NE (13.6, NE)	40/ 149 (26.8)	30.2 (NE , NE)	1.02 (0.67, 1.56)	0.9219	
No	22/ 86 (25.6)	NE (NE , NE)	19/ 80 (23.8)	NE (14.5, NE)	0.79 (0.42, 1.48)	0.4654	
Side of Tumor							0.8135
Left	27/ 88 (30.7)	NE (NE , NE)	21/ 90 (23.3)	NE (NE , NE)	0.97 (0.54, 1.74)	0.9238	
Right	45/ 144 (31.3)	NE (21.8, NE)	38/ 139 (27.3)	30.2 (14.5, NE)	0.93 (0.60, 1.44)	0.7459	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.
[4] P-Value for interaction from Cox proportional hazards model using ties=exact option with treatment, subgroup and treatment*subgroup interaction as covariates.
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Kaplan Meier Plot of Serious AE excluding events related to underlying disease progression
Safety Analysis Set



Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
Kaplan-Meier Plots for subgroups only created if p-value for interaction < 0.05.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Severe AE
Safety Analysis Set

	EC+FOLFOX (N=232)	Control 1 (N=229)
Number of subjects with events, n (%)	199 (85.8)	163 (71.2)
Number of censored subjects, n (%)	33 (14.2)	66 (28.8)
Kaplan-Meier estimates of Time to Event (months) [1]		
25%-ile (95% CI)	0.5 (0.5, 0.5)	0.8 (0.5, 1.0)
Median (95% CI)	1.5 (1.0, 1.9)	2.3 (1.7, 3.6)
75%-ile (95% CI)	5.1 (3.6, 6.7)	8.3 (6.0, 13.9)
Unstratified analysis		
Hazard Ratio (95% CI) [2]	1.31 (1.07, 1.61)	
p-value [3]	0.0113	

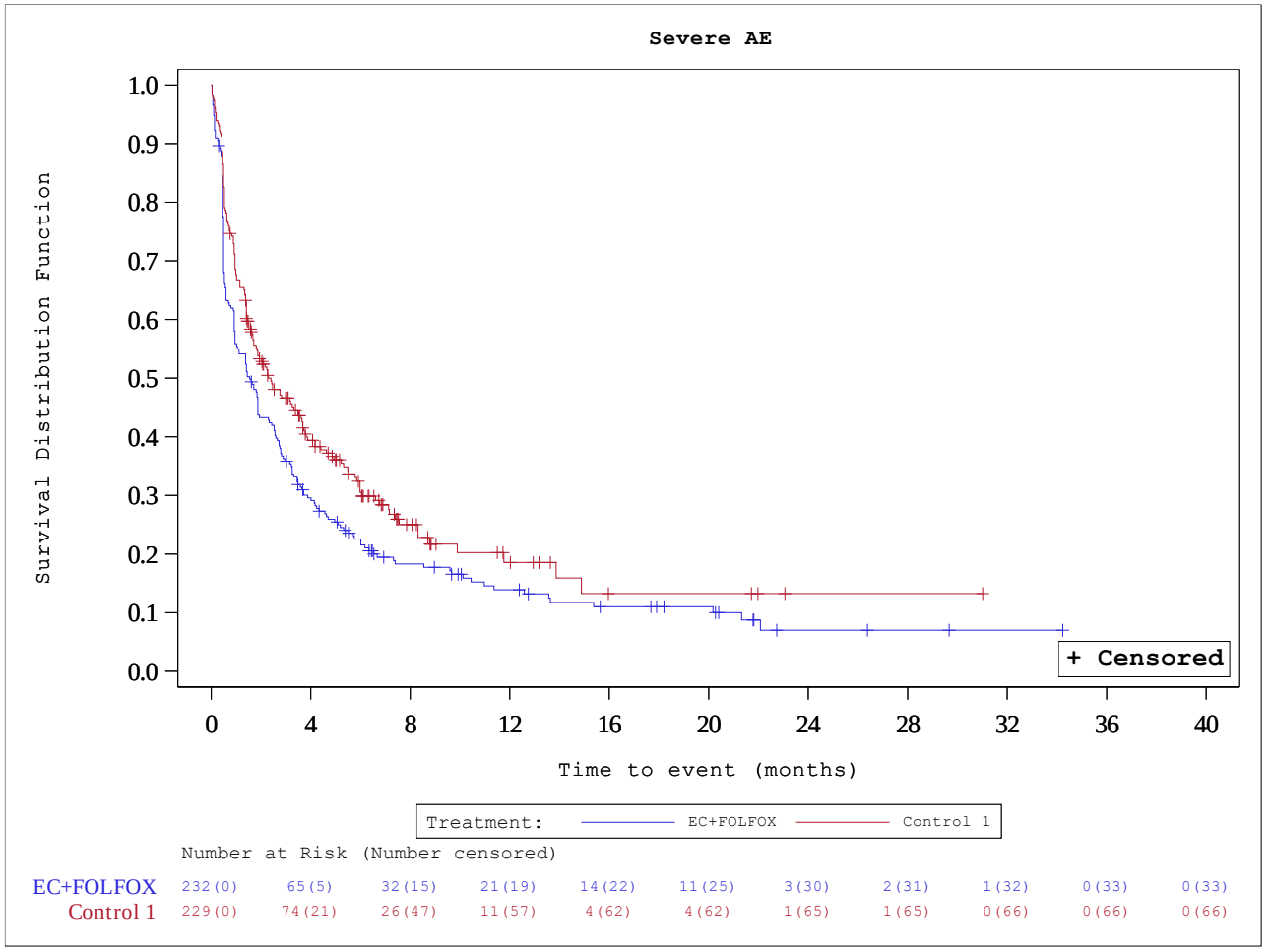
Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Severe AE - Subgroup analysis
Safety Analysis Set

Subgroup Level	EC+FOLFOX (N=232) n/ N (%)	EC+FOLFOX (N=232) Median (95% CI)[1]	Control 1 (N=229) n/ N (%)	Control 1 (N=229) Median (95% CI)[1]	Unstratified analysis Hazard Ratio (95% CI)[2]	Unstratified analysis p-Value[3]	Interaction p-Value[4]
Age (Years)							0.8481
< 65	124/ 148 (83.8)	1.8 (1.4, 2.7)	89/ 131 (67.9)	2.8 (1.9, 3.8)	1.31 (0.99, 1.72)	0.0577	
>= 65	75/ 84 (89.3)	1.0 (0.6, 1.9)	74/ 98 (75.5)	1.8 (1.4, 3.7)	1.37 (0.99, 1.89)	0.0629	
Sex							0.5855
Male	98/ 121 (81.0)	2.3 (1.7, 3.2)	76/ 112 (67.9)	3.7 (2.3, 5.2)	1.26 (0.93, 1.70)	0.1351	
Female	101/ 111 (91.0)	0.6 (0.5, 1.4)	87/ 117 (74.4)	1.5 (1.0, 2.4)	1.42 (1.07, 1.90)	0.0188	
Region							0.5399
Europe	90/ 108 (83.3)	1.9 (1.0, 2.8)	68/ 103 (66.0)	3.7 (1.9, 5.8)	1.50 (1.09, 2.05)	0.0130	
USA/Canada	14/ 15 (93.3)	0.5 (0.3, 0.9)	15/ 17 (88.2)	0.5 (0.3, 1.5)	1.14 (0.55, 2.38)	0.7718	
Rest of World	95/ 109 (87.2)	1.4 (1.0, 2.6)	80/ 109 (73.4)	2.2 (1.4, 3.6)	1.21 (0.90, 1.64)	0.2088	
ECOG-PS at Randomization							0.0758
0	108/ 130 (83.1)	2.6 (1.6, 3.4)	90/ 130 (69.2)	2.3 (1.5, 3.8)	1.13 (0.85, 1.49)	0.4071	
1	91/ 102 (89.2)	0.8 (0.5, 1.4)	73/ 99 (73.7)	2.4 (1.5, 3.6)	1.63 (1.20, 2.23)	0.0020	
Number of Organs Involved							0.6952
<= 2	103/ 116 (88.8)	1.8 (1.0, 2.7)	85/ 119 (71.4)	2.4 (1.5, 4.2)	1.37 (1.03, 1.83)	0.0329	
>= 3	96/ 116 (82.8)	1.4 (0.9, 2.3)	78/ 110 (70.9)	2.3 (1.4, 3.7)	1.25 (0.93, 1.69)	0.1531	
Presence of Liver Metastases							0.7378
Yes	125/ 146 (85.6)	1.4 (0.9, 1.9)	109/ 149 (73.2)	2.2 (1.6, 3.3)	1.36 (1.05, 1.76)	0.0213	
No	74/ 86 (86.0)	2.3 (1.0, 3.6)	54/ 80 (67.5)	2.8 (1.4, 5.5)	1.27 (0.89, 1.80)	0.1953	
Side of Tumor							0.5135
Left	76/ 88 (86.4)	2.6 (1.6, 3.3)	64/ 90 (71.1)	2.8 (1.4, 4.9)	1.19 (0.85, 1.66)	0.3233	
Right	123/ 144 (85.4)	1.0 (0.7, 1.8)	99/ 139 (71.2)	2.2 (1.5, 3.6)	1.39 (1.06, 1.81)	0.0164	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.
[4] P-Value for interaction from Cox proportional hazards model using ties=exact option with treatment, subgroup and treatment*subgroup interaction as covariates.
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Kaplan Meier Plot of Severe AE
Safety Analysis Set



Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
Kaplan-Meier Plots for subgroups only created if p-value for interaction < 0.05.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Severe AE excluding events related to underlying disease progression
Safety Analysis Set

	EC+FOLFOX (N=232)	Control 1 (N=229)
Number of subjects with events, n (%)	139 (59.9)	90 (39.3)
Number of censored subjects, n (%)	93 (40.1)	139 (60.7)
Kaplan-Meier estimates of Time to Event (months) [1]		
25%-ile (95% CI)	2.6 (1.7, 3.5)	2.2 (1.5, 3.6)
Median (95% CI)	6.2 (5.4, 10.1)	NE (6.8, NE)
75%-ile (95% CI)	28.8 (20.2, NE)	NE (NE, NE)
Unstratified analysis		
Hazard Ratio (95% CI) [2]	1.28 (0.98, 1.67)	
p-value [3]	0.0679	

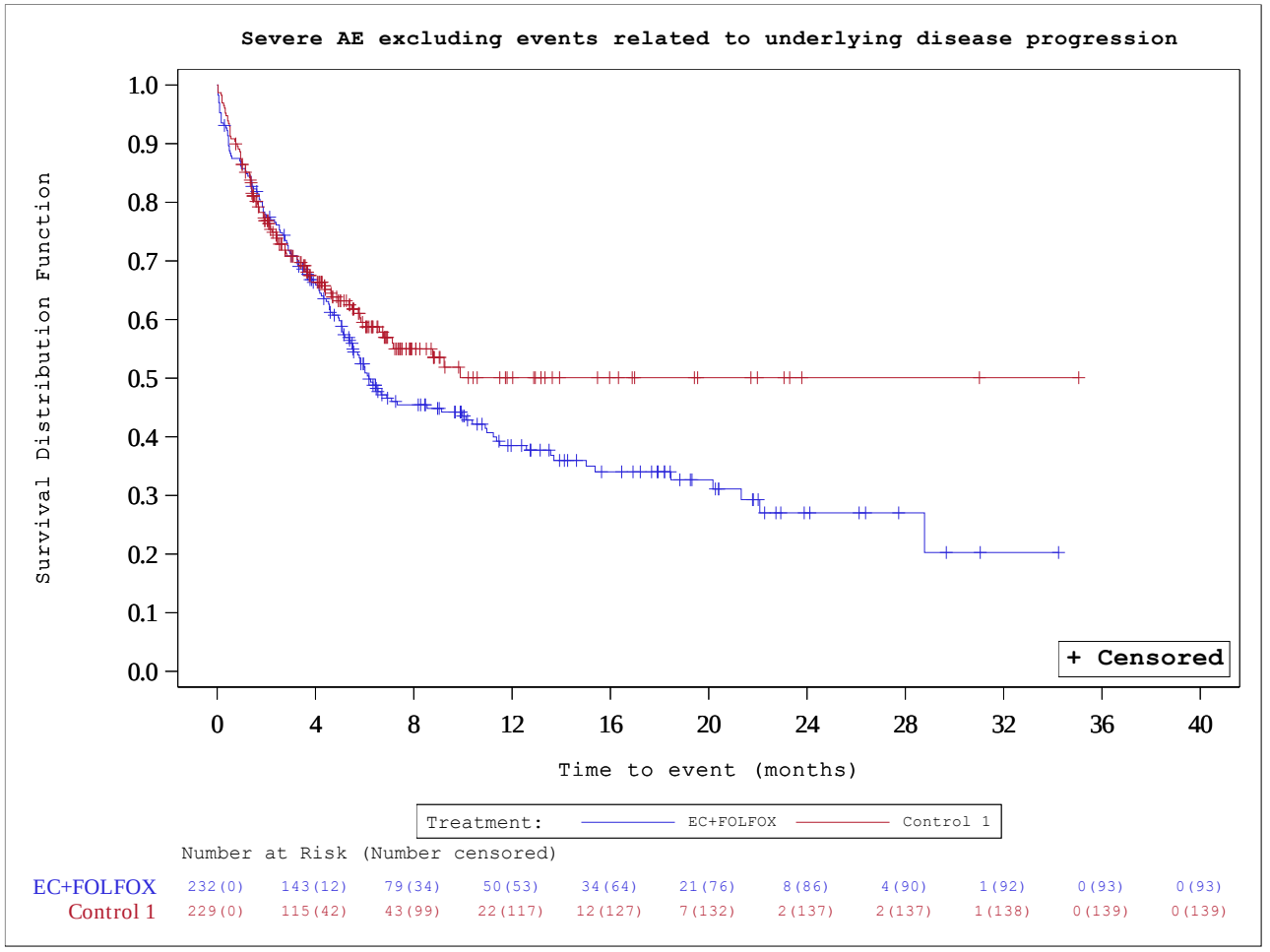
Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Severe AE excluding events related to underlying disease progression - Subgroup analysis
Safety Analysis Set

Subgroup Level	EC+FOLFOX (N=232) n/ N (%)	EC+FOLFOX (N=232) Median (95% CI)[1]	Control 1 (N=229) n/ N (%)	Control 1 (N=229) Median (95% CI)[1]	Unstratified analysis Hazard Ratio (95% CI)[2]	Unstratified analysis p-Value[3]	Interaction p-Value[4]
Age (Years)							0.7482
< 65	88/ 148 (59.5)	6.2 (5.2, 11.0)	51/ 131 (38.9)	9.9 (6.0, NE)	1.22 (0.86, 1.73)	0.2532	
>= 65	51/ 84 (60.7)	5.8 (4.7, 11.5)	39/ 98 (39.8)	NE (5.8, NE)	1.37 (0.90, 2.08)	0.1423	
Sex							0.0852
Male	64/ 121 (52.9)	7.3 (6.1, 21.3)	46/ 112 (41.1)	8.8 (5.5, NE)	1.00 (0.68, 1.47)	0.9951	
Female	75/ 111 (67.6)	5.1 (4.4, 9.1)	44/ 117 (37.6)	NE (6.0, NE)	1.64 (1.13, 2.39)	0.0086	
Region							0.2713
Europe	66/ 108 (61.1)	6.1 (4.7, 10.0)	40/ 103 (38.8)	9.9 (5.8, NE)	1.30 (0.87, 1.93)	0.1938	
USA/Canada	10/ 15 (66.7)	3.0 (1.9, NE)	12/ 17 (70.6)	1.3 (0.9, 2.8)	0.65 (0.28, 1.53)	0.3254	
Rest of World	63/ 109 (57.8)	6.9 (5.6, 15.4)	38/ 109 (34.9)	NE (7.1, NE)	1.38 (0.92, 2.07)	0.1190	
ECOG-PS at Randomization							0.7439
0	76/ 130 (58.5)	6.7 (5.2, 15.0)	47/ 130 (36.2)	NE (8.8, NE)	1.34 (0.93, 1.94)	0.1118	
1	63/ 102 (61.8)	6.0 (4.6, 10.0)	43/ 99 (43.4)	7.1 (4.9, NE)	1.21 (0.82, 1.79)	0.3280	
Number of Organs Involved							0.8977
<= 2	64/ 116 (55.2)	11.0 (5.6, 20.2)	43/ 119 (36.1)	NE (7.2, NE)	1.30 (0.88, 1.92)	0.1854	
>= 3	75/ 116 (64.7)	5.8 (4.6, 6.9)	47/ 110 (42.7)	6.8 (4.4, NE)	1.24 (0.86, 1.79)	0.2545	
Presence of Liver Metastases							0.5306
Yes	83/ 146 (56.8)	7.1 (5.4, 12.6)	58/ 149 (38.9)	NE (5.8, NE)	1.19 (0.85, 1.67)	0.3009	
No	56/ 86 (65.1)	5.5 (4.2, 7.3)	32/ 80 (40.0)	9.9 (5.8, NE)	1.46 (0.94, 2.26)	0.0892	
Side of Tumor							0.8859
Left	50/ 88 (56.8)	7.3 (5.4, 22.1)	32/ 90 (35.6)	9.9 (7.2, NE)	1.21 (0.77, 1.90)	0.4105	
Right	89/ 144 (61.8)	6.0 (5.0, 9.1)	58/ 139 (41.7)	NE (5.4, NE)	1.30 (0.93, 1.81)	0.1174	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.
[4] P-Value for interaction from Cox proportional hazards model using ties=exact option with treatment, subgroup and treatment*subgroup interaction as covariates.
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Kaplan Meier Plot of Severe AE excluding events related to underlying disease progression
Safety Analysis Set



Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
Kaplan-Meier Plots for subgroups only created if p-value for interaction < 0.05.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
AE leading to discontinuation of Encorafenib
Safety Analysis Set

	EC+FOLFOX (N=232)	Control 1 (N=229)
Number of subjects with events, n (%)	32 (13.8)	0 (0.0)
Number of censored subjects, n (%)	200 (86.2)	229 (100.0)
Kaplan-Meier estimates of Time to Event (months) [1]		
25%-ile (95% CI)	NE (30.8, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
Unstratified analysis		
Hazard Ratio (95% CI) [2]	NE	
p-value [3]		

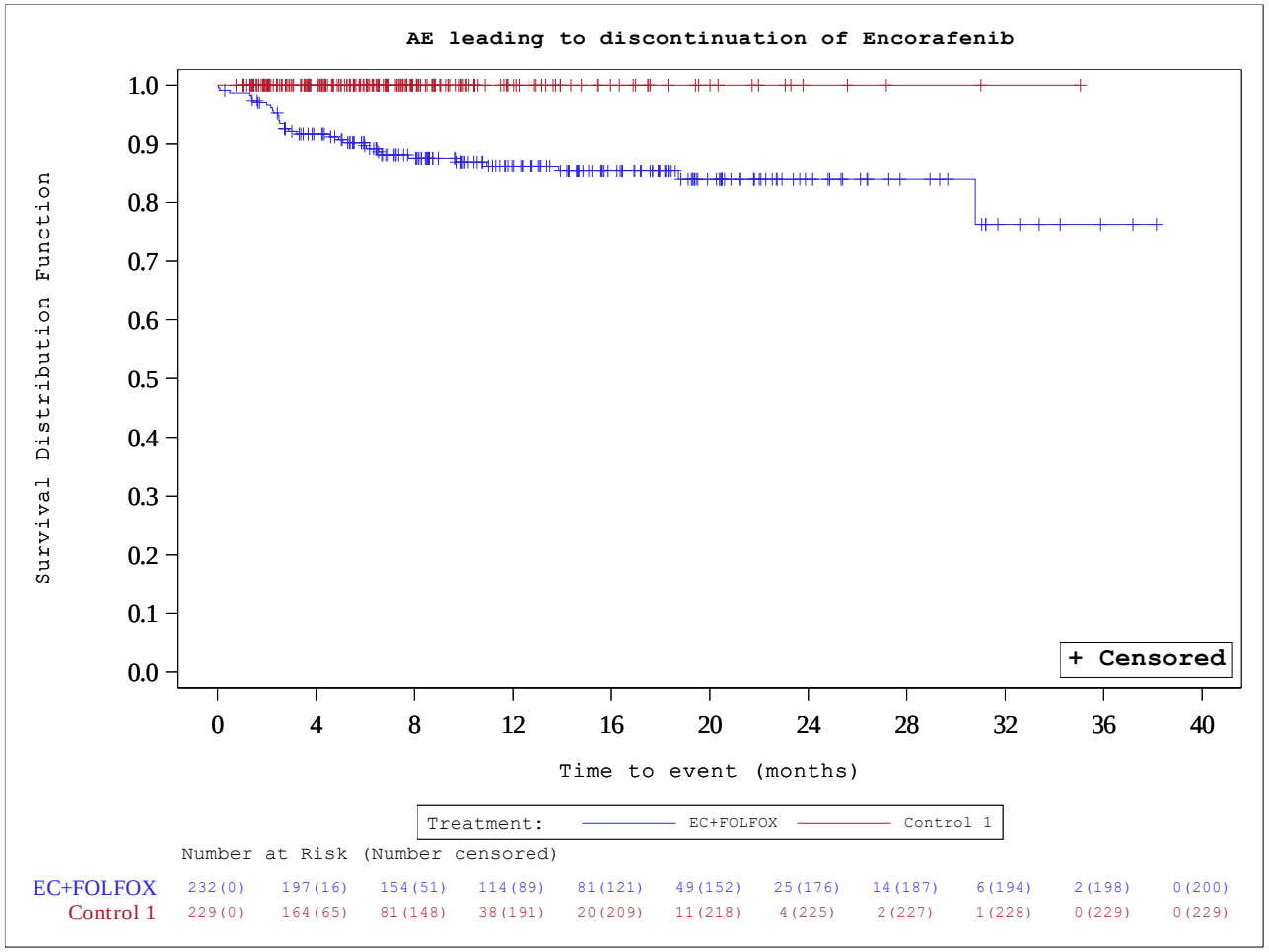
Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
AE leading to discontinuation of Encorafenib - Subgroup analysis
Safety Analysis Set

Subgroup Level	EC+FOLFOX (N=232) n/ N (%)	EC+FOLFOX (N=232) Median (95% CI)[1]	Control 1 (N=229) n/ N (%)	Control 1 (N=229) Median (95% CI)[1]	Unstratified analysis Hazard Ratio (95% CI)[2]	Unstratified analysis p-Value[3]	Interaction p-Value[4]
Age (Years)							0.9998
< 65	17/ 148 (11.5)	NE (NE , NE)	0/ 131 (0.0)	NE (NE , NE)	NE		
>= 65	15/ 84 (17.9)	NE (30.8, NE)	0/ 98 (0.0)	NE (NE , NE)	NE		
Sex							1.0000
Male	16/ 121 (13.2)	NE (NE , NE)	0/ 112 (0.0)	NE (NE , NE)	NE		
Female	16/ 111 (14.4)	NE (NE , NE)	0/ 117 (0.0)	NE (NE , NE)	NE		
Region							1.0000
Europe	12/ 108 (11.1)	NE (NE , NE)	0/ 103 (0.0)	NE (NE , NE)	NE		
USA/Canada	1/ 15 (6.7)	NE (NE , NE)	0/ 17 (0.0)	NE (NE , NE)	NE		
Rest of World	19/ 109 (17.4)	NE (NE , NE)	0/ 109 (0.0)	NE (NE , NE)	NE		
ECOG-PS at Randomization							0.9998
0	15/ 130 (11.5)	NE (NE , NE)	0/ 130 (0.0)	NE (NE , NE)	NE		
1	17/ 102 (16.7)	NE (NE , NE)	0/ 99 (0.0)	NE (NE , NE)	NE		
Number of Organs Involved							0.9998
<= 2	12/ 116 (10.3)	NE (NE , NE)	0/ 119 (0.0)	NE (NE , NE)	NE		
>= 3	20/ 116 (17.2)	NE (NE , NE)	0/ 110 (0.0)	NE (NE , NE)	NE		
Presence of Liver Metastases							0.9996
Yes	26/ 146 (17.8)	NE (NE , NE)	0/ 149 (0.0)	NE (NE , NE)	NE		
No	6/ 86 (7.0)	NE (30.8, NE)	0/ 80 (0.0)	NE (NE , NE)	NE		
Side of Tumor							0.9999
Left	14/ 88 (15.9)	NE (NE , NE)	0/ 90 (0.0)	NE (NE , NE)	NE		
Right	18/ 144 (12.5)	NE (30.8, NE)	0/ 139 (0.0)	NE (NE , NE)	NE		

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.
[4] P-Value for interaction from Cox proportional hazards model using ties=exact option with treatment, subgroup and treatment*subgroup interaction as covariates.
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Kaplan Meier Plot of AE leading to discontinuation of Encorafenib
Safety Analysis Set



Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
Kaplan-Meier Plots for subgroups only created if p-value for interaction < 0.05.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
AE leading to discontinuation of Encorafenib excluding events related to underlying disease progression
Safety Analysis Set

	EC+FOLFOX (N=232)	Control 1 (N=229)
Number of subjects with events, n (%)	18 (7.8)	0 (0.0)
Number of censored subjects, n (%)	214 (92.2)	229 (100.0)
Kaplan-Meier estimates of Time to Event (months) [1]		
25%-ile (95% CI)	NE (30.8, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
Unstratified analysis		
Hazard Ratio (95% CI) [2]	NE	
p-value [3]		

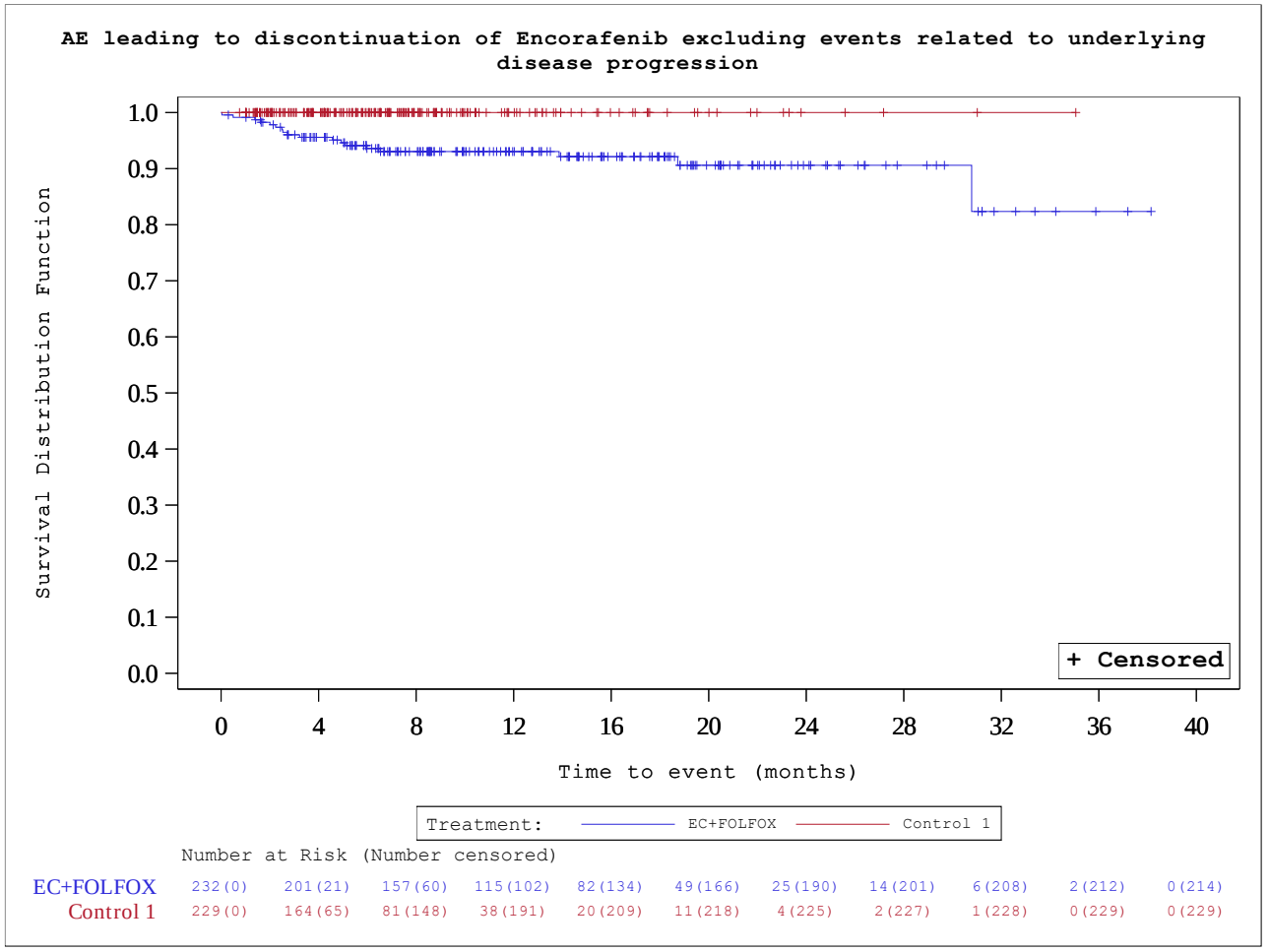
Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
AE leading to discontinuation of Encorafenib excluding events related to underlying disease progression - Subgroup analysis
Safety Analysis Set

Subgroup Level	EC+FOLFOX (N=232) n/ N (%)	EC+FOLFOX (N=232) Median (95% CI)[1]	Control 1 (N=229) n/ N (%)	Control 1 (N=229) Median (95% CI)[1]	Unstratified analysis Hazard Ratio (95% CI)[2]	Unstratified analysis p-Value[3]	Interaction p-Value[4]
Age (Years)							
< 65	9/ 148 (6.1)		0/ 131 (0.0)				
>= 65	9/ 84 (10.7)		0/ 98 (0.0)				
Sex							0.9998
Male	7/ 121 (5.8)	NE (NE , NE)	0/ 112 (0.0)	NE (NE , NE)	NE		
Female	11/ 111 (9.9)	NE (NE , NE)	0/ 117 (0.0)	NE (NE , NE)	NE		
Region							
Europe	8/ 108 (7.4)		0/ 103 (0.0)				
USA/Canada	1/ 15 (6.7)		0/ 17 (0.0)				
Rest of World	9/ 109 (8.3)		0/ 109 (0.0)				
ECOG-PS at Randomization							0.9998
0	8/ 130 (6.2)	NE (NE , NE)	0/ 130 (0.0)	NE (NE , NE)	NE		
1	10/ 102 (9.8)	NE (NE , NE)	0/ 99 (0.0)	NE (NE , NE)	NE		
Number of Organs Involved							0.9999
<= 2	8/ 116 (6.9)	NE (NE , NE)	0/ 119 (0.0)	NE (NE , NE)	NE		
>= 3	10/ 116 (8.6)	NE (NE , NE)	0/ 110 (0.0)	NE (NE , NE)	NE		
Presence of Liver Metastases							0.9998
Yes	14/ 146 (9.6)	NE (NE , NE)	0/ 149 (0.0)	NE (NE , NE)	NE		
No	4/ 86 (4.7)	NE (30.8, NE)	0/ 80 (0.0)	NE (NE , NE)	NE		
Side of Tumor							0.9999
Left	6/ 88 (6.8)	NE (NE , NE)	0/ 90 (0.0)	NE (NE , NE)	NE		
Right	12/ 144 (8.3)	NE (30.8, NE)	0/ 139 (0.0)	NE (NE , NE)	NE		

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.
[4] P-Value for interaction from Cox proportional hazards model using ties=exact option with treatment, subgroup and treatment*subgroup interaction as covariates.
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Kaplan Meier Plot of AE leading to discontinuation of Encorafenib excluding events related to underlying disease progression
Safety Analysis Set



Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
Kaplan-Meier Plots for subgroups only created if p-value for interaction < 0.05.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
AE leading to discontinuation of Cetuximab
Safety Analysis Set

	EC+FOLFOX (N=232)	Control 1 (N=229)
Number of subjects with events, n (%)	34 (14.7)	0 (0.0)
Number of censored subjects, n (%)	198 (85.3)	229 (100.0)
Kaplan-Meier estimates of Time to Event (months) [1]		
25%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
Unstratified analysis		
Hazard Ratio (95% CI) [2]	NE	
p-value [3]		

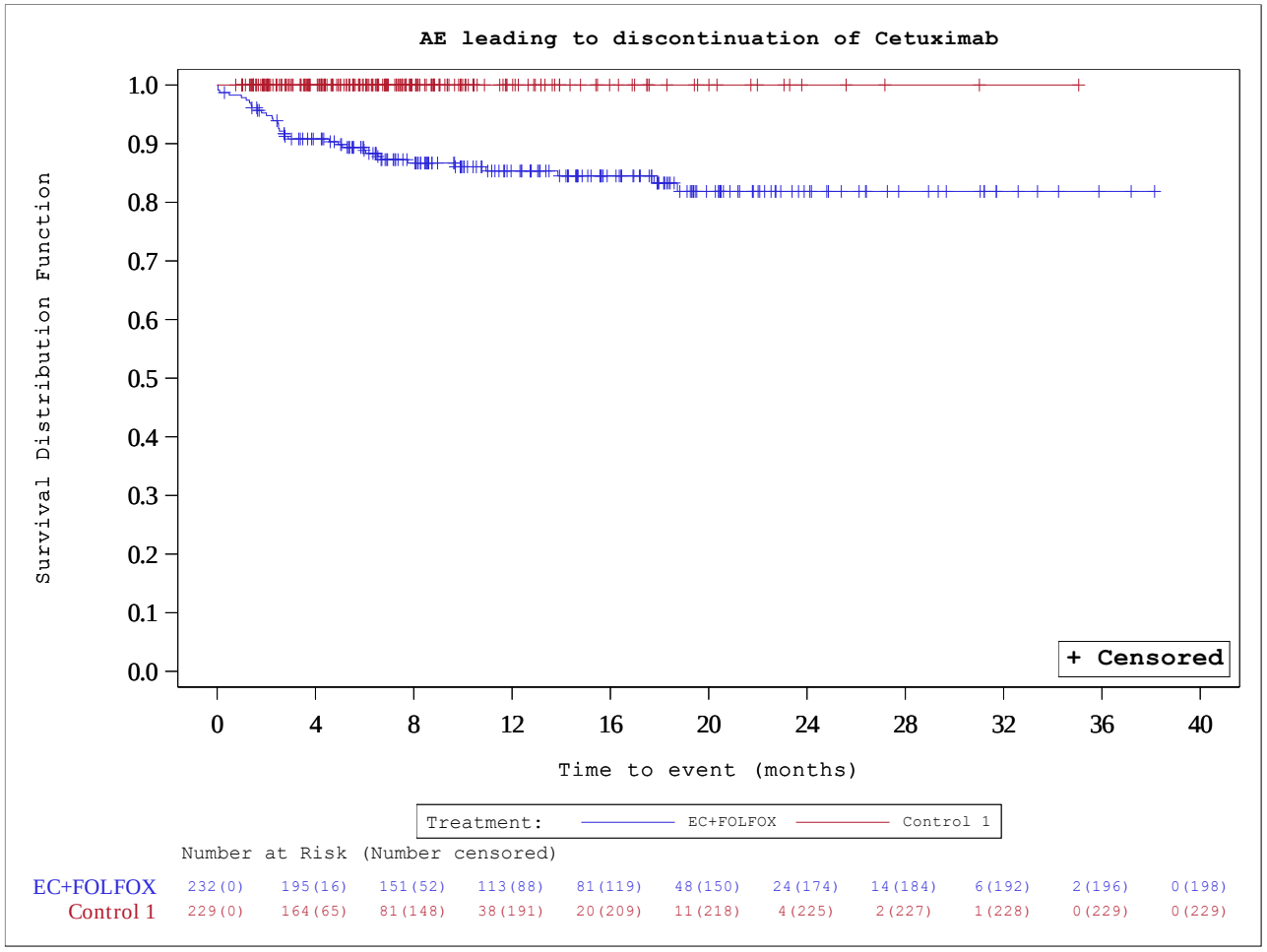
Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
AE leading to discontinuation of Cetuximab - Subgroup analysis
Safety Analysis Set

Subgroup Level	EC+FOLFOX (N=232) n/ N (%)	EC+FOLFOX (N=232) Median (95% CI)[1]	Control 1 (N=229) n/ N (%)	Control 1 (N=229) Median (95% CI)[1]	Unstratified analysis Hazard Ratio (95% CI)[2]	Unstratified analysis p-Value[3]	Interaction p-Value[4]
Age (Years)							0.9999
< 65	19/ 148 (12.8)	NE (NE , NE)	0/ 131 (0.0)	NE (NE , NE)	NE		
>= 65	15/ 84 (17.9)	NE (NE , NE)	0/ 98 (0.0)	NE (NE , NE)	NE		
Sex							0.9999
Male	16/ 121 (13.2)	NE (NE , NE)	0/ 112 (0.0)	NE (NE , NE)	NE		
Female	18/ 111 (16.2)	NE (NE , NE)	0/ 117 (0.0)	NE (NE , NE)	NE		
Region							1.0000
Europe	12/ 108 (11.1)	NE (NE , NE)	0/ 103 (0.0)	NE (NE , NE)	NE		
USA/Canada	1/ 15 (6.7)	NE (NE , NE)	0/ 17 (0.0)	NE (NE , NE)	NE		
Rest of World	21/ 109 (19.3)	NE (NE , NE)	0/ 109 (0.0)	NE (NE , NE)	NE		
ECOG-PS at Randomization							0.9997
0	14/ 130 (10.8)	NE (NE , NE)	0/ 130 (0.0)	NE (NE , NE)	NE		
1	20/ 102 (19.6)	NE (NE , NE)	0/ 99 (0.0)	NE (NE , NE)	NE		
Number of Organs Involved							0.9997
<= 2	12/ 116 (10.3)	NE (NE , NE)	0/ 119 (0.0)	NE (NE , NE)	NE		
>= 3	22/ 116 (19.0)	NE (NE , NE)	0/ 110 (0.0)	NE (NE , NE)	NE		
Presence of Liver Metastases							0.9996
Yes	28/ 146 (19.2)	NE (NE , NE)	0/ 149 (0.0)	NE (NE , NE)	NE		
No	6/ 86 (7.0)	NE (NE , NE)	0/ 80 (0.0)	NE (NE , NE)	NE		
Side of Tumor							1.0000
Left	14/ 88 (15.9)	NE (NE , NE)	0/ 90 (0.0)	NE (NE , NE)	NE		
Right	20/ 144 (13.9)	NE (NE , NE)	0/ 139 (0.0)	NE (NE , NE)	NE		

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.
[4] P-Value for interaction from Cox proportional hazards model using ties=exact option with treatment, subgroup and treatment*subgroup interaction as covariates.
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Kaplan Meier Plot of AE leading to discontinuation of Cetuximab
Safety Analysis Set



Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
Kaplan-Meier Plots for subgroups only created if p-value for interaction < 0.05.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
AE leading to discontinuation of Cetuximab excluding events related to underlying disease progression
Safety Analysis Set

	EC+FOLFOX (N=232)	Control 1 (N=229)
Number of subjects with events, n (%)	21 (9.1)	0 (0.0)
Number of censored subjects, n (%)	211 (90.9)	229 (100.0)
Kaplan-Meier estimates of Time to Event (months) [1]		
25%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
Unstratified analysis		
Hazard Ratio (95% CI) [2]	NE	
p-value [3]		

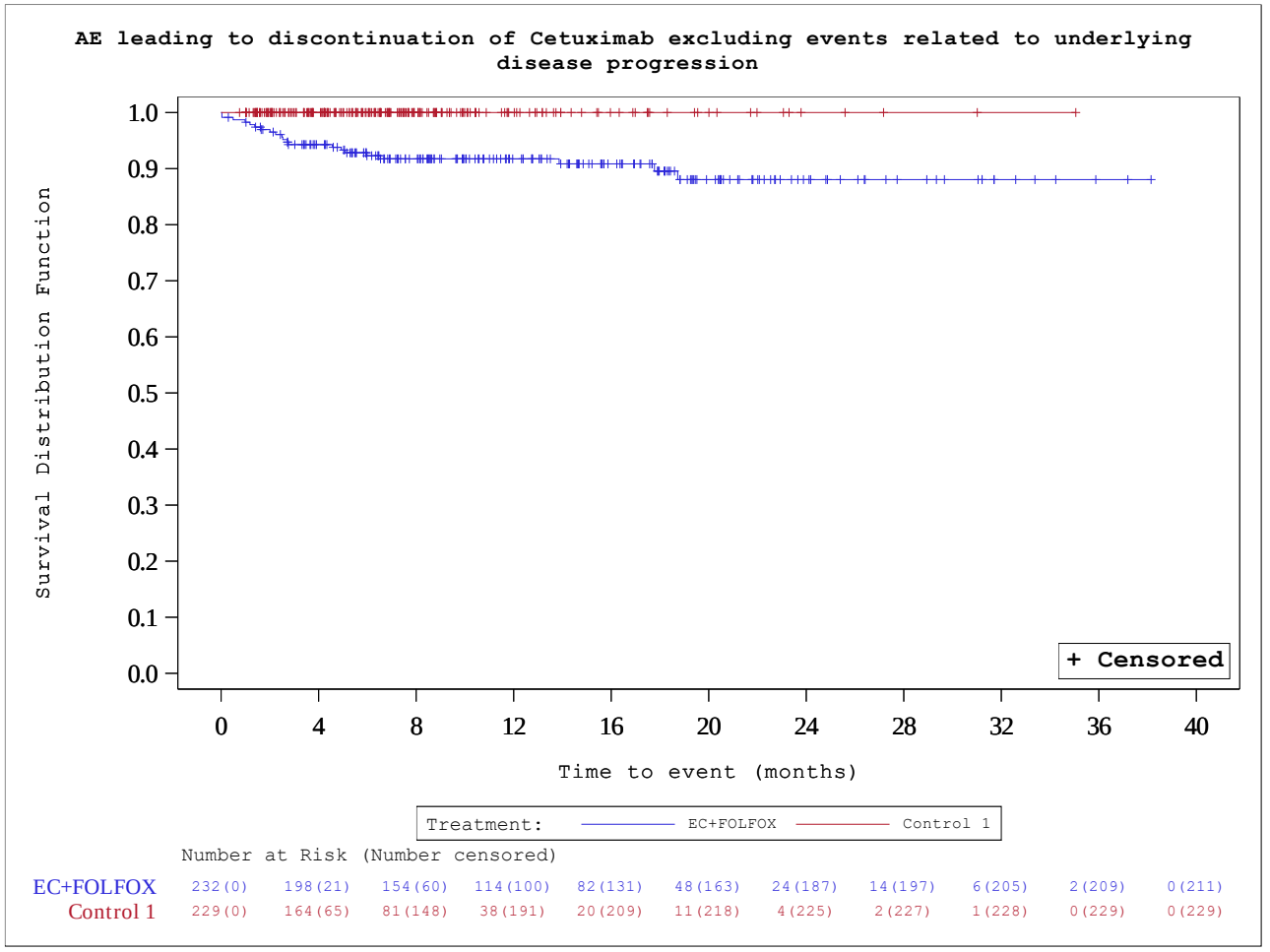
Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
AE leading to discontinuation of Cetuximab excluding events related to underlying disease progression - Subgroup analysis
Safety Analysis Set

Subgroup Level	EC+FOLFOX (N=232) n/ N (%)	EC+FOLFOX (N=232) Median (95% CI)[1]	Control 1 (N=229) n/ N (%)	Control 1 (N=229) Median (95% CI)[1]	Unstratified analysis Hazard Ratio (95% CI)[2]	Unstratified analysis p-Value[3]	Interaction p-Value[4]
Age (Years)							0.9998
< 65	11/ 148 (7.4)	NE (NE , NE)	0/ 131 (0.0)	NE (NE , NE)	NE		
>= 65	10/ 84 (11.9)	NE (NE , NE)	0/ 98 (0.0)	NE (NE , NE)	NE		
Sex							0.9998
Male	8/ 121 (6.6)	NE (NE , NE)	0/ 112 (0.0)	NE (NE , NE)	NE		
Female	13/ 111 (11.7)	NE (NE , NE)	0/ 117 (0.0)	NE (NE , NE)	NE		
Region							1.0000
Europe	8/ 108 (7.4)	NE (NE , NE)	0/ 103 (0.0)	NE (NE , NE)	NE		
USA/Canada	1/ 15 (6.7)	NE (NE , NE)	0/ 17 (0.0)	NE (NE , NE)	NE		
Rest of World	12/ 109 (11.0)	NE (NE , NE)	0/ 109 (0.0)	NE (NE , NE)	NE		
ECOG-PS at Randomization							0.9998
0	8/ 130 (6.2)	NE (NE , NE)	0/ 130 (0.0)	NE (NE , NE)	NE		
1	13/ 102 (12.7)	NE (NE , NE)	0/ 99 (0.0)	NE (NE , NE)	NE		
Number of Organs Involved							0.9998
<= 2	8/ 116 (6.9)	NE (NE , NE)	0/ 119 (0.0)	NE (NE , NE)	NE		
>= 3	13/ 116 (11.2)	NE (NE , NE)	0/ 110 (0.0)	NE (NE , NE)	NE		
Presence of Liver Metastases							0.9997
Yes	17/ 146 (11.6)	NE (NE , NE)	0/ 149 (0.0)	NE (NE , NE)	NE		
No	4/ 86 (4.7)	NE (NE , NE)	0/ 80 (0.0)	NE (NE , NE)	NE		
Side of Tumor							0.9999
Left	6/ 88 (6.8)	NE (NE , NE)	0/ 90 (0.0)	NE (NE , NE)	NE		
Right	15/ 144 (10.4)	NE (NE , NE)	0/ 139 (0.0)	NE (NE , NE)	NE		

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.
[4] P-Value for interaction from Cox proportional hazards model using ties=exact option with treatment, subgroup and treatment*subgroup interaction as covariates.
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Kaplan Meier Plot of AE leading to discontinuation of Cetuximab excluding events related to underlying disease progression
Safety Analysis Set



Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
Kaplan-Meier Plots for subgroups only created if p-value for interaction < 0.05.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
AE leading to discontinuation of other study intervention
Safety Analysis Set

	EC+FOLFOX (N=232)	Control 1 (N=229)
Number of subjects with events, n (%)	48 (20.7)	40 (17.5)
Number of censored subjects, n (%)	184 (79.3)	189 (82.5)
Kaplan-Meier estimates of Time to Event (months) [1]		
25%-ile (95% CI)	20.6 (10.9, NE)	11.4 (9.2, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
Unstratified analysis		
Hazard Ratio (95% CI) [2]	0.87 (0.57, 1.33)	
p-value [3]	0.5180	

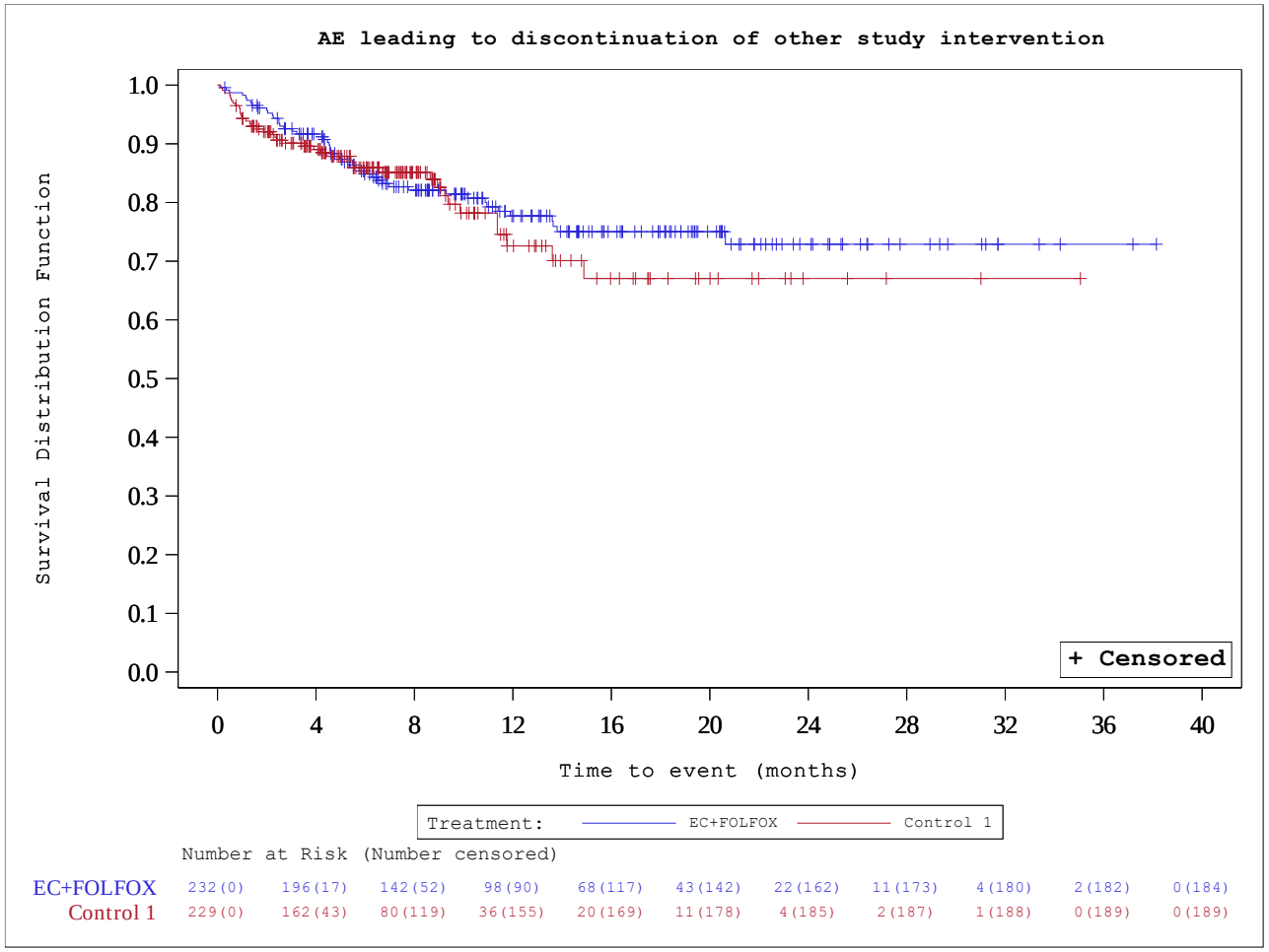
Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
AE leading to discontinuation of other study intervention - Subgroup analysis
Safety Analysis Set

Subgroup Level	EC+FOLFOX (N=232) n/ N (%)	EC+FOLFOX (N=232) Median (95% CI)[1]	Control 1 (N=229) n/ N (%)	Control 1 (N=229) Median (95% CI)[1]	Unstratified analysis Hazard Ratio (95% CI)[2]	Unstratified analysis p-Value[3]	Interaction p-Value[4]
Age (Years)							0.7579
< 65	28/ 148 (18.9)	NE (NE , NE)	19/ 131 (14.5)	NE (NE , NE)	0.96 (0.53, 1.73)	0.8893	
>= 65	20/ 84 (23.8)	NE (NE , NE)	21/ 98 (21.4)	NE (13.6, NE)	0.81 (0.43, 1.50)	0.4952	
Sex							0.7824
Male	24/ 121 (19.8)	NE (NE , NE)	20/ 112 (17.9)	NE (14.9, NE)	0.80 (0.44, 1.46)	0.4627	
Female	24/ 111 (21.6)	NE (NE , NE)	20/ 117 (17.1)	NE (NE , NE)	0.94 (0.51, 1.71)	0.8313	
Region							0.2182
Europe	19/ 108 (17.6)	NE (NE , NE)	20/ 103 (19.4)	NE (NE , NE)	0.60 (0.32, 1.15)	0.1187	
USA/Canada	3/ 15 (20.0)	NE (NE , NE)	4/ 17 (23.5)	NE (9.4, NE)	0.75 (0.17, 3.35)	0.7037	
Rest of World	26/ 109 (23.9)	NE (NE , NE)	16/ 109 (14.7)	NE (14.9, NE)	1.30 (0.69, 2.43)	0.4127	
ECOG-PS at Randomization							0.1677
0	28/ 130 (21.5)	NE (NE , NE)	18/ 130 (13.8)	NE (NE , NE)	1.10 (0.60, 2.00)	0.7598	
1	20/ 102 (19.6)	NE (NE , NE)	22/ 99 (22.2)	NE (NE , NE)	0.67 (0.37, 1.25)	0.2061	
Number of Organs Involved							0.1146
<= 2	29/ 116 (25.0)	NE (NE , NE)	18/ 119 (15.1)	NE (NE , NE)	1.20 (0.66, 2.19)	0.5430	
>= 3	19/ 116 (16.4)	NE (NE , NE)	22/ 110 (20.0)	NE (14.9, NE)	0.61 (0.33, 1.14)	0.1217	
Presence of Liver Metastases							0.1807
Yes	29/ 146 (19.9)	NE (NE , NE)	30/ 149 (20.1)	NE (14.9, NE)	0.72 (0.43, 1.21)	0.2206	
No	19/ 86 (22.1)	NE (NE , NE)	10/ 80 (12.5)	NE (NE , NE)	1.31 (0.60, 2.85)	0.4980	
Side of Tumor							0.8181
Left	18/ 88 (20.5)	NE (NE , NE)	14/ 90 (15.6)	NE (14.9, NE)	0.93 (0.46, 1.90)	0.8459	
Right	30/ 144 (20.8)	NE (NE , NE)	26/ 139 (18.7)	NE (NE , NE)	0.84 (0.49, 1.43)	0.5207	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.
[4] P-Value for interaction from Cox proportional hazards model using ties=exact option with treatment, subgroup and treatment*subgroup interaction as covariates.
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Kaplan Meier Plot of AE leading to discontinuation of other study intervention
Safety Analysis Set



Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
Kaplan-Meier Plots for subgroups only created if p-value for interaction < 0.05.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
AE leading to discontinuation of other study intervention excluding events related to underlying disease progression
Safety Analysis Set

	EC+FOLFOX (N=232)	Control 1 (N=229)
Number of subjects with events, n (%)	30 (12.9)	22 (9.6)
Number of censored subjects, n (%)	202 (87.1)	207 (90.4)
Kaplan-Meier estimates of Time to Event (months) [1]		
25%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
Unstratified analysis		
Hazard Ratio (95% CI) [2]	0.99 (0.57, 1.73)	
p-value [3]	0.9791	

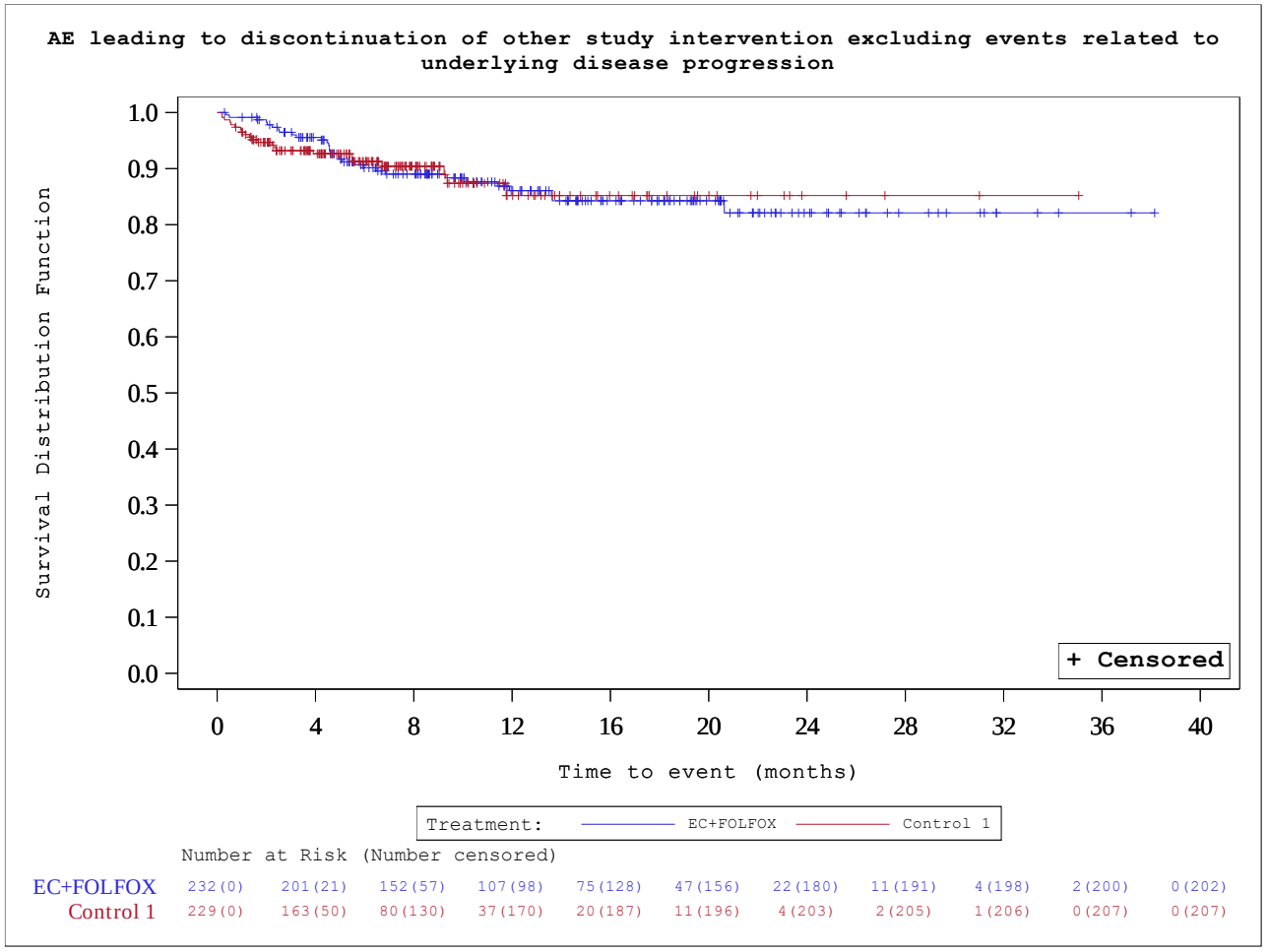
Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
AE leading to discontinuation of other study intervention excluding events related to underlying disease progression - Subgroup analysis
Safety Analysis Set

Subgroup Level	EC+FOLFOX (N=232) n/ N (%)	EC+FOLFOX (N=232) Median (95% CI)[1]	Control 1 (N=229) n/ N (%)	Control 1 (N=229) Median (95% CI)[1]	Unstratified analysis Hazard Ratio (95% CI)[2]	Unstratified analysis p-Value[3]	Interaction p-Value[4]
Age (Years)							0.0856
< 65	19/ 148 (12.8)	NE (NE , NE)	7/ 131 (5.3)	NE (NE , NE)	1.81 (0.76, 4.35)	0.1752	
>= 65	11/ 84 (13.1)	NE (NE , NE)	15/ 98 (15.3)	NE (NE , NE)	0.61 (0.28, 1.34)	0.2140	
Sex							0.3322
Male	17/ 121 (14.0)	NE (NE , NE)	9/ 112 (8.0)	NE (NE , NE)	1.27 (0.56, 2.88)	0.5690	
Female	13/ 111 (11.7)	NE (NE , NE)	13/ 117 (11.1)	NE (NE , NE)	0.79 (0.36, 1.71)	0.5412	
Region							0.0967
Europe	13/ 108 (12.0)	NE (NE , NE)	13/ 103 (12.6)	NE (NE , NE)	0.68 (0.31, 1.48)	0.3265	
USA/Canada	2/ 15 (13.3)	NE (NE , NE)	4/ 17 (23.5)	NE (9.4, NE)	0.49 (0.09, 2.66)	0.3951	
Rest of World	15/ 109 (13.8)	NE (NE , NE)	5/ 109 (4.6)	NE (NE , NE)	2.32 (0.84, 6.44)	0.0954	
ECOG-PS at Randomization							0.4095
0	17/ 130 (13.1)	NE (NE , NE)	10/ 130 (7.7)	NE (NE , NE)	1.15 (0.52, 2.54)	0.7311	
1	13/ 102 (12.7)	NE (NE , NE)	12/ 99 (12.1)	NE (NE , NE)	0.86 (0.39, 1.90)	0.7131	
Number of Organs Involved							0.1864
<= 2	20/ 116 (17.2)	NE (NE , NE)	11/ 119 (9.2)	NE (NE , NE)	1.31 (0.62, 2.77)	0.4774	
>= 3	10/ 116 (8.6)	NE (NE , NE)	11/ 110 (10.0)	NE (NE , NE)	0.69 (0.29, 1.64)	0.4002	
Presence of Liver Metastases							0.2619
Yes	17/ 146 (11.6)	NE (NE , NE)	16/ 149 (10.7)	NE (NE , NE)	0.84 (0.42, 1.68)	0.6286	
No	13/ 86 (15.1)	NE (NE , NE)	6/ 80 (7.5)	NE (NE , NE)	1.38 (0.52, 3.71)	0.5183	
Side of Tumor							0.3077
Left	12/ 88 (13.6)	NE (NE , NE)	6/ 90 (6.7)	NE (NE , NE)	1.46 (0.54, 3.96)	0.4543	
Right	18/ 144 (12.5)	NE (NE , NE)	16/ 139 (11.5)	NE (NE , NE)	0.82 (0.42, 1.62)	0.5736	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.
[4] P-Value for interaction from Cox proportional hazards model using ties=exact option with treatment, subgroup and treatment*subgroup interaction as covariates.
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Kaplan Meier Plot of AE leading to discontinuation of other study intervention excluding events related to underlying disease progression
Safety Analysis Set



Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
Kaplan-Meier Plots for subgroups only created if p-value for interaction < 0.05.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
AE leading to discontinuation of Encorafenib or Cetuximab
Safety Analysis Set

	EC+FOLFOX (N=232)	Control 1 (N=229)
Number of subjects with events, n (%)	36 (15.5)	0 (0.0)
Number of censored subjects, n (%)	196 (84.5)	229 (100.0)
Kaplan-Meier estimates of Time to Event (months) [1]		
25%-ile (95% CI)	30.8 (30.8, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
Unstratified analysis		
Hazard Ratio (95% CI) [2]	NE	
p-value [3]		

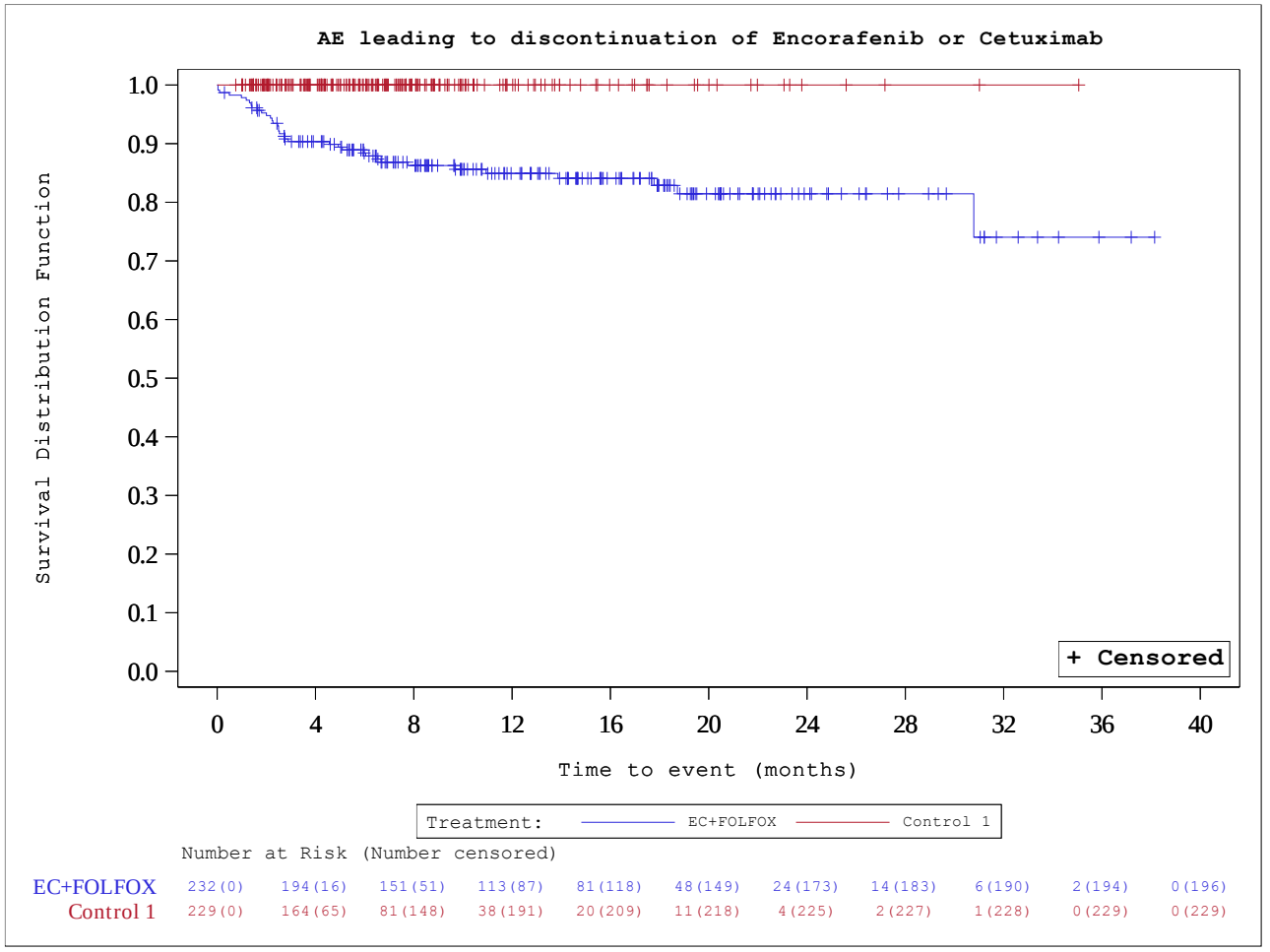
Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
AE leading to discontinuation of Encorafenib or Cetuximab - Subgroup analysis
Safety Analysis Set

Subgroup Level	EC+FOLFOX (N=232) n/ N (%)	EC+FOLFOX (N=232) Median (95% CI)[1]	Control 1 (N=229) n/ N (%)	Control 1 (N=229) Median (95% CI)[1]	Unstratified analysis Hazard Ratio (95% CI)[2]	Unstratified analysis p-Value[3]	Interaction p-Value[4]
Age (Years)							0.9998
< 65	19/ 148 (12.8)	NE (NE , NE)	0/ 131 (0.0)	NE (NE , NE)	NE		
>= 65	17/ 84 (20.2)	NE (30.8, NE)	0/ 98 (0.0)	NE (NE , NE)	NE		
Sex							1.0000
Male	18/ 121 (14.9)	NE (NE , NE)	0/ 112 (0.0)	NE (NE , NE)	NE		
Female	18/ 111 (16.2)	NE (NE , NE)	0/ 117 (0.0)	NE (NE , NE)	NE		
Region							1.0000
Europe	13/ 108 (12.0)	NE (30.8, NE)	0/ 103 (0.0)	NE (NE , NE)	NE		
USA/Canada	1/ 15 (6.7)	NE (NE , NE)	0/ 17 (0.0)	NE (NE , NE)	NE		
Rest of World	22/ 109 (20.2)	NE (NE , NE)	0/ 109 (0.0)	NE (NE , NE)	NE		
ECOG-PS at Randomization							0.9998
0	16/ 130 (12.3)	NE (NE , NE)	0/ 130 (0.0)	NE (NE , NE)	NE		
1	20/ 102 (19.6)	NE (NE , NE)	0/ 99 (0.0)	NE (NE , NE)	NE		
Number of Organs Involved							0.9997
<= 2	13/ 116 (11.2)	NE (NE , NE)	0/ 119 (0.0)	NE (NE , NE)	NE		
>= 3	23/ 116 (19.8)	NE (NE , NE)	0/ 110 (0.0)	NE (NE , NE)	NE		
Presence of Liver Metastases							0.9996
Yes	29/ 146 (19.9)	NE (NE , NE)	0/ 149 (0.0)	NE (NE , NE)	NE		
No	7/ 86 (8.1)	NE (30.8, NE)	0/ 80 (0.0)	NE (NE , NE)	NE		
Side of Tumor							1.0000
Left	14/ 88 (15.9)	NE (NE , NE)	0/ 90 (0.0)	NE (NE , NE)	NE		
Right	22/ 144 (15.3)	NE (30.8, NE)	0/ 139 (0.0)	NE (NE , NE)	NE		

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.
[4] P-Value for interaction from Cox proportional hazards model using ties=exact option with treatment, subgroup and treatment*subgroup interaction as covariates.
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Kaplan Meier Plot of AE leading to discontinuation of Encorafenib or Cetuximab
Safety Analysis Set



Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
Kaplan-Meier Plots for subgroups only created if p-value for interaction < 0.05.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
AE leading to discontinuation of Encorafenib or Cetuximab excluding events related to underlying disease progression
Safety Analysis Set

	EC+FOLFOX (N=232)	Control 1 (N=229)
Number of subjects with events, n (%)	22 (9.5)	0 (0.0)
Number of censored subjects, n (%)	210 (90.5)	229 (100.0)
Kaplan-Meier estimates of Time to Event (months) [1]		
25%-ile (95% CI)	NE (30.8, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
Unstratified analysis		
Hazard Ratio (95% CI) [2]	NE	
p-value [3]		

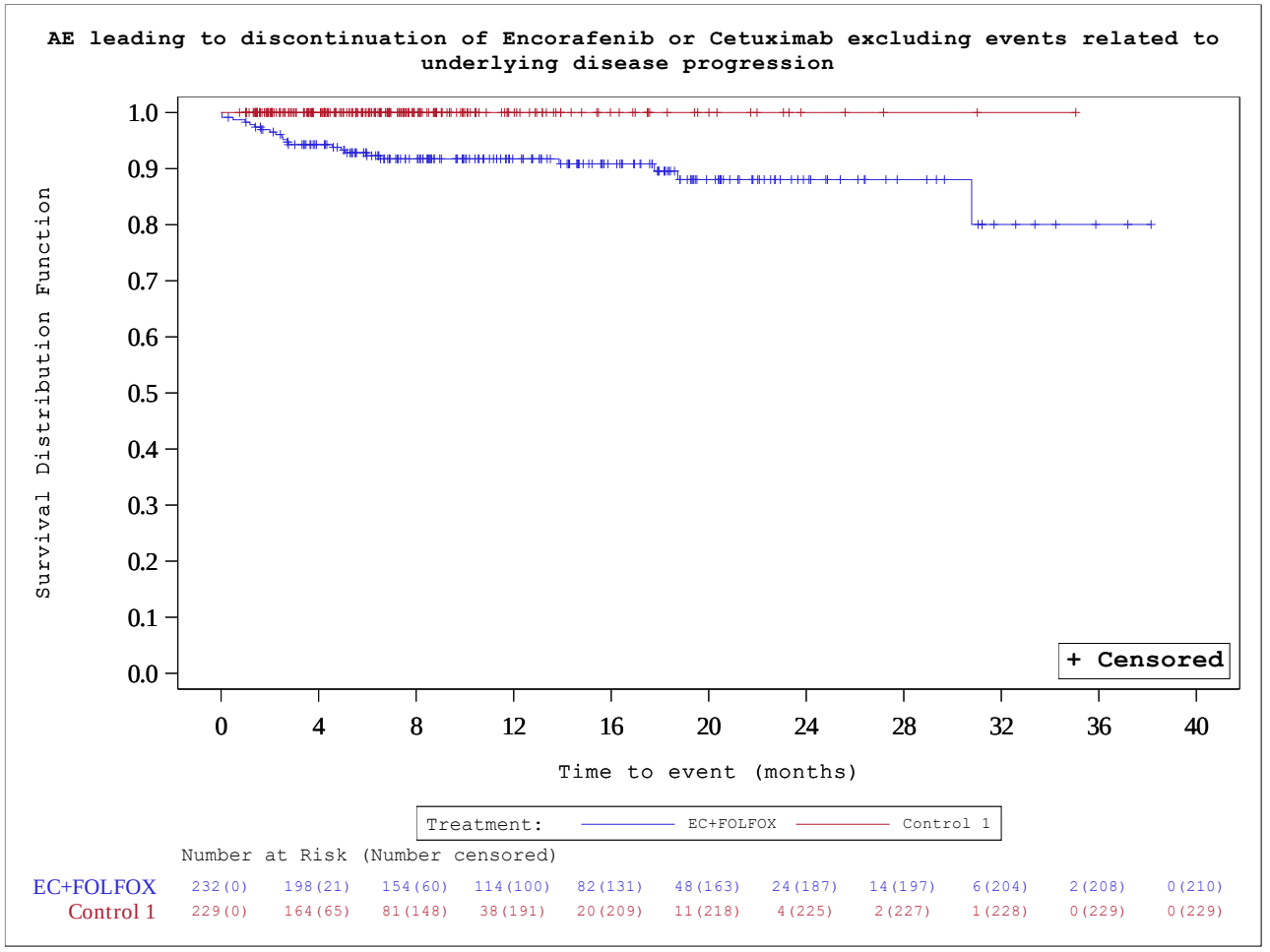
Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
AE leading to discontinuation of Encorafenib or Cetuximab excluding events related to underlying disease progression - Subgroup analysis
Safety Analysis Set

Subgroup Level	EC+FOLFOX (N=232) n/ N (%)	EC+FOLFOX (N=232) Median (95% CI)[1]	Control 1 (N=229) n/ N (%)	Control 1 (N=229) Median (95% CI)[1]	Unstratified analysis Hazard Ratio (95% CI)[2]	Unstratified analysis p-Value[3]	Interaction p-Value[4]
Age (Years)							0.9998
< 65	11/ 148 (7.4)	NE (NE , NE)	0/ 131 (0.0)	NE (NE , NE)	NE		
>= 65	11/ 84 (13.1)	NE (30.8, NE)	0/ 98 (0.0)	NE (NE , NE)	NE		
Sex							0.9999
Male	9/ 121 (7.4)	NE (NE , NE)	0/ 112 (0.0)	NE (NE , NE)	NE		
Female	13/ 111 (11.7)	NE (NE , NE)	0/ 117 (0.0)	NE (NE , NE)	NE		
Region							1.0000
Europe	9/ 108 (8.3)	NE (NE , NE)	0/ 103 (0.0)	NE (NE , NE)	NE		
USA/Canada	1/ 15 (6.7)	NE (NE , NE)	0/ 17 (0.0)	NE (NE , NE)	NE		
Rest of World	12/ 109 (11.0)	NE (NE , NE)	0/ 109 (0.0)	NE (NE , NE)	NE		
ECOG-PS at Randomization							0.9998
0	9/ 130 (6.9)	NE (NE , NE)	0/ 130 (0.0)	NE (NE , NE)	NE		
1	13/ 102 (12.7)	NE (NE , NE)	0/ 99 (0.0)	NE (NE , NE)	NE		
Number of Organs Involved							0.9998
<= 2	9/ 116 (7.8)	NE (NE , NE)	0/ 119 (0.0)	NE (NE , NE)	NE		
>= 3	13/ 116 (11.2)	NE (NE , NE)	0/ 110 (0.0)	NE (NE , NE)	NE		
Presence of Liver Metastases							0.9998
Yes	17/ 146 (11.6)	NE (NE , NE)	0/ 149 (0.0)	NE (NE , NE)	NE		
No	5/ 86 (5.8)	NE (30.8, NE)	0/ 80 (0.0)	NE (NE , NE)	NE		
Side of Tumor							0.9998
Left	6/ 88 (6.8)	NE (NE , NE)	0/ 90 (0.0)	NE (NE , NE)	NE		
Right	16/ 144 (11.1)	NE (30.8, NE)	0/ 139 (0.0)	NE (NE , NE)	NE		

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.
[4] P-Value for interaction from Cox proportional hazards model using ties=exact option with treatment, subgroup and treatment*subgroup interaction as covariates.
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Kaplan Meier Plot of AE leading to discontinuation of Encorafenib or Cetuximab excluding events related to underlying disease progression
Safety Analysis Set



Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
Kaplan-Meier Plots for subgroups only created if p-value for interaction < 0.05.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
AE leading to discontinuation of Encorafenib or Cetuximab or other study intervention
Safety Analysis Set

	EC+FOLFOX (N=232)	Control 1 (N=229)
Number of subjects with events, n (%)	62 (26.7)	40 (17.5)
Number of censored subjects, n (%)	170 (73.3)	189 (82.5)
Kaplan-Meier estimates of Time to Event (months) [1]		
25%-ile (95% CI)	10.9 (6.3, 20.6)	11.4 (9.2, NE)
Median (95% CI)	NE (30.8, NE)	NE (NE, NE)
75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
Unstratified analysis		
Hazard Ratio (95% CI) [2]	1.16 (0.78, 1.74)	
p-value [3]	0.4668	

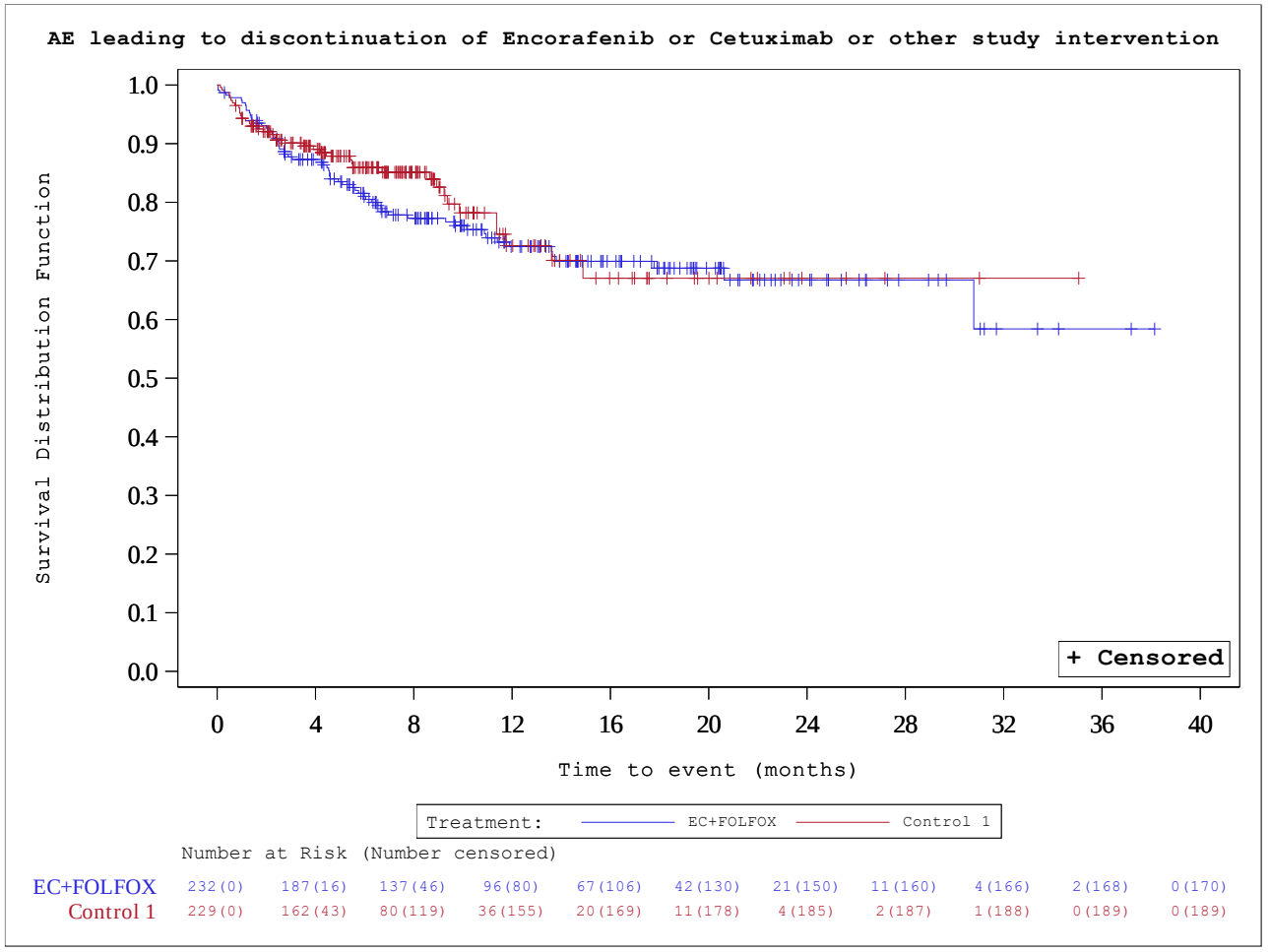
Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
AE leading to discontinuation of Encorafenib or Cetuximab or other study intervention - Subgroup analysis
Safety Analysis Set

Subgroup Level	EC+FOLFOX (N=232) n/ N (%)	EC+FOLFOX (N=232) Median (95% CI)[1]	Control 1 (N=229) n/ N (%)	Control 1 (N=229) Median (95% CI)[1]	Unstratified analysis Hazard Ratio (95% CI)[2]	Unstratified analysis p-Value[3]	Interaction p-Value[4]
Age (Years)							0.7783
< 65	36/ 148 (24.3)	NE (NE , NE)	19/ 131 (14.5)	NE (NE , NE)	1.26 (0.72, 2.20)	0.4260	
>= 65	26/ 84 (31.0)	NE (30.8, NE)	21/ 98 (21.4)	NE (13.6, NE)	1.10 (0.61, 1.98)	0.7461	
Sex							0.9286
Male	32/ 121 (26.4)	NE (30.8, NE)	20/ 112 (17.9)	NE (14.9, NE)	1.13 (0.64, 1.99)	0.6714	
Female	30/ 111 (27.0)	NE (NE , NE)	20/ 117 (17.1)	NE (NE , NE)	1.18 (0.67, 2.10)	0.5699	
Region							0.0765
Europe	23/ 108 (21.3)	NE (30.8, NE)	20/ 103 (19.4)	NE (NE , NE)	0.74 (0.40, 1.37)	0.3367	
USA/Canada	3/ 15 (20.0)	NE (NE , NE)	4/ 17 (23.5)	NE (9.4, NE)	0.75 (0.17, 3.35)	0.7037	
Rest of World	36/ 109 (33.0)	NE (NE , NE)	16/ 109 (14.7)	NE (14.9, NE)	1.87 (1.03, 3.39)	0.0358	
ECOG-PS at Randomization							0.2831
0	34/ 130 (26.2)	NE (30.8, NE)	18/ 130 (13.8)	NE (NE , NE)	1.37 (0.77, 2.44)	0.2854	
1	28/ 102 (27.5)	NE (NE , NE)	22/ 99 (22.2)	NE (NE , NE)	0.99 (0.56, 1.75)	0.9791	
Number of Organs Involved							0.4338
<= 2	32/ 116 (27.6)	NE (30.8, NE)	18/ 119 (15.1)	NE (NE , NE)	1.36 (0.76, 2.44)	0.3022	
>= 3	30/ 116 (25.9)	NE (NE , NE)	22/ 110 (20.0)	NE (14.9, NE)	1.01 (0.58, 1.76)	0.9740	
Presence of Liver Metastases							0.3255
Yes	40/ 146 (27.4)	NE (NE , NE)	30/ 149 (20.1)	NE (14.9, NE)	1.04 (0.64, 1.67)	0.8787	
No	22/ 86 (25.6)	30.8 (30.8, NE)	10/ 80 (12.5)	NE (NE , NE)	1.55 (0.72, 3.31)	0.2562	
Side of Tumor							0.9087
Left	23/ 88 (26.1)	NE (NE , NE)	14/ 90 (15.6)	NE (14.9, NE)	1.21 (0.62, 2.39)	0.5741	
Right	39/ 144 (27.1)	30.8 (30.8, NE)	26/ 139 (18.7)	NE (NE , NE)	1.15 (0.69, 1.90)	0.5899	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.
[4] P-Value for interaction from Cox proportional hazards model using ties=exact option with treatment, subgroup and treatment*subgroup interaction as covariates.
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Kaplan Meier Plot of AE leading to discontinuation of Encorafenib or Cetuximab or other study intervention
Safety Analysis Set



Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
Kaplan-Meier Plots for subgroups only created if p-value for interaction < 0.05.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
AE leading to discontinuation of Encorafenib or Cetuximab or other study intervention excluding events related to underlying disease progression
Safety Analysis Set

	EC+FOLFOX (N=232)	Control 1 (N=229)
Number of subjects with events, n (%)	38 (16.4)	22 (9.6)
Number of censored subjects, n (%)	194 (83.6)	207 (90.4)
Kaplan-Meier estimates of Time to Event (months) [1]		
25%-ile (95% CI)	30.8 (17.8, NE)	NE (NE, NE)
Median (95% CI)	NE (30.8, NE)	NE (NE, NE)
75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
Unstratified analysis		
Hazard Ratio (95% CI) [2]	1.24 (0.72, 2.11)	
p-value [3]	0.4378	

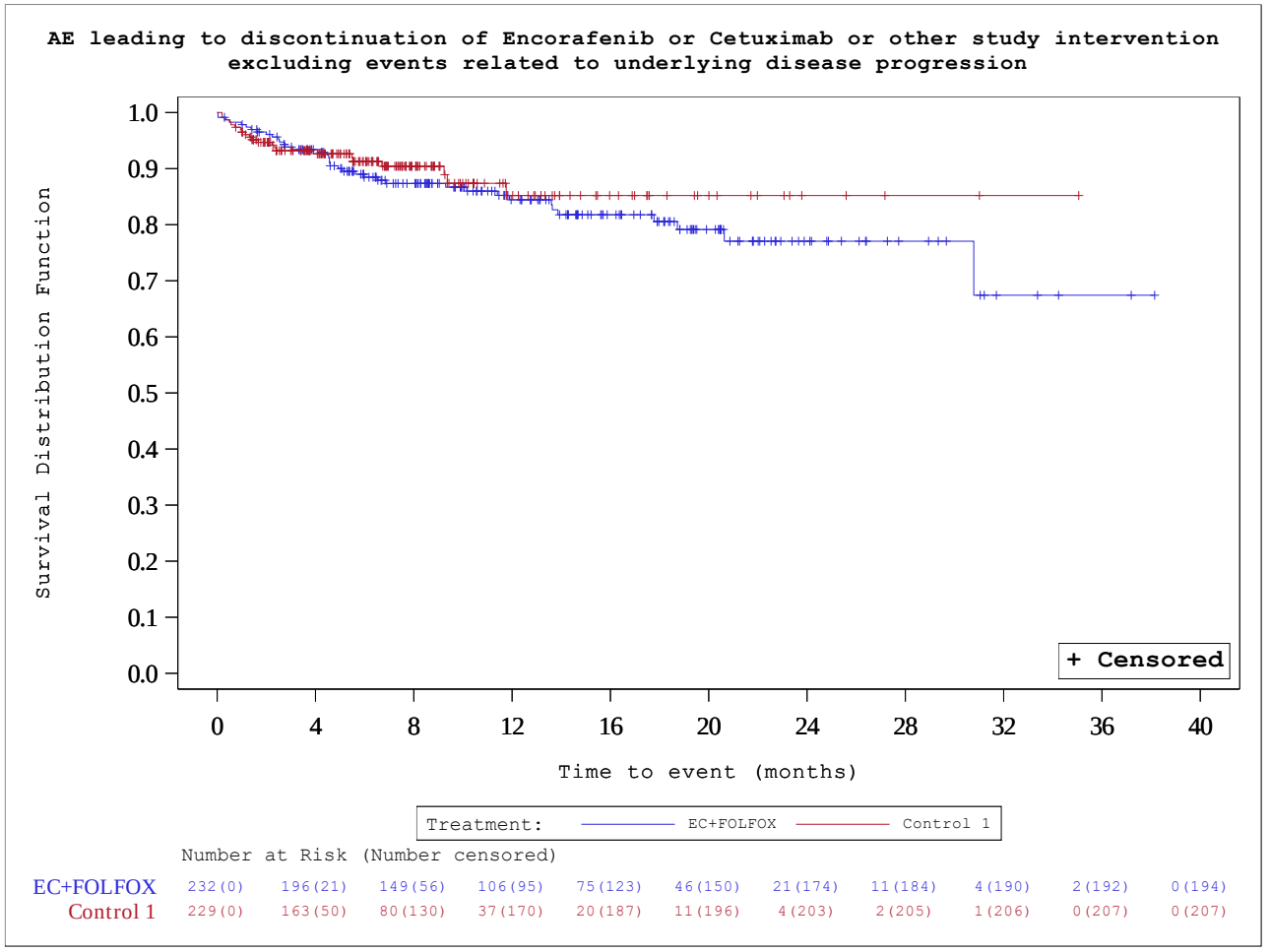
Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
AE leading to discontinuation of Encorafenib or Cetuximab or other study intervention excluding events related to underlying disease progression - Subgroup analysis
Safety Analysis Set

Subgroup Level	EC+FOLFOX (N=232) n/ N (%)	EC+FOLFOX (N=232) Median (95% CI)[1]	Control 1 (N=229) n/ N (%)	Control 1 (N=229) Median (95% CI)[1]	Unstratified analysis Hazard Ratio (95% CI)[2]	Unstratified analysis p-Value[3]	Interaction p-Value[4]
Age (Years)							0.2316
< 65	21/ 148 (14.2)	NE (NE , NE)	7/ 131 (5.3)	NE (NE , NE)	1.98 (0.84, 4.71)	0.1137	
>= 65	17/ 84 (20.2)	NE (30.8, NE)	15/ 98 (15.3)	NE (NE , NE)	0.93 (0.46, 1.89)	0.8379	
Sex							0.4729
Male	20/ 121 (16.5)	NE (30.8, NE)	9/ 112 (8.0)	NE (NE , NE)	1.52 (0.68, 3.37)	0.3047	
Female	18/ 111 (16.2)	NE (NE , NE)	13/ 117 (11.1)	NE (NE , NE)	1.02 (0.49, 2.12)	0.9530	
Region							0.0629
Europe	17/ 108 (15.7)	NE (30.8, NE)	13/ 103 (12.6)	NE (NE , NE)	0.85 (0.40, 1.80)	0.6701	
USA/Canada	2/ 15 (13.3)	NE (NE , NE)	4/ 17 (23.5)	NE (9.4, NE)	0.49 (0.09, 2.66)	0.3951	
Rest of World	19/ 109 (17.4)	NE (NE , NE)	5/ 109 (4.6)	NE (NE , NE)	2.88 (1.07, 7.80)	0.0293	
ECOG-PS at Randomization							0.4880
0	21/ 130 (16.2)	NE (30.8, NE)	10/ 130 (7.7)	NE (NE , NE)	1.36 (0.63, 2.93)	0.4342	
1	17/ 102 (16.7)	NE (NE , NE)	12/ 99 (12.1)	NE (NE , NE)	1.15 (0.54, 2.42)	0.7207	
Number of Organs Involved							0.5006
<= 2	22/ 116 (19.0)	NE (30.8, NE)	11/ 119 (9.2)	NE (NE , NE)	1.45 (0.70, 3.03)	0.3166	
>= 3	16/ 116 (13.8)	NE (NE , NE)	11/ 110 (10.0)	NE (NE , NE)	1.05 (0.48, 2.29)	0.9092	
Presence of Liver Metastases							0.3016
Yes	22/ 146 (15.1)	NE (NE , NE)	16/ 149 (10.7)	NE (NE , NE)	1.05 (0.55, 2.02)	0.8786	
No	16/ 86 (18.6)	NE (30.8, NE)	6/ 80 (7.5)	NE (NE , NE)	1.76 (0.68, 4.58)	0.2402	
Side of Tumor							0.5796
Left	13/ 88 (14.8)	NE (NE , NE)	6/ 90 (6.7)	NE (NE , NE)	1.63 (0.61, 4.36)	0.3251	
Right	25/ 144 (17.4)	NE (30.8, NE)	16/ 139 (11.5)	NE (NE , NE)	1.12 (0.59, 2.11)	0.7342	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.
[4] P-Value for interaction from Cox proportional hazards model using ties=exact option with treatment, subgroup and treatment*subgroup interaction as covariates.
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Kaplan Meier Plot of AE leading to discontinuation of Encorafenib or Cetuximab or other study intervention excluding events related to underlying disease progression
Safety Analysis Set



Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
Kaplan-Meier Plots for subgroups only created if p-value for interaction < 0.05.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
AE leading to death
Safety Analysis Set

	EC+FOLFOX (N=232)	Control 1 (N=229)
Number of subjects with events, n (%)	10 (4.3)	10 (4.4)
Number of censored subjects, n (%)	222 (95.7)	219 (95.6)
Kaplan-Meier estimates of Time to Event (months) [1]		
25%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
Unstratified analysis		
Hazard Ratio (95% CI) [2]	0.68 (0.28, 1.67)	
p-value [3]	0.4023	

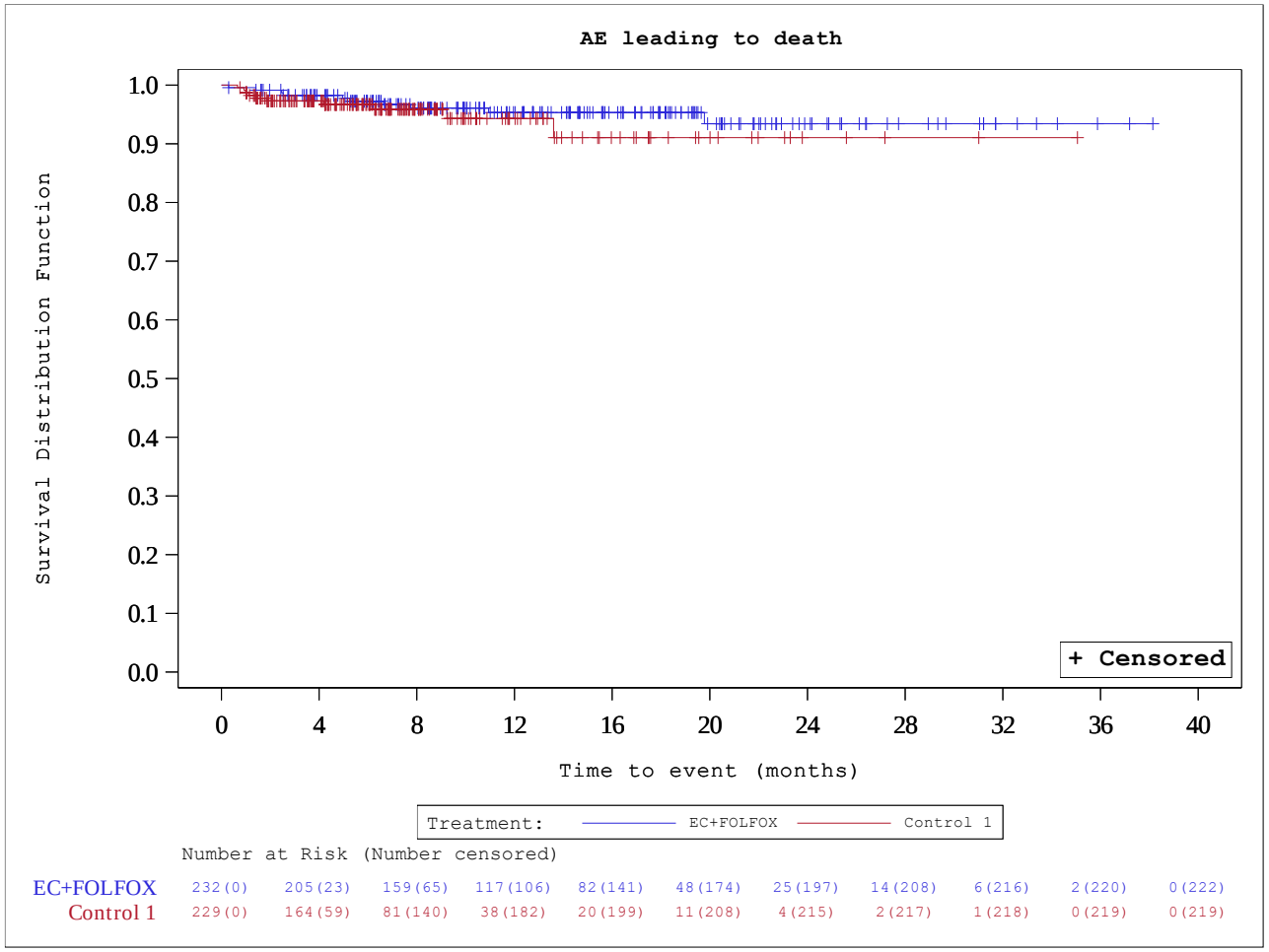
Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
AE leading to death - Subgroup analysis
Safety Analysis Set

Subgroup Level	EC+FOLFOX (N=232) n/ N (%)	EC+FOLFOX (N=232) Median (95% CI)[1]	Control 1 (N=229) n/ N (%)	Control 1 (N=229) Median (95% CI)[1]	Unstratified analysis Hazard Ratio (95% CI)[2]	Unstratified analysis p-Value[3]	Interaction p-Value[4]
Age (Years)							0.9371
< 65	5/ 148 (3.4)	NE (NE , NE)	4/ 131 (3.1)	NE (NE , NE)	0.85 (0.23, 3.18)	0.8066	
>= 65	5/ 84 (6.0)	NE (NE , NE)	6/ 98 (6.1)	NE (NE , NE)	0.64 (0.19, 2.16)	0.4707	
Sex							0.4178
Male	6/ 121 (5.0)	NE (NE , NE)	4/ 112 (3.6)	NE (NE , NE)	1.05 (0.29, 3.80)	0.9353	
Female	4/ 111 (3.6)	NE (NE , NE)	6/ 117 (5.1)	NE (NE , NE)	0.46 (0.13, 1.66)	0.2245	
Region							0.9771
Europe	5/ 108 (4.6)	NE (NE , NE)	5/ 103 (4.9)	NE (NE , NE)	0.60 (0.17, 2.13)	0.4225	
USA/Canada	1/ 15 (6.7)	NE (NE , NE)	1/ 17 (5.9)	NE (NE , NE)	0.92 (0.06, 14.87)	0.9554	
Rest of World	4/ 109 (3.7)	NE (NE , NE)	4/ 109 (3.7)	NE (NE , NE)	0.74 (0.18, 3.03)	0.6761	
ECOG-PS at Randomization							0.6594
0	6/ 130 (4.6)	NE (NE , NE)	5/ 130 (3.8)	NE (NE , NE)	0.84 (0.25, 2.79)	0.7704	
1	4/ 102 (3.9)	NE (NE , NE)	5/ 99 (5.1)	NE (NE , NE)	0.55 (0.14, 2.11)	0.3746	
Number of Organs Involved							0.9871
<= 2	2/ 116 (1.7)	NE (NE , NE)	2/ 119 (1.7)	NE (NE , NE)	0.37 (0.05, 2.69)	0.3080	
>= 3	8/ 116 (6.9)	NE (NE , NE)	8/ 110 (7.3)	NE (NE , NE)	0.73 (0.27, 1.98)	0.5390	
Presence of Liver Metastases							0.6908
Yes	7/ 146 (4.8)	NE (NE , NE)	8/ 149 (5.4)	NE (NE , NE)	0.62 (0.22, 1.74)	0.3569	
No	3/ 86 (3.5)	NE (NE , NE)	2/ 80 (2.5)	NE (NE , NE)	0.96 (0.15, 6.03)	0.9638	
Side of Tumor							0.3574
Left	5/ 88 (5.7)	NE (NE , NE)	7/ 90 (7.8)	NE (NE , NE)	0.48 (0.15, 1.59)	0.2240	
Right	5/ 144 (3.5)	NE (NE , NE)	3/ 139 (2.2)	NE (NE , NE)	1.11 (0.26, 4.75)	0.8908	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.
[4] P-Value for interaction from Cox proportional hazards model using ties=exact option with treatment, subgroup and treatment*subgroup interaction as covariates.
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Kaplan Meier Plot of AE leading to death
Safety Analysis Set



Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
Kaplan-Meier Plots for subgroups only created if p-value for interaction < 0.05.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
AE leading to death excluding events related to underlying disease progression
Safety Analysis Set

	EC+FOLFOX (N=232)	Control 1 (N=229)
Number of subjects with events, n (%)	0 (0.0)	5 (2.2)
Number of censored subjects, n (%)	232 (100.0)	224 (97.8)
Kaplan-Meier estimates of Time to Event (months) [1]		
25%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
Unstratified analysis		
Hazard Ratio (95% CI) [2]	NE	
p-value [3]		

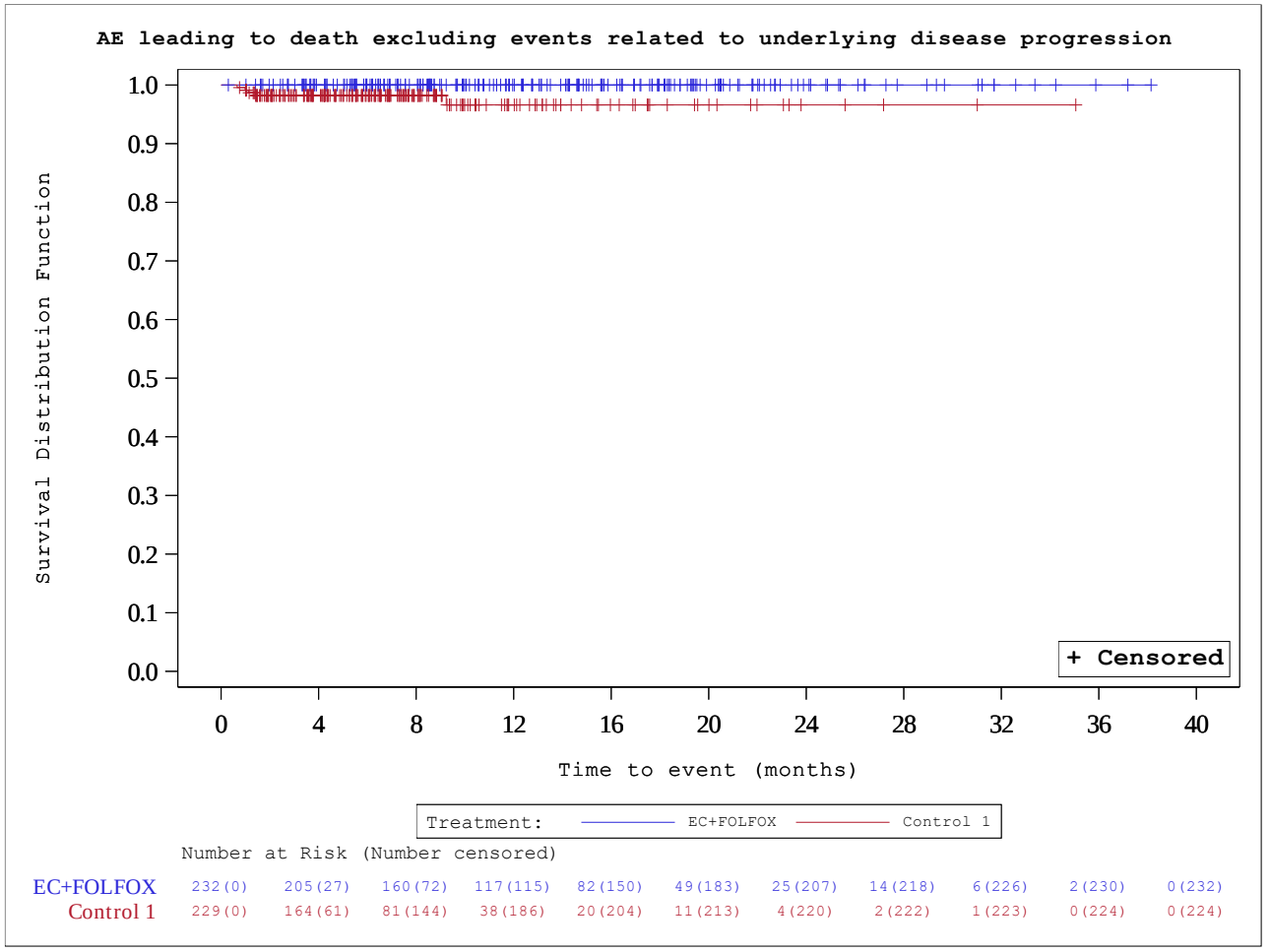
Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
AE leading to death excluding events related to underlying disease progression - Subgroup analysis
Safety Analysis Set

Subgroup Level	EC+FOLFOX (N=232) n/ N (%)	EC+FOLFOX (N=232) Median (95% CI)[1]	Control 1 (N=229) n/ N (%)	Control 1 (N=229) Median (95% CI)[1]	Unstratified analysis Hazard Ratio (95% CI)[2]	Unstratified analysis p-Value[3]	Interaction p-Value[4]
Age (Years)							
< 65	0/ 148 (0.0)		1/ 131 (0.8)				
>= 65	0/ 84 (0.0)		4/ 98 (4.1)				
Sex							
Male	0/ 121 (0.0)		1/ 112 (0.9)				
Female	0/ 111 (0.0)		4/ 117 (3.4)				
Region							
Europe	0/ 108 (0.0)		2/ 103 (1.9)				
USA/Canada	0/ 15 (0.0)		1/ 17 (5.9)				
Rest of World	0/ 109 (0.0)		2/ 109 (1.8)				
ECOG-PS at Randomization							
0	0/ 130 (0.0)		2/ 130 (1.5)				
1	0/ 102 (0.0)		3/ 99 (3.0)				
Number of Organs Involved							
<= 2	0/ 116 (0.0)		1/ 119 (0.8)				
>= 3	0/ 116 (0.0)		4/ 110 (3.6)				
Presence of Liver Metastases							
Yes	0/ 146 (0.0)		4/ 149 (2.7)				
No	0/ 86 (0.0)		1/ 80 (1.3)				
Side of Tumor							
Left	0/ 88 (0.0)		4/ 90 (4.4)				
Right	0/ 144 (0.0)		1/ 139 (0.7)				

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.
[4] P-Value for interaction from Cox proportional hazards model using ties=exact option with treatment, subgroup and treatment*subgroup interaction as covariates.
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Kaplan Meier Plot of AE leading to death excluding events related to underlying disease progression
Safety Analysis Set



Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
Kaplan-Meier Plots for subgroups only created if p-value for interaction < 0.05.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Incidence of AE leading to discontinuation of Encorafenib by SOC, PT
Safety Analysis Set

System Organ Class (SOC) Preferred Term (PT)	EC+FOLFOX (N=232) n (%)	Control 1 (N=229) n (%)
Blood and lymphatic system disorders	1 (0.4)	0 (0.0)
Anaemia	1 (0.4)	0 (0.0)
Eye disorders	1 (0.4)	0 (0.0)
Orbital haematoma	1 (0.4)	0 (0.0)
Gastrointestinal disorders	8 (3.4)	0 (0.0)
Abdominal pain upper	1 (0.4)	0 (0.0)
Diarrhoea	1 (0.4)	0 (0.0)
Gastrointestinal perforation	1 (0.4)	0 (0.0)
Intestinal obstruction	2 (0.9)	0 (0.0)
Large intestine perforation	1 (0.4)	0 (0.0)
Nausea	1 (0.4)	0 (0.0)
Vomiting	1 (0.4)	0 (0.0)
General disorders and administration site conditions	5 (2.2)	0 (0.0)
Asthenia	2 (0.9)	0 (0.0)
Disease progression	3 (1.3)	0 (0.0)
Mucosal inflammation	1 (0.4)	0 (0.0)
Hepatobiliary disorders	1 (0.4)	0 (0.0)
Jaundice	1 (0.4)	0 (0.0)
Immune system disorders	2 (0.9)	0 (0.0)
Hypersensitivity	2 (0.9)	0 (0.0)
Infections and infestations	4 (1.7)	0 (0.0)
Abdominal sepsis	1 (0.4)	0 (0.0)
COVID-19	1 (0.4)	0 (0.0)
Peritonitis	1 (0.4)	0 (0.0)
Pneumonia	1 (0.4)	0 (0.0)
Sepsis	1 (0.4)	0 (0.0)
Septic shock	1 (0.4)	0 (0.0)
Injury, poisoning and procedural complications	1 (0.4)	0 (0.0)
Infusion related reaction	1 (0.4)	0 (0.0)
Investigations	6 (2.6)	0 (0.0)
Lipase increased	5 (2.2)	0 (0.0)
Weight decreased	1 (0.4)	0 (0.0)
Metabolism and nutrition disorders	2 (0.9)	0 (0.0)
Decreased appetite	1 (0.4)	0 (0.0)
Hyperlipasaemia	1 (0.4)	0 (0.0)
Musculoskeletal and connective tissue disorders	2 (0.9)	0 (0.0)
Arthralgia	1 (0.4)	0 (0.0)
Joint stiffness	1 (0.4)	0 (0.0)
Myalgia	1 (0.4)	0 (0.0)
Temporomandibular pain and dysfunction syndrome	1 (0.4)	0 (0.0)
Nervous system disorders	4 (1.7)	0 (0.0)
Cerebrovascular accident	1 (0.4)	0 (0.0)
Lacunar infarction	1 (0.4)	0 (0.0)
Peripheral sensory neuropathy	2 (0.9)	0 (0.0)
Respiratory, thoracic and mediastinal disorders	2 (0.9)	0 (0.0)
Interstitial lung disease	1 (0.4)	0 (0.0)
Pneumonitis	1 (0.4)	0 (0.0)

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Incidence of AE leading to discontinuation of Encorafenib by SOC, PT
Safety Analysis Set

System Organ Class (SOC) Preferred Term (PT)	EC+FOLFOX (N=232) n (%)	Control 1 (N=229) n (%)
Skin and subcutaneous tissue disorders	3 (1.3)	0 (0.0)
Pruritus	1 (0.4)	0 (0.0)
Rash	1 (0.4)	0 (0.0)
Skin disorder	1 (0.4)	0 (0.0)

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Incidence of AE leading to discontinuation of Cetuximab by SOC, PT
Safety Analysis Set

System Organ Class (SOC) Preferred Term (PT)	EC+FOLFOX (N=232) n (%)	Control 1 (N=229) n (%)
Blood and lymphatic system disorders	2 (0.9)	0 (0.0)
Anaemia	2 (0.9)	0 (0.0)
Neutropenia	1 (0.4)	0 (0.0)
Eye disorders	1 (0.4)	0 (0.0)
Orbital haematoma	1 (0.4)	0 (0.0)
Gastrointestinal disorders	7 (3.0)	0 (0.0)
Abdominal pain upper	1 (0.4)	0 (0.0)
Gastrointestinal perforation	1 (0.4)	0 (0.0)
Intestinal obstruction	2 (0.9)	0 (0.0)
Large intestine perforation	1 (0.4)	0 (0.0)
Nausea	1 (0.4)	0 (0.0)
Vomiting	1 (0.4)	0 (0.0)
General disorders and administration site conditions	5 (2.2)	0 (0.0)
Asthenia	2 (0.9)	0 (0.0)
Disease progression	3 (1.3)	0 (0.0)
Mucosal inflammation	1 (0.4)	0 (0.0)
Hepatobiliary disorders	1 (0.4)	0 (0.0)
Jaundice	1 (0.4)	0 (0.0)
Immune system disorders	2 (0.9)	0 (0.0)
Hypersensitivity	2 (0.9)	0 (0.0)
Infections and infestations	5 (2.2)	0 (0.0)
Abdominal sepsis	1 (0.4)	0 (0.0)
COVID-19	1 (0.4)	0 (0.0)
Paronychia	1 (0.4)	0 (0.0)
Peritonitis	1 (0.4)	0 (0.0)
Pneumonia	1 (0.4)	0 (0.0)
Sepsis	1 (0.4)	0 (0.0)
Septic shock	1 (0.4)	0 (0.0)
Injury, poisoning and procedural complications	3 (1.3)	0 (0.0)
Infusion related reaction	3 (1.3)	0 (0.0)
Investigations	6 (2.6)	0 (0.0)
Lipase increased	5 (2.2)	0 (0.0)
Weight decreased	1 (0.4)	0 (0.0)
Metabolism and nutrition disorders	2 (0.9)	0 (0.0)
Decreased appetite	1 (0.4)	0 (0.0)
Hyperlipasaemia	1 (0.4)	0 (0.0)
Musculoskeletal and connective tissue disorders	2 (0.9)	0 (0.0)
Arthralgia	1 (0.4)	0 (0.0)
Joint stiffness	1 (0.4)	0 (0.0)
Myalgia	1 (0.4)	0 (0.0)
Temporomandibular pain and dysfunction syndrome	1 (0.4)	0 (0.0)
Nervous system disorders	4 (1.7)	0 (0.0)
Cerebrovascular accident	1 (0.4)	0 (0.0)
Lacunar infarction	1 (0.4)	0 (0.0)
Peripheral sensory neuropathy	2 (0.9)	0 (0.0)
Respiratory, thoracic and mediastinal disorders	2 (0.9)	0 (0.0)
Interstitial lung disease	1 (0.4)	0 (0.0)
Pneumonitis	1 (0.4)	0 (0.0)

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Incidence of AE leading to discontinuation of Cetuximab by SOC, PT
Safety Analysis Set

System Organ Class (SOC) Preferred Term (PT)	EC+FOLFOX (N=232) n (%)	Control 1 (N=229) n (%)
Skin and subcutaneous tissue disorders	3 (1.3)	0 (0.0)
Pruritus	1 (0.4)	0 (0.0)
Rash	1 (0.4)	0 (0.0)
Rash maculo-papular	1 (0.4)	0 (0.0)
Skin disorder	1 (0.4)	0 (0.0)

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Incidence of AE leading to discontinuation of other study intervention by SOC, PT
Safety Analysis Set

System Organ Class (SOC) Preferred Term (PT)	EC+FOLFOX (N=232) n (%)	Control 1 (N=229) n (%)
Blood and lymphatic system disorders	5 (2.2)	2 (0.9)
Anaemia	5 (2.2)	0 (0.0)
Febrile neutropenia	0 (0.0)	1 (0.4)
Thrombotic microangiopathy	0 (0.0)	1 (0.4)
Cardiac disorders	1 (0.4)	3 (1.3)
Acute coronary syndrome	1 (0.4)	0 (0.0)
Cardiac arrest	0 (0.0)	1 (0.4)
Myocardial infarction	0 (0.0)	2 (0.9)
Ear and labyrinth disorders	0 (0.0)	1 (0.4)
Deafness bilateral	0 (0.0)	1 (0.4)
Eye disorders	1 (0.4)	0 (0.0)
Orbital haematoma	1 (0.4)	0 (0.0)
Gastrointestinal disorders	7 (3.0)	13 (5.7)
Abdominal distension	0 (0.0)	1 (0.4)
Abdominal pain	1 (0.4)	1 (0.4)
Diarrhoea	1 (0.4)	1 (0.4)
Enterocolitis	0 (0.0)	1 (0.4)
Gastrointestinal perforation	1 (0.4)	1 (0.4)
Intestinal obstruction	2 (0.9)	5 (2.2)
Intestinal perforation	0 (0.0)	1 (0.4)
Large intestine perforation	1 (0.4)	0 (0.0)
Nausea	2 (0.9)	1 (0.4)
Vomiting	0 (0.0)	1 (0.4)
General disorders and administration site conditions	16 (6.9)	7 (3.1)
Asthenia	6 (2.6)	1 (0.4)
Chest pain	1 (0.4)	0 (0.0)
Disease progression	3 (1.3)	1 (0.4)
Fatigue	2 (0.9)	1 (0.4)
General physical health deterioration	0 (0.0)	3 (1.3)
Impaired healing	0 (0.0)	1 (0.4)
Malaise	1 (0.4)	1 (0.4)
Mucosal inflammation	1 (0.4)	0 (0.0)
Pyrexia	2 (0.9)	0 (0.0)
Immune system disorders	0 (0.0)	1 (0.4)
Anaphylactic reaction	0 (0.0)	1 (0.4)
Infections and infestations	8 (3.4)	7 (3.1)
Abdominal sepsis	1 (0.4)	1 (0.4)
COVID-19	1 (0.4)	0 (0.0)
Cellulitis	1 (0.4)	0 (0.0)
Peritonitis	1 (0.4)	0 (0.0)
Pneumonia	1 (0.4)	2 (0.9)
Sepsis	2 (0.9)	1 (0.4)
Septic shock	1 (0.4)	2 (0.9)
Urinary tract infection	3 (1.3)	1 (0.4)
Injury, poisoning and procedural complications	1 (0.4)	1 (0.4)
Fall	0 (0.0)	1 (0.4)
Infusion related reaction	1 (0.4)	0 (0.0)
Investigations	6 (2.6)	4 (1.7)
Carbon dioxide decreased	0 (0.0)	1 (0.4)
Lipase increased	1 (0.4)	1 (0.4)
Neutrophil count decreased	2 (0.9)	1 (0.4)

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Incidence of AE leading to discontinuation of other study intervention by SOC, PT
Safety Analysis Set

System Organ Class (SOC) Preferred Term (PT)	EC+FOLFOX (N=232) n (%)	Control 1 (N=229) n (%)
Platelet count decreased	3 (1.3)	1 (0.4)
Weight decreased	1 (0.4)	0 (0.0)
White blood cell count decreased	1 (0.4)	1 (0.4)
Metabolism and nutrition disorders	3 (1.3)	0 (0.0)
Decreased appetite	3 (1.3)	0 (0.0)
Musculoskeletal and connective tissue disorders	2 (0.9)	1 (0.4)
Arthralgia	1 (0.4)	0 (0.0)
Back pain	0 (0.0)	1 (0.4)
Joint stiffness	1 (0.4)	0 (0.0)
Myalgia	1 (0.4)	0 (0.0)
Nervous system disorders	7 (3.0)	4 (1.7)
Cerebrovascular accident	1 (0.4)	0 (0.0)
Hyperammonaemic encephalopathy	0 (0.0)	1 (0.4)
Lacunar infarction	1 (0.4)	0 (0.0)
Neuropathy peripheral	1 (0.4)	1 (0.4)
Neurotoxicity	0 (0.0)	1 (0.4)
Paraesthesia	1 (0.4)	0 (0.0)
Peripheral sensory neuropathy	3 (1.3)	0 (0.0)
Status epilepticus	0 (0.0)	1 (0.4)
Renal and urinary disorders	0 (0.0)	1 (0.4)
Acute kidney injury	0 (0.0)	1 (0.4)
Respiratory, thoracic and mediastinal disorders	2 (0.9)	3 (1.3)
Dyspnoea	0 (0.0)	1 (0.4)
Interstitial lung disease	2 (0.9)	0 (0.0)
Pneumonitis	0 (0.0)	1 (0.4)
Respiratory failure	0 (0.0)	1 (0.4)
Skin and subcutaneous tissue disorders	2 (0.9)	0 (0.0)
Palmar-plantar erythrodysaesthesia syndrome	1 (0.4)	0 (0.0)
Skin disorder	1 (0.4)	0 (0.0)
Vascular disorders	1 (0.4)	0 (0.0)
Peripheral arterial occlusive disease	1 (0.4)	0 (0.0)

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Incidence of AE leading to discontinuation of Encorafenib or Cetuximab by SOC, PT
Safety Analysis Set

System Organ Class (SOC) Preferred Term (PT)	EC+FOLFOX (N=232) n (%)	Control 1 (N=229) n (%)
Blood and lymphatic system disorders	2 (0.9)	0 (0.0)
Anaemia	2 (0.9)	0 (0.0)
Neutropenia	1 (0.4)	0 (0.0)
Eye disorders	1 (0.4)	0 (0.0)
Orbital haematoma	1 (0.4)	0 (0.0)
Gastrointestinal disorders	8 (3.4)	0 (0.0)
Abdominal pain upper	1 (0.4)	0 (0.0)
Diarrhoea	1 (0.4)	0 (0.0)
Gastrointestinal perforation	1 (0.4)	0 (0.0)
Intestinal obstruction	2 (0.9)	0 (0.0)
Large intestine perforation	1 (0.4)	0 (0.0)
Nausea	1 (0.4)	0 (0.0)
Vomiting	1 (0.4)	0 (0.0)
General disorders and administration site conditions	5 (2.2)	0 (0.0)
Asthenia	2 (0.9)	0 (0.0)
Disease progression	3 (1.3)	0 (0.0)
Mucosal inflammation	1 (0.4)	0 (0.0)
Hepatobiliary disorders	1 (0.4)	0 (0.0)
Jaundice	1 (0.4)	0 (0.0)
Immune system disorders	3 (1.3)	0 (0.0)
Hypersensitivity	3 (1.3)	0 (0.0)
Infections and infestations	5 (2.2)	0 (0.0)
Abdominal sepsis	1 (0.4)	0 (0.0)
COVID-19	1 (0.4)	0 (0.0)
Paronychia	1 (0.4)	0 (0.0)
Peritonitis	1 (0.4)	0 (0.0)
Pneumonia	1 (0.4)	0 (0.0)
Sepsis	1 (0.4)	0 (0.0)
Septic shock	1 (0.4)	0 (0.0)
Injury, poisoning and procedural complications	3 (1.3)	0 (0.0)
Infusion related reaction	3 (1.3)	0 (0.0)
Investigations	6 (2.6)	0 (0.0)
Lipase increased	5 (2.2)	0 (0.0)
Weight decreased	1 (0.4)	0 (0.0)
Metabolism and nutrition disorders	2 (0.9)	0 (0.0)
Decreased appetite	1 (0.4)	0 (0.0)
Hyperlipasaemia	1 (0.4)	0 (0.0)
Musculoskeletal and connective tissue disorders	2 (0.9)	0 (0.0)
Arthralgia	1 (0.4)	0 (0.0)
Joint stiffness	1 (0.4)	0 (0.0)
Myalgia	1 (0.4)	0 (0.0)
Temporomandibular pain and dysfunction syndrome	1 (0.4)	0 (0.0)
Nervous system disorders	4 (1.7)	0 (0.0)
Cerebrovascular accident	1 (0.4)	0 (0.0)
Lacunar infarction	1 (0.4)	0 (0.0)
Peripheral sensory neuropathy	2 (0.9)	0 (0.0)
Respiratory, thoracic and mediastinal disorders	2 (0.9)	0 (0.0)
Interstitial lung disease	1 (0.4)	0 (0.0)

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Incidence of AE leading to discontinuation of Encorafenib or Cetuximab by SOC, PT
Safety Analysis Set

System Organ Class (SOC) Preferred Term (PT)	EC+FOLFOX (N=232) n (%)	Control 1 (N=229) n (%)
Pneumonitis	1 (0.4)	0 (0.0)
Skin and subcutaneous tissue disorders	3 (1.3)	0 (0.0)
Pruritus	1 (0.4)	0 (0.0)
Rash	1 (0.4)	0 (0.0)
Rash maculo-papular	1 (0.4)	0 (0.0)
Skin disorder	1 (0.4)	0 (0.0)

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Frequent AE by SOC, PT (incidence >= 10% or >=10 patients and incidence >= 1%)
Safety Analysis Set

		EC+FOLFOX (N=232)	Control 1 (N=229)
SOC: Blood and lymphatic system disorders	Number of subjects with events, n (%)	145 (62.5)	113 (49.3)
	Number of censored subjects, n (%)	87 (37.5)	116 (50.7)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	1.0 (0.5, 1.8)	1.0 (0.9, 1.4)
	Median (95% CI)	4.4 (3.2, 6.3)	5.1 (3.4, 11.8)
	75%-ile (95% CI)	22.3 (15.6, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	1.11 (0.87, 1.43)	
	p-value [3]	0.4027	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.

		EC+FOLFOX (N=232)	Control 1 (N=229)
SOC: Blood and lymphatic system disorders, PT: Anaemia	Number of subjects with events, n (%)	107 (46.1)	58 (25.3)
	Number of censored subjects, n (%)	125 (53.9)	171 (74.7)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	3.6 (2.7, 4.6)	6.0 (2.9, NE)
	Median (95% CI)	12.6 (7.6, 21.2)	NE (NE, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	1.57 (1.14, 2.16)	
	p-value [3]	0.0056	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.

		EC+FOLFOX (N=232)	Control 1 (N=229)
SOC: Blood and lymphatic system disorders, PT: Febrile neutropenia	Number of subjects with events, n (%)	5 (2.2)	11 (4.8)
	Number of censored subjects, n (%)	227 (97.8)	218 (95.2)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Median (95% CI)	NE (NE, NE)	NE (NE, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	0.43 (0.15, 1.23)	
	p-value [3]	0.1035	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.

		EC+FOLFOX (N=232)	Control 1 (N=229)
SOC: Blood and lymphatic system disorders, PT: Neutropenia	Number of subjects with events, n (%)	56 (24.1)	57 (24.9)
	Number of censored subjects, n (%)	176 (75.9)	172 (75.1)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	26.7 (2.8, NE)	4.4 (3.2, NE)
	Median (95% CI)	NE (NE, NE)	NE (NE, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	0.90 (0.62, 1.30)	
	p-value [3]	0.5504	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.

		EC+FOLFOX (N=232)	Control 1 (N=229)
SOC: Blood and lymphatic system disorders, PT: Thrombocytopenia	Number of subjects with events, n (%)	32 (13.8)	21 (9.2)
	Number of censored subjects, n (%)	200 (86.2)	208 (90.8)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Median (95% CI)	NE (NE, NE)	NE (NE, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	1.21 (0.70, 2.11)	
	p-value [3]	0.4973	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.

		EC+FOLFOX (N=232)	Control 1 (N=229)
SOC: Cardiac disorders	Number of subjects with events, n (%)	26 (11.2)	19 (8.3)
	Number of censored subjects, n (%)	206 (88.8)	210 (91.7)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	NE (NE, NE)	NE (15.0, NE)
	Median (95% CI)	NE (NE, NE)	NE (NE, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	1.07 (0.59, 1.97)	
	p-value [3]	0.8145	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.

		EC+FOLFOX (N=232)	Control 1 (N=229)
SOC: Ear and labyrinth disorders	Number of subjects with events, n (%)	5 (2.2)	10 (4.4)
	Number of censored subjects, n (%)	227 (97.8)	219 (95.6)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	NE (NE, NE)	27.6 (27.6, NE)
	Median (95% CI)	NE (NE, NE)	27.6 (27.6, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (27.6, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	0.28 (0.09, 0.86)	
	p-value [3]	0.0192	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.

		EC+FOLFOX (N=232)	Control 1 (N=229)
SOC: Eye disorders	Number of subjects with events, n (%)	34 (14.7)	13 (5.7)
	Number of censored subjects, n (%)	198 (85.3)	216 (94.3)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	NE (20.5, NE)	30.2 (30.2, NE)
	Median (95% CI)	NE (NE, NE)	30.2 (30.2, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (30.2, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	1.97 (1.03, 3.75)	
	p-value [3]	0.0369	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.

		EC+FOLFOX (N=232)	Control 1 (N=229)
SOC: Gastrointestinal disorders	Number of subjects with events, n (%)	202 (87.1)	196 (85.6)
	Number of censored subjects, n (%)	30 (12.9)	33 (14.4)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	0.1 (0.1, 0.1)	0.1 (0.1, 0.1)
	Median (95% CI)	0.5 (0.2, 0.5)	0.3 (0.2, 0.5)
	75%-ile (95% CI)	2.1 (1.2, 3.3)	1.6 (1.0, 3.3)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	0.93 (0.77, 1.14)	
	p-value [3]	0.4872	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.

		EC+FOLFOX (N=232)	Control 1 (N=229)
SOC: Gastrointestinal disorders, PT: Abdominal discomfort	Number of subjects with events, n (%)	10 (4.3)	3 (1.3)
	Number of censored subjects, n (%)	222 (95.7)	226 (98.7)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Median (95% CI)	NE (NE, NE)	NE (NE, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	2.05 (0.55, 7.59)	
	p-value [3]	0.2749	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.

		EC+FOLFOX (N=232)	Control 1 (N=229)
SOC: Gastrointestinal disorders, PT: Abdominal distension	Number of subjects with events, n (%)	14 (6.0)	8 (3.5)
	Number of censored subjects, n (%)	218 (94.0)	221 (96.5)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Median (95% CI)	NE (NE, NE)	NE (NE, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	1.41 (0.59, 3.39)	
	p-value [3]	0.4413	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.

		EC+FOLFOX (N=232)	Control 1 (N=229)
SOC: Gastrointestinal disorders, PT: Abdominal pain	Number of subjects with events, n (%)	47 (20.3)	53 (23.1)
	Number of censored subjects, n (%)	185 (79.7)	176 (76.9)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	25.2 (10.7, NE)	7.4 (4.3, NE)
	Median (95% CI)	NE (NE, NE)	NE (23.2, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	0.65 (0.43, 0.96)	
	p-value [3]	0.0306	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.

		EC+FOLFOX (N=232)	Control 1 (N=229)
SOC: Gastrointestinal disorders, PT: Abdominal pain upper	Number of subjects with events, n (%)	24 (10.3)	19 (8.3)
	Number of censored subjects, n (%)	208 (89.7)	210 (91.7)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Median (95% CI)	NE (NE, NE)	NE (NE, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	0.98 (0.53, 1.82)	
	p-value [3]	0.9561	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.

		EC+FOLFOX (N=232)	Control 1 (N=229)
SOC: Gastrointestinal disorders, PT: Constipation	Number of subjects with events, n (%)	63 (27.2)	52 (22.7)
	Number of censored subjects, n (%)	169 (72.8)	177 (77.3)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	8.4 (5.7, 17.4)	8.7 (3.3, NE)
	Median (95% CI)	NE (NE, NE)	NE (NE, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	0.93 (0.64, 1.35)	
	p-value [3]	0.7119	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Frequent AE by SOC, PT (incidence >= 10% or >=10 patients and incidence >= 1%)
Safety Analysis Set

		EC+FOLFOX (N=232)	Control 1 (N=229)
SOC: Gastrointestinal disorders, PT: Diarrhoea	Number of subjects with events, n (%)	97 (41.8)	115 (50.2)
	Number of censored subjects, n (%)	135 (58.2)	114 (49.8)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	2.6 (1.4, 5.1)	0.5 (0.3, 0.7)
	Median (95% CI)	21.1 (11.0, NE)	3.7 (2.3, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	0.59 (0.45, 0.78)	
	p-value [3]	0.0001	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Frequent AE by SOC, PT (incidence >= 10% or >=10 patients and incidence >= 1%)
Safety Analysis Set

		EC+FOLFOX (N=232)	Control 1 (N=229)
SOC: Gastrointestinal disorders, PT: Gastrooesophageal reflux disease	Number of subjects with events, n (%)	6 (2.6)	11 (4.8)
	Number of censored subjects, n (%)	226 (97.4)	218 (95.2)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Median (95% CI)	NE (NE, NE)	NE (NE, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	0.35 (0.13, 0.97)	
	p-value [3]	0.0354	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.

		EC+FOLFOX (N=232)	Control 1 (N=229)
SOC: Gastrointestinal disorders, PT: Gingival bleeding	Number of subjects with events, n (%)	10 (4.3)	2 (0.9)
	Number of censored subjects, n (%)	222 (95.7)	227 (99.1)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Median (95% CI)	NE (NE, NE)	NE (NE, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	3.44 (0.74, 15.92)	
	p-value [3]	0.0928	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Frequent AE by SOC, PT (incidence >= 10% or >=10 patients and incidence >= 1%)
Safety Analysis Set

		EC+FOLFOX (N=232)	Control 1 (N=229)
SOC: Gastrointestinal disorders, PT: Haemorrhoids	Number of subjects with events, n (%)	24 (10.3)	8 (3.5)
	Number of censored subjects, n (%)	208 (89.7)	221 (96.5)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	NE (30.9, NE)	NE (NE, NE)
	Median (95% CI)	NE (NE, NE)	NE (NE, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	2.40 (1.07, 5.38)	
	p-value [3]	0.0290	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Frequent AE by SOC, PT (incidence >= 10% or >=10 patients and incidence >= 1%)
Safety Analysis Set

		EC+FOLFOX (N=232)	Control 1 (N=229)
SOC: Gastrointestinal disorders, PT: Intestinal obstruction	Number of subjects with events, n (%)	13 (5.6)	9 (3.9)
	Number of censored subjects, n (%)	219 (94.4)	220 (96.1)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Median (95% CI)	NE (NE, NE)	NE (NE, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	0.86 (0.36, 2.07)	
	p-value [3]	0.7441	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.

		EC+FOLFOX (N=232)	Control 1 (N=229)
SOC: Gastrointestinal disorders, PT: Nausea	Number of subjects with events, n (%)	125 (53.9)	114 (49.8)
	Number of censored subjects, n (%)	107 (46.1)	115 (50.2)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	0.1 (0.1, 0.5)	0.1 (0.1, 0.3)
	Median (95% CI)	5.3 (1.8, 17.5)	3.7 (1.5, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	0.99 (0.77, 1.28)	
	p-value [3]	0.9719	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.

		EC+FOLFOX (N=232)	Control 1 (N=229)
SOC: Gastrointestinal disorders, PT: Stomatitis	Number of subjects with events, n (%)	35 (15.1)	33 (14.4)
	Number of censored subjects, n (%)	197 (84.9)	196 (85.6)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	NE (20.1, NE)	NE (NE, NE)
	Median (95% CI)	NE (NE, NE)	NE (NE, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	0.87 (0.54, 1.40)	
	p-value [3]	0.5593	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.

		EC+FOLFOX (N=232)	Control 1 (N=229)
SOC: Gastrointestinal disorders, PT: Vomiting	Number of subjects with events, n (%)	84 (36.2)	51 (22.3)
	Number of censored subjects, n (%)	148 (63.8)	178 (77.7)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	1.8 (0.6, 4.4)	9.1 (3.2, NE)
	Median (95% CI)	NE (18.3, NE)	NE (NE, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	1.59 (1.12, 2.26)	
	p-value [3]	0.0091	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.

		EC+FOLFOX (N=232)	Control 1 (N=229)
SOC: General disorders and administration site conditions	Number of subjects with events, n (%)	187 (80.6)	148 (64.6)
	Number of censored subjects, n (%)	45 (19.4)	81 (35.4)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	0.1 (0.1, 0.3)	0.3 (0.1, 0.5)
	Median (95% CI)	1.0 (0.5, 1.8)	1.8 (1.1, 3.3)
	75%-ile (95% CI)	5.4 (3.9, 11.6)	NE (7.2, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	1.29 (1.04, 1.60)	
	p-value [3]	0.0227	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.

		EC+FOLFOX (N=232)	Control 1 (N=229)
SOC: General disorders and administration site conditions, PT: Asthenia	Number of subjects with events, n (%)	68 (29.3)	34 (14.8)
	Number of censored subjects, n (%)	164 (70.7)	195 (85.2)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	5.1 (2.9, 20.6)	NE (NE, NE)
	Median (95% CI)	NE (NE, NE)	NE (NE, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	1.86 (1.23, 2.81)	
	p-value [3]	0.0030	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.

		EC+FOLFOX (N=232)	Control 1 (N=229)
SOC: General disorders and administration site conditions, PT: Chest pain	Number of subjects with events, n (%)	10 (4.3)	5 (2.2)
	Number of censored subjects, n (%)	222 (95.7)	224 (97.8)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Median (95% CI)	NE (NE, NE)	NE (NE, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	1.36 (0.45, 4.08)	
	p-value [3]	0.5845	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Frequent AE by SOC, PT (incidence >= 10% or >=10 patients and incidence >= 1%)
Safety Analysis Set

		EC+FOLFOX (N=232)	Control 1 (N=229)
SOC: General disorders and administration site conditions, PT: Fatigue	Number of subjects with events, n (%)	61 (26.3)	64 (27.9)
	Number of censored subjects, n (%)	171 (73.7)	165 (72.1)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	7.4 (2.2, NE)	4.2 (1.4, 8.7)
	Median (95% CI)	NE (NE, NE)	NE (NE, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	0.84 (0.59, 1.19)	
	p-value [3]	0.3204	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Frequent AE by SOC, PT (incidence >= 10% or >=10 patients and incidence >= 1%)
Safety Analysis Set

		EC+FOLFOX (N=232)	Control 1 (N=229)
SOC: General disorders and administration site conditions, PT: Malaise	Number of subjects with events, n (%)	20 (8.6)	23 (10.0)
	Number of censored subjects, n (%)	212 (91.4)	206 (90.0)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Median (95% CI)	NE (NE, NE)	NE (NE, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	0.75 (0.41, 1.37)	
	p-value [3]	0.3439	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.

		EC+FOLFOX (N=232)	Control 1 (N=229)
SOC: General disorders and administration site conditions, PT: Mucosal inflammation	Number of subjects with events, n (%)	34 (14.7)	24 (10.5)
	Number of censored subjects, n (%)	198 (85.3)	205 (89.5)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Median (95% CI)	NE (NE, NE)	NE (NE, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	1.29 (0.77, 2.18)	
	p-value [3]	0.3369	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.

		EC+FOLFOX (N=232)	Control 1 (N=229)
SOC: General disorders and administration site conditions, PT: Oedema peripheral	Number of subjects with events, n (%)	16 (6.9)	9 (3.9)
	Number of censored subjects, n (%)	216 (93.1)	220 (96.1)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Median (95% CI)	NE (NE, NE)	NE (NE, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	1.21 (0.53, 2.79)	
	p-value [3]	0.6483	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.

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Frequent AE by SOC, PT (incidence >= 10% or >=10 patients and incidence >= 1%)
Safety Analysis Set

		EC+FOLFOX (N=232)	Control 1 (N=229)
SOC: General disorders and administration site conditions, PT: Pain	Number of subjects with events, n (%)	19 (8.2)	5 (2.2)
	Number of censored subjects, n (%)	213 (91.8)	224 (97.8)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Median (95% CI)	NE (NE, NE)	NE (NE, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	2.77 (1.02, 7.53)	
	p-value [3]	0.0378	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.

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Encorafenib (PF-07263896) Protocol C4221015
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Datacut: 06JAN2025
Frequent AE by SOC, PT (incidence >= 10% or >=10 patients and incidence >= 1%)
Safety Analysis Set

		EC+FOLFOX (N=232)	Control 1 (N=229)
SOC: General disorders and administration site conditions, PT: Pyrexia	Number of subjects with events, n (%)	67 (28.9)	36 (15.7)
	Number of censored subjects, n (%)	165 (71.1)	193 (84.3)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	7.5 (4.1, 15.5)	NE (9.5, NE)
	Median (95% CI)	NE (26.7, NE)	NE (NE, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	1.58 (1.05, 2.38)	
	p-value [3]	0.0263	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.

		EC+FOLFOX (N=232)	Control 1 (N=229)
SOC: Hepatobiliary disorders	Number of subjects with events, n (%)	17 (7.3)	13 (5.7)
	Number of censored subjects, n (%)	215 (92.7)	216 (94.3)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	NE (NE, NE)	24.6 (24.6, NE)
	Median (95% CI)	NE (NE, NE)	NE (24.6, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	0.96 (0.46, 2.01)	
	p-value [3]	0.9197	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.

		EC+FOLFOX (N=232)	Control 1 (N=229)
SOC: Immune system disorders	Number of subjects with events, n (%)	25 (10.8)	15 (6.6)
	Number of censored subjects, n (%)	207 (89.2)	214 (93.4)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	29.9 (25.3, NE)	NE (NE, NE)
	Median (95% CI)	NE (29.9, NE)	NE (NE, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	1.24 (0.65, 2.38)	
	p-value [3]	0.5123	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.

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Frequent AE by SOC, PT (incidence >= 10% or >=10 patients and incidence >= 1%)
Safety Analysis Set

		EC+FOLFOX (N=232)	Control 1 (N=229)
SOC: Immune system disorders, PT: Drug hypersensitivity	Number of subjects with events, n (%)	11 (4.7)	3 (1.3)
	Number of censored subjects, n (%)	221 (95.3)	226 (98.7)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	NE (29.9, NE)	NE (NE, NE)
	Median (95% CI)	NE (NE, NE)	NE (NE, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	2.53 (0.69, 9.23)	
	p-value [3]	0.1457	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.

		EC+FOLFOX (N=232)	Control 1 (N=229)
SOC: Infections and infestations	Number of subjects with events, n (%)	123 (53.0)	98 (42.8)
	Number of censored subjects, n (%)	109 (47.0)	131 (57.2)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	2.7 (2.1, 3.7)	3.4 (2.8, 4.1)
	Median (95% CI)	9.5 (7.4, 14.1)	8.5 (7.4, 9.4)
	75%-ile (95% CI)	NE (19.8, NE)	17.7 (10.2, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	0.90 (0.69, 1.18)	
	p-value [3]	0.4553	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.

		EC+FOLFOX (N=232)	Control 1 (N=229)
SOC: Infections and infestations, PT: COVID-19	Number of subjects with events, n (%)	34 (14.7)	28 (12.2)
	Number of censored subjects, n (%)	198 (85.3)	201 (87.8)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	26.2 (23.2, NE)	16.1 (10.3, NE)
	Median (95% CI)	NE (NE, NE)	NE (16.7, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	0.76 (0.45, 1.26)	
	p-value [3]	0.2851	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.

		EC+FOLFOX (N=232)	Control 1 (N=229)
SOC: Infections and infestations, PT: Nasopharyngitis	Number of subjects with events, n (%)	12 (5.2)	8 (3.5)
	Number of censored subjects, n (%)	220 (94.8)	221 (96.5)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	NE (NE, NE)	NE (18.8, NE)
	Median (95% CI)	NE (NE, NE)	NE (NE, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	0.94 (0.38, 2.35)	
	p-value [3]	0.8946	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.

		EC+FOLFOX (N=232)	Control 1 (N=229)
SOC: Infections and infestations, PT: Paronychia	Number of subjects with events, n (%)	20 (8.6)	5 (2.2)
	Number of censored subjects, n (%)	212 (91.4)	224 (97.8)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	NE (22.7, NE)	NE (NE, NE)
	Median (95% CI)	NE (NE, NE)	NE (NE, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	2.46 (0.91, 6.68)	
	p-value [3]	0.0678	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.

		EC+FOLFOX (N=232)	Control 1 (N=229)
SOC: Infections and infestations, PT: Upper respiratory tract infection	Number of subjects with events, n (%)	16 (6.9)	19 (8.3)
	Number of censored subjects, n (%)	216 (93.1)	210 (91.7)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	NE (NE, NE)	NE (14.0, NE)
	Median (95% CI)	NE (NE, NE)	NE (NE, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	0.52 (0.26, 1.02)	
	p-value [3]	0.0548	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.

		EC+FOLFOX (N=232)	Control 1 (N=229)
SOC: Infections and infestations, PT: Urinary tract infection	Number of subjects with events, n (%)	23 (9.9)	16 (7.0)
	Number of censored subjects, n (%)	209 (90.1)	213 (93.0)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	26.5 (25.4, NE)	24.7 (17.7, NE)
	Median (95% CI)	NE (30.0, NE)	NE (24.7, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	0.84 (0.44, 1.64)	
	p-value [3]	0.6177	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.

		EC+FOLFOX (N=232)	Control 1 (N=229)
SOC: Injury, poisoning and procedural complications	Number of subjects with events, n (%)	45 (19.4)	29 (12.7)
	Number of censored subjects, n (%)	187 (80.6)	200 (87.3)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	22.9 (12.0, NE)	NE (11.1, NE)
	Median (95% CI)	NE (NE, NE)	NE (NE, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	1.11 (0.69, 1.79)	
	p-value [3]	0.6574	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.

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Frequent AE by SOC, PT (incidence >= 10% or >=10 patients and incidence >= 1%)
Safety Analysis Set

		EC+FOLFOX (N=232)	Control 1 (N=229)
SOC: Injury, poisoning and procedural complications, PT: Fall	Number of subjects with events, n (%)	11 (4.7)	4 (1.7)
	Number of censored subjects, n (%)	221 (95.3)	225 (98.3)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	NE (29.8, NE)	NE (NE, NE)
	Median (95% CI)	NE (NE, NE)	NE (NE, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	2.00 (0.63, 6.37)	
	p-value [3]	0.2336	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.

		EC+FOLFOX (N=232)	Control 1 (N=229)
SOC: Injury, poisoning and procedural complications, PT: Infusion related reaction	Number of subjects with events, n (%)	16 (6.9)	10 (4.4)
	Number of censored subjects, n (%)	216 (93.1)	219 (95.6)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Median (95% CI)	NE (NE, NE)	NE (NE, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	1.34 (0.60, 2.96)	
	p-value [3]	0.4692	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.

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Datacut: 06JAN2025
Frequent AE by SOC, PT (incidence >= 10% or >=10 patients and incidence >= 1%)
Safety Analysis Set

		EC+FOLFOX (N=232)	Control 1 (N=229)
SOC: Investigations	Number of subjects with events, n (%)	164 (70.7)	138 (60.3)
	Number of censored subjects, n (%)	68 (29.3)	91 (39.7)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	0.5 (0.5, 0.5)	1.0 (0.6, 1.3)
	Median (95% CI)	1.4 (0.9, 2.4)	2.8 (2.1, 3.7)
	75%-ile (95% CI)	18.9 (6.2, NE)	21.8 (7.9, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	1.28 (1.02, 1.61)	
	p-value [3]	0.0363	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.

		EC+FOLFOX (N=232)	Control 1 (N=229)
SOC: Investigations, PT: Alanine aminotransferase increased	Number of subjects with events, n (%)	29 (12.5)	28 (12.2)
	Number of censored subjects, n (%)	203 (87.5)	201 (87.8)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Median (95% CI)	NE (NE, NE)	NE (NE, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	0.91 (0.54, 1.54)	
	p-value [3]	0.7290	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.

		EC+FOLFOX (N=232)	Control 1 (N=229)
SOC: Investigations, PT: Aspartate aminotransferase increased	Number of subjects with events, n (%)	31 (13.4)	33 (14.4)
	Number of censored subjects, n (%)	201 (86.6)	196 (85.6)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	NE (NE, NE)	NE (9.4, NE)
	Median (95% CI)	NE (NE, NE)	NE (NE, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	0.81 (0.50, 1.33)	
	p-value [3]	0.4060	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.

		EC+FOLFOX (N=232)	Control 1 (N=229)
SOC: Investigations, PT: Blood alkaline phosphatase increased	Number of subjects with events, n (%)	16 (6.9)	11 (4.8)
	Number of censored subjects, n (%)	216 (93.1)	218 (95.2)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Median (95% CI)	NE (NE, NE)	NE (NE, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	1.14 (0.53, 2.47)	
	p-value [3]	0.7404	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.

		EC+FOLFOX (N=232)	Control 1 (N=229)
SOC: Investigations, PT: Blood bilirubin increased	Number of subjects with events, n (%)	9 (3.9)	10 (4.4)
	Number of censored subjects, n (%)	223 (96.1)	219 (95.6)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Median (95% CI)	NE (NE, NE)	NE (NE, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	0.73 (0.30, 1.81)	
	p-value [3]	0.4973	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.

		EC+FOLFOX (N=232)	Control 1 (N=229)
SOC: Investigations, PT: Electrocardiogram QT prolonged	Number of subjects with events, n (%)	11 (4.7)	1 (0.4)
	Number of censored subjects, n (%)	221 (95.3)	228 (99.6)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Median (95% CI)	NE (NE, NE)	NE (NE, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	9.73 (1.25, 75.40)	
	p-value [3]	0.0075	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.

		EC+FOLFOX (N=232)	Control 1 (N=229)
SOC: Investigations, PT: Lipase increased	Number of subjects with events, n (%)	52 (22.4)	27 (11.8)
	Number of censored subjects, n (%)	180 (77.6)	202 (88.2)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	NE (3.4, NE)	NE (NE, NE)
	Median (95% CI)	NE (NE, NE)	NE (NE, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	1.86 (1.17, 2.97)	
	p-value [3]	0.0077	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.

		EC+FOLFOX (N=232)	Control 1 (N=229)
SOC: Investigations, PT: Lymphocyte count decreased	Number of subjects with events, n (%)	11 (4.7)	6 (2.6)
	Number of censored subjects, n (%)	221 (95.3)	223 (97.4)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Median (95% CI)	NE (NE, NE)	NE (NE, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	1.63 (0.60, 4.43)	
	p-value [3]	0.3351	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.

		EC+FOLFOX (N=232)	Control 1 (N=229)
SOC: Investigations, PT: Neutrophil count decreased	Number of subjects with events, n (%)	79 (34.1)	67 (29.3)
	Number of censored subjects, n (%)	153 (65.9)	162 (70.7)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	1.8 (0.6, 4.8)	2.8 (1.8, 6.9)
	Median (95% CI)	NE (NE, NE)	NE (21.8, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	1.14 (0.82, 1.58)	
	p-value [3]	0.4528	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.

		EC+FOLFOX (N=232)	Control 1 (N=229)
SOC: Investigations, PT: Platelet count decreased	Number of subjects with events, n (%)	53 (22.8)	32 (14.0)
	Number of censored subjects, n (%)	179 (77.2)	197 (86.0)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	25.5 (4.0, NE)	25.8 (25.8, NE)
	Median (95% CI)	NE (NE, NE)	NE (25.8, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (25.8, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	1.48 (0.95, 2.29)	
	p-value [3]	0.0818	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.

		EC+FOLFOX (N=232)	Control 1 (N=229)
SOC: Investigations, PT: Weight decreased	Number of subjects with events, n (%)	44 (19.0)	22 (9.6)
	Number of censored subjects, n (%)	188 (81.0)	207 (90.4)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	NE (9.4, NE)	NE (19.5, NE)
	Median (95% CI)	NE (NE, NE)	NE (NE, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	1.78 (1.07, 2.99)	
	p-value [3]	0.0256	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.

		EC+FOLFOX (N=232)	Control 1 (N=229)
SOC: Investigations, PT: White blood cell count decreased	Number of subjects with events, n (%)	43 (18.5)	32 (14.0)
	Number of censored subjects, n (%)	189 (81.5)	197 (86.0)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Median (95% CI)	NE (NE, NE)	NE (NE, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	1.30 (0.82, 2.06)	
	p-value [3]	0.2595	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.

		EC+FOLFOX (N=232)	Control 1 (N=229)
SOC: Metabolism and nutrition disorders	Number of subjects with events, n (%)	144 (62.1)	99 (43.2)
	Number of censored subjects, n (%)	88 (37.9)	130 (56.8)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	0.5 (0.4, 0.7)	1.0 (0.6, 1.9)
	Median (95% CI)	3.4 (2.1, 4.8)	13.9 (6.9, NE)
	75%-ile (95% CI)	24.3 (22.3, NE)	NE (17.4, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	1.48 (1.15, 1.92)	
	p-value [3]	0.0026	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.

		EC+FOLFOX (N=232)	Control 1 (N=229)
SOC: Metabolism and nutrition disorders, PT: Decreased appetite	Number of subjects with events, n (%)	87 (37.5)	62 (27.1)
	Number of censored subjects, n (%)	145 (62.5)	167 (72.9)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	1.1 (0.5, 3.7)	3.5 (1.6, NE)
	Median (95% CI)	24.3 (22.3, NE)	NE (NE, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	1.32 (0.95, 1.84)	
	p-value [3]	0.0948	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.

		EC+FOLFOX (N=232)	Control 1 (N=229)
SOC: Metabolism and nutrition disorders, PT: Hyperglycaemia	Number of subjects with events, n (%)	20 (8.6)	4 (1.7)
	Number of censored subjects, n (%)	212 (91.4)	225 (98.3)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Median (95% CI)	NE (NE, NE)	NE (NE, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	4.10 (1.39, 12.07)	
	p-value [3]	0.0057	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.

		EC+FOLFOX (N=232)	Control 1 (N=229)
SOC: Metabolism and nutrition disorders, PT: Hypoalbuminaemia	Number of subjects with events, n (%)	30 (12.9)	14 (6.1)
	Number of censored subjects, n (%)	202 (87.1)	215 (93.9)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Median (95% CI)	NE (NE, NE)	NE (NE, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	1.93 (1.02, 3.64)	
	p-value [3]	0.0392	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.

		EC+FOLFOX (N=232)	Control 1 (N=229)
SOC: Metabolism and nutrition disorders, PT: Hypocalcaemia	Number of subjects with events, n (%)	11 (4.7)	7 (3.1)
	Number of censored subjects, n (%)	221 (95.3)	222 (96.9)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Median (95% CI)	NE (NE, NE)	NE (NE, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	1.31 (0.50, 3.40)	
	p-value [3]	0.5821	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.

		EC+FOLFOX (N=232)	Control 1 (N=229)
SOC: Metabolism and nutrition disorders, PT: Hypokalaemia	Number of subjects with events, n (%)	41 (17.7)	26 (11.4)
	Number of censored subjects, n (%)	191 (82.3)	203 (88.6)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	NE (16.8, NE)	NE (NE, NE)
	Median (95% CI)	NE (NE, NE)	NE (NE, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	1.34 (0.81, 2.19)	
	p-value [3]	0.2505	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.

		EC+FOLFOX (N=232)	Control 1 (N=229)
SOC: Metabolism and nutrition disorders, PT: Hypomagnesaemia	Number of subjects with events, n (%)	38 (16.4)	11 (4.8)
	Number of censored subjects, n (%)	194 (83.6)	218 (95.2)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	NE (20.7, NE)	NE (NE, NE)
	Median (95% CI)	NE (NE, NE)	NE (NE, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	2.82 (1.43, 5.54)	
	p-value [3]	0.0017	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.

		EC+FOLFOX (N=232)	Control 1 (N=229)
SOC: Metabolism and nutrition disorders, PT: Hyponatraemia	Number of subjects with events, n (%)	11 (4.7)	11 (4.8)
	Number of censored subjects, n (%)	221 (95.3)	218 (95.2)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Median (95% CI)	NE (NE, NE)	NE (NE, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	0.87 (0.38, 2.01)	
	p-value [3]	0.7450	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.

		EC+FOLFOX (N=232)	Control 1 (N=229)
SOC: Metabolism and nutrition disorders, PT: Hypophosphataemia	Number of subjects with events, n (%)	14 (6.0)	3 (1.3)
	Number of censored subjects, n (%)	218 (94.0)	226 (98.7)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Median (95% CI)	NE (NE, NE)	NE (NE, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	4.08 (1.17, 14.24)	
	p-value [3]	0.0171	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.

		EC+FOLFOX (N=232)	Control 1 (N=229)
SOC: Musculoskeletal and connective tissue disorders	Number of subjects with events, n (%)	133 (57.3)	50 (21.8)
	Number of censored subjects, n (%)	99 (42.7)	179 (78.2)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	2.6 (1.8, 3.3)	10.6 (5.3, NE)
	Median (95% CI)	8.6 (6.6, 11.3)	NE (17.2, NE)
	75%-ile (95% CI)	NE (16.5, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	2.37 (1.71, 3.29)	
	p-value [3]	<.0001	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.

		EC+FOLFOX (N=232)	Control 1 (N=229)
SOC: Musculoskeletal and connective tissue disorders, PT: Arthralgia	Number of subjects with events, n (%)	73 (31.5)	12 (5.2)
	Number of censored subjects, n (%)	159 (68.5)	217 (94.8)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	8.5 (6.4, 11.3)	NE (20.8, NE)
	Median (95% CI)	NE (18.9, NE)	NE (NE, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	4.67 (2.52, 8.62)	
	p-value [3]	<.0001	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.

		EC+FOLFOX (N=232)	Control 1 (N=229)
SOC: Musculoskeletal and connective tissue disorders, PT: Back pain	Number of subjects with events, n (%)	24 (10.3)	16 (7.0)
	Number of censored subjects, n (%)	208 (89.7)	213 (93.0)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	NE (27.2, NE)	NE (17.2, NE)
	Median (95% CI)	NE (NE, NE)	NE (NE, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	1.01 (0.53, 1.93)	
	p-value [3]	0.9766	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Frequent AE by SOC, PT (incidence >= 10% or >=10 patients and incidence >= 1%)
Safety Analysis Set

		EC+FOLFOX (N=232)	Control 1 (N=229)
SOC: Musculoskeletal and connective tissue disorders, PT: Myalgia	Number of subjects with events, n (%)	38 (16.4)	9 (3.9)
	Number of censored subjects, n (%)	194 (83.6)	220 (96.1)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	NE (13.1, NE)	NE (NE, NE)
	Median (95% CI)	NE (NE, NE)	NE (NE, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	3.25 (1.56, 6.76)	
	p-value [3]	0.0009	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.

		EC+FOLFOX (N=232)	Control 1 (N=229)
SOC: Musculoskeletal and connective tissue disorders, PT: Pain in extremity	Number of subjects with events, n (%)	21 (9.1)	8 (3.5)
	Number of censored subjects, n (%)	211 (90.9)	221 (96.5)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Median (95% CI)	NE (NE, NE)	NE (NE, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	1.88 (0.82, 4.31)	
	p-value [3]	0.1289	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.

		EC+FOLFOX (N=232)	Control 1 (N=229)
SOC: Neoplasms benign, malignant and unspecified (incl cysts and polyps)	Number of subjects with events, n (%)	43 (18.5)	9 (3.9)
	Number of censored subjects, n (%)	189 (81.5)	220 (96.1)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	NE (12.9, NE)	NE (NE, NE)
	Median (95% CI)	NE (NE, NE)	NE (NE, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	4.08 (1.98, 8.40)	
	p-value [3]	<.0001	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.

		EC+FOLFOX (N=232)	Control 1 (N=229)
SOC: Neoplasms benign, malignant and unspecified (incl cysts and polyps), PT: Melanocytic naevus	Number of subjects with events, n (%)	13 (5.6)	0 (0.0)
	Number of censored subjects, n (%)	219 (94.4)	229 (100.0)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Median (95% CI)	NE (NE, NE)	NE (NE, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	NE	
	p-value [3]		

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.

		EC+FOLFOX (N=232)	Control 1 (N=229)
SOC: Nervous system disorders	Number of subjects with events, n (%)	191 (82.3)	165 (72.1)
	Number of censored subjects, n (%)	41 (17.7)	64 (27.9)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	0.4 (0.2, 0.5)	0.4 (0.1, 0.5)
	Median (95% CI)	1.4 (1.1, 1.8)	1.8 (1.0, 2.3)
	75%-ile (95% CI)	4.6 (3.4, 5.5)	5.7 (4.1, 6.5)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	1.13 (0.92, 1.39)	
	p-value [3]	0.2349	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.

		EC+FOLFOX (N=232)	Control 1 (N=229)
SOC: Nervous system disorders, PT: Dizziness	Number of subjects with events, n (%)	23 (9.9)	21 (9.2)
	Number of censored subjects, n (%)	209 (90.1)	208 (90.8)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	29.2 (29.2, NE)	NE (NE, NE)
	Median (95% CI)	NE (NE, NE)	NE (NE, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	0.91 (0.50, 1.66)	
	p-value [3]	0.7657	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.

		EC+FOLFOX (N=232)	Control 1 (N=229)
SOC: Nervous system disorders, PT: Dysgeusia	Number of subjects with events, n (%)	35 (15.1)	32 (14.0)
	Number of censored subjects, n (%)	197 (84.9)	197 (86.0)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	NE (NE, NE)	NE (17.4, NE)
	Median (95% CI)	NE (NE, NE)	NE (NE, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	0.93 (0.58, 1.51)	
	p-value [3]	0.7830	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.

		EC+FOLFOX (N=232)	Control 1 (N=229)
SOC: Nervous system disorders, PT: Headache	Number of subjects with events, n (%)	35 (15.1)	20 (8.7)
	Number of censored subjects, n (%)	197 (84.9)	209 (91.3)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	NE (NE, NE)	NE (14.9, NE)
	Median (95% CI)	NE (NE, NE)	NE (NE, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	1.53 (0.88, 2.68)	
	p-value [3]	0.1313	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Frequent AE by SOC, PT (incidence >= 10% or >=10 patients and incidence >= 1%)
Safety Analysis Set

		EC+FOLFOX (N=232)	Control 1 (N=229)
SOC: Nervous system disorders, PT: Neuropathy peripheral	Number of subjects with events, n (%)	64 (27.6)	54 (23.6)
	Number of censored subjects, n (%)	168 (72.4)	175 (76.4)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	5.7 (4.7, NE)	6.3 (3.3, NE)
	Median (95% CI)	NE (NE, NE)	NE (NE, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	0.99 (0.68, 1.42)	
	p-value [3]	0.9429	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.

		EC+FOLFOX (N=232)	Control 1 (N=229)
SOC: Nervous system disorders, PT: Neurotoxicity	Number of subjects with events, n (%)	26 (11.2)	19 (8.3)
	Number of censored subjects, n (%)	206 (88.8)	210 (91.7)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Median (95% CI)	NE (NE, NE)	NE (NE, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	1.31 (0.72, 2.36)	
	p-value [3]	0.3767	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.

		EC+FOLFOX (N=232)	Control 1 (N=229)
SOC: Nervous system disorders, PT: Paraesthesia	Number of subjects with events, n (%)	34 (14.7)	19 (8.3)
	Number of censored subjects, n (%)	198 (85.3)	210 (91.7)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	NE (23.0, NE)	NE (NE, NE)
	Median (95% CI)	NE (NE, NE)	NE (NE, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	1.53 (0.87, 2.70)	
	p-value [3]	0.1341	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Frequent AE by SOC, PT (incidence >= 10% or >=10 patients and incidence >= 1%)
Safety Analysis Set

		EC+FOLFOX (N=232)	Control 1 (N=229)
SOC: Nervous system disorders, PT: Peripheral sensory neuropathy	Number of subjects with events, n (%)	62 (26.7)	54 (23.6)
	Number of censored subjects, n (%)	170 (73.3)	175 (76.4)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	5.1 (3.2, NE)	5.2 (4.1, NE)
	Median (95% CI)	NE (NE, NE)	NE (NE, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	1.01 (0.70, 1.45)	
	p-value [3]	0.9718	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.

		EC+FOLFOX (N=232)	Control 1 (N=229)
SOC: Psychiatric disorders	Number of subjects with events, n (%)	43 (18.5)	38 (16.6)
	Number of censored subjects, n (%)	189 (81.5)	191 (83.4)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	NE (15.4, NE)	16.3 (12.3, NE)
	Median (95% CI)	NE (NE, NE)	NE (NE, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	0.90 (0.58, 1.40)	
	p-value [3]	0.6437	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.

		EC+FOLFOX (N=232)	Control 1 (N=229)
SOC: Psychiatric disorders, PT: Insomnia	Number of subjects with events, n (%)	29 (12.5)	17 (7.4)
	Number of censored subjects, n (%)	203 (87.5)	212 (92.6)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Median (95% CI)	NE (NE, NE)	NE (NE, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	1.36 (0.74, 2.49)	
	p-value [3]	0.3186	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.

		EC+FOLFOX (N=232)	Control 1 (N=229)
SOC: Renal and urinary disorders	Number of subjects with events, n (%)	43 (18.5)	31 (13.5)
	Number of censored subjects, n (%)	189 (81.5)	198 (86.5)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	21.6 (16.3, NE)	13.3 (10.2, NE)
	Median (95% CI)	NE (NE, NE)	NE (NE, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	1.03 (0.64, 1.65)	
	p-value [3]	0.8991	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.

		EC+FOLFOX (N=232)	Control 1 (N=229)
SOC: Renal and urinary disorders, PT: Haematuria	Number of subjects with events, n (%)	10 (4.3)	4 (1.7)
	Number of censored subjects, n (%)	222 (95.7)	225 (98.3)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Median (95% CI)	NE (NE, NE)	NE (NE, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	1.82 (0.56, 5.90)	
	p-value [3]	0.3115	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.

		EC+FOLFOX (N=232)	Control 1 (N=229)
SOC: Renal and urinary disorders, PT: Proteinuria	Number of subjects with events, n (%)	6 (2.6)	18 (7.9)
	Number of censored subjects, n (%)	226 (97.4)	211 (92.1)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	NE (NE, NE)	18.0 (16.8, NE)
	Median (95% CI)	NE (NE, NE)	NE (18.0, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	0.18 (0.07, 0.47)	
	p-value [3]	0.0001	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.

		EC+FOLFOX (N=232)	Control 1 (N=229)
SOC: Reproductive system and breast disorders	Number of subjects with events, n (%)	21 (9.1)	10 (4.4)
	Number of censored subjects, n (%)	211 (90.9)	219 (95.6)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	NE (NE, NE)	32.2 (NE, NE)
	Median (95% CI)	NE (NE, NE)	32.2 (NE, NE)
	75%-ile (95% CI)	NE (NE, NE)	32.2 (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	1.39 (0.65, 2.99)	
	p-value [3]	0.3987	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.

		EC+FOLFOX (N=232)	Control 1 (N=229)
SOC: Respiratory, thoracic and mediastinal disorders	Number of subjects with events, n (%)	112 (48.3)	89 (38.9)
	Number of censored subjects, n (%)	120 (51.7)	140 (61.1)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	2.3 (1.5, 3.2)	1.8 (1.2, 2.8)
	Median (95% CI)	12.6 (7.3, NE)	12.2 (8.3, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	1.01 (0.76, 1.34)	
	p-value [3]	0.9512	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.

		EC+FOLFOX (N=232)	Control 1 (N=229)
SOC: Respiratory, thoracic and mediastinal disorders, PT: Cough	Number of subjects with events, n (%)	24 (10.3)	12 (5.2)
	Number of censored subjects, n (%)	208 (89.7)	217 (94.8)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	34.9 (34.9, NE)	NE (NE, NE)
	Median (95% CI)	NE (34.9, NE)	NE (NE, NE)
	75%-ile (95% CI)	NE (34.9, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	1.55 (0.77, 3.12)	
	p-value [3]	0.2193	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Frequent AE by SOC, PT (incidence >= 10% or >=10 patients and incidence >= 1%)
Safety Analysis Set

		EC+FOLFOX (N=232)	Control 1 (N=229)
SOC: Respiratory, thoracic and mediastinal disorders, PT: Dysphonia	Number of subjects with events, n (%)	8 (3.4)	11 (4.8)
	Number of censored subjects, n (%)	224 (96.6)	218 (95.2)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Median (95% CI)	NE (NE, NE)	NE (NE, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	0.59 (0.23, 1.49)	
	p-value [3]	0.2547	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.

		EC+FOLFOX (N=232)	Control 1 (N=229)
SOC: Respiratory, thoracic and mediastinal disorders, PT: Dyspnoea	Number of subjects with events, n (%)	23 (9.9)	19 (8.3)
	Number of censored subjects, n (%)	209 (90.1)	210 (91.7)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Median (95% CI)	NE (NE, NE)	NE (NE, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	0.92 (0.50, 1.71)	
	p-value [3]	0.8029	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Frequent AE by SOC, PT (incidence >= 10% or >=10 patients and incidence >= 1%)
Safety Analysis Set

		EC+FOLFOX (N=232)	Control 1 (N=229)
SOC: Respiratory, thoracic and mediastinal disorders, PT: Epistaxis	Number of subjects with events, n (%)	41 (17.7)	32 (14.0)
	Number of censored subjects, n (%)	191 (82.3)	197 (86.0)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	NE (14.0, NE)	NE (12.9, NE)
	Median (95% CI)	NE (NE, NE)	NE (NE, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	0.96 (0.60, 1.53)	
	p-value [3]	0.8551	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.

		EC+FOLFOX (N=232)	Control 1 (N=229)
SOC: Respiratory, thoracic and mediastinal disorders, PT: Hiccups	Number of subjects with events, n (%)	6 (2.6)	13 (5.7)
	Number of censored subjects, n (%)	226 (97.4)	216 (94.3)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Median (95% CI)	NE (NE, NE)	NE (NE, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	0.42 (0.16, 1.09)	
	p-value [3]	0.0671	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.

		EC+FOLFOX (N=232)	Control 1 (N=229)
SOC: Respiratory, thoracic and mediastinal disorders, PT: Pulmonary embolism	Number of subjects with events, n (%)	9 (3.9)	10 (4.4)
	Number of censored subjects, n (%)	223 (96.1)	219 (95.6)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Median (95% CI)	NE (NE, NE)	NE (NE, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	0.76 (0.31, 1.88)	
	p-value [3]	0.5490	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.

		EC+FOLFOX (N=232)	Control 1 (N=229)
SOC: Respiratory, thoracic and mediastinal disorders, PT: Rhinorrhoea	Number of subjects with events, n (%)	11 (4.7)	9 (3.9)
	Number of censored subjects, n (%)	221 (95.3)	220 (96.1)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	35.0 (35.0, NE)	NE (NE, NE)
	Median (95% CI)	NE (35.0, NE)	NE (NE, NE)
	75%-ile (95% CI)	NE (35.0, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	0.87 (0.36, 2.14)	
	p-value [3]	0.7674	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.

		EC+FOLFOX (N=232)	Control 1 (N=229)
SOC: Skin and subcutaneous tissue disorders	Number of subjects with events, n (%)	188 (81.0)	79 (34.5)
	Number of censored subjects, n (%)	44 (19.0)	150 (65.5)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	0.5 (0.4, 0.5)	2.7 (1.9, 3.9)
	Median (95% CI)	1.0 (0.9, 1.6)	34.3 (8.3, 34.3)
	75%-ile (95% CI)	4.2 (3.0, 8.1)	34.3 (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	3.56 (2.73, 4.65)	
	p-value [3]	<.0001	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.

		EC+FOLFOX (N=232)	Control 1 (N=229)
SOC: Skin and subcutaneous tissue disorders, PT: Alopecia	Number of subjects with events, n (%)	53 (22.8)	26 (11.4)
	Number of censored subjects, n (%)	179 (77.2)	203 (88.6)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	12.8 (4.6, NE)	NE (NE, NE)
	Median (95% CI)	NE (NE, NE)	NE (NE, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	1.86 (1.16, 2.97)	
	p-value [3]	0.0087	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.

		EC+FOLFOX (N=232)	Control 1 (N=229)
SOC: Skin and subcutaneous tissue disorders, PT: Dermatitis acneiform	Number of subjects with events, n (%)	43 (18.5)	2 (0.9)
	Number of censored subjects, n (%)	189 (81.5)	227 (99.1)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	NE (15.5, NE)	NE (NE, NE)
	Median (95% CI)	NE (NE, NE)	NE (NE, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	19.53 (4.73, 80.73)	
	p-value [3]	<.0001	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.

		EC+FOLFOX (N=232)	Control 1 (N=229)
SOC: Skin and subcutaneous tissue disorders, PT: Dry skin	Number of subjects with events, n (%)	38 (16.4)	11 (4.8)
	Number of censored subjects, n (%)	194 (83.6)	218 (95.2)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	23.7 (18.6, NE)	NE (NE, NE)
	Median (95% CI)	NE (NE, NE)	NE (NE, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	2.72 (1.38, 5.36)	
	p-value [3]	0.0027	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.

		EC+FOLFOX (N=232)	Control 1 (N=229)
SOC: Skin and subcutaneous tissue disorders, PT: Nail disorder	Number of subjects with events, n (%)	10 (4.3)	0 (0.0)
	Number of censored subjects, n (%)	222 (95.7)	229 (100.0)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Median (95% CI)	NE (NE, NE)	NE (NE, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	NE	
	p-value [3]		

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.

		EC+FOLFOX (N=232)	Control 1 (N=229)
SOC: Skin and subcutaneous tissue disorders, PT: Palmar-plantar erythrodysaesthesia syndrome	Number of subjects with events, n (%)	37 (15.9)	23 (10.0)
	Number of censored subjects, n (%)	195 (84.1)	206 (90.0)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	NE (14.8, NE)	NE (NE, NE)
	Median (95% CI)	NE (NE, NE)	NE (NE, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	1.21 (0.72, 2.06)	
	p-value [3]	0.4693	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.

		EC+FOLFOX (N=232)	Control 1 (N=229)
SOC: Skin and subcutaneous tissue disorders, PT: Pigmentation disorder	Number of subjects with events, n (%)	17 (7.3)	2 (0.9)
	Number of censored subjects, n (%)	215 (92.7)	227 (99.1)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Median (95% CI)	NE (NE, NE)	NE (NE, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	8.65 (2.00, 37.45)	
	p-value [3]	0.0005	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.

		EC+FOLFOX (N=232)	Control 1 (N=229)
SOC: Skin and subcutaneous tissue disorders, PT: Pruritus	Number of subjects with events, n (%)	32 (13.8)	7 (3.1)
	Number of censored subjects, n (%)	200 (86.2)	222 (96.9)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	28.1 (21.9, NE)	NE (NE, NE)
	Median (95% CI)	NE (NE, NE)	NE (NE, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	3.41 (1.49, 7.79)	
	p-value [3]	0.0021	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.

		EC+FOLFOX (N=232)	Control 1 (N=229)
SOC: Skin and subcutaneous tissue disorders, PT: Rash	Number of subjects with events, n (%)	70 (30.2)	9 (3.9)
	Number of censored subjects, n (%)	162 (69.8)	220 (96.1)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	7.6 (3.3, 14.0)	NE (NE, NE)
	Median (95% CI)	NE (24.0, NE)	NE (NE, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	6.88 (3.42, 13.81)	
	p-value [3]	<.0001	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Frequent AE by SOC, PT (incidence >= 10% or >=10 patients and incidence >= 1%)
Safety Analysis Set

		EC+FOLFOX (N=232)	Control 1 (N=229)
SOC: Skin and subcutaneous tissue disorders, PT: Skin hyperpigmentation	Number of subjects with events, n (%)	43 (18.5)	7 (3.1)
	Number of censored subjects, n (%)	189 (81.5)	222 (96.9)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	NE (15.2, NE)	NE (NE, NE)
	Median (95% CI)	NE (NE, NE)	NE (NE, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	5.80 (2.60, 12.91)	
	p-value [3]	<.0001	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.

		EC+FOLFOX (N=232)	Control 1 (N=229)
SOC: Skin and subcutaneous tissue disorders, PT: Skin lesion	Number of subjects with events, n (%)	13 (5.6)	2 (0.9)
	Number of censored subjects, n (%)	219 (94.4)	227 (99.1)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Median (95% CI)	NE (NE, NE)	NE (NE, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	4.22 (0.94, 19.00)	
	p-value [3]	0.0424	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.

		EC+FOLFOX (N=232)	Control 1 (N=229)
SOC: Vascular disorders	Number of subjects with events, n (%)	36 (15.5)	51 (22.3)
	Number of censored subjects, n (%)	196 (84.5)	178 (77.7)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	NE (20.6, NE)	7.5 (3.9, NE)
	Median (95% CI)	NE (NE, NE)	27.9 (27.9, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (27.9, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	0.51 (0.33, 0.80)	
	p-value [3]	0.0024	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.

		EC+FOLFOX (N=232)	Control 1 (N=229)
SOC: Vascular disorders, PT: Hypertension	Number of subjects with events, n (%)	9 (3.9)	35 (15.3)
	Number of censored subjects, n (%)	223 (96.1)	194 (84.7)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	NE (NE, NE)	NE (10.4, NE)
	Median (95% CI)	NE (NE, NE)	NE (NE, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	0.19 (0.09, 0.39)	
	p-value [3]	<.0001	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.

		EC+FOLFOX (N=232)	Control 1 (N=229)
SOC: Vascular disorders, PT: Hypotension	Number of subjects with events, n (%)	11 (4.7)	3 (1.3)
	Number of censored subjects, n (%)	221 (95.3)	226 (98.7)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Median (95% CI)	NE (NE, NE)	NE (NE, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	2.92 (0.81, 10.54)	
	p-value [3]	0.0877	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Frequent AE by SOC, PT (incidence >= 10% or >=10 patients and incidence >= 1%) - Subgroup analysis
Safety Analysis Set

SOC/PT	Subgroup Level	EC+FOLFOX (N=232) n/ N (%)	EC+FOLFOX (N=232) Median (95% CI)[1]	Control 1 (N=229) n/ N (%)	Control 1 (N=229) Median (95% CI)[1]	Unstratified analysis Hazard Ratio (95% CI)[2]	Unstratified analysis p-Value[3]	Interaction p-Value[4]
SOC: Blood and lymphatic system disorders, PT: Anaemia	Age (Years)							0.7344
	< 65	64/ 148 (43.2)	15.6 (11.5, NE)	28/ 131 (21.4)	NE (NE , NE)	1.70 (1.08, 2.65)	0.0196	
	>= 65	43/ 84 (51.2)	7.5 (5.5, 16.3)	30/ 98 (30.6)	NE (11.0, NE)	1.53 (0.96, 2.44)	0.0733	
	Sex							0.1345
	Male	46/ 121 (38.0)	21.2 (12.5, NE)	28/ 112 (25.0)	NE (NE , NE)	1.22 (0.76, 1.96)	0.4049	
	Female	61/ 111 (55.0)	6.9 (5.1, 14.3)	30/ 117 (25.6)	NE (NE , NE)	1.98 (1.28, 3.07)	0.0019	
	Region							0.1918
	Europe	46/ 108 (42.6)	17.3 (10.4, NE)	17/ 103 (16.5)	NE (NE , NE)	2.15 (1.23, 3.76)	0.0061	
	USA/Canada	8/ 15 (53.3)	5.9 (1.3, NE)	9/ 17 (52.9)	11.8 (0.5, NE)	0.90 (0.35, 2.34)	0.8283	
	Rest of World	53/ 109 (48.6)	12.5 (5.8, NE)	32/ 109 (29.4)	NE (NE , NE)	1.47 (0.95, 2.29)	0.0851	
	ECOG-PS at Randomization							0.4041
	0	54/ 130 (41.5)	17.3 (11.5, NE)	25/ 130 (19.2)	NE (NE , NE)	1.81 (1.12, 2.92)	0.0134	
	1	53/ 102 (52.0)	7.6 (4.7, 12.6)	33/ 99 (33.3)	NE (11.0, NE)	1.37 (0.88, 2.12)	0.1564	
	Number of Organs Involved							0.1526
	<= 2	59/ 116 (50.9)	11.3 (6.7, 17.3)	27/ 119 (22.7)	NE (NE , NE)	1.96 (1.24, 3.09)	0.0034	
	>= 3	48/ 116 (41.4)	15.6 (6.9, NE)	31/ 110 (28.2)	NE (11.0, NE)	1.26 (0.80, 1.99)	0.3236	
	Presence of Liver Metastases							0.2849
	Yes	69/ 146 (47.3)	11.9 (6.3, NE)	43/ 149 (28.9)	NE (NE , NE)	1.41 (0.96, 2.07)	0.0771	
	No	38/ 86 (44.2)	16.3 (9.7, NE)	15/ 80 (18.8)	NE (NE , NE)	1.98 (1.08, 3.62)	0.0242	
	Side of Tumor							0.3582
	Left	39/ 88 (44.3)	14.9 (7.5, NE)	25/ 90 (27.8)	NE (NE , NE)	1.33 (0.80, 2.21)	0.2674	
	Right	68/ 144 (47.2)	12.6 (6.9, 21.2)	33/ 139 (23.7)	NE (NE , NE)	1.76 (1.16, 2.67)	0.0072	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
Subgroup analysis was done for SOCs / PTs with significant overall treatment effect (significant log-rank).
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.
[4] P-Value for interaction from Cox proportional hazards model using ties=exact option with treatment, subgroup and treatment*subgroup interaction as covariates.
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Frequent AE by SOC, PT (incidence >= 10% or >=10 patients and incidence >= 1%) - Subgroup analysis
Safety Analysis Set

SOC/PT	Subgroup Level	EC+FOLFOX (N=232) n/ N (%)	EC+FOLFOX (N=232) Median (95% CI)[1]	Control 1 (N=229) n/ N (%)	Control 1 (N=229) Median (95% CI)[1]	Unstratified analysis Hazard Ratio (95% CI)[2]	Unstratified analysis p-Value[3]	Interaction p-Value[4]
SOC: Ear and labyrinth disorders	Age (Years)							
	< 65	4/ 148 (2.7)		3/ 131 (2.3)				
	>= 65	1/ 84 (1.2)		7/ 98 (7.1)				
	Sex							
	Male	3/ 121 (2.5)		5/ 112 (4.5)				
	Female	2/ 111 (1.8)		5/ 117 (4.3)				
	Region							
	Europe	3/ 108 (2.8)		6/ 103 (5.8)				
	USA/Canada	0/ 15 (0.0)		0/ 17 (0.0)				
	Rest of World	2/ 109 (1.8)		4/ 109 (3.7)				
	ECOG-PS at Randomization							
	0	3/ 130 (2.3)		5/ 130 (3.8)				
	1	2/ 102 (2.0)		5/ 99 (5.1)				
	Number of Organs Involved							0.6498
	<= 2	3/ 116 (2.6)	NE (NE , NE)	7/ 119 (5.9)	27.6 (27.6, NE)	0.19 (0.05, 0.79)	0.0135	
	>= 3	2/ 116 (1.7)	NE (NE , NE)	3/ 110 (2.7)	NE (NE , NE)	0.58 (0.10, 3.47)	0.5448	
	Presence of Liver Metastases							
	Yes	3/ 146 (2.1)		6/ 149 (4.0)				
	No	2/ 86 (2.3)		4/ 80 (5.0)				
	Side of Tumor							0.4881
	Left	2/ 88 (2.3)	NE (NE , NE)	2/ 90 (2.2)	NE (NE , NE)	0.62 (0.08, 4.88)	0.6452	
	Right	3/ 144 (2.1)	NE (NE , NE)	8/ 139 (5.8)	27.6 (27.6, NE)	0.22 (0.06, 0.86)	0.0185	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
Subgroup analysis was done for SOCs / PTs with significant overall treatment effect (significant log-rank).
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.
[4] P-Value for interaction from Cox proportional hazards model using ties=exact option with treatment, subgroup and treatment*subgroup interaction as covariates.
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Frequent AE by SOC, PT (incidence >= 10% or >=10 patients and incidence >= 1%) - Subgroup analysis
Safety Analysis Set

SOC/PT	Subgroup Level	EC+FOLFOX (N=232) n/ N (%)	EC+FOLFOX (N=232) Median (95% CI)[1]	Control 1 (N=229) n/ N (%)	Control 1 (N=229) Median (95% CI)[1]	Unstratified analysis Hazard Ratio (95% CI)[2]	Unstratified analysis p-Value[3]	Interaction p-Value[4]
SOC: Eye disorders	Age (Years)							0.5515
	< 65	19/ 148 (12.8)	NE (NE , NE)	5/ 131 (3.8)	NE (NE , NE)	2.71 (1.01, 7.31)	0.0403	
	>= 65	15/ 84 (17.9)	NE (22.7, NE)	8/ 98 (8.2)	30.2 (NE , NE)	1.64 (0.69, 3.90)	0.2607	
	Sex							0.9785
	Male	14/ 121 (11.6)	NE (NE , NE)	5/ 112 (4.5)	30.2 (NE , NE)	1.73 (0.61, 4.91)	0.2970	
	Female	20/ 111 (18.0)	NE (NE , NE)	8/ 117 (6.8)	NE (NE , NE)	2.18 (0.96, 4.96)	0.0576	
	Region							0.5718
	Europe	20/ 108 (18.5)	NE (NE , NE)	8/ 103 (7.8)	NE (NE , NE)	1.83 (0.80, 4.19)	0.1477	
	USA/Canada	0/ 15 (0.0)	NE (NE , NE)	2/ 17 (11.8)	NE (NE , NE)	NE		
	Rest of World	14/ 109 (12.8)	NE (NE , NE)	3/ 109 (2.8)	30.2 (30.2, NE)	3.55 (1.01, 12.48)	0.0352	
	ECOG-PS at Randomization							0.8512
	0	22/ 130 (16.9)	NE (NE , NE)	8/ 130 (6.2)	30.2 (30.2, NE)	2.04 (0.90, 4.63)	0.0821	
	1	12/ 102 (11.8)	NE (NE , NE)	5/ 99 (5.1)	NE (NE , NE)	1.86 (0.65, 5.32)	0.2393	
	Number of Organs Involved							0.9384
	<= 2	21/ 116 (18.1)	NE (NE , NE)	8/ 119 (6.7)	30.2 (30.2, NE)	1.87 (0.82, 4.28)	0.1325	
	>= 3	13/ 116 (11.2)	NE (NE , NE)	5/ 110 (4.5)	NE (NE , NE)	2.14 (0.76, 6.01)	0.1411	
	Presence of Liver Metastases							0.6937
	Yes	18/ 146 (12.3)	NE (NE , NE)	8/ 149 (5.4)	30.2 (NE , NE)	1.85 (0.80, 4.28)	0.1469	
	No	16/ 86 (18.6)	NE (NE , NE)	5/ 80 (6.3)	NE (NE , NE)	2.09 (0.75, 5.82)	0.1493	
	Side of Tumor							0.3865
	Left	9/ 88 (10.2)	NE (NE , NE)	5/ 90 (5.6)	NE (NE , NE)	1.27 (0.41, 3.89)	0.6748	
	Right	25/ 144 (17.4)	NE (NE , NE)	8/ 139 (5.8)	30.2 (30.2, NE)	2.42 (1.09, 5.40)	0.0256	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
Subgroup analysis was done for SOCs / PTs with significant overall treatment effect (significant log-rank).
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.
[4] P-Value for interaction from Cox proportional hazards model using ties=exact option with treatment, subgroup and treatment*subgroup interaction as covariates.
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Frequent AE by SOC, PT (incidence >= 10% or >=10 patients and incidence >= 1%) - Subgroup analysis
Safety Analysis Set

SOC/PT	Subgroup Level	EC+FOLFOX (N=232) n/ N (%)	EC+FOLFOX (N=232) Median (95% CI)[1]	Control 1 (N=229) n/ N (%)	Control 1 (N=229) Median (95% CI)[1]	Unstratified analysis Hazard Ratio (95% CI)[2]	Unstratified analysis p-Value[3]	Interaction p-Value[4]
SOC: Gastrointestinal disorders, PT: Abdominal pain	Age (Years)							0.7507
	< 65	34/ 148 (23.0)	NE (NE , NE)	34/ 131 (26.0)	23.2 (23.2, NE)	0.66 (0.40, 1.07)	0.0868	
	>= 65	13/ 84 (15.5)	NE (NE , NE)	19/ 98 (19.4)	NE (NE , NE)	0.57 (0.28, 1.18)	0.1246	
	Sex							0.7219
	Male	19/ 121 (15.7)	NE (NE , NE)	22/ 112 (19.6)	NE (23.2, NE)	0.63 (0.34, 1.17)	0.1417	
	Female	28/ 111 (25.2)	NE (25.2, NE)	31/ 117 (26.5)	NE (14.1, NE)	0.67 (0.40, 1.13)	0.1333	
	Region							0.7115
	Europe	24/ 108 (22.2)	NE (NE , NE)	27/ 103 (26.2)	23.2 (23.2, NE)	0.61 (0.35, 1.07)	0.0824	
	USA/Canada	5/ 15 (33.3)	NE (7.5, NE)	8/ 17 (47.1)	14.1 (2.3, 14.1)	0.52 (0.17, 1.63)	0.2548	
	Rest of World	18/ 109 (16.5)	NE (NE , NE)	18/ 109 (16.5)	NE (NE , NE)	0.75 (0.38, 1.45)	0.3866	
	ECOG-PS at Randomization							0.8460
	0	25/ 130 (19.2)	NE (NE , NE)	29/ 130 (22.3)	23.2 (23.2, NE)	0.62 (0.36, 1.07)	0.0807	
	1	22/ 102 (21.6)	NE (25.2, NE)	24/ 99 (24.2)	NE (NE , NE)	0.68 (0.38, 1.23)	0.1997	
	Number of Organs Involved							0.9452
	<= 2	23/ 116 (19.8)	NE (NE , NE)	26/ 119 (21.8)	NE (NE , NE)	0.67 (0.38, 1.19)	0.1669	
	>= 3	24/ 116 (20.7)	NE (25.2, NE)	27/ 110 (24.5)	23.2 (14.1, NE)	0.62 (0.36, 1.09)	0.0965	
	Presence of Liver Metastases							0.2043
	Yes	30/ 146 (20.5)	NE (25.2, NE)	30/ 149 (20.1)	NE (NE , NE)	0.80 (0.48, 1.34)	0.4047	
	No	17/ 86 (19.8)	NE (NE , NE)	23/ 80 (28.8)	23.2 (14.1, NE)	0.46 (0.24, 0.88)	0.0169	
	Side of Tumor							0.2864
	Left	13/ 88 (14.8)	NE (NE , NE)	20/ 90 (22.2)	23.2 (NE , NE)	0.44 (0.21, 0.90)	0.0220	
	Right	34/ 144 (23.6)	NE (NE , NE)	33/ 139 (23.7)	NE (14.1, NE)	0.77 (0.47, 1.25)	0.2886	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
Subgroup analysis was done for SOCs / PTs with significant overall treatment effect (significant log-rank).
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.
[4] P-Value for interaction from Cox proportional hazards model using ties=exact option with treatment, subgroup and treatment*subgroup interaction as covariates.
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

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Frequent AE by SOC, PT (incidence >= 10% or >=10 patients and incidence >= 1%) - Subgroup analysis
Safety Analysis Set

SOC/PT	Subgroup Level	EC+FOLFOX (N=232) n/ N (%)	EC+FOLFOX (N=232) Median (95% CI)[1]	Control 1 (N=229) n/ N (%)	Control 1 (N=229) Median (95% CI)[1]	Unstratified analysis Hazard Ratio (95% CI)[2]	Unstratified analysis p-Value[3]	Interaction p-Value[4]
SOC: Gastrointestinal disorders, PT: Diarrhoea	Age (Years)							0.3053
	< 65	56/ 148 (37.8)	NE (14.8, NE)	65/ 131 (49.6)	3.7 (2.3, NE)	0.52 (0.36, 0.76)	0.0004	
	>= 65	41/ 84 (48.8)	11.0 (5.6, NE)	50/ 98 (51.0)	4.0 (1.2, NE)	0.71 (0.47, 1.08)	0.1132	
	Sex							0.1392
	Male	51/ 121 (42.1)	17.1 (9.2, NE)	48/ 112 (42.9)	NE (3.2, NE)	0.70 (0.47, 1.05)	0.0814	
	Female	46/ 111 (41.4)	NE (9.9, NE)	67/ 117 (57.3)	2.3 (1.0, 4.5)	0.51 (0.35, 0.75)	0.0004	
	Region							0.0035
	Europe	54/ 108 (50.0)	9.9 (6.3, 21.1)	48/ 103 (46.6)	NE (1.9, NE)	0.78 (0.53, 1.16)	0.2295	
	USA/Canada	10/ 15 (66.7)	2.3 (0.4, NE)	8/ 17 (47.1)	4.5 (0.7, NE)	1.39 (0.55, 3.53)	0.4823	
	Rest of World	33/ 109 (30.3)	NE (NE , NE)	59/ 109 (54.1)	3.5 (1.7, NE)	0.37 (0.24, 0.57)	<.0001	
	ECOG-PS at Randomization							0.7422
	0	51/ 130 (39.2)	NE (14.8, NE)	59/ 130 (45.4)	NE (2.6, NE)	0.60 (0.41, 0.88)	0.0082	
	1	46/ 102 (45.1)	10.8 (5.8, NE)	56/ 99 (56.6)	2.6 (0.8, 10.9)	0.57 (0.39, 0.85)	0.0050	
	Number of Organs Involved							0.1824
	<= 2	46/ 116 (39.7)	NE (11.7, NE)	64/ 119 (53.8)	3.5 (1.7, NE)	0.48 (0.33, 0.71)	0.0002	
	>= 3	51/ 116 (44.0)	21.1 (7.7, NE)	51/ 110 (46.4)	7.2 (1.9, NE)	0.72 (0.49, 1.07)	0.1078	
	Presence of Liver Metastases							0.2462
	Yes	60/ 146 (41.1)	NE (9.0, NE)	69/ 149 (46.3)	7.2 (2.6, NE)	0.68 (0.48, 0.96)	0.0298	
	No	37/ 86 (43.0)	21.1 (9.9, NE)	46/ 80 (57.5)	2.3 (1.2, 10.9)	0.46 (0.29, 0.72)	0.0005	
	Side of Tumor							0.9053
	Left	34/ 88 (38.6)	NE (9.7, NE)	41/ 90 (45.6)	NE (2.1, NE)	0.62 (0.39, 0.99)	0.0420	
	Right	63/ 144 (43.8)	17.1 (8.9, NE)	74/ 139 (53.2)	3.5 (1.7, NE)	0.57 (0.40, 0.80)	0.0010	

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Subgroup analysis was done for SOCs / PTs with significant overall treatment effect (significant log-rank).
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.
[4] P-Value for interaction from Cox proportional hazards model using ties=exact option with treatment, subgroup and treatment*subgroup interaction as covariates.
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Frequent AE by SOC, PT (incidence >= 10% or >=10 patients and incidence >= 1%) - Subgroup analysis
Safety Analysis Set

SOC/PT	Subgroup Level	EC+FOLFOX (N=232) n/ N (%)	EC+FOLFOX (N=232) Median (95% CI)[1]	Control 1 (N=229) n/ N (%)	Control 1 (N=229) Median (95% CI)[1]	Unstratified analysis Hazard Ratio (95% CI)[2]	Unstratified analysis p-Value[3]	Interaction p-Value[4]
SOC: Gastrointestinal disorders, PT: Gastrooesophageal reflux disease	Age (Years)							
	< 65	2/ 148 (1.4)		7/ 131 (5.3)				
	>= 65	4/ 84 (4.8)		4/ 98 (4.1)				
	Sex							0.2797
	Male	5/ 121 (4.1)	NE (NE , NE)	6/ 112 (5.4)	NE (NE , NE)	0.54 (0.16, 1.81)	0.3110	
	Female	1/ 111 (0.9)	NE (NE , NE)	5/ 117 (4.3)	NE (NE , NE)	0.12 (0.01, 1.08)	0.0263	
	Region							0.3112
	Europe	1/ 108 (0.9)	NE (NE , NE)	3/ 103 (2.9)	NE (NE , NE)	0.20 (0.02, 1.97)	0.1276	
	USA/Canada	2/ 15 (13.3)	NE (NE , NE)	1/ 17 (5.9)	NE (NE , NE)	2.16 (0.20, 23.92)	0.5199	
	Rest of World	3/ 109 (2.8)	NE (NE , NE)	7/ 109 (6.4)	NE (NE , NE)	0.26 (0.07, 1.03)	0.0401	
	ECOG-PS at Randomization							0.6141
	0	3/ 130 (2.3)	NE (NE , NE)	7/ 130 (5.4)	NE (NE , NE)	0.27 (0.07, 1.06)	0.0453	
	1	3/ 102 (2.9)	NE (NE , NE)	4/ 99 (4.0)	NE (NE , NE)	0.51 (0.11, 2.36)	0.3837	
	Number of Organs Involved							0.4001
	<= 2	5/ 116 (4.3)	NE (NE , NE)	7/ 119 (5.9)	NE (NE , NE)	0.52 (0.16, 1.68)	0.2687	
	>= 3	1/ 116 (0.9)	NE (NE , NE)	4/ 110 (3.6)	NE (NE , NE)	0.13 (0.01, 1.20)	0.0353	
	Presence of Liver Metastases							0.8076
	Yes	4/ 146 (2.7)	NE (NE , NE)	8/ 149 (5.4)	NE (NE , NE)	0.34 (0.10, 1.16)	0.0724	
	No	2/ 86 (2.3)	NE (NE , NE)	3/ 80 (3.8)	NE (NE , NE)	0.35 (0.06, 2.20)	0.2451	
	Side of Tumor							
	Left	1/ 88 (1.1)		8/ 90 (8.9)				
	Right	5/ 144 (3.5)		3/ 139 (2.2)				

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
Subgroup analysis was done for SOCs / PTs with significant overall treatment effect (significant log-rank).
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.
[4] P-Value for interaction from Cox proportional hazards model using ties=exact option with treatment, subgroup and treatment*subgroup interaction as covariates.
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Frequent AE by SOC, PT (incidence >= 10% or >=10 patients and incidence >= 1%) - Subgroup analysis
Safety Analysis Set

SOC/PT	Subgroup Level	EC+FOLFOX (N=232) n/ N (%)	EC+FOLFOX (N=232) Median (95% CI)[1]	Control 1 (N=229) n/ N (%)	Control 1 (N=229) Median (95% CI)[1]	Unstratified analysis Hazard Ratio (95% CI)[2]	Unstratified analysis p-Value[3]	Interaction p-Value[4]
SOC: Gastrointestinal disorders, PT: Haemorrhoids	Age (Years)							0.6724
	< 65	18/ 148 (12.2)	NE (NE , NE)	5/ 131 (3.8)	NE (NE , NE)	2.78 (1.02, 7.54)	0.0364	
	>= 65	6/ 84 (7.1)	NE (30.9, NE)	3/ 98 (3.1)	NE (NE , NE)	1.45 (0.35, 6.04)	0.6067	
	Sex							0.1399
	Male	11/ 121 (9.1)	NE (NE , NE)	1/ 112 (0.9)	NE (NE , NE)	8.77 (1.13, 68.27)	0.0126	
	Female	13/ 111 (11.7)	NE (30.9, NE)	7/ 117 (6.0)	NE (NE , NE)	1.51 (0.59, 3.85)	0.3852	
	Region							0.2882
	Europe	8/ 108 (7.4)	NE (30.9, NE)	1/ 103 (1.0)	NE (NE , NE)	5.46 (0.67, 44.74)	0.0759	
	USA/Canada	1/ 15 (6.7)	NE (NE , NE)	2/ 17 (11.8)	NE (NE , NE)	0.49 (0.04, 5.47)	0.5574	
	Rest of World	15/ 109 (13.8)	NE (NE , NE)	5/ 109 (4.6)	NE (NE , NE)	2.54 (0.92, 7.07)	0.0636	
	ECOG-PS at Randomization							0.2888
	0	16/ 130 (12.3)	NE (30.9, NE)	7/ 130 (5.4)	NE (NE , NE)	2.03 (0.83, 4.97)	0.1140	
	1	8/ 102 (7.8)	NE (NE , NE)	1/ 99 (1.0)	NE (NE , NE)	4.97 (0.61, 40.45)	0.0983	
	Number of Organs Involved							0.8876
	<= 2	14/ 116 (12.1)	NE (30.9, NE)	5/ 119 (4.2)	NE (NE , NE)	2.37 (0.84, 6.69)	0.0922	
	>= 3	10/ 116 (8.6)	NE (NE , NE)	3/ 110 (2.7)	NE (NE , NE)	2.53 (0.69, 9.28)	0.1460	
	Presence of Liver Metastases							0.2685
	Yes	19/ 146 (13.0)	NE (NE , NE)	5/ 149 (3.4)	NE (NE , NE)	3.27 (1.21, 8.82)	0.0133	
	No	5/ 86 (5.8)	NE (30.9, NE)	3/ 80 (3.8)	NE (NE , NE)	1.20 (0.28, 5.15)	0.8019	
	Side of Tumor							0.1353
	Left	8/ 88 (9.1)	NE (30.9, NE)	5/ 90 (5.6)	NE (NE , NE)	1.07 (0.33, 3.54)	0.9057	
	Right	16/ 144 (11.1)	NE (NE , NE)	3/ 139 (2.2)	NE (NE , NE)	4.42 (1.28, 15.22)	0.0101	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
Subgroup analysis was done for SOCs / PTs with significant overall treatment effect (significant log-rank).
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.
[4] P-Value for interaction from Cox proportional hazards model using ties=exact option with treatment, subgroup and treatment*subgroup interaction as covariates.
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Frequent AE by SOC, PT (incidence >= 10% or >=10 patients and incidence >= 1%) - Subgroup analysis
Safety Analysis Set

SOC/PT	Subgroup Level	EC+FOLFOX (N=232) n/ N (%)	EC+FOLFOX (N=232) Median (95% CI)[1]	Control 1 (N=229) n/ N (%)	Control 1 (N=229) Median (95% CI)[1]	Unstratified analysis Hazard Ratio (95% CI)[2]	Unstratified analysis p-Value[3]	Interaction p-Value[4]
SOC: Gastrointestinal disorders, PT: Vomiting	Age (Years)							0.5416
	< 65	62/ 148 (41.9)	NE (13.9, NE)	38/ 131 (29.0)	NE (NE , NE)	1.45 (0.96, 2.17)	0.0764	
	>= 65	22/ 84 (26.2)	NE (NE , NE)	13/ 98 (13.3)	NE (NE , NE)	1.84 (0.92, 3.67)	0.0785	
	Sex							0.3565
	Male	32/ 121 (26.4)	NE (NE , NE)	21/ 112 (18.8)	NE (NE , NE)	1.35 (0.77, 2.34)	0.2903	
	Female	52/ 111 (46.8)	17.3 (5.3, NE)	30/ 117 (25.6)	NE (NE , NE)	1.84 (1.17, 2.90)	0.0074	
	Region							0.0504
	Europe	31/ 108 (28.7)	NE (NE , NE)	22/ 103 (21.4)	NE (NE , NE)	1.22 (0.70, 2.11)	0.4864	
	USA/Canada	12/ 15 (80.0)	2.3 (0.2, 4.4)	2/ 17 (11.8)	NE (NE , NE)	8.35 (1.86, 37.53)	0.0010	
	Rest of World	41/ 109 (37.6)	NE (17.3, NE)	27/ 109 (24.8)	NE (NE , NE)	1.54 (0.94, 2.50)	0.0859	
	ECOG-PS at Randomization							0.5911
	0	46/ 130 (35.4)	NE (18.3, NE)	25/ 130 (19.2)	NE (NE , NE)	1.72 (1.05, 2.81)	0.0290	
	1	38/ 102 (37.3)	NE (14.9, NE)	26/ 99 (26.3)	NE (NE , NE)	1.47 (0.89, 2.43)	0.1306	
	Number of Organs Involved							0.1527
	<= 2	40/ 116 (34.5)	NE (18.3, NE)	18/ 119 (15.1)	NE (NE , NE)	2.09 (1.19, 3.66)	0.0084	
	>= 3	44/ 116 (37.9)	NE (14.9, NE)	33/ 110 (30.0)	NE (NE , NE)	1.31 (0.83, 2.06)	0.2507	
	Presence of Liver Metastases							0.6252
	Yes	51/ 146 (34.9)	NE (17.3, NE)	34/ 149 (22.8)	NE (NE , NE)	1.46 (0.95, 2.27)	0.0858	
	No	33/ 86 (38.4)	NE (14.9, NE)	17/ 80 (21.3)	NE (NE , NE)	1.84 (1.02, 3.32)	0.0386	
	Side of Tumor							0.2232
	Left	29/ 88 (33.0)	NE (NE , NE)	23/ 90 (25.6)	NE (NE , NE)	1.26 (0.73, 2.17)	0.4175	
	Right	55/ 144 (38.2)	NE (17.2, NE)	28/ 139 (20.1)	NE (NE , NE)	1.87 (1.18, 2.95)	0.0070	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
Subgroup analysis was done for SOCs / PTs with significant overall treatment effect (significant log-rank).
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.
[4] P-Value for interaction from Cox proportional hazards model using ties=exact option with treatment, subgroup and treatment*subgroup interaction as covariates.
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Frequent AE by SOC, PT (incidence >= 10% or >=10 patients and incidence >= 1%) - Subgroup analysis
Safety Analysis Set

SOC/PT	Subgroup Level	EC+FOLFOX (N=232) n/ N (%)	EC+FOLFOX (N=232) Median (95% CI)[1]	Control 1 (N=229) n/ N (%)	Control 1 (N=229) Median (95% CI)[1]	Unstratified analysis Hazard Ratio (95% CI)[2]	Unstratified analysis p-Value[3]	Interaction p-Value[4]
SOC: General disorders and administration site conditions	Age (Years)							0.4768
	< 65	117/ 148 (79.1)	1.0 (0.5, 2.1)	86/ 131 (65.6)	2.1 (1.1, 3.7)	1.20 (0.91, 1.59)	0.2080	
	>= 65	70/ 84 (83.3)	0.7 (0.5, 2.5)	62/ 98 (63.3)	1.4 (0.7, 4.2)	1.42 (1.01, 2.00)	0.0455	
	Sex							0.7643
	Male	96/ 121 (79.3)	1.0 (0.5, 2.8)	69/ 112 (61.6)	2.3 (1.3, 4.4)	1.34 (0.98, 1.82)	0.0664	
	Female	91/ 111 (82.0)	0.7 (0.5, 1.9)	79/ 117 (67.5)	1.4 (0.7, 2.9)	1.25 (0.93, 1.70)	0.1472	
	Region							0.9618
	Europe	90/ 108 (83.3)	0.5 (0.5, 1.0)	73/ 103 (70.9)	1.4 (0.9, 2.8)	1.32 (0.97, 1.80)	0.0843	
	USA/Canada	13/ 15 (86.7)	0.5 (0.2, 1.5)	13/ 17 (76.5)	0.6 (0.1, 1.4)	1.21 (0.55, 2.68)	0.6438	
	Rest of World	84/ 109 (77.1)	2.7 (1.1, 3.9)	62/ 109 (56.9)	3.9 (1.2, 10.1)	1.31 (0.94, 1.82)	0.1024	
	ECOG-PS at Randomization							0.8510
	0	103/ 130 (79.2)	1.0 (0.5, 2.2)	82/ 130 (63.1)	2.5 (1.4, 4.2)	1.29 (0.97, 1.73)	0.0862	
	1	84/ 102 (82.4)	0.8 (0.5, 2.5)	66/ 99 (66.7)	1.2 (0.7, 2.8)	1.25 (0.90, 1.72)	0.1775	
	Number of Organs Involved							0.8449
	<= 2	96/ 116 (82.8)	0.8 (0.5, 2.3)	79/ 119 (66.4)	1.3 (0.8, 3.3)	1.27 (0.94, 1.71)	0.1209	
	>= 3	91/ 116 (78.4)	1.0 (0.5, 2.5)	69/ 110 (62.7)	2.3 (1.4, 3.9)	1.32 (0.96, 1.80)	0.0877	
	Presence of Liver Metastases							0.3778
	Yes	114/ 146 (78.1)	1.0 (0.5, 2.4)	97/ 149 (65.1)	1.6 (1.0, 3.3)	1.19 (0.91, 1.57)	0.2085	
	No	73/ 86 (84.9)	0.6 (0.5, 2.3)	51/ 80 (63.8)	2.1 (1.0, 4.9)	1.46 (1.02, 2.09)	0.0376	
	Side of Tumor							0.5545
	Left	70/ 88 (79.5)	1.3 (0.5, 3.2)	58/ 90 (64.4)	2.2 (1.0, 3.9)	1.15 (0.81, 1.63)	0.4340	
	Right	117/ 144 (81.3)	0.8 (0.5, 2.1)	90/ 139 (64.7)	1.4 (1.0, 3.7)	1.35 (1.03, 1.78)	0.0311	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
Subgroup analysis was done for SOCs / PTs with significant overall treatment effect (significant log-rank).
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.
[4] P-Value for interaction from Cox proportional hazards model using ties=exact option with treatment, subgroup and treatment*subgroup interaction as covariates.
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Frequent AE by SOC, PT (incidence >= 10% or >=10 patients and incidence >= 1%) - Subgroup analysis
Safety Analysis Set

SOC/PT	Subgroup Level	EC+FOLFOX (N=232) n/ N (%)	EC+FOLFOX (N=232) Median (95% CI)[1]	Control 1 (N=229) n/ N (%)	Control 1 (N=229) Median (95% CI)[1]	Unstratified analysis Hazard Ratio (95% CI)[2]	Unstratified analysis p-Value[3]	Interaction p-Value[4]
SOC: General disorders and administration site conditions, PT: Asthenia	Age (Years)							0.5443
	< 65	39/ 148 (26.4)	NE (NE , NE)	19/ 131 (14.5)	NE (NE , NE)	1.67 (0.96, 2.90)	0.0675	
	>= 65	29/ 84 (34.5)	NE (15.1, NE)	15/ 98 (15.3)	NE (NE , NE)	2.18 (1.17, 4.07)	0.0122	
	Sex							0.2576
	Male	31/ 121 (25.6)	NE (NE , NE)	18/ 112 (16.1)	NE (NE , NE)	1.46 (0.82, 2.62)	0.1997	
	Female	37/ 111 (33.3)	NE (20.6, NE)	16/ 117 (13.7)	NE (NE , NE)	2.35 (1.30, 4.24)	0.0036	
	Region							0.5221
	Europe	48/ 108 (44.4)	15.1 (6.4, NE)	27/ 103 (26.2)	NE (NE , NE)	1.64 (1.02, 2.63)	0.0407	
	USA/Canada	1/ 15 (6.7)	NE (NE , NE)	1/ 17 (5.9)	NE (NE , NE)	0.99 (0.06, 15.86)	0.9918	
	Rest of World	19/ 109 (17.4)	NE (NE , NE)	6/ 109 (5.5)	NE (NE , NE)	2.92 (1.16, 7.33)	0.0171	
	ECOG-PS at Randomization							0.7940
	0	37/ 130 (28.5)	NE (NE , NE)	18/ 130 (13.8)	NE (NE , NE)	1.95 (1.11, 3.43)	0.0190	
	1	31/ 102 (30.4)	NE (NE , NE)	16/ 99 (16.2)	NE (NE , NE)	1.73 (0.94, 3.18)	0.0719	
	Number of Organs Involved							0.6872
	<= 2	34/ 116 (29.3)	NE (NE , NE)	16/ 119 (13.4)	NE (NE , NE)	2.02 (1.11, 3.67)	0.0189	
	>= 3	34/ 116 (29.3)	NE (21.4, NE)	18/ 110 (16.4)	NE (NE , NE)	1.72 (0.97, 3.04)	0.0615	
	Presence of Liver Metastases							0.7276
	Yes	41/ 146 (28.1)	NE (21.4, NE)	20/ 149 (13.4)	NE (NE , NE)	1.95 (1.14, 3.34)	0.0127	
	No	27/ 86 (31.4)	NE (NE , NE)	14/ 80 (17.5)	NE (NE , NE)	1.71 (0.89, 3.27)	0.1022	
	Side of Tumor							0.6577
	Left	26/ 88 (29.5)	NE (NE , NE)	12/ 90 (13.3)	NE (NE , NE)	2.10 (1.06, 4.16)	0.0311	
	Right	42/ 144 (29.2)	NE (21.4, NE)	22/ 139 (15.8)	NE (NE , NE)	1.73 (1.03, 2.90)	0.0361	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
Subgroup analysis was done for SOCs / PTs with significant overall treatment effect (significant log-rank).
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.
[4] P-Value for interaction from Cox proportional hazards model using ties=exact option with treatment, subgroup and treatment*subgroup interaction as covariates.
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Frequent AE by SOC, PT (incidence >= 10% or >=10 patients and incidence >= 1%) - Subgroup analysis
Safety Analysis Set

SOC/PT	Subgroup Level	EC+FOLFOX (N=232) n/ N (%)	EC+FOLFOX (N=232) Median (95% CI)[1]	Control 1 (N=229) n/ N (%)	Control 1 (N=229) Median (95% CI)[1]	Unstratified analysis Hazard Ratio (95% CI)[2]	Unstratified analysis p-Value[3]	Interaction p-Value[4]
SOC: General disorders and administration site conditions, PT: Pain	Age (Years)							0.0848
	< 65	14/ 148 (9.5)	NE (NE , NE)	1/ 131 (0.8)	NE (NE , NE)	9.39 (1.22, 72.23)	0.0089	
	>= 65	5/ 84 (6.0)	NE (NE , NE)	4/ 98 (4.1)	NE (NE , NE)	0.99 (0.26, 3.83)	0.9882	
	Sex							0.3295
	Male	9/ 121 (7.4)	NE (NE , NE)	1/ 112 (0.9)	NE (NE , NE)	5.32 (0.66, 43.05)	0.0819	
	Female	10/ 111 (9.0)	NE (NE , NE)	4/ 117 (3.4)	NE (NE , NE)	2.10 (0.65, 6.81)	0.2080	
	Region							0.4591
	Europe	12/ 108 (11.1)	NE (NE , NE)	1/ 103 (1.0)	NE (NE , NE)	7.00 (0.89, 54.90)	0.0326	
	USA/Canada	0/ 15 (0.0)	NE (NE , NE)	1/ 17 (5.9)	NE (NE , NE)	NE		
	Rest of World	7/ 109 (6.4)	NE (NE , NE)	3/ 109 (2.8)	NE (NE , NE)	2.03 (0.52, 8.01)	0.3001	
	ECOG-PS at Randomization							0.9143
	0	11/ 130 (8.5)	NE (NE , NE)	3/ 130 (2.3)	NE (NE , NE)	2.75 (0.75, 10.05)	0.1128	
	1	8/ 102 (7.8)	NE (NE , NE)	2/ 99 (2.0)	NE (NE , NE)	2.70 (0.56, 13.06)	0.2003	
	Number of Organs Involved							0.1564
	<= 2	8/ 116 (6.9)	NE (NE , NE)	4/ 119 (3.4)	NE (NE , NE)	1.47 (0.43, 5.07)	0.5374	
	>= 3	11/ 116 (9.5)	NE (NE , NE)	1/ 110 (0.9)	NE (NE , NE)	7.86 (1.01, 61.47)	0.0205	
	Presence of Liver Metastases							0.1759
	Yes	13/ 146 (8.9)	NE (NE , NE)	2/ 149 (1.3)	NE (NE , NE)	5.02 (1.12, 22.46)	0.0193	
	No	6/ 86 (7.0)	NE (NE , NE)	3/ 80 (3.8)	NE (NE , NE)	1.18 (0.28, 5.08)	0.8203	
	Side of Tumor							0.9193
	Left	8/ 88 (9.1)	NE (NE , NE)	2/ 90 (2.2)	NE (NE , NE)	2.79 (0.58, 13.49)	0.1852	
	Right	11/ 144 (7.6)	NE (NE , NE)	3/ 139 (2.2)	NE (NE , NE)	2.75 (0.76, 10.02)	0.1103	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
Subgroup analysis was done for SOCs / PTs with significant overall treatment effect (significant log-rank).
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.
[4] P-Value for interaction from Cox proportional hazards model using ties=exact option with treatment, subgroup and treatment*subgroup interaction as covariates.
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Frequent AE by SOC, PT (incidence >= 10% or >=10 patients and incidence >= 1%) - Subgroup analysis
Safety Analysis Set

SOC/PT	Subgroup Level	EC+FOLFOX (N=232) n/ N (%)	EC+FOLFOX (N=232) Median (95% CI)[1]	Control 1 (N=229) n/ N (%)	Control 1 (N=229) Median (95% CI)[1]	Unstratified analysis Hazard Ratio (95% CI)[2]	Unstratified analysis p-Value[3]	Interaction p-Value[4]
SOC: General disorders and administration site conditions, PT: Pyrexia	Age (Years)							0.9306
	< 65	45/ 148 (30.4)	NE (26.7, NE)	22/ 131 (16.8)	NE (NE , NE)	1.51 (0.90, 2.53)	0.1161	
	>= 65	22/ 84 (26.2)	NE (NE , NE)	14/ 98 (14.3)	NE (NE , NE)	1.62 (0.83, 3.18)	0.1536	
	Sex							0.7307
	Male	34/ 121 (28.1)	NE (26.7, NE)	16/ 112 (14.3)	NE (NE , NE)	1.66 (0.91, 3.02)	0.0949	
	Female	33/ 111 (29.7)	NE (NE , NE)	20/ 117 (17.1)	NE (NE , NE)	1.52 (0.87, 2.66)	0.1425	
	Region							0.5684
	Europe	29/ 108 (26.9)	NE (NE , NE)	17/ 103 (16.5)	NE (NE , NE)	1.38 (0.76, 2.53)	0.2892	
	USA/Canada	3/ 15 (20.0)	NE (NE , NE)	3/ 17 (17.6)	NE (NE , NE)	1.06 (0.21, 5.31)	0.9404	
	Rest of World	35/ 109 (32.1)	26.7 (18.7, NE)	16/ 109 (14.7)	NE (NE , NE)	1.91 (1.05, 3.47)	0.0306	
	ECOG-PS at Randomization							0.8463
	0	41/ 130 (31.5)	26.7 (26.7, NE)	23/ 130 (17.7)	NE (NE , NE)	1.51 (0.90, 2.53)	0.1140	
	1	26/ 102 (25.5)	NE (NE , NE)	13/ 99 (13.1)	NE (NE , NE)	1.70 (0.87, 3.33)	0.1155	
	Number of Organs Involved							0.4963
	<= 2	38/ 116 (32.8)	NE (18.7, NE)	19/ 119 (16.0)	NE (NE , NE)	1.83 (1.05, 3.19)	0.0300	
	>= 3	29/ 116 (25.0)	26.7 (26.7, NE)	17/ 110 (15.5)	NE (NE , NE)	1.33 (0.72, 2.43)	0.3581	
	Presence of Liver Metastases							0.0032
	Yes	31/ 146 (21.2)	NE (NE , NE)	27/ 149 (18.1)	NE (NE , NE)	0.95 (0.56, 1.60)	0.8472	
	No	36/ 86 (41.9)	26.7 (13.0, NE)	9/ 80 (11.3)	NE (NE , NE)	3.53 (1.69, 7.38)	0.0003	
	Side of Tumor							0.5110
	Left	25/ 88 (28.4)	NE (26.7, NE)	11/ 90 (12.2)	NE (NE , NE)	1.90 (0.93, 3.91)	0.0743	
	Right	42/ 144 (29.2)	NE (NE , NE)	25/ 139 (18.0)	NE (NE , NE)	1.43 (0.87, 2.35)	0.1595	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
Subgroup analysis was done for SOCs / PTs with significant overall treatment effect (significant log-rank).
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.
[4] P-Value for interaction from Cox proportional hazards model using ties=exact option with treatment, subgroup and treatment*subgroup interaction as covariates.
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Frequent AE by SOC, PT (incidence >= 10% or >=10 patients and incidence >= 1%) - Subgroup analysis
Safety Analysis Set

SOC/PT	Subgroup Level	EC+FOLFOX (N=232) n/ N (%)	EC+FOLFOX (N=232) Median (95% CI)[1]	Control 1 (N=229) n/ N (%)	Control 1 (N=229) Median (95% CI)[1]	Unstratified analysis Hazard Ratio (95% CI)[2]	Unstratified analysis p-Value[3]	Interaction p-Value[4]
SOC: Investigations	Age (Years)							0.7398
	< 65	108/ 148 (73.0)	1.4 (0.9, 2.4)	82/ 131 (62.6)	2.8 (1.9, 3.7)	1.31 (0.98, 1.75)	0.0714	
	>= 65	56/ 84 (66.7)	1.9 (0.9, 4.6)	56/ 98 (57.1)	3.3 (1.9, 4.9)	1.21 (0.83, 1.75)	0.3265	
	Sex							0.7183
	Male	85/ 121 (70.2)	1.9 (1.0, 3.0)	69/ 112 (61.6)	3.3 (2.0, 4.3)	1.22 (0.89, 1.68)	0.2311	
	Female	79/ 111 (71.2)	1.2 (0.6, 2.5)	69/ 117 (59.0)	2.7 (1.9, 5.6)	1.37 (0.99, 1.90)	0.0643	
	Region							0.3165
	Europe	63/ 108 (58.3)	4.6 (3.0, 16.4)	50/ 103 (48.5)	6.3 (3.3, 21.8)	1.16 (0.80, 1.69)	0.4505	
	USA/Canada	15/ 15 (100.0)	0.5 (0.5, 0.9)	12/ 17 (70.6)	1.0 (0.5, 3.7)	2.51 (1.10, 5.74)	0.0272	
	Rest of World	86/ 109 (78.9)	0.9 (0.5, 1.3)	76/ 109 (69.7)	1.9 (1.4, 2.8)	1.38 (1.01, 1.88)	0.0451	
	ECOG-PS at Randomization							0.4697
	0	97/ 130 (74.6)	1.6 (0.9, 2.8)	84/ 130 (64.6)	2.3 (1.5, 3.7)	1.19 (0.89, 1.59)	0.2579	
	1	67/ 102 (65.7)	1.4 (0.8, 3.0)	54/ 99 (54.5)	4.3 (2.5, 6.6)	1.41 (0.98, 2.01)	0.0701	
	Number of Organs Involved							0.5972
	<= 2	86/ 116 (74.1)	1.6 (0.9, 3.4)	78/ 119 (65.5)	2.5 (1.9, 3.4)	1.20 (0.88, 1.63)	0.2691	
	>= 3	78/ 116 (67.2)	1.4 (0.9, 2.7)	60/ 110 (54.5)	3.7 (2.1, 6.3)	1.39 (0.99, 1.95)	0.0574	
	Presence of Liver Metastases							0.4798
	Yes	100/ 146 (68.5)	1.4 (0.9, 2.8)	84/ 149 (56.4)	3.4 (2.1, 5.6)	1.37 (1.02, 1.83)	0.0365	
	No	64/ 86 (74.4)	1.5 (0.8, 3.0)	54/ 80 (67.5)	2.3 (1.5, 3.3)	1.15 (0.80, 1.66)	0.4838	
	Side of Tumor							0.4691
	Left	60/ 88 (68.2)	1.9 (1.0, 3.3)	57/ 90 (63.3)	3.1 (1.9, 4.4)	1.13 (0.78, 1.62)	0.5521	
	Right	104/ 144 (72.2)	1.1 (0.9, 2.5)	81/ 139 (58.3)	2.8 (1.9, 4.3)	1.38 (1.03, 1.85)	0.0306	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
Subgroup analysis was done for SOCs / PTs with significant overall treatment effect (significant log-rank).
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.
[4] P-Value for interaction from Cox proportional hazards model using ties=exact option with treatment, subgroup and treatment*subgroup interaction as covariates.
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Frequent AE by SOC, PT (incidence >= 10% or >=10 patients and incidence >= 1%) - Subgroup analysis
Safety Analysis Set

SOC/PT	Subgroup Level	EC+FOLFOX (N=232) n/ N (%)	EC+FOLFOX (N=232) Median (95% CI)[1]	Control 1 (N=229) n/ N (%)	Control 1 (N=229) Median (95% CI)[1]	Unstratified analysis Hazard Ratio (95% CI)[2]	Unstratified analysis p-Value[3]	Interaction p-Value[4]
SOC: Investigations, PT: Electrocardiogram QT prolonged	Age (Years)							
	< 65	6/ 148 (4.1)		1/ 131 (0.8)				
	>= 65	5/ 84 (6.0)		0/ 98 (0.0)				
	Sex							
	Male	6/ 121 (5.0)		0/ 112 (0.0)				
	Female	5/ 111 (4.5)		1/ 117 (0.9)				
	Region							
	Europe	2/ 108 (1.9)		1/ 103 (1.0)				
	USA/Canada	0/ 15 (0.0)		0/ 17 (0.0)				
	Rest of World	9/ 109 (8.3)		0/ 109 (0.0)				
	ECOG-PS at Randomization							
	0	3/ 130 (2.3)		1/ 130 (0.8)				
	1	8/ 102 (7.8)		0/ 99 (0.0)				
	Number of Organs Involved							
	<= 2	5/ 116 (4.3)		0/ 119 (0.0)				
	>= 3	6/ 116 (5.2)		1/ 110 (0.9)				
	Presence of Liver Metastases							0.9934
	Yes	9/ 146 (6.2)	NE (NE , NE)	1/ 149 (0.7)	NE (NE , NE)	8.04 (1.02, 63.57)	0.0187	
	No	2/ 86 (2.3)	NE (NE , NE)	0/ 80 (0.0)	NE (NE , NE)	NE		
	Side of Tumor							0.9932
	Left	2/ 88 (2.3)	NE (NE , NE)	0/ 90 (0.0)	NE (NE , NE)	NE		
	Right	9/ 144 (6.3)	NE (NE , NE)	1/ 139 (0.7)	NE (NE , NE)	7.96 (1.01, 62.87)	0.0194	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
Subgroup analysis was done for SOCs / PTs with significant overall treatment effect (significant log-rank).
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.
[4] P-Value for interaction from Cox proportional hazards model using ties=exact option with treatment, subgroup and treatment*subgroup interaction as covariates.
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Frequent AE by SOC, PT (incidence >= 10% or >=10 patients and incidence >= 1%) - Subgroup analysis
Safety Analysis Set

SOC/PT	Subgroup Level	EC+FOLFOX (N=232) n/ N (%)	EC+FOLFOX (N=232) Median (95% CI)[1]	Control 1 (N=229) n/ N (%)	Control 1 (N=229) Median (95% CI)[1]	Unstratified analysis Hazard Ratio (95% CI)[2]	Unstratified analysis p-Value[3]	Interaction p-Value[4]
SOC: Investigations, PT: Lipase increased	Age (Years)							0.4524
	< 65	37/ 148 (25.0)	NE (NE , NE)	20/ 131 (15.3)	NE (NE , NE)	1.62 (0.94, 2.80)	0.0784	
	>= 65	15/ 84 (17.9)	NE (NE , NE)	7/ 98 (7.1)	NE (NE , NE)	2.40 (0.98, 5.90)	0.0484	
	Sex							0.4274
	Male	31/ 121 (25.6)	NE (NE , NE)	13/ 112 (11.6)	NE (NE , NE)	2.20 (1.15, 4.20)	0.0146	
	Female	21/ 111 (18.9)	NE (NE , NE)	14/ 117 (12.0)	NE (NE , NE)	1.56 (0.79, 3.07)	0.1961	
	Region							0.2241
	Europe	18/ 108 (16.7)	NE (NE , NE)	12/ 103 (11.7)	NE (NE , NE)	1.31 (0.63, 2.73)	0.4695	
	USA/Canada	7/ 15 (46.7)	NE (1.9, NE)	1/ 17 (5.9)	NE (NE , NE)	8.73 (1.07, 70.94)	0.0145	
	Rest of World	27/ 109 (24.8)	NE (NE , NE)	14/ 109 (12.8)	NE (NE , NE)	2.00 (1.05, 3.81)	0.0323	
	ECOG-PS at Randomization							0.2275
	0	30/ 130 (23.1)	NE (NE , NE)	19/ 130 (14.6)	NE (NE , NE)	1.49 (0.84, 2.65)	0.1725	
	1	22/ 102 (21.6)	NE (NE , NE)	8/ 99 (8.1)	NE (NE , NE)	2.74 (1.22, 6.17)	0.0109	
	Number of Organs Involved							0.1167
	<= 2	28/ 116 (24.1)	NE (NE , NE)	20/ 119 (16.8)	NE (NE , NE)	1.40 (0.79, 2.49)	0.2446	
	>= 3	24/ 116 (20.7)	NE (NE , NE)	7/ 110 (6.4)	NE (NE , NE)	3.23 (1.39, 7.50)	0.0039	
	Presence of Liver Metastases							0.6700
	Yes	30/ 146 (20.5)	NE (NE , NE)	17/ 149 (11.4)	NE (NE , NE)	1.72 (0.95, 3.12)	0.0725	
	No	22/ 86 (25.6)	NE (NE , NE)	10/ 80 (12.5)	NE (NE , NE)	2.11 (1.00, 4.46)	0.0452	
	Side of Tumor							0.5787
	Left	21/ 88 (23.9)	NE (NE , NE)	13/ 90 (14.4)	NE (NE , NE)	1.64 (0.82, 3.28)	0.1542	
	Right	31/ 144 (21.5)	NE (NE , NE)	14/ 139 (10.1)	NE (NE , NE)	2.08 (1.11, 3.91)	0.0204	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
Subgroup analysis was done for SOCs / PTs with significant overall treatment effect (significant log-rank).
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.
[4] P-Value for interaction from Cox proportional hazards model using ties=exact option with treatment, subgroup and treatment*subgroup interaction as covariates.
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Frequent AE by SOC, PT (incidence >= 10% or >=10 patients and incidence >= 1%) - Subgroup analysis
Safety Analysis Set

SOC/PT	Subgroup Level	EC+FOLFOX (N=232) n/ N (%)	EC+FOLFOX (N=232) Median (95% CI)[1]	Control 1 (N=229) n/ N (%)	Control 1 (N=229) Median (95% CI)[1]	Unstratified analysis Hazard Ratio (95% CI)[2]	Unstratified analysis p-Value[3]	Interaction p-Value[4]
SOC: Investigations, PT: Weight decreased	Age (Years)							0.0116
	< 65	21/ 148 (14.2)	NE (NE , NE)	16/ 131 (12.2)	NE (19.5, NE)	1.00 (0.52, 1.94)	0.9941	
	>= 65	23/ 84 (27.4)	NE (NE , NE)	6/ 98 (6.1)	NE (NE , NE)	4.21 (1.71, 10.36)	0.0007	
	Sex							0.7390
	Male	21/ 121 (17.4)	NE (NE , NE)	11/ 112 (9.8)	NE (NE , NE)	1.57 (0.76, 3.28)	0.2221	
	Female	23/ 111 (20.7)	NE (NE , NE)	11/ 117 (9.4)	NE (NE , NE)	2.02 (0.98, 4.15)	0.0527	
	Region							0.0398
	Europe	13/ 108 (12.0)	NE (NE , NE)	12/ 103 (11.7)	NE (NE , NE)	0.82 (0.37, 1.82)	0.6270	
	USA/Canada	6/ 15 (40.0)	NE (1.8, NE)	1/ 17 (5.9)	NE (NE , NE)	7.68 (0.92, 63.80)	0.0257	
	Rest of World	25/ 109 (22.9)	NE (NE , NE)	9/ 109 (8.3)	NE (19.5, NE)	2.74 (1.28, 5.90)	0.0070	
	ECOG-PS at Randomization							0.2700
	0	26/ 130 (20.0)	NE (NE , NE)	10/ 130 (7.7)	NE (NE , NE)	2.37 (1.14, 4.93)	0.0178	
	1	18/ 102 (17.6)	NE (NE , NE)	12/ 99 (12.1)	NE (19.5, NE)	1.31 (0.63, 2.72)	0.4739	
	Number of Organs Involved							0.0948
	<= 2	30/ 116 (25.9)	NE (NE , NE)	11/ 119 (9.2)	NE (NE , NE)	2.61 (1.30, 5.22)	0.0051	
	>= 3	14/ 116 (12.1)	NE (NE , NE)	11/ 110 (10.0)	NE (NE , NE)	1.08 (0.49, 2.38)	0.8546	
	Presence of Liver Metastases							0.9705
	Yes	22/ 146 (15.1)	NE (NE , NE)	11/ 149 (7.4)	NE (NE , NE)	1.86 (0.90, 3.83)	0.0893	
	No	22/ 86 (25.6)	NE (NE , NE)	11/ 80 (13.8)	NE (19.5, NE)	1.68 (0.80, 3.50)	0.1672	
	Side of Tumor							0.6548
	Left	13/ 88 (14.8)	NE (NE , NE)	8/ 90 (8.9)	NE (19.5, NE)	1.48 (0.61, 3.60)	0.3855	
	Right	31/ 144 (21.5)	NE (NE , NE)	14/ 139 (10.1)	NE (NE , NE)	1.95 (1.03, 3.67)	0.0360	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
Subgroup analysis was done for SOCs / PTs with significant overall treatment effect (significant log-rank).
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.
[4] P-Value for interaction from Cox proportional hazards model using ties=exact option with treatment, subgroup and treatment*subgroup interaction as covariates.
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Frequent AE by SOC, PT (incidence >= 10% or >=10 patients and incidence >= 1%) - Subgroup analysis
Safety Analysis Set

SOC/PT	Subgroup Level	EC+FOLFOX (N=232) n/ N (%)	EC+FOLFOX (N=232) Median (95% CI)[1]	Control 1 (N=229) n/ N (%)	Control 1 (N=229) Median (95% CI)[1]	Unstratified analysis Hazard Ratio (95% CI)[2]	Unstratified analysis p-Value[3]	Interaction p-Value[4]
SOC: Metabolism and nutrition disorders	Age (Years)							0.5706
	< 65	86/ 148 (58.1)	4.5 (2.5, 16.8)	51/ 131 (38.9)	NE (7.6, NE)	1.43 (1.01, 2.03)	0.0446	
	>= 65	58/ 84 (69.0)	1.3 (0.7, 3.5)	48/ 98 (49.0)	11.8 (3.5, 17.4)	1.67 (1.14, 2.46)	0.0086	
	Sex							0.7989
	Male	74/ 121 (61.2)	2.3 (1.2, 6.1)	49/ 112 (43.8)	8.7 (3.7, NE)	1.46 (1.01, 2.10)	0.0410	
	Female	70/ 111 (63.1)	3.7 (1.6, 12.4)	50/ 117 (42.7)	13.9 (4.6, NE)	1.51 (1.04, 2.17)	0.0286	
	Region							0.7011
	Europe	60/ 108 (55.6)	4.5 (2.8, 22.3)	34/ 103 (33.0)	13.9 (11.8, NE)	1.66 (1.08, 2.53)	0.0186	
	USA/Canada	13/ 15 (86.7)	0.5 (0.2, 2.8)	10/ 17 (58.8)	1.0 (0.4, NE)	1.75 (0.76, 4.00)	0.1803	
	Rest of World	71/ 109 (65.1)	2.3 (0.9, 5.8)	55/ 109 (50.5)	6.9 (3.5, NE)	1.36 (0.96, 1.95)	0.0873	
	ECOG-PS at Randomization							0.4197
	0	72/ 130 (55.4)	6.1 (2.8, 20.3)	43/ 130 (33.1)	NE (NE , NE)	1.69 (1.15, 2.47)	0.0067	
	1	72/ 102 (70.6)	1.5 (0.8, 3.5)	56/ 99 (56.6)	3.5 (1.6, 11.8)	1.34 (0.94, 1.90)	0.1050	
	Number of Organs Involved							0.8971
	<= 2	76/ 116 (65.5)	3.0 (1.1, 4.6)	53/ 119 (44.5)	9.7 (3.9, NE)	1.53 (1.07, 2.18)	0.0183	
	>= 3	68/ 116 (58.6)	3.5 (2.1, 13.8)	46/ 110 (41.8)	13.9 (4.4, NE)	1.44 (0.99, 2.09)	0.0577	
	Presence of Liver Metastases							0.4764
	Yes	90/ 146 (61.6)	3.3 (1.5, 6.1)	60/ 149 (40.3)	13.9 (9.7, NE)	1.56 (1.12, 2.17)	0.0074	
	No	54/ 86 (62.8)	3.4 (1.3, 6.7)	39/ 80 (48.8)	7.6 (3.2, NE)	1.38 (0.91, 2.10)	0.1233	
	Side of Tumor							0.9016
	Left	55/ 88 (62.5)	3.5 (2.3, 7.7)	39/ 90 (43.3)	9.7 (4.4, NE)	1.51 (1.00, 2.28)	0.0498	
	Right	89/ 144 (61.8)	2.8 (1.1, 6.1)	60/ 139 (43.2)	13.9 (4.6, NE)	1.48 (1.06, 2.06)	0.0204	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
Subgroup analysis was done for SOCs / PTs with significant overall treatment effect (significant log-rank).
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.
[4] P-Value for interaction from Cox proportional hazards model using ties=exact option with treatment, subgroup and treatment*subgroup interaction as covariates.
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

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Population: arm B vs. arm C
Datacut: 06JAN2025
Frequent AE by SOC, PT (incidence >= 10% or >=10 patients and incidence >= 1%) - Subgroup analysis
Safety Analysis Set

SOC/PT	Subgroup Level	EC+FOLFOX (N=232) n/ N (%)	EC+FOLFOX (N=232) Median (95% CI)[1]	Control 1 (N=229) n/ N (%)	Control 1 (N=229) Median (95% CI)[1]	Unstratified analysis Hazard Ratio (95% CI)[2]	Unstratified analysis p-Value[3]	Interaction p-Value[4]
SOC: Metabolism and nutrition disorders, PT: Hyperglycaemia	Age (Years)							0.9873
	< 65	13/ 148 (8.8)	NE (NE , NE)	4/ 131 (3.1)	NE (NE , NE)	2.33 (0.75, 7.24)	0.1338	
	>= 65	7/ 84 (8.3)	NE (NE , NE)	0/ 98 (0.0)	NE (NE , NE)	NE		
	Sex							0.9910
	Male	10/ 121 (8.3)	NE (NE , NE)	4/ 112 (3.6)	NE (NE , NE)	1.92 (0.59, 6.22)	0.2678	
	Female	10/ 111 (9.0)	NE (NE , NE)	0/ 117 (0.0)	NE (NE , NE)	NE		
	Region							0.9377
	Europe	7/ 108 (6.5)	NE (NE , NE)	1/ 103 (1.0)	NE (NE , NE)	4.54 (0.54, 38.05)	0.1280	
	USA/Canada	5/ 15 (33.3)	NE (5.9, NE)	1/ 17 (5.9)	NE (NE , NE)	5.28 (0.62, 45.21)	0.0879	
	Rest of World	8/ 109 (7.3)	NE (NE , NE)	2/ 109 (1.8)	NE (NE , NE)	3.76 (0.80, 17.73)	0.0720	
	ECOG-PS at Randomization							0.3533
	0	10/ 130 (7.7)	NE (NE , NE)	3/ 130 (2.3)	NE (NE , NE)	2.62 (0.71, 9.69)	0.1357	
	1	10/ 102 (9.8)	NE (NE , NE)	1/ 99 (1.0)	NE (NE , NE)	8.43 (1.07, 66.17)	0.0152	
	Number of Organs Involved							0.1478
	<= 2	13/ 116 (11.2)	NE (NE , NE)	1/ 119 (0.8)	NE (NE , NE)	10.69 (1.38, 82.59)	0.0048	
	>= 3	7/ 116 (6.0)	NE (NE , NE)	3/ 110 (2.7)	NE (NE , NE)	1.89 (0.49, 7.32)	0.3501	
	Presence of Liver Metastases							0.2648
	Yes	15/ 146 (10.3)	NE (NE , NE)	2/ 149 (1.3)	NE (NE , NE)	6.51 (1.48, 28.58)	0.0043	
	No	5/ 86 (5.8)	NE (NE , NE)	2/ 80 (2.5)	NE (NE , NE)	1.63 (0.30, 8.93)	0.5685	
	Side of Tumor							0.9902
	Left	8/ 88 (9.1)	NE (NE , NE)	4/ 90 (4.4)	NE (NE , NE)	1.61 (0.48, 5.45)	0.4355	
	Right	12/ 144 (8.3)	NE (NE , NE)	0/ 139 (0.0)	NE (NE , NE)	NE		

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
Subgroup analysis was done for SOCs / PTs with significant overall treatment effect (significant log-rank).
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.
[4] P-Value for interaction from Cox proportional hazards model using ties=exact option with treatment, subgroup and treatment*subgroup interaction as covariates.
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Frequent AE by SOC, PT (incidence >= 10% or >=10 patients and incidence >= 1%) - Subgroup analysis
Safety Analysis Set

SOC/PT	Subgroup Level	EC+FOLFOX (N=232) n/ N (%)	EC+FOLFOX (N=232) Median (95% CI)[1]	Control 1 (N=229) n/ N (%)	Control 1 (N=229) Median (95% CI)[1]	Unstratified analysis Hazard Ratio (95% CI)[2]	Unstratified analysis p-Value[3]	Interaction p-Value[4]
SOC: Metabolism and nutrition disorders, PT: Hypoalbuminaemia	Age (Years)							0.8072
	< 65	16/ 148 (10.8)	NE (NE , NE)	7/ 131 (5.3)	NE (NE , NE)	1.84 (0.75, 4.47)	0.1745	
	>= 65	14/ 84 (16.7)	NE (NE , NE)	7/ 98 (7.1)	NE (NE , NE)	2.13 (0.86, 5.29)	0.0939	
	Sex							0.1185
	Male	15/ 121 (12.4)	NE (NE , NE)	10/ 112 (8.9)	NE (NE , NE)	1.23 (0.55, 2.74)	0.6126	
	Female	15/ 111 (13.5)	NE (NE , NE)	4/ 117 (3.4)	NE (NE , NE)	3.71 (1.23, 11.20)	0.0125	
	Region							0.9995
	Europe	4/ 108 (3.7)	NE (NE , NE)	0/ 103 (0.0)	NE (NE , NE)	NE		
	USA/Canada	5/ 15 (33.3)	NE (5.1, NE)	3/ 17 (17.6)	NE (NE , NE)	1.75 (0.42, 7.34)	0.4376	
	Rest of World	21/ 109 (19.3)	NE (NE , NE)	11/ 109 (10.1)	NE (NE , NE)	1.83 (0.88, 3.80)	0.1001	
	ECOG-PS at Randomization							0.3037
	0	11/ 130 (8.5)	NE (NE , NE)	3/ 130 (2.3)	NE (NE , NE)	3.40 (0.95, 12.20)	0.0459	
	1	19/ 102 (18.6)	NE (NE , NE)	11/ 99 (11.1)	NE (NE , NE)	1.52 (0.72, 3.20)	0.2681	
	Number of Organs Involved							0.2889
	<= 2	15/ 116 (12.9)	NE (NE , NE)	5/ 119 (4.2)	NE (NE , NE)	2.88 (1.05, 7.93)	0.0322	
	>= 3	15/ 116 (12.9)	NE (NE , NE)	9/ 110 (8.2)	NE (NE , NE)	1.41 (0.61, 3.23)	0.4160	
	Presence of Liver Metastases							0.6633
	Yes	23/ 146 (15.8)	NE (NE , NE)	10/ 149 (6.7)	NE (NE , NE)	2.10 (1.00, 4.43)	0.0452	
	No	7/ 86 (8.1)	NE (NE , NE)	4/ 80 (5.0)	NE (NE , NE)	1.54 (0.45, 5.26)	0.4886	
	Side of Tumor							0.1410
	Left	12/ 88 (13.6)	NE (NE , NE)	9/ 90 (10.0)	NE (NE , NE)	1.18 (0.49, 2.80)	0.7137	
	Right	18/ 144 (12.5)	NE (NE , NE)	5/ 139 (3.6)	NE (NE , NE)	3.27 (1.21, 8.81)	0.0132	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
Subgroup analysis was done for SOCs / PTs with significant overall treatment effect (significant log-rank).
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.
[4] P-Value for interaction from Cox proportional hazards model using ties=exact option with treatment, subgroup and treatment*subgroup interaction as covariates.
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Frequent AE by SOC, PT (incidence >= 10% or >=10 patients and incidence >= 1%) - Subgroup analysis
Safety Analysis Set

SOC/PT	Subgroup Level	EC+FOLFOX (N=232) n/ N (%)	EC+FOLFOX (N=232) Median (95% CI)[1]	Control 1 (N=229) n/ N (%)	Control 1 (N=229) Median (95% CI)[1]	Unstratified analysis Hazard Ratio (95% CI)[2]	Unstratified analysis p-Value[3]	Interaction p-Value[4]
SOC: Metabolism and nutrition disorders, PT: Hypomagnesaemia	Age (Years)							0.1403
	< 65	18/ 148 (12.2)	NE (NE , NE)	7/ 131 (5.3)	NE (NE , NE)	1.71 (0.70, 4.15)	0.2318	
	>= 65	20/ 84 (23.8)	NE (NE , NE)	4/ 98 (4.1)	NE (NE , NE)	5.29 (1.80, 15.49)	0.0007	
	Sex							0.2021
	Male	17/ 121 (14.0)	NE (NE , NE)	7/ 112 (6.3)	NE (NE , NE)	2.01 (0.83, 4.87)	0.1120	
	Female	21/ 111 (18.9)	NE (NE , NE)	4/ 117 (3.4)	NE (NE , NE)	4.27 (1.45, 12.55)	0.0041	
	Region							0.4588
	Europe	15/ 108 (13.9)	NE (NE , NE)	4/ 103 (3.9)	NE (NE , NE)	2.90 (0.95, 8.81)	0.0497	
	USA/Canada	8/ 15 (53.3)	6.3 (2.8, NE)	1/ 17 (5.9)	NE (NE , NE)	8.88 (1.11, 71.17)	0.0129	
	Rest of World	15/ 109 (13.8)	NE (NE , NE)	6/ 109 (5.5)	NE (NE , NE)	2.05 (0.79, 5.33)	0.1332	
	ECOG-PS at Randomization							0.7581
	0	16/ 130 (12.3)	NE (NE , NE)	4/ 130 (3.1)	NE (NE , NE)	3.04 (1.01, 9.18)	0.0386	
	1	22/ 102 (21.6)	NE (NE , NE)	7/ 99 (7.1)	NE (NE , NE)	2.67 (1.14, 6.28)	0.0191	
	Number of Organs Involved							0.2233
	<= 2	21/ 116 (18.1)	NE (NE , NE)	4/ 119 (3.4)	NE (NE , NE)	4.21 (1.43, 12.36)	0.0046	
	>= 3	17/ 116 (14.7)	NE (NE , NE)	7/ 110 (6.4)	NE (NE , NE)	1.99 (0.82, 4.81)	0.1210	
	Presence of Liver Metastases							0.4250
	Yes	25/ 146 (17.1)	NE (NE , NE)	6/ 149 (4.0)	NE (NE , NE)	3.36 (1.37, 8.23)	0.0051	
	No	13/ 86 (15.1)	NE (NE , NE)	5/ 80 (6.3)	NE (NE , NE)	2.22 (0.79, 6.23)	0.1207	
	Side of Tumor							0.1156
	Left	11/ 88 (12.5)	NE (NE , NE)	6/ 90 (6.7)	NE (NE , NE)	1.32 (0.48, 3.68)	0.5879	
	Right	27/ 144 (18.8)	NE (NE , NE)	5/ 139 (3.6)	NE (NE , NE)	4.59 (1.76, 11.95)	0.0006	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
Subgroup analysis was done for SOCs / PTs with significant overall treatment effect (significant log-rank).
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.
[4] P-Value for interaction from Cox proportional hazards model using ties=exact option with treatment, subgroup and treatment*subgroup interaction as covariates.
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Frequent AE by SOC, PT (incidence >= 10% or >=10 patients and incidence >= 1%) - Subgroup analysis
Safety Analysis Set

SOC/PT	Subgroup Level	EC+FOLFOX (N=232) n/ N (%)	EC+FOLFOX (N=232) Median (95% CI)[1]	Control 1 (N=229) n/ N (%)	Control 1 (N=229) Median (95% CI)[1]	Unstratified analysis Hazard Ratio (95% CI)[2]	Unstratified analysis p-Value[3]	Interaction p-Value[4]
SOC: Metabolism and nutrition disorders, PT: Hypophosphataemia	Age (Years)							
	< 65	7/ 148 (4.7)		1/ 131 (0.8)				
	>= 65	7/ 84 (8.3)		2/ 98 (2.0)				
	Sex							0.7036
	Male	11/ 121 (9.1)	NE (NE , NE)	2/ 112 (1.8)	NE (NE , NE)	4.87 (1.08, 21.99)	0.0227	
	Female	3/ 111 (2.7)	NE (NE , NE)	1/ 117 (0.9)	NE (NE , NE)	2.13 (0.22, 21.05)	0.5075	
	Region							0.5781
	Europe	9/ 108 (8.3)	NE (NE , NE)	1/ 103 (1.0)	NE (NE , NE)	6.96 (0.88, 55.36)	0.0332	
	USA/Canada	1/ 15 (6.7)	NE (NE , NE)	0/ 17 (0.0)	NE (NE , NE)	NE		
	Rest of World	4/ 109 (3.7)	NE (NE , NE)	2/ 109 (1.8)	NE (NE , NE)	1.90 (0.35, 10.38)	0.4517	
	ECOG-PS at Randomization							0.7494
	0	6/ 130 (4.6)	NE (NE , NE)	1/ 130 (0.8)	NE (NE , NE)	5.77 (0.69, 48.01)	0.0661	
	1	8/ 102 (7.8)	NE (NE , NE)	2/ 99 (2.0)	NE (NE , NE)	3.22 (0.68, 15.26)	0.1204	
	Number of Organs Involved							0.9921
	<= 2	7/ 116 (6.0)	NE (NE , NE)	0/ 119 (0.0)	NE (NE , NE)	NE		
	>= 3	7/ 116 (6.0)	NE (NE , NE)	3/ 110 (2.7)	NE (NE , NE)	1.77 (0.45, 6.90)	0.4036	
	Presence of Liver Metastases							
	Yes	7/ 146 (4.8)		2/ 149 (1.3)				
	No	7/ 86 (8.1)		1/ 80 (1.3)				
	Side of Tumor							0.3397
	Left	5/ 88 (5.7)	NE (NE , NE)	2/ 90 (2.2)	NE (NE , NE)	2.11 (0.41, 10.92)	0.3621	
	Right	9/ 144 (6.3)	NE (NE , NE)	1/ 139 (0.7)	NE (NE , NE)	8.00 (1.01, 63.43)	0.0194	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
Subgroup analysis was done for SOCs / PTs with significant overall treatment effect (significant log-rank).
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.
[4] P-Value for interaction from Cox proportional hazards model using ties=exact option with treatment, subgroup and treatment*subgroup interaction as covariates.
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Frequent AE by SOC, PT (incidence >= 10% or >=10 patients and incidence >= 1%) - Subgroup analysis
Safety Analysis Set

SOC/PT	Subgroup Level	EC+FOLFOX (N=232) n/ N (%)	EC+FOLFOX (N=232) Median (95% CI)[1]	Control 1 (N=229) n/ N (%)	Control 1 (N=229) Median (95% CI)[1]	Unstratified analysis Hazard Ratio (95% CI)[2]	Unstratified analysis p-Value[3]	Interaction p-Value[4]
SOC: Musculoskeletal and connective tissue disorders	Age (Years)							0.7532
	< 65	92/ 148 (62.2)	7.0 (5.7, 10.0)	31/ 131 (23.7)	NE (NE , NE)	2.46 (1.63, 3.71)	<.0001	
	>= 65	41/ 84 (48.8)	12.4 (6.9, 15.6)	19/ 98 (19.4)	NE (17.2, NE)	2.08 (1.20, 3.60)	0.0073	
	Sex							0.9133
	Male	64/ 121 (52.9)	10.0 (6.4, 16.5)	23/ 112 (20.5)	NE (17.2, NE)	2.39 (1.48, 3.86)	0.0002	
	Female	69/ 111 (62.2)	7.2 (5.7, 11.1)	27/ 117 (23.1)	NE (14.7, NE)	2.36 (1.51, 3.69)	0.0001	
	Region							0.0585
	Europe	63/ 108 (58.3)	10.8 (6.9, 11.5)	24/ 103 (23.3)	NE (10.6, NE)	1.87 (1.16, 3.01)	0.0086	
	USA/Canada	9/ 15 (60.0)	3.9 (2.8, NE)	9/ 17 (52.9)	8.6 (1.4, NE)	1.17 (0.45, 3.00)	0.7455	
	Rest of World	61/ 109 (56.0)	7.4 (5.8, 13.4)	17/ 109 (15.6)	NE (17.2, NE)	3.74 (2.18, 6.43)	<.0001	
	ECOG-PS at Randomization							0.2945
	0	69/ 130 (53.1)	10.9 (7.6, 16.5)	30/ 130 (23.1)	NE (17.2, NE)	2.05 (1.33, 3.16)	0.0009	
	1	64/ 102 (62.7)	6.4 (4.5, 11.1)	20/ 99 (20.2)	NE (10.6, NE)	2.84 (1.71, 4.71)	<.0001	
	Number of Organs Involved							0.6573
	<= 2	64/ 116 (55.2)	11.1 (7.2, 16.5)	24/ 119 (20.2)	NE (17.2, NE)	2.23 (1.39, 3.58)	0.0007	
	>= 3	69/ 116 (59.5)	6.7 (4.9, 9.4)	26/ 110 (23.6)	NE (11.2, NE)	2.54 (1.61, 3.98)	<.0001	
	Presence of Liver Metastases							0.4431
	Yes	79/ 146 (54.1)	8.6 (6.7, 12.4)	29/ 149 (19.5)	NE (17.2, NE)	2.63 (1.72, 4.04)	<.0001	
	No	54/ 86 (62.8)	7.4 (5.8, 11.5)	21/ 80 (26.3)	NE (11.2, NE)	2.02 (1.21, 3.36)	0.0059	
	Side of Tumor							0.3132
	Left	49/ 88 (55.7)	9.6 (6.9, 13.4)	21/ 90 (23.3)	NE (14.7, NE)	1.89 (1.13, 3.18)	0.0141	
	Right	84/ 144 (58.3)	7.6 (5.4, 11.3)	29/ 139 (20.9)	NE (17.2, NE)	2.72 (1.78, 4.16)	<.0001	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
Subgroup analysis was done for SOCs / PTs with significant overall treatment effect (significant log-rank).
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.
[4] P-Value for interaction from Cox proportional hazards model using ties=exact option with treatment, subgroup and treatment*subgroup interaction as covariates.
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

Pierre Fabre Pharma GmbH: Final
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Population: arm B vs. arm C
Datacut: 06JAN2025
Frequent AE by SOC, PT (incidence >= 10% or >=10 patients and incidence >= 1%) - Subgroup analysis
Safety Analysis Set

SOC/PT	Subgroup Level	EC+FOLFOX (N=232) n/ N (%)	EC+FOLFOX (N=232) Median (95% CI)[1]	Control 1 (N=229) n/ N (%)	Control 1 (N=229) Median (95% CI)[1]	Unstratified analysis Hazard Ratio (95% CI)[2]	Unstratified analysis p-Value[3]	Interaction p-Value[4]
SOC: Musculoskeletal and connective tissue disorders, PT: Arthralgia	Age (Years)							0.2147
	< 65	49/ 148 (33.1)	NE (18.9, NE)	5/ 131 (3.8)	NE (NE , NE)	7.02 (2.79, 17.69)	<.0001	
	>= 65	24/ 84 (28.6)	NE (13.4, NE)	7/ 98 (7.1)	NE (20.8, NE)	2.85 (1.22, 6.67)	0.0116	
	Sex							0.1791
	Male	35/ 121 (28.9)	NE (17.4, NE)	3/ 112 (2.7)	NE (20.8, NE)	9.14 (2.80, 29.81)	<.0001	
	Female	38/ 111 (34.2)	20.7 (13.3, NE)	9/ 117 (7.7)	NE (NE , NE)	3.17 (1.52, 6.59)	0.0012	
	Region							0.5812
	Europe	39/ 108 (36.1)	18.9 (12.5, NE)	4/ 103 (3.9)	NE (NE , NE)	6.33 (2.25, 17.82)	<.0001	
	USA/Canada	4/ 15 (26.7)	NE (5.0, NE)	1/ 17 (5.9)	NE (NE , NE)	3.66 (0.41, 32.81)	0.2149	
	Rest of World	30/ 109 (27.5)	NE (20.3, NE)	7/ 109 (6.4)	NE (20.8, NE)	3.51 (1.53, 8.06)	0.0016	
	ECOG-PS at Randomization							0.5282
	0	38/ 130 (29.2)	NE (18.9, NE)	5/ 130 (3.8)	NE (NE , NE)	5.56 (2.17, 14.23)	<.0001	
	1	35/ 102 (34.3)	NE (11.3, NE)	7/ 99 (7.1)	NE (NE , NE)	3.94 (1.74, 8.89)	0.0004	
	Number of Organs Involved							0.2525
	<= 2	37/ 116 (31.9)	NE (17.4, NE)	8/ 119 (6.7)	NE (20.8, NE)	3.29 (1.52, 7.13)	0.0015	
	>= 3	36/ 116 (31.0)	NE (13.4, NE)	4/ 110 (3.6)	NE (NE , NE)	7.36 (2.62, 20.73)	<.0001	
	Presence of Liver Metastases							0.1776
	Yes	43/ 146 (29.5)	NE (16.5, NE)	5/ 149 (3.4)	NE (NE , NE)	7.29 (2.88, 18.46)	<.0001	
	No	30/ 86 (34.9)	20.3 (17.3, NE)	7/ 80 (8.8)	NE (NE , NE)	2.83 (1.23, 6.51)	0.0106	
	Side of Tumor							0.5042
	Left	26/ 88 (29.5)	NE (17.3, NE)	3/ 90 (3.3)	NE (NE , NE)	6.90 (2.07, 22.95)	0.0003	
	Right	47/ 144 (32.6)	20.7 (14.0, NE)	9/ 139 (6.5)	NE (NE , NE)	3.96 (1.93, 8.10)	<.0001	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
Subgroup analysis was done for SOCs / PTs with significant overall treatment effect (significant log-rank).
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.
[4] P-Value for interaction from Cox proportional hazards model using ties=exact option with treatment, subgroup and treatment*subgroup interaction as covariates.
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Frequent AE by SOC, PT (incidence >= 10% or >=10 patients and incidence >= 1%) - Subgroup analysis
Safety Analysis Set

SOC/PT	Subgroup Level	EC+FOLFOX (N=232) n/ N (%)	EC+FOLFOX (N=232) Median (95% CI)[1]	Control 1 (N=229) n/ N (%)	Control 1 (N=229) Median (95% CI)[1]	Unstratified analysis Hazard Ratio (95% CI)[2]	Unstratified analysis p-Value[3]	Interaction p-Value[4]
SOC: Musculoskeletal and connective tissue disorders, PT: Myalgia	Age (Years)							0.3599
	< 65	29/ 148 (19.6)	NE (NE , NE)	5/ 131 (3.8)	NE (NE , NE)	3.92 (1.50, 10.21)	0.0026	
	>= 65	9/ 84 (10.7)	NE (NE , NE)	4/ 98 (4.1)	NE (NE , NE)	2.18 (0.67, 7.12)	0.1862	
	Sex							0.5144
	Male	18/ 121 (14.9)	NE (NE , NE)	5/ 112 (4.5)	NE (NE , NE)	2.67 (0.98, 7.26)	0.0459	
	Female	20/ 111 (18.0)	NE (NE , NE)	4/ 117 (3.4)	NE (NE , NE)	3.97 (1.34, 11.71)	0.0072	
	Region							0.1469
	Europe	20/ 108 (18.5)	NE (NE , NE)	8/ 103 (7.8)	NE (NE , NE)	1.35 (0.58, 3.15)	0.4808	
	USA/Canada	1/ 15 (6.7)	NE (NE , NE)	0/ 17 (0.0)	NE (NE , NE)	NE		
	Rest of World	17/ 109 (15.6)	NE (NE , NE)	1/ 109 (0.9)	NE (NE , NE)	17.09 (2.28, 128.38)	0.0002	
	ECOG-PS at Randomization							0.6372
	0	18/ 130 (13.8)	NE (NE , NE)	5/ 130 (3.8)	NE (NE , NE)	2.63 (0.97, 7.18)	0.0496	
	1	20/ 102 (19.6)	NE (NE , NE)	4/ 99 (4.0)	NE (NE , NE)	4.02 (1.36, 11.83)	0.0064	
	Number of Organs Involved							0.0252
	<= 2	16/ 116 (13.8)	NE (NE , NE)	8/ 119 (6.7)	NE (NE , NE)	1.62 (0.69, 3.81)	0.2678	
	>= 3	22/ 116 (19.0)	NE (23.7, NE)	1/ 110 (0.9)	NE (NE , NE)	16.54 (2.22, 123.23)	0.0002	
	Presence of Liver Metastases							0.3218
	Yes	26/ 146 (17.8)	NE (NE , NE)	5/ 149 (3.4)	NE (NE , NE)	4.27 (1.63, 11.18)	0.0013	
	No	12/ 86 (14.0)	NE (NE , NE)	4/ 80 (5.0)	NE (NE , NE)	2.04 (0.64, 6.49)	0.2174	
	Side of Tumor							0.9555
	Left	16/ 88 (18.2)	NE (NE , NE)	4/ 90 (4.4)	NE (NE , NE)	3.24 (1.07, 9.80)	0.0277	
	Right	22/ 144 (15.3)	NE (NE , NE)	5/ 139 (3.6)	NE (NE , NE)	3.27 (1.23, 8.70)	0.0122	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
Subgroup analysis was done for SOCs / PTs with significant overall treatment effect (significant log-rank).
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.
[4] P-Value for interaction from Cox proportional hazards model using ties=exact option with treatment, subgroup and treatment*subgroup interaction as covariates.
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Frequent AE by SOC, PT (incidence >= 10% or >=10 patients and incidence >= 1%) - Subgroup analysis
Safety Analysis Set

SOC/PT	Subgroup Level	EC+FOLFOX (N=232) n/ N (%)	EC+FOLFOX (N=232) Median (95% CI)[1]	Control 1 (N=229) n/ N (%)	Control 1 (N=229) Median (95% CI)[1]	Unstratified analysis Hazard Ratio (95% CI)[2]	Unstratified analysis p-Value[3]	Interaction p-Value[4]
SOC: Neoplasms benign, malignant and unspecified (incl cysts and polyps)	Age (Years)							0.3008
	< 65	24/ 148 (16.2)	NE (NE , NE)	6/ 131 (4.6)	NE (NE , NE)	2.99 (1.22, 7.37)	0.0124	
	>= 65	19/ 84 (22.6)	NE (NE , NE)	3/ 98 (3.1)	NE (NE , NE)	6.60 (1.95, 22.37)	0.0005	
	Sex							0.7672
	Male	23/ 121 (19.0)	NE (NE , NE)	5/ 112 (4.5)	NE (NE , NE)	3.58 (1.36, 9.47)	0.0060	
	Female	20/ 111 (18.0)	NE (NE , NE)	4/ 117 (3.4)	NE (NE , NE)	4.61 (1.56, 13.57)	0.0024	
	Region							0.9777
	Europe	22/ 108 (20.4)	NE (NE , NE)	5/ 103 (4.9)	NE (NE , NE)	3.36 (1.26, 8.94)	0.0101	
	USA/Canada	3/ 15 (20.0)	NE (NE , NE)	0/ 17 (0.0)	NE (NE , NE)	NE		
	Rest of World	18/ 109 (16.5)	NE (NE , NE)	4/ 109 (3.7)	NE (NE , NE)	4.10 (1.38, 12.18)	0.0061	
	ECOG-PS at Randomization							0.7157
	0	26/ 130 (20.0)	NE (NE , NE)	6/ 130 (4.6)	NE (NE , NE)	3.47 (1.42, 8.50)	0.0038	
	1	17/ 102 (16.7)	NE (NE , NE)	3/ 99 (3.0)	NE (NE , NE)	5.30 (1.55, 18.11)	0.0029	
	Number of Organs Involved							0.1133
	<= 2	22/ 116 (19.0)	NE (NE , NE)	2/ 119 (1.7)	NE (NE , NE)	9.84 (2.30, 42.04)	0.0002	
	>= 3	21/ 116 (18.1)	NE (NE , NE)	7/ 110 (6.4)	NE (NE , NE)	2.44 (1.04, 5.77)	0.0352	
	Presence of Liver Metastases							0.6080
	Yes	29/ 146 (19.9)	NE (NE , NE)	7/ 149 (4.7)	NE (NE , NE)	3.58 (1.56, 8.21)	0.0013	
	No	14/ 86 (16.3)	NE (NE , NE)	2/ 80 (2.5)	NE (NE , NE)	5.98 (1.35, 26.41)	0.0073	
	Side of Tumor							0.8347
	Left	13/ 88 (14.8)	NE (NE , NE)	3/ 90 (3.3)	NE (NE , NE)	3.60 (1.01, 12.75)	0.0345	
	Right	30/ 144 (20.8)	NE (NE , NE)	6/ 139 (4.3)	NE (NE , NE)	4.32 (1.79, 10.40)	0.0004	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
Subgroup analysis was done for SOCs / PTs with significant overall treatment effect (significant log-rank).
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.
[4] P-Value for interaction from Cox proportional hazards model using ties=exact option with treatment, subgroup and treatment*subgroup interaction as covariates.
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Frequent AE by SOC, PT (incidence >= 10% or >=10 patients and incidence >= 1%) - Subgroup analysis
Safety Analysis Set

SOC/PT	Subgroup Level	EC+FOLFOX (N=232) n/ N (%)	EC+FOLFOX (N=232) Median (95% CI)[1]	Control 1 (N=229) n/ N (%)	Control 1 (N=229) Median (95% CI)[1]	Unstratified analysis Hazard Ratio (95% CI)[2]	Unstratified analysis p-Value[3]	Interaction p-Value[4]
SOC: Renal and urinary disorders, PT: Proteinuria	Age (Years)							0.9453
	< 65	3/ 148 (2.0)	NE (NE , NE)	8/ 131 (6.1)	NE (16.8, NE)	0.19 (0.05, 0.74)	0.0093	
	>= 65	3/ 84 (3.6)	NE (NE , NE)	10/ 98 (10.2)	NE (18.0, NE)	0.19 (0.05, 0.72)	0.0081	
	Sex							0.1235
	Male	2/ 121 (1.7)	NE (NE , NE)	12/ 112 (10.7)	NE (16.8, NE)	0.07 (0.01, 0.32)	<.0001	
	Female	4/ 111 (3.6)	NE (NE , NE)	6/ 117 (5.1)	NE (18.0, NE)	0.44 (0.12, 1.65)	0.2111	
	Region							0.9175
	Europe	0/ 108 (0.0)	NE (NE , NE)	7/ 103 (6.8)	NE (16.8, NE)	NE		
	USA/Canada	2/ 15 (13.3)	NE (NE , NE)	3/ 17 (17.6)	NE (NE , NE)	0.66 (0.11, 3.97)	0.6499	
	Rest of World	4/ 109 (3.7)	NE (NE , NE)	8/ 109 (7.3)	NE (NE , NE)	0.29 (0.08, 1.02)	0.0434	
	ECOG-PS at Randomization							0.9910
	0	6/ 130 (4.6)	NE (NE , NE)	10/ 130 (7.7)	NE (18.0, NE)	0.28 (0.10, 0.83)	0.0159	
	1	0/ 102 (0.0)	NE (NE , NE)	8/ 99 (8.1)	NE (NE , NE)	NE		
	Number of Organs Involved							0.9914
	<= 2	6/ 116 (5.2)	NE (NE , NE)	12/ 119 (10.1)	NE (18.0, NE)	0.26 (0.09, 0.75)	0.0083	
	>= 3	0/ 116 (0.0)	NE (NE , NE)	6/ 110 (5.5)	NE (NE , NE)	NE		
	Presence of Liver Metastases							0.2823
	Yes	4/ 146 (2.7)	NE (NE , NE)	9/ 149 (6.0)	NE (18.0, NE)	0.25 (0.07, 0.85)	0.0179	
	No	2/ 86 (2.3)	NE (NE , NE)	9/ 80 (11.3)	NE (16.8, NE)	0.10 (0.02, 0.53)	0.0020	
	Side of Tumor							0.8139
	Left	3/ 88 (3.4)	NE (NE , NE)	8/ 90 (8.9)	NE (16.8, NE)	0.22 (0.05, 0.87)	0.0212	
	Right	3/ 144 (2.1)	NE (NE , NE)	10/ 139 (7.2)	NE (18.0, NE)	0.15 (0.04, 0.59)	0.0023	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
Subgroup analysis was done for SOCs / PTs with significant overall treatment effect (significant log-rank).
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.
[4] P-Value for interaction from Cox proportional hazards model using ties=exact option with treatment, subgroup and treatment*subgroup interaction as covariates.
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Frequent AE by SOC, PT (incidence >= 10% or >=10 patients and incidence >= 1%) - Subgroup analysis
Safety Analysis Set

SOC/PT	Subgroup Level	EC+FOLFOX (N=232) n/ N (%)	EC+FOLFOX (N=232) Median (95% CI)[1]	Control 1 (N=229) n/ N (%)	Control 1 (N=229) Median (95% CI)[1]	Unstratified analysis Hazard Ratio (95% CI)[2]	Unstratified analysis p-Value[3]	Interaction p-Value[4]
SOC: Skin and subcutaneous tissue disorders	Age (Years)							0.1156
	< 65	118/ 148 (79.7)	1.0 (0.7, 1.9)	50/ 131 (38.2)	10.8 (5.4, NE)	2.89 (2.07, 4.04)	<.0001	
	>= 65	70/ 84 (83.3)	1.2 (0.9, 1.8)	29/ 98 (29.6)	34.3 (8.3, 34.3)	4.90 (3.15, 7.62)	<.0001	
	Sex							0.2678
	Male	94/ 121 (77.7)	1.0 (0.8, 1.8)	34/ 112 (30.4)	34.3 (10.8, 34.3)	4.11 (2.76, 6.12)	<.0001	
	Female	94/ 111 (84.7)	1.0 (0.8, 1.9)	45/ 117 (38.5)	10.0 (5.1, NE)	3.15 (2.20, 4.51)	<.0001	
	Region							0.8633
	Europe	91/ 108 (84.3)	1.3 (0.9, 2.0)	35/ 103 (34.0)	NE (8.0, NE)	3.38 (2.28, 5.00)	<.0001	
	USA/Canada	13/ 15 (86.7)	0.8 (0.4, 2.8)	6/ 17 (35.3)	NE (2.7, NE)	4.39 (1.55, 12.40)	0.0023	
	Rest of World	84/ 109 (77.1)	1.0 (0.6, 1.8)	38/ 109 (34.9)	34.3 (8.1, 34.3)	3.61 (2.44, 5.34)	<.0001	
	ECOG-PS at Randomization							0.3861
	0	105/ 130 (80.8)	1.0 (0.9, 1.8)	41/ 130 (31.5)	34.3 (8.1, 34.3)	3.96 (2.74, 5.72)	<.0001	
	1	83/ 102 (81.4)	1.2 (0.8, 1.9)	38/ 99 (38.4)	10.0 (6.2, NE)	3.13 (2.13, 4.61)	<.0001	
	Number of Organs Involved							0.3489
	<= 2	97/ 116 (83.6)	0.8 (0.5, 1.0)	43/ 119 (36.1)	34.3 (8.0, 34.3)	3.95 (2.74, 5.70)	<.0001	
	>= 3	91/ 116 (78.4)	1.6 (1.0, 2.4)	36/ 110 (32.7)	NE (8.1, NE)	3.19 (2.17, 4.71)	<.0001	
	Presence of Liver Metastases							0.8608
	Yes	121/ 146 (82.9)	1.0 (0.8, 1.6)	54/ 149 (36.2)	34.3 (8.0, 34.3)	3.54 (2.56, 4.89)	<.0001	
	No	67/ 86 (77.9)	1.1 (0.9, 1.9)	25/ 80 (31.3)	NE (8.3, NE)	3.68 (2.32, 5.85)	<.0001	
	Side of Tumor							0.2911
	Left	64/ 88 (72.7)	1.9 (1.0, 3.0)	28/ 90 (31.1)	NE (10.8, NE)	2.98 (1.91, 4.67)	<.0001	
	Right	124/ 144 (86.1)	0.9 (0.7, 1.2)	51/ 139 (36.7)	34.3 (8.0, 34.3)	4.05 (2.91, 5.64)	<.0001	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
Subgroup analysis was done for SOCs / PTs with significant overall treatment effect (significant log-rank).
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.
[4] P-Value for interaction from Cox proportional hazards model using ties=exact option with treatment, subgroup and treatment*subgroup interaction as covariates.
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Frequent AE by SOC, PT (incidence >= 10% or >=10 patients and incidence >= 1%) - Subgroup analysis
Safety Analysis Set

SOC/PT	Subgroup Level	EC+FOLFOX (N=232) n/ N (%)	EC+FOLFOX (N=232) Median (95% CI)[1]	Control 1 (N=229) n/ N (%)	Control 1 (N=229) Median (95% CI)[1]	Unstratified analysis Hazard Ratio (95% CI)[2]	Unstratified analysis p-Value[3]	Interaction p-Value[4]
SOC: Skin and subcutaneous tissue disorders, PT: Alopecia	Age (Years)							0.8057
	< 65	39/ 148 (26.4)	NE (NE , NE)	17/ 131 (13.0)	NE (NE , NE)	1.89 (1.07, 3.34)	0.0266	
	>= 65	14/ 84 (16.7)	NE (NE , NE)	9/ 98 (9.2)	NE (NE , NE)	1.64 (0.71, 3.79)	0.2433	
	Sex							0.4583
	Male	18/ 121 (14.9)	NE (NE , NE)	6/ 112 (5.4)	NE (NE , NE)	2.63 (1.04, 6.63)	0.0333	
	Female	35/ 111 (31.5)	NE (NE , NE)	20/ 117 (17.1)	NE (NE , NE)	1.69 (0.97, 2.93)	0.0588	
	Region							0.1939
	Europe	20/ 108 (18.5)	NE (NE , NE)	14/ 103 (13.6)	NE (NE , NE)	1.13 (0.57, 2.24)	0.7333	
	USA/Canada	7/ 15 (46.7)	NE (2.1, NE)	3/ 17 (17.6)	NE (NE , NE)	2.67 (0.69, 10.35)	0.1389	
	Rest of World	26/ 109 (23.9)	NE (NE , NE)	9/ 109 (8.3)	NE (NE , NE)	2.85 (1.33, 6.08)	0.0047	
	ECOG-PS at Randomization							0.6849
	0	29/ 130 (22.3)	NE (NE , NE)	13/ 130 (10.0)	NE (NE , NE)	2.00 (1.04, 3.86)	0.0345	
	1	24/ 102 (23.5)	NE (NE , NE)	13/ 99 (13.1)	NE (NE , NE)	1.71 (0.87, 3.36)	0.1161	
	Number of Organs Involved							0.4942
	<= 2	27/ 116 (23.3)	NE (NE , NE)	16/ 119 (13.4)	NE (NE , NE)	1.60 (0.86, 2.97)	0.1360	
	>= 3	26/ 116 (22.4)	NE (NE , NE)	10/ 110 (9.1)	NE (NE , NE)	2.27 (1.10, 4.72)	0.0235	
	Presence of Liver Metastases							0.4047
	Yes	38/ 146 (26.0)	NE (NE , NE)	17/ 149 (11.4)	NE (NE , NE)	2.18 (1.23, 3.86)	0.0063	
	No	15/ 86 (17.4)	NE (NE , NE)	9/ 80 (11.3)	NE (NE , NE)	1.35 (0.59, 3.10)	0.4779	
	Side of Tumor							0.8689
	Left	17/ 88 (19.3)	NE (NE , NE)	9/ 90 (10.0)	NE (NE , NE)	1.79 (0.79, 4.01)	0.1550	
	Right	36/ 144 (25.0)	NE (NE , NE)	17/ 139 (12.2)	NE (NE , NE)	1.89 (1.06, 3.37)	0.0280	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
Subgroup analysis was done for SOCs / PTs with significant overall treatment effect (significant log-rank).
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.
[4] P-Value for interaction from Cox proportional hazards model using ties=exact option with treatment, subgroup and treatment*subgroup interaction as covariates.
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Frequent AE by SOC, PT (incidence >= 10% or >=10 patients and incidence >= 1%) - Subgroup analysis
Safety Analysis Set

SOC/PT	Subgroup Level	EC+FOLFOX (N=232) n/ N (%)	EC+FOLFOX (N=232) Median (95% CI)[1]	Control 1 (N=229) n/ N (%)	Control 1 (N=229) Median (95% CI)[1]	Unstratified analysis Hazard Ratio (95% CI)[2]	Unstratified analysis p-Value[3]	Interaction p-Value[4]
SOC: Skin and subcutaneous tissue disorders, PT: Dermatitis acneiform	Age (Years)							0.9878
	< 65	36/ 148 (24.3)	NE (NE , NE)	2/ 131 (1.5)	NE (NE , NE)	15.84 (3.81, 65.84)	<.0001	
	>= 65	7/ 84 (8.3)	NE (NE , NE)	0/ 98 (0.0)	NE (NE , NE)	NE		
	Sex							0.8481
	Male	25/ 121 (20.7)	NE (NE , NE)	1/ 112 (0.9)	NE (NE , NE)	22.43 (3.04, 165.74)	<.0001	
	Female	18/ 111 (16.2)	NE (NE , NE)	1/ 117 (0.9)	NE (NE , NE)	16.29 (2.17, 122.35)	0.0002	
	Region							0.7407
	Europe	14/ 108 (13.0)	NE (NE , NE)	0/ 103 (0.0)	NE (NE , NE)	NE		
	USA/Canada	6/ 15 (40.0)	NE (3.7, NE)	1/ 17 (5.9)	NE (NE , NE)	7.28 (0.88, 60.42)	0.0312	
	Rest of World	23/ 109 (21.1)	NE (NE , NE)	1/ 109 (0.9)	NE (NE , NE)	22.33 (3.01, 165.69)	<.0001	
	ECOG-PS at Randomization							0.7894
	0	25/ 130 (19.2)	NE (NE , NE)	1/ 130 (0.8)	NE (NE , NE)	23.52 (3.18, 173.84)	<.0001	
	1	18/ 102 (17.6)	NE (NE , NE)	1/ 99 (1.0)	NE (NE , NE)	15.50 (2.07, 116.31)	0.0004	
	Number of Organs Involved							0.8997
	<= 2	22/ 116 (19.0)	NE (NE , NE)	1/ 119 (0.8)	NE (NE , NE)	21.88 (2.94, 162.70)	<.0001	
	>= 3	21/ 116 (18.1)	NE (NE , NE)	1/ 110 (0.9)	NE (NE , NE)	17.10 (2.30, 127.22)	0.0001	
	Presence of Liver Metastases							0.5770
	Yes	29/ 146 (19.9)	NE (NE , NE)	1/ 149 (0.7)	NE (NE , NE)	27.51 (3.75, 202.06)	<.0001	
	No	14/ 86 (16.3)	NE (NE , NE)	1/ 80 (1.3)	NE (NE , NE)	11.64 (1.52, 89.06)	0.0028	
	Side of Tumor							0.9472
	Left	20/ 88 (22.7)	NE (NE , NE)	1/ 90 (1.1)	NE (NE , NE)	17.36 (2.32, 129.98)	0.0001	
	Right	23/ 144 (16.0)	NE (NE , NE)	1/ 139 (0.7)	NE (NE , NE)	21.65 (2.92, 160.32)	<.0001	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
Subgroup analysis was done for SOCs / PTs with significant overall treatment effect (significant log-rank).
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.
[4] P-Value for interaction from Cox proportional hazards model using ties=exact option with treatment, subgroup and treatment*subgroup interaction as covariates.
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

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Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Frequent AE by SOC, PT (incidence >= 10% or >=10 patients and incidence >= 1%) - Subgroup analysis
Safety Analysis Set

SOC/PT	Subgroup Level	EC+FOLFOX (N=232) n/ N (%)	EC+FOLFOX (N=232) Median (95% CI)[1]	Control 1 (N=229) n/ N (%)	Control 1 (N=229) Median (95% CI)[1]	Unstratified analysis Hazard Ratio (95% CI)[2]	Unstratified analysis p-Value[3]	Interaction p-Value[4]
SOC: Skin and subcutaneous tissue disorders, PT: Dry skin	Age (Years)							0.6498
	< 65	24/ 148 (16.2)	NE (NE , NE)	7/ 131 (5.3)	NE (NE , NE)	2.59 (1.11, 6.06)	0.0226	
	>= 65	14/ 84 (16.7)	NE (23.7, NE)	4/ 98 (4.1)	NE (NE , NE)	2.89 (0.93, 8.94)	0.0546	
	Sex							0.7817
	Male	20/ 121 (16.5)	NE (NE , NE)	5/ 112 (4.5)	NE (NE , NE)	3.08 (1.15, 8.28)	0.0191	
	Female	18/ 111 (16.2)	NE (NE , NE)	6/ 117 (5.1)	NE (NE , NE)	2.39 (0.93, 6.13)	0.0615	
	Region							0.2450
	Europe	21/ 108 (19.4)	NE (NE , NE)	3/ 103 (2.9)	NE (NE , NE)	5.43 (1.60, 18.43)	0.0024	
	USA/Canada	4/ 15 (26.7)	NE (6.9, NE)	1/ 17 (5.9)	NE (NE , NE)	3.58 (0.40, 32.14)	0.2238	
	Rest of World	13/ 109 (11.9)	NE (NE , NE)	7/ 109 (6.4)	NE (NE , NE)	1.42 (0.56, 3.63)	0.4554	
	ECOG-PS at Randomization							0.5991
	0	24/ 130 (18.5)	NE (NE , NE)	6/ 130 (4.6)	NE (NE , NE)	2.94 (1.18, 7.30)	0.0151	
	1	14/ 102 (13.7)	NE (NE , NE)	5/ 99 (5.1)	NE (NE , NE)	2.46 (0.88, 6.85)	0.0754	
	Number of Organs Involved							0.5092
	<= 2	18/ 116 (15.5)	NE (NE , NE)	4/ 119 (3.4)	NE (NE , NE)	3.76 (1.26, 11.22)	0.0113	
	>= 3	20/ 116 (17.2)	23.7 (23.7, NE)	7/ 110 (6.4)	NE (NE , NE)	2.16 (0.90, 5.16)	0.0757	
	Presence of Liver Metastases							0.1652
	Yes	25/ 146 (17.1)	NE (23.7, NE)	10/ 149 (6.7)	NE (NE , NE)	2.08 (0.99, 4.37)	0.0479	
	No	13/ 86 (15.1)	NE (NE , NE)	1/ 80 (1.3)	NE (NE , NE)	9.13 (1.18, 70.64)	0.0106	
	Side of Tumor							0.7343
	Left	15/ 88 (17.0)	NE (NE , NE)	5/ 90 (5.6)	NE (NE , NE)	2.48 (0.88, 6.97)	0.0744	
	Right	23/ 144 (16.0)	NE (NE , NE)	6/ 139 (4.3)	NE (NE , NE)	2.91 (1.18, 7.21)	0.0158	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
Subgroup analysis was done for SOCs / PTs with significant overall treatment effect (significant log-rank).
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.
[4] P-Value for interaction from Cox proportional hazards model using ties=exact option with treatment, subgroup and treatment*subgroup interaction as covariates.
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Frequent AE by SOC, PT (incidence >= 10% or >=10 patients and incidence >= 1%) - Subgroup analysis
Safety Analysis Set

SOC/PT	Subgroup Level	EC+FOLFOX (N=232) n/ N (%)	EC+FOLFOX (N=232) Median (95% CI)[1]	Control 1 (N=229) n/ N (%)	Control 1 (N=229) Median (95% CI)[1]	Unstratified analysis Hazard Ratio (95% CI)[2]	Unstratified analysis p-Value[3]	Interaction p-Value[4]
SOC: Skin and subcutaneous tissue disorders, PT: Pigmentation disorder	Age (Years)							0.5345
	< 65	13/ 148 (8.8)	NE (NE , NE)	1/ 131 (0.8)	NE (NE , NE)	12.06 (1.58, 92.15)	0.0022	
	>= 65	4/ 84 (4.8)	NE (NE , NE)	1/ 98 (1.0)	NE (NE , NE)	4.59 (0.51, 41.07)	0.1341	
	Sex							0.9886
	Male	8/ 121 (6.6)	NE (NE , NE)	0/ 112 (0.0)	NE (NE , NE)	NE		
	Female	9/ 111 (8.1)	NE (NE , NE)	2/ 117 (1.7)	NE (NE , NE)	4.89 (1.06, 22.63)	0.0246	
	Region							1.0000
	Europe	0/ 108 (0.0)	NE (NE , NE)	0/ 103 (0.0)	NE (NE , NE)	NE		
	USA/Canada	0/ 15 (0.0)	NE (NE , NE)	0/ 17 (0.0)	NE (NE , NE)	NE		
	Rest of World	17/ 109 (15.6)	NE (NE , NE)	2/ 109 (1.8)	NE (NE , NE)	9.14 (2.11, 39.56)	0.0003	
	ECOG-PS at Randomization							0.7822
	0	10/ 130 (7.7)	NE (NE , NE)	1/ 130 (0.8)	NE (NE , NE)	10.35 (1.33, 80.88)	0.0056	
	1	7/ 102 (6.9)	NE (NE , NE)	1/ 99 (1.0)	NE (NE , NE)	6.94 (0.85, 56.40)	0.0350	
	Number of Organs Involved							0.9890
	<= 2	10/ 116 (8.6)	NE (NE , NE)	2/ 119 (1.7)	NE (NE , NE)	5.33 (1.17, 24.33)	0.0154	
	>= 3	7/ 116 (6.0)	NE (NE , NE)	0/ 110 (0.0)	NE (NE , NE)	NE		
	Presence of Liver Metastases							0.3964
	Yes	13/ 146 (8.9)	NE (NE , NE)	1/ 149 (0.7)	NE (NE , NE)	13.74 (1.80, 104.99)	0.0009	
	No	4/ 86 (4.7)	NE (NE , NE)	1/ 80 (1.3)	NE (NE , NE)	3.81 (0.43, 34.09)	0.1979	
	Side of Tumor							0.9896
	Left	8/ 88 (9.1)	NE (NE , NE)	0/ 90 (0.0)	NE (NE , NE)	NE		
	Right	9/ 144 (6.3)	NE (NE , NE)	2/ 139 (1.4)	NE (NE , NE)	4.47 (0.97, 20.69)	0.0357	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
Subgroup analysis was done for SOCs / PTs with significant overall treatment effect (significant log-rank).
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.
[4] P-Value for interaction from Cox proportional hazards model using ties=exact option with treatment, subgroup and treatment*subgroup interaction as covariates.
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

SOC/PT	Subgroup Level	EC+FOLFOX (N=232) n/ N (%)	EC+FOLFOX (N=232) Median (95% CI)[1]	Control 1 (N=229) n/ N (%)	Control 1 (N=229) Median (95% CI)[1]	Unstratified analysis Hazard Ratio (95% CI)[2]	Unstratified analysis p-Value[3]	Interaction p-Value[4]
SOC: Skin and subcutaneous tissue disorders, PT: Pruritus	Age (Years)							0.7984
	< 65	22/ 148 (14.9)	NE (NE , NE)	4/ 131 (3.1)	NE (NE , NE)	3.70 (1.26, 10.83)	0.0108	
	>= 65	10/ 84 (11.9)	NE (28.1, NE)	3/ 98 (3.1)	NE (NE , NE)	2.78 (0.74, 10.37)	0.1136	
	Sex							0.3590
	Male	16/ 121 (13.2)	NE (28.1, NE)	2/ 112 (1.8)	NE (NE , NE)	5.42 (1.23, 23.89)	0.0126	
	Female	16/ 111 (14.4)	NE (NE , NE)	5/ 117 (4.3)	NE (NE , NE)	2.60 (0.94, 7.19)	0.0558	
	Region							0.6697
	Europe	16/ 108 (14.8)	NE (28.1, NE)	2/ 103 (1.9)	NE (NE , NE)	5.26 (1.19, 23.33)	0.0151	
	USA/Canada	1/ 15 (6.7)	NE (NE , NE)	0/ 17 (0.0)	NE (NE , NE)	NE		
	Rest of World	15/ 109 (13.8)	NE (NE , NE)	5/ 109 (4.6)	NE (NE , NE)	2.47 (0.89, 6.86)	0.0731	
	ECOG-PS at Randomization							0.7701
	0	17/ 130 (13.1)	NE (NE , NE)	4/ 130 (3.1)	NE (NE , NE)	3.05 (1.01, 9.22)	0.0381	
	1	15/ 102 (14.7)	NE (NE , NE)	3/ 99 (3.0)	NE (NE , NE)	3.91 (1.13, 13.62)	0.0208	
	Number of Organs Involved							0.8800
	<= 2	19/ 116 (16.4)	NE (NE , NE)	4/ 119 (3.4)	NE (NE , NE)	3.64 (1.22, 10.84)	0.0134	
	>= 3	13/ 116 (11.2)	NE (21.9, NE)	3/ 110 (2.7)	NE (NE , NE)	3.20 (0.90, 11.34)	0.0570	
	Presence of Liver Metastases							0.2249
	Yes	18/ 146 (12.3)	NE (NE , NE)	6/ 149 (4.0)	NE (NE , NE)	2.28 (0.90, 5.81)	0.0750	
	No	14/ 86 (16.3)	NE (28.1, NE)	1/ 80 (1.3)	NE (NE , NE)	10.13 (1.31, 78.07)	0.0063	
	Side of Tumor							0.4003
	Left	9/ 88 (10.2)	NE (NE , NE)	3/ 90 (3.3)	NE (NE , NE)	1.87 (0.49, 7.18)	0.3555	
	Right	23/ 144 (16.0)	NE (28.1, NE)	4/ 139 (2.9)	NE (NE , NE)	4.60 (1.58, 13.37)	0.0021	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
Subgroup analysis was done for SOCs / PTs with significant overall treatment effect (significant log-rank).
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.
[4] P-Value for interaction from Cox proportional hazards model using ties=exact option with treatment, subgroup and treatment*subgroup interaction as covariates.
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Frequent AE by SOC, PT (incidence >= 10% or >=10 patients and incidence >= 1%) - Subgroup analysis
Safety Analysis Set

SOC/PT	Subgroup Level	EC+FOLFOX (N=232) n/ N (%)	EC+FOLFOX (N=232) Median (95% CI)[1]	Control 1 (N=229) n/ N (%)	Control 1 (N=229) Median (95% CI)[1]	Unstratified analysis Hazard Ratio (95% CI)[2]	Unstratified analysis p-Value[3]	Interaction p-Value[4]
SOC: Skin and subcutaneous tissue disorders, PT: Rash	Age (Years)							0.2344
	< 65	44/ 148 (29.7)	NE (24.0, NE)	7/ 131 (5.3)	NE (NE , NE)	4.84 (2.17, 10.80)	<.0001	
	>= 65	26/ 84 (31.0)	NE (30.0, NE)	2/ 98 (2.0)	NE (NE , NE)	13.97 (3.30, 59.08)	<.0001	
	Sex							0.5596
	Male	33/ 121 (27.3)	NE (24.0, NE)	3/ 112 (2.7)	NE (NE , NE)	8.54 (2.60, 28.00)	<.0001	
	Female	37/ 111 (33.3)	30.0 (30.0, NE)	6/ 117 (5.1)	NE (NE , NE)	6.11 (2.57, 14.52)	<.0001	
	Region							0.1971
	Europe	38/ 108 (35.2)	NE (18.4, NE)	2/ 103 (1.9)	NE (NE , NE)	16.21 (3.90, 67.42)	<.0001	
	USA/Canada	5/ 15 (33.3)	19.8 (19.8, NE)	0/ 17 (0.0)	NE (NE , NE)	NE		
	Rest of World	27/ 109 (24.8)	NE (30.0, NE)	7/ 109 (6.4)	NE (NE , NE)	3.38 (1.46, 7.79)	0.0025	
	ECOG-PS at Randomization							0.3585
	0	43/ 130 (33.1)	NE (24.0, NE)	7/ 130 (5.4)	NE (NE , NE)	5.46 (2.45, 12.20)	<.0001	
	1	27/ 102 (26.5)	30.0 (19.8, NE)	2/ 99 (2.0)	NE (NE , NE)	11.87 (2.81, 50.12)	<.0001	
	Number of Organs Involved							0.0670
	<= 2	33/ 116 (28.4)	NE (NE , NE)	1/ 119 (0.8)	NE (NE , NE)	29.39 (4.01, 215.62)	<.0001	
	>= 3	37/ 116 (31.9)	30.0 (18.4, NE)	8/ 110 (7.3)	NE (NE , NE)	3.94 (1.82, 8.50)	0.0002	
	Presence of Liver Metastases							0.2428
	Yes	40/ 146 (27.4)	30.0 (24.0, NE)	7/ 149 (4.7)	NE (NE , NE)	4.74 (2.11, 10.64)	<.0001	
	No	30/ 86 (34.9)	NE (14.9, NE)	2/ 80 (2.5)	NE (NE , NE)	14.30 (3.41, 59.99)	<.0001	
	Side of Tumor							0.5450
	Left	25/ 88 (28.4)	NE (19.8, NE)	4/ 90 (4.4)	NE (NE , NE)	4.79 (1.65, 13.95)	0.0016	
	Right	45/ 144 (31.3)	NE (24.0, NE)	5/ 139 (3.6)	NE (NE , NE)	8.42 (3.33, 21.25)	<.0001	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
Subgroup analysis was done for SOCs / PTs with significant overall treatment effect (significant log-rank).
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.
[4] P-Value for interaction from Cox proportional hazards model using ties=exact option with treatment, subgroup and treatment*subgroup interaction as covariates.
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Frequent AE by SOC, PT (incidence >= 10% or >=10 patients and incidence >= 1%) - Subgroup analysis
Safety Analysis Set

SOC/PT	Subgroup Level	EC+FOLFOX (N=232) n/ N (%)	EC+FOLFOX (N=232) Median (95% CI)[1]	Control 1 (N=229) n/ N (%)	Control 1 (N=229) Median (95% CI)[1]	Unstratified analysis Hazard Ratio (95% CI)[2]	Unstratified analysis p-Value[3]	Interaction p-Value[4]
SOC: Skin and subcutaneous tissue disorders, PT: Skin hyperpigmentation	Age (Years)							0.2776
	< 65	30/ 148 (20.3)	NE (NE , NE)	6/ 131 (4.6)	NE (NE , NE)	4.24 (1.76, 10.23)	0.0005	
	>= 65	13/ 84 (15.5)	NE (NE , NE)	1/ 98 (1.0)	NE (NE , NE)	14.44 (1.88, 110.63)	0.0007	
	Sex							0.5551
	Male	24/ 121 (19.8)	NE (NE , NE)	3/ 112 (2.7)	NE (NE , NE)	7.56 (2.27, 25.13)	0.0001	
	Female	19/ 111 (17.1)	NE (NE , NE)	4/ 117 (3.4)	NE (NE , NE)	4.35 (1.47, 12.88)	0.0038	
	Region							0.4077
	Europe	13/ 108 (12.0)	NE (NE , NE)	2/ 103 (1.9)	NE (NE , NE)	4.63 (1.03, 20.76)	0.0279	
	USA/Canada	4/ 15 (26.7)	NE (NE , NE)	2/ 17 (11.8)	NE (NE , NE)	2.20 (0.40, 12.08)	0.3516	
	Rest of World	26/ 109 (23.9)	NE (NE , NE)	3/ 109 (2.8)	NE (NE , NE)	9.31 (2.81, 30.80)	<.0001	
	ECOG-PS at Randomization							0.9573
	0	25/ 130 (19.2)	NE (NE , NE)	4/ 130 (3.1)	NE (NE , NE)	6.13 (2.13, 17.63)	0.0001	
	1	18/ 102 (17.6)	NE (NE , NE)	3/ 99 (3.0)	NE (NE , NE)	5.46 (1.60, 18.61)	0.0023	
	Number of Organs Involved							0.6161
	<= 2	22/ 116 (19.0)	NE (NE , NE)	3/ 119 (2.5)	NE (NE , NE)	7.15 (2.13, 23.96)	0.0002	
	>= 3	21/ 116 (18.1)	NE (NE , NE)	4/ 110 (3.6)	NE (NE , NE)	4.76 (1.63, 13.90)	0.0017	
	Presence of Liver Metastases							0.2395
	Yes	26/ 146 (17.8)	NE (NE , NE)	6/ 149 (4.0)	NE (NE , NE)	3.94 (1.62, 9.63)	0.0012	
	No	17/ 86 (19.8)	NE (NE , NE)	1/ 80 (1.3)	NE (NE , NE)	16.84 (2.24, 126.43)	0.0002	
	Side of Tumor							0.2461
	Left	16/ 88 (18.2)	NE (NE , NE)	1/ 90 (1.1)	NE (NE , NE)	15.71 (2.08, 118.54)	0.0003	
	Right	27/ 144 (18.8)	NE (NE , NE)	6/ 139 (4.3)	NE (NE , NE)	4.14 (1.70, 10.06)	0.0007	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
Subgroup analysis was done for SOCs / PTs with significant overall treatment effect (significant log-rank).
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.
[4] P-Value for interaction from Cox proportional hazards model using ties=exact option with treatment, subgroup and treatment*subgroup interaction as covariates.
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Frequent AE by SOC, PT (incidence >= 10% or >=10 patients and incidence >= 1%) - Subgroup analysis
Safety Analysis Set

SOC/PT	Subgroup Level	EC+FOLFOX (N=232) n/ N (%)	EC+FOLFOX (N=232) Median (95% CI)[1]	Control 1 (N=229) n/ N (%)	Control 1 (N=229) Median (95% CI)[1]	Unstratified analysis Hazard Ratio (95% CI)[2]	Unstratified analysis p-Value[3]	Interaction p-Value[4]
SOC: Skin and subcutaneous tissue disorders, PT: Skin lesion	Age (Years)							
	< 65	8/ 148 (5.4)		1/ 131 (0.8)				
	>= 65	5/ 84 (6.0)		1/ 98 (1.0)				
	Sex							
	Male	8/ 121 (6.6)		0/ 112 (0.0)				
	Female	5/ 111 (4.5)		2/ 117 (1.7)				
	Region							0.4573
	Europe	10/ 108 (9.3)	NE (NE , NE)	1/ 103 (1.0)	NE (NE , NE)	5.74 (0.72, 45.69)	0.0636	
	USA/Canada	2/ 15 (13.3)	NE (19.1, NE)	0/ 17 (0.0)	NE (NE , NE)	NE		
	Rest of World	1/ 109 (0.9)	NE (NE , NE)	1/ 109 (0.9)	NE (NE , NE)	0.81 (0.05, 13.12)	0.8848	
	ECOG-PS at Randomization							
	0	6/ 130 (4.6)		1/ 130 (0.8)				
	1	7/ 102 (6.9)		1/ 99 (1.0)				
	Number of Organs Involved							
	<= 2	5/ 116 (4.3)		1/ 119 (0.8)				
	>= 3	8/ 116 (6.9)		1/ 110 (0.9)				
	Presence of Liver Metastases							0.5060
	Yes	9/ 146 (6.2)	NE (NE , NE)	1/ 149 (0.7)	NE (NE , NE)	6.25 (0.78, 49.96)	0.0492	
	No	4/ 86 (4.7)	NE (NE , NE)	1/ 80 (1.3)	NE (NE , NE)	2.37 (0.25, 22.34)	0.4383	
	Side of Tumor							
	Left	7/ 88 (8.0)		1/ 90 (1.1)				
	Right	6/ 144 (4.2)		1/ 139 (0.7)				

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
Subgroup analysis was done for SOCs / PTs with significant overall treatment effect (significant log-rank).
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.
[4] P-Value for interaction from Cox proportional hazards model using ties=exact option with treatment, subgroup and treatment*subgroup interaction as covariates.
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Frequent AE by SOC, PT (incidence >= 10% or >=10 patients and incidence >= 1%) - Subgroup analysis
Safety Analysis Set

SOC/PT	Subgroup Level	EC+FOLFOX (N=232) n/ N (%)	EC+FOLFOX (N=232) Median (95% CI)[1]	Control 1 (N=229) n/ N (%)	Control 1 (N=229) Median (95% CI)[1]	Unstratified analysis Hazard Ratio (95% CI)[2]	Unstratified analysis p-Value[3]	Interaction p-Value[4]
SOC: Vascular disorders	Age (Years)							0.6034
	< 65	19/ 148 (12.8)	NE (NE , NE)	27/ 131 (20.6)	27.9 (NE , NE)	0.44 (0.24, 0.81)	0.0066	
	>= 65	17/ 84 (20.2)	NE (NE , NE)	24/ 98 (24.5)	NE (NE , NE)	0.64 (0.34, 1.20)	0.1603	
	Sex							0.1494
	Male	15/ 121 (12.4)	NE (NE , NE)	28/ 112 (25.0)	NE (NE , NE)	0.35 (0.18, 0.67)	0.0009	
	Female	21/ 111 (18.9)	NE (NE , NE)	23/ 117 (19.7)	27.9 (NE , NE)	0.73 (0.40, 1.34)	0.3081	
	Region							0.4208
	Europe	17/ 108 (15.7)	NE (NE , NE)	23/ 103 (22.3)	NE (NE , NE)	0.48 (0.25, 0.92)	0.0236	
	USA/Canada	4/ 15 (26.7)	NE (NE , NE)	10/ 17 (58.8)	2.8 (0.5, NE)	0.33 (0.10, 1.05)	0.0480	
	Rest of World	15/ 109 (13.8)	NE (NE , NE)	18/ 109 (16.5)	27.9 (27.9, NE)	0.65 (0.32, 1.30)	0.2143	
	ECOG-PS at Randomization							0.1541
	0	17/ 130 (13.1)	NE (NE , NE)	31/ 130 (23.8)	27.9 (27.9, NE)	0.38 (0.20, 0.69)	0.0012	
	1	19/ 102 (18.6)	NE (NE , NE)	20/ 99 (20.2)	NE (NE , NE)	0.74 (0.39, 1.39)	0.3435	
	Number of Organs Involved							0.8682
	<= 2	18/ 116 (15.5)	NE (NE , NE)	25/ 119 (21.0)	27.9 (27.9, NE)	0.53 (0.28, 0.98)	0.0412	
	>= 3	18/ 116 (15.5)	NE (NE , NE)	26/ 110 (23.6)	NE (NE , NE)	0.50 (0.27, 0.92)	0.0231	
	Presence of Liver Metastases							0.7630
	Yes	21/ 146 (14.4)	NE (NE , NE)	32/ 149 (21.5)	NE (NE , NE)	0.48 (0.27, 0.84)	0.0086	
	No	15/ 86 (17.4)	NE (NE , NE)	19/ 80 (23.8)	27.9 (NE , NE)	0.58 (0.29, 1.15)	0.1144	
	Side of Tumor							0.6969
	Left	13/ 88 (14.8)	NE (NE , NE)	17/ 90 (18.9)	NE (NE , NE)	0.63 (0.30, 1.30)	0.2075	
	Right	23/ 144 (16.0)	NE (NE , NE)	34/ 139 (24.5)	27.9 (27.9, NE)	0.47 (0.27, 0.81)	0.0052	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
Subgroup analysis was done for SOCs / PTs with significant overall treatment effect (significant log-rank).
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.
[4] P-Value for interaction from Cox proportional hazards model using ties=exact option with treatment, subgroup and treatment*subgroup interaction as covariates.
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Frequent AE by SOC, PT (incidence >= 10% or >=10 patients and incidence >= 1%) - Subgroup analysis
Safety Analysis Set

SOC/PT	Subgroup Level	EC+FOLFOX (N=232) n/ N (%)	EC+FOLFOX (N=232) Median (95% CI)[1]	Control 1 (N=229) n/ N (%)	Control 1 (N=229) Median (95% CI)[1]	Unstratified analysis Hazard Ratio (95% CI)[2]	Unstratified analysis p-Value[3]	Interaction p-Value[4]
SOC: Vascular disorders, PT: Hypertension	Age (Years)							0.6029
	< 65	4/ 148 (2.7)	NE (NE , NE)	17/ 131 (13.0)	NE (NE , NE)	0.16 (0.05, 0.49)	0.0002	
	>= 65	5/ 84 (6.0)	NE (NE , NE)	18/ 98 (18.4)	NE (NE , NE)	0.23 (0.08, 0.63)	0.0021	
	Sex							0.0266
	Male	2/ 121 (1.7)	NE (NE , NE)	22/ 112 (19.6)	NE (NE , NE)	0.06 (0.01, 0.26)	<.0001	
	Female	7/ 111 (6.3)	NE (NE , NE)	13/ 117 (11.1)	NE (NE , NE)	0.43 (0.17, 1.09)	0.0680	
	Region							0.8142
	Europe	5/ 108 (4.6)	NE (NE , NE)	15/ 103 (14.6)	NE (NE , NE)	0.21 (0.08, 0.60)	0.0014	
	USA/Canada	1/ 15 (6.7)	NE (NE , NE)	7/ 17 (41.2)	NE (2.3, NE)	0.12 (0.02, 1.02)	0.0216	
	Rest of World	3/ 109 (2.8)	NE (NE , NE)	13/ 109 (11.9)	NE (NE , NE)	0.17 (0.05, 0.61)	0.0023	
	ECOG-PS at Randomization							0.9974
	0	6/ 130 (4.6)	NE (NE , NE)	23/ 130 (17.7)	NE (NE , NE)	0.18 (0.07, 0.45)	<.0001	
	1	3/ 102 (2.9)	NE (NE , NE)	12/ 99 (12.1)	NE (NE , NE)	0.20 (0.06, 0.71)	0.0056	
	Number of Organs Involved							0.9026
	<= 2	5/ 116 (4.3)	NE (NE , NE)	19/ 119 (16.0)	NE (NE , NE)	0.19 (0.07, 0.53)	0.0004	
	>= 3	4/ 116 (3.4)	NE (NE , NE)	16/ 110 (14.5)	NE (NE , NE)	0.18 (0.06, 0.54)	0.0006	
	Presence of Liver Metastases							0.9233
	Yes	5/ 146 (3.4)	NE (NE , NE)	21/ 149 (14.1)	NE (NE , NE)	0.17 (0.06, 0.46)	<.0001	
	No	4/ 86 (4.7)	NE (NE , NE)	14/ 80 (17.5)	NE (NE , NE)	0.21 (0.07, 0.64)	0.0025	
	Side of Tumor							0.2169
	Left	1/ 88 (1.1)	NE (NE , NE)	12/ 90 (13.3)	NE (NE , NE)	0.07 (0.01, 0.57)	0.0011	
	Right	8/ 144 (5.6)	NE (NE , NE)	23/ 139 (16.5)	NE (NE , NE)	0.24 (0.10, 0.54)	0.0002	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
Subgroup analysis was done for SOCs / PTs with significant overall treatment effect (significant log-rank).
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.
[4] P-Value for interaction from Cox proportional hazards model using ties=exact option with treatment, subgroup and treatment*subgroup interaction as covariates.
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

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Encorafenib (PF-07263896) Protocol C4221015
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Datacut: 06JAN2025
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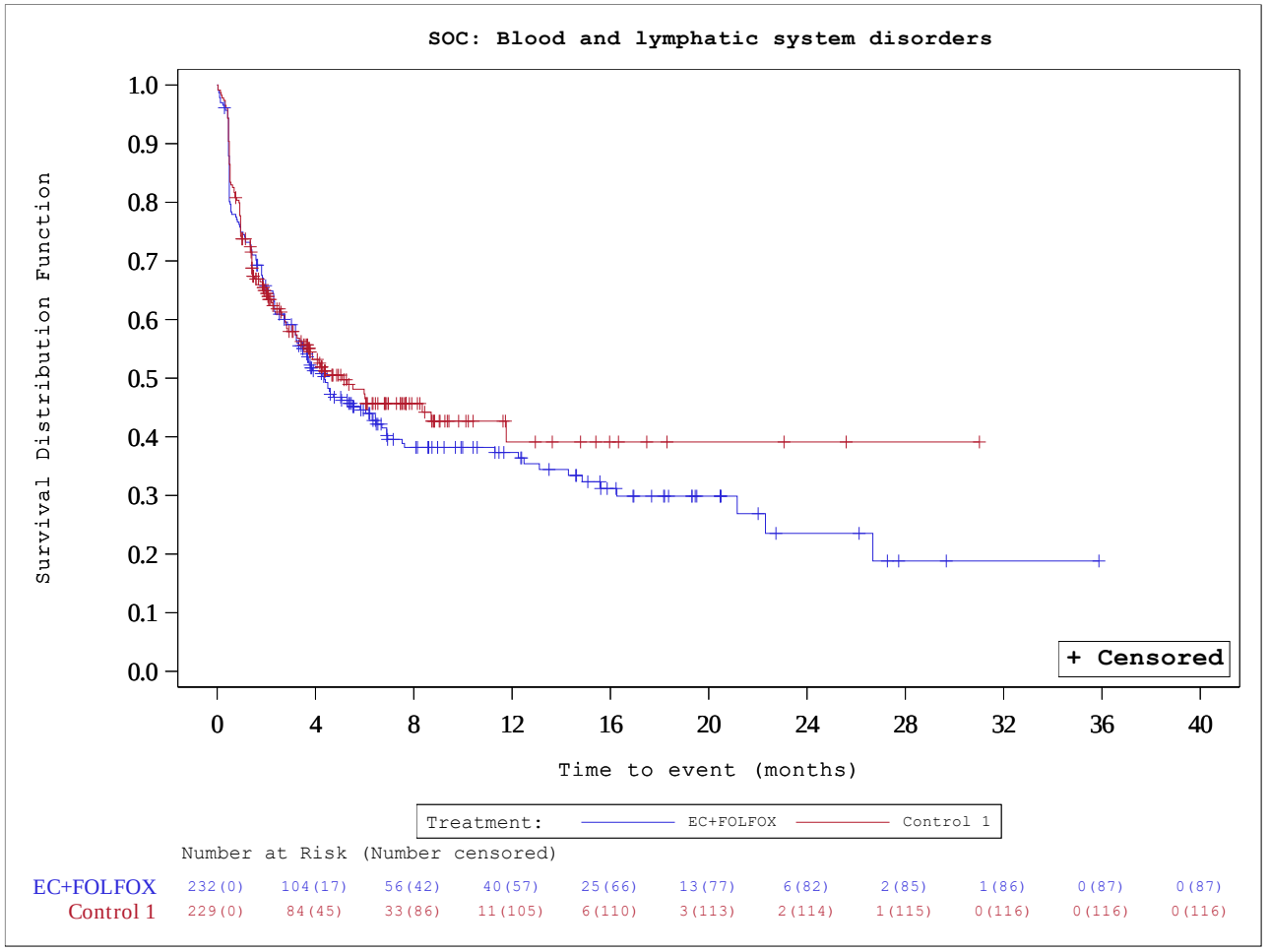
Safety Analysis Set



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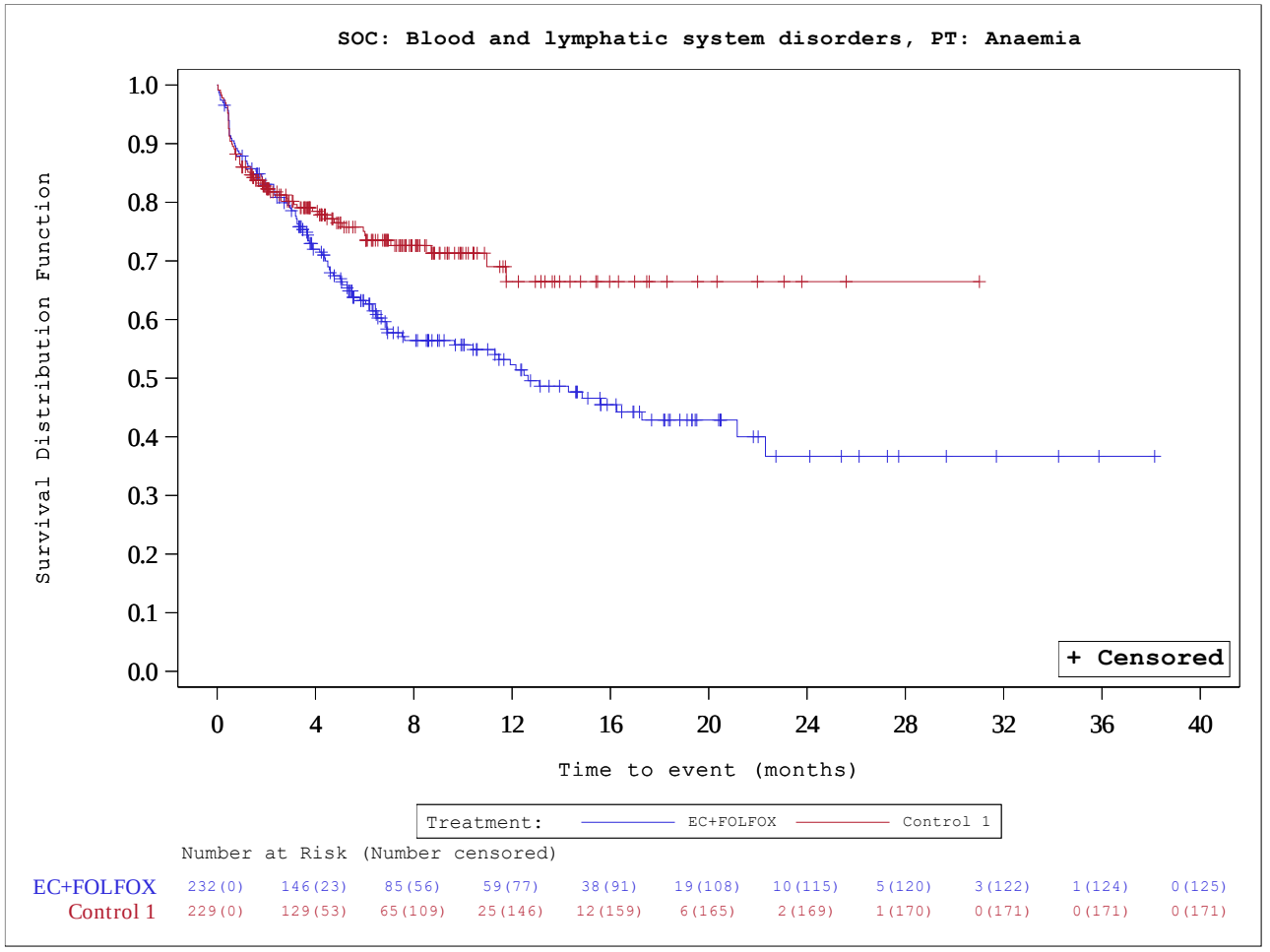

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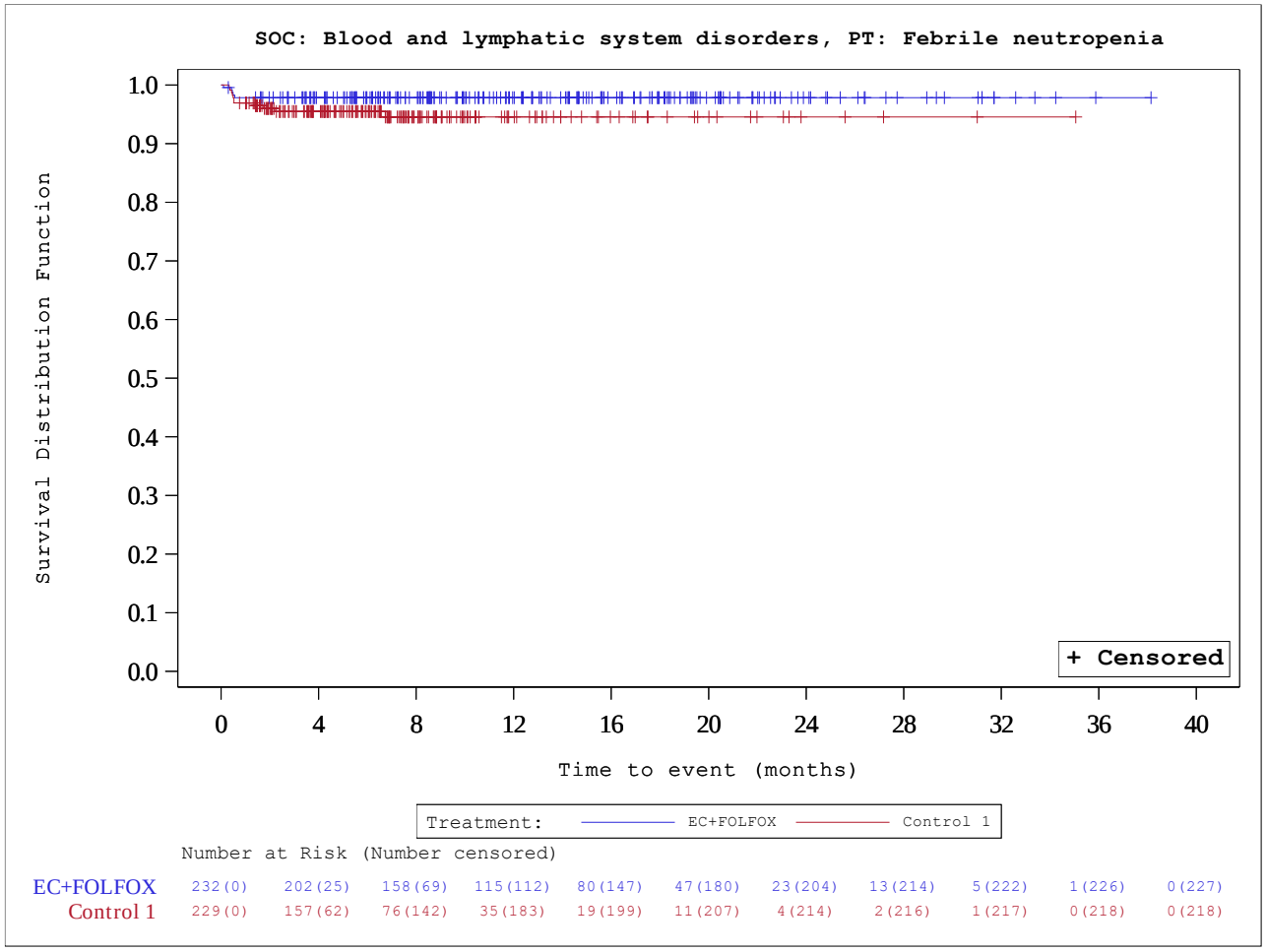

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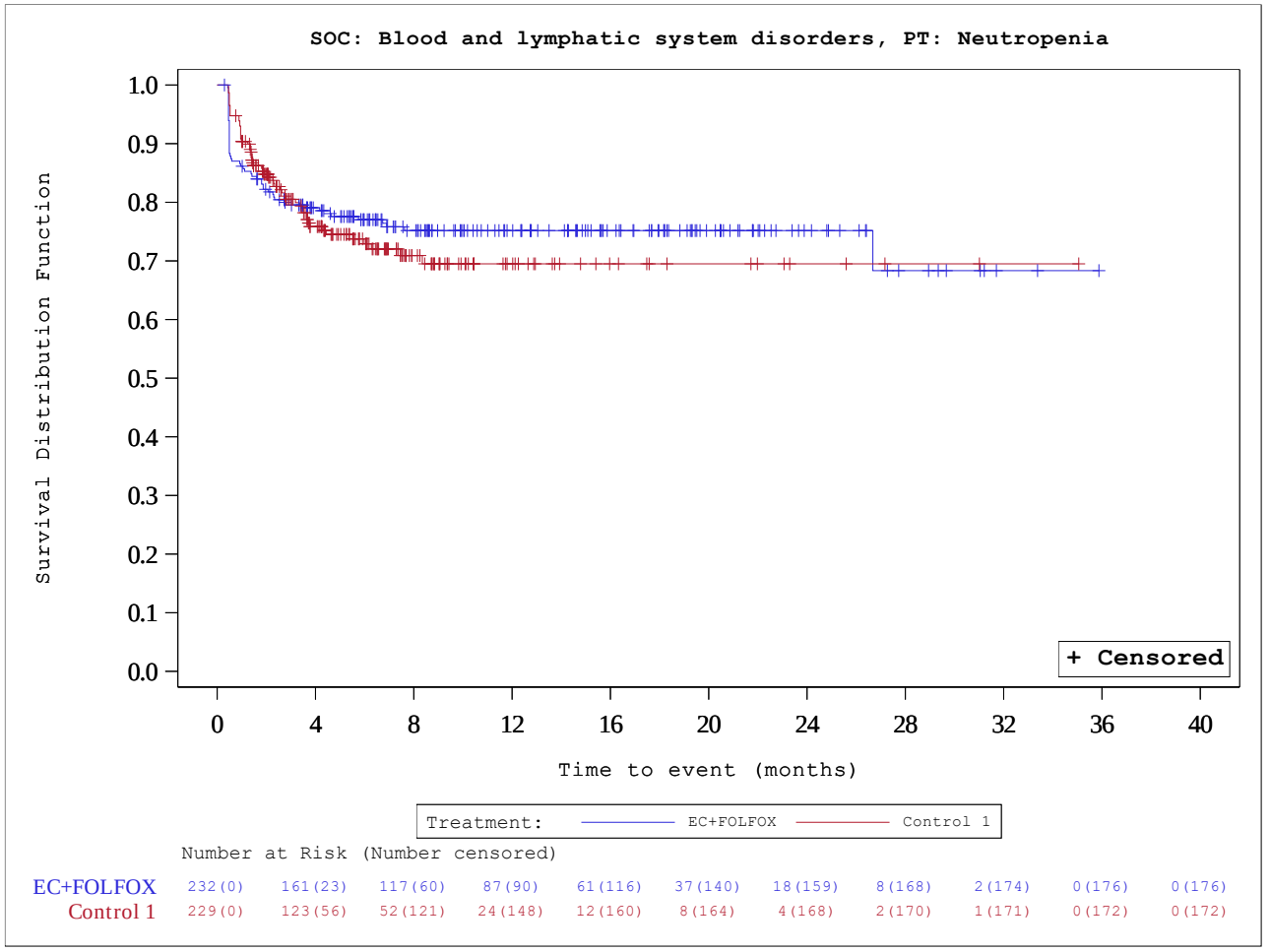

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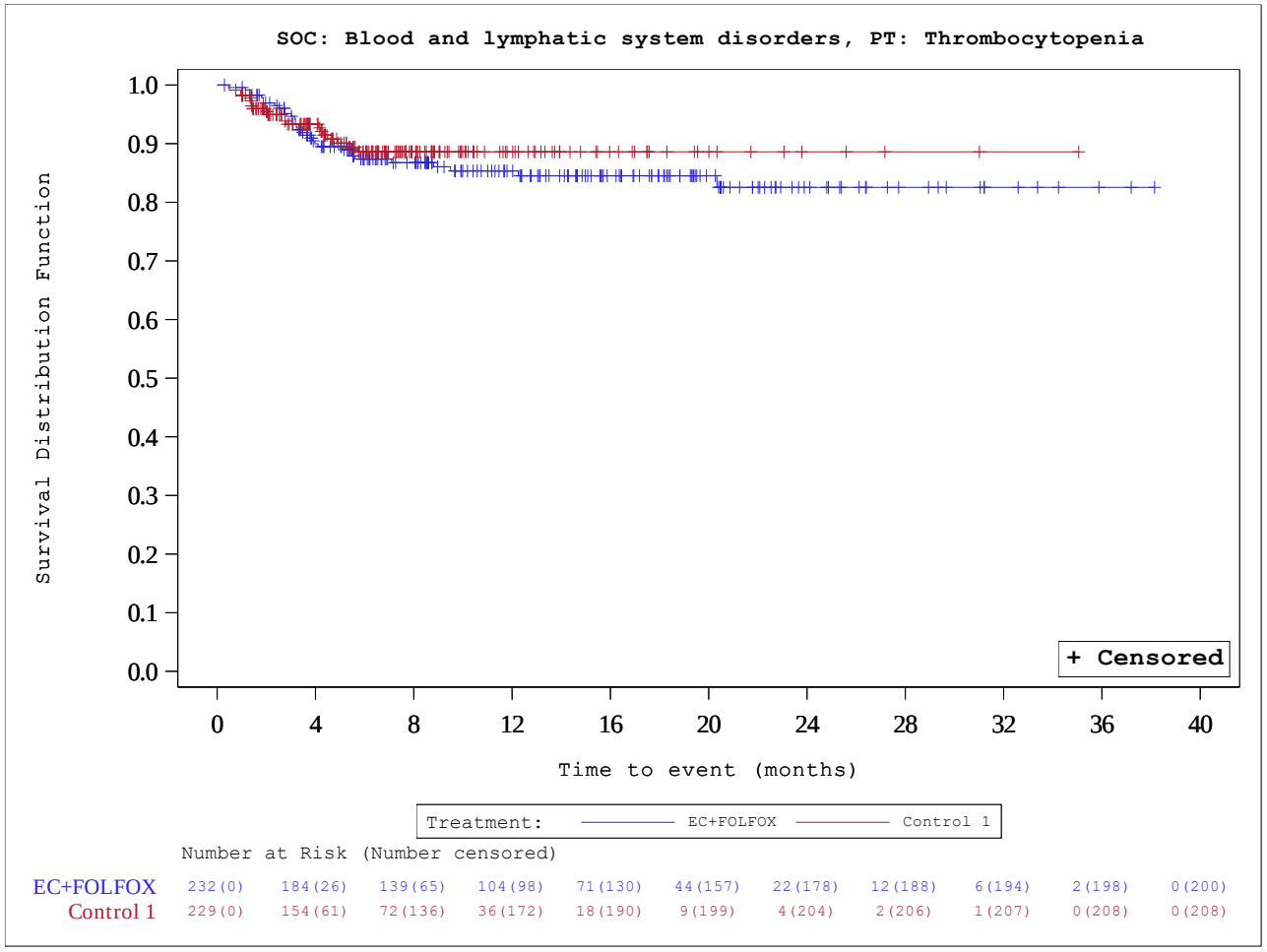

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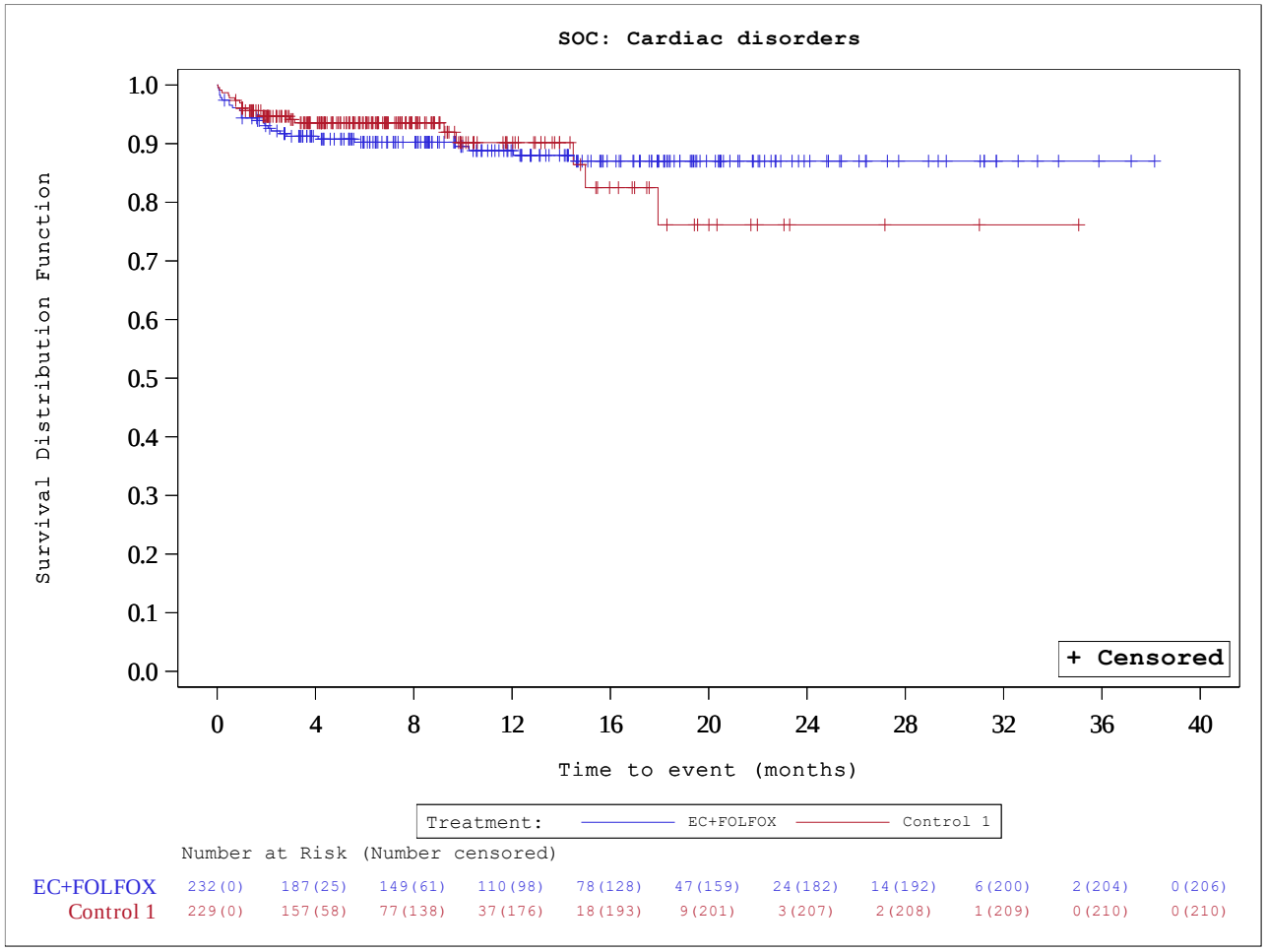

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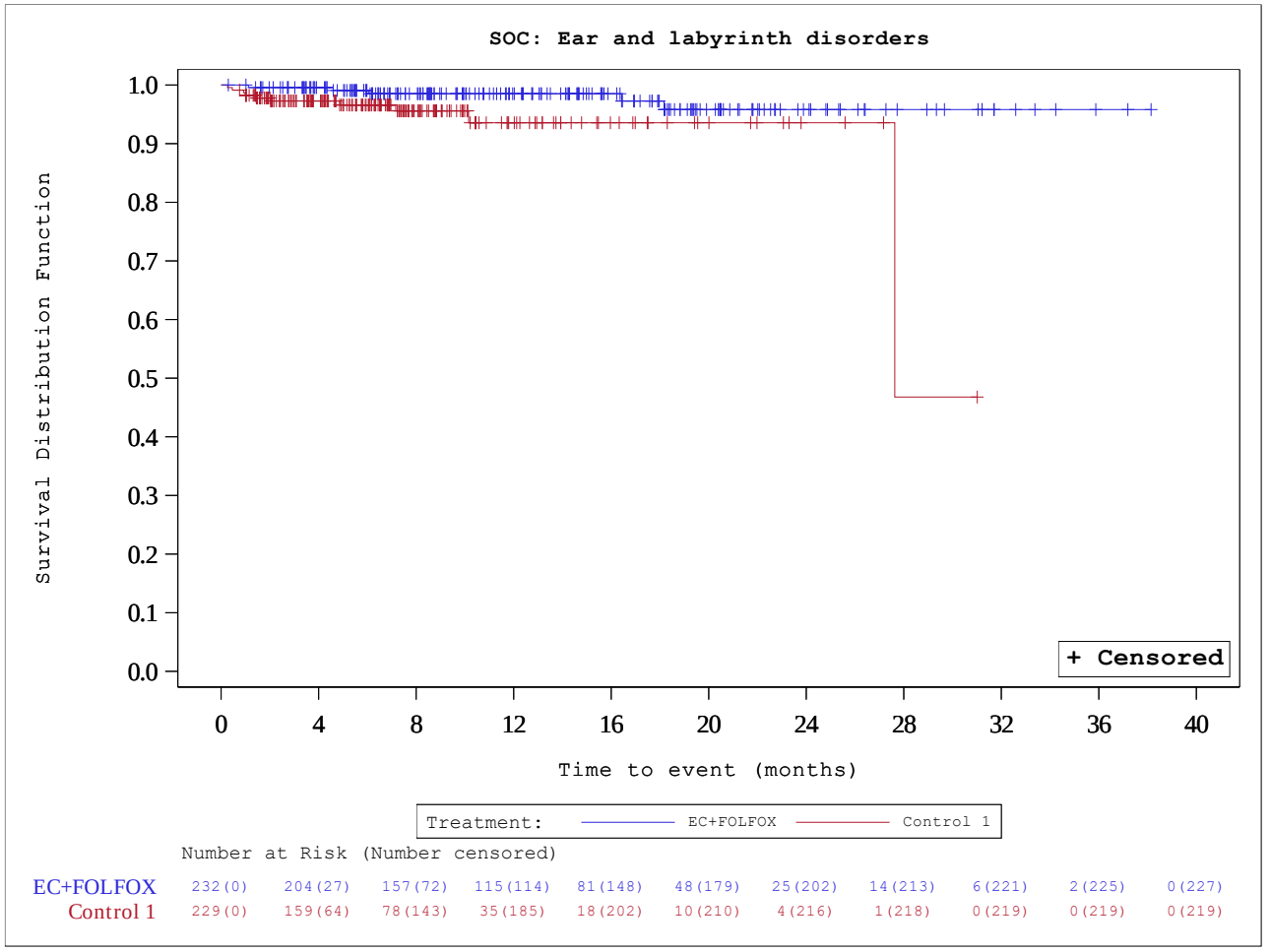

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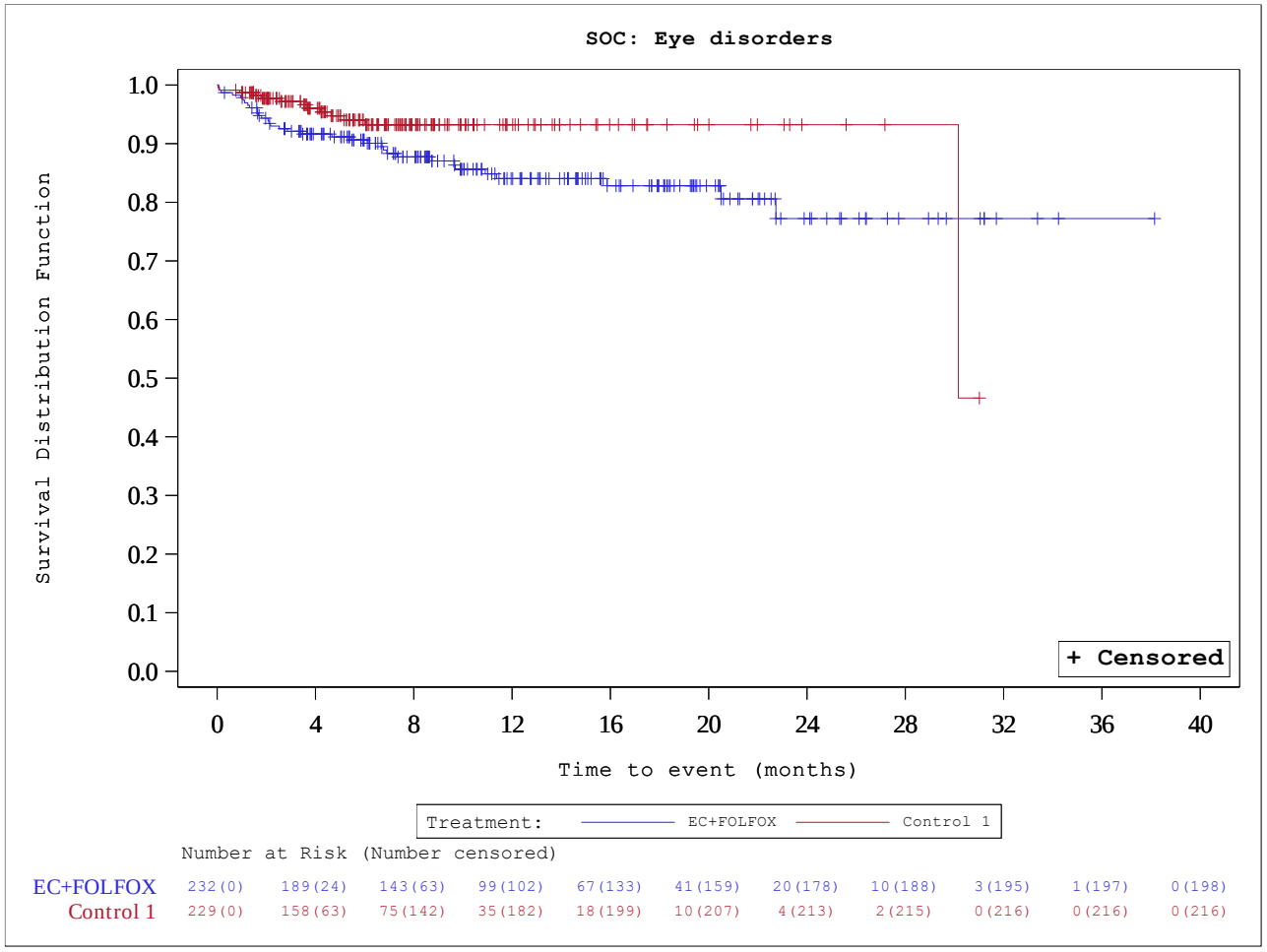

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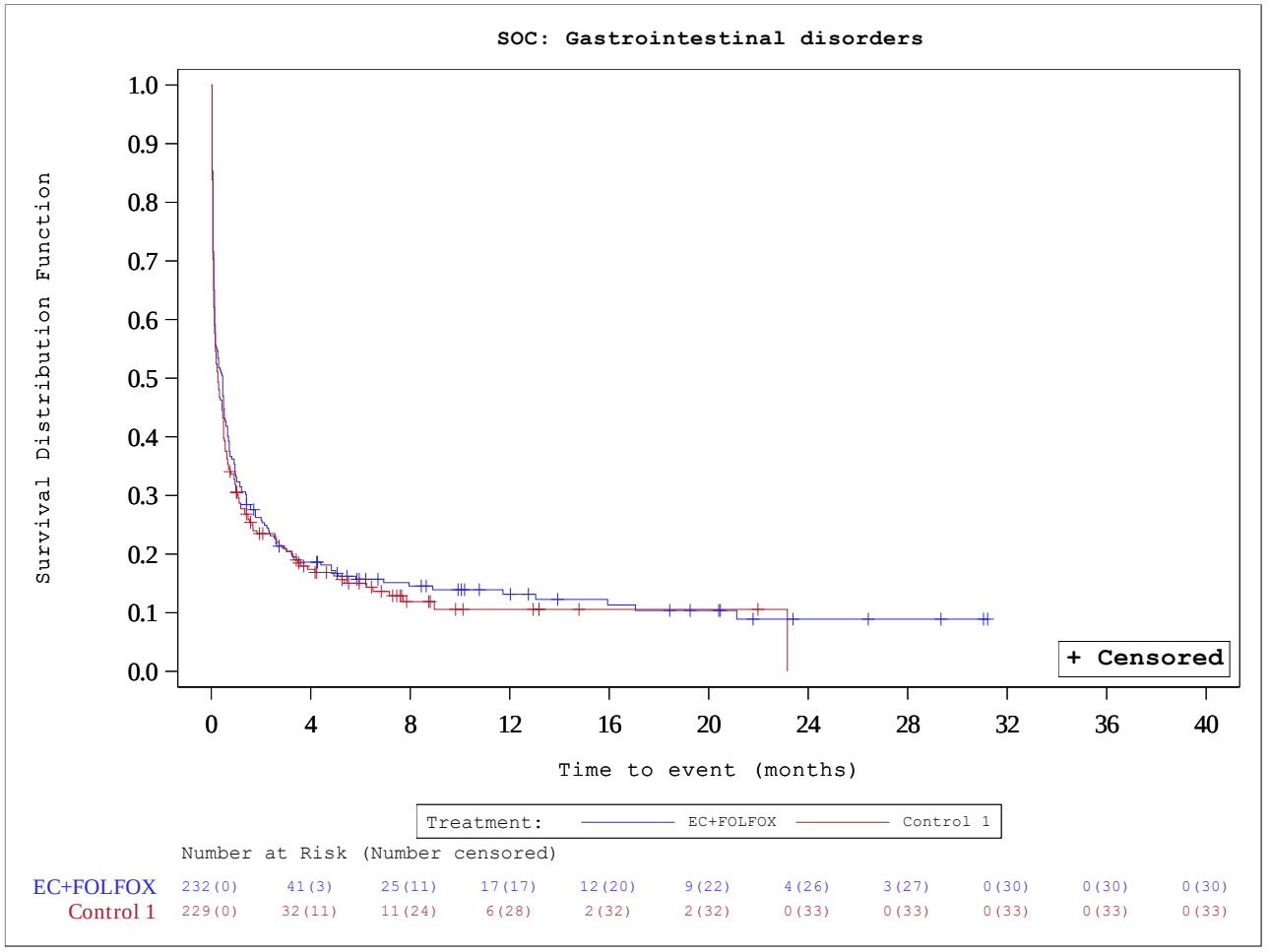

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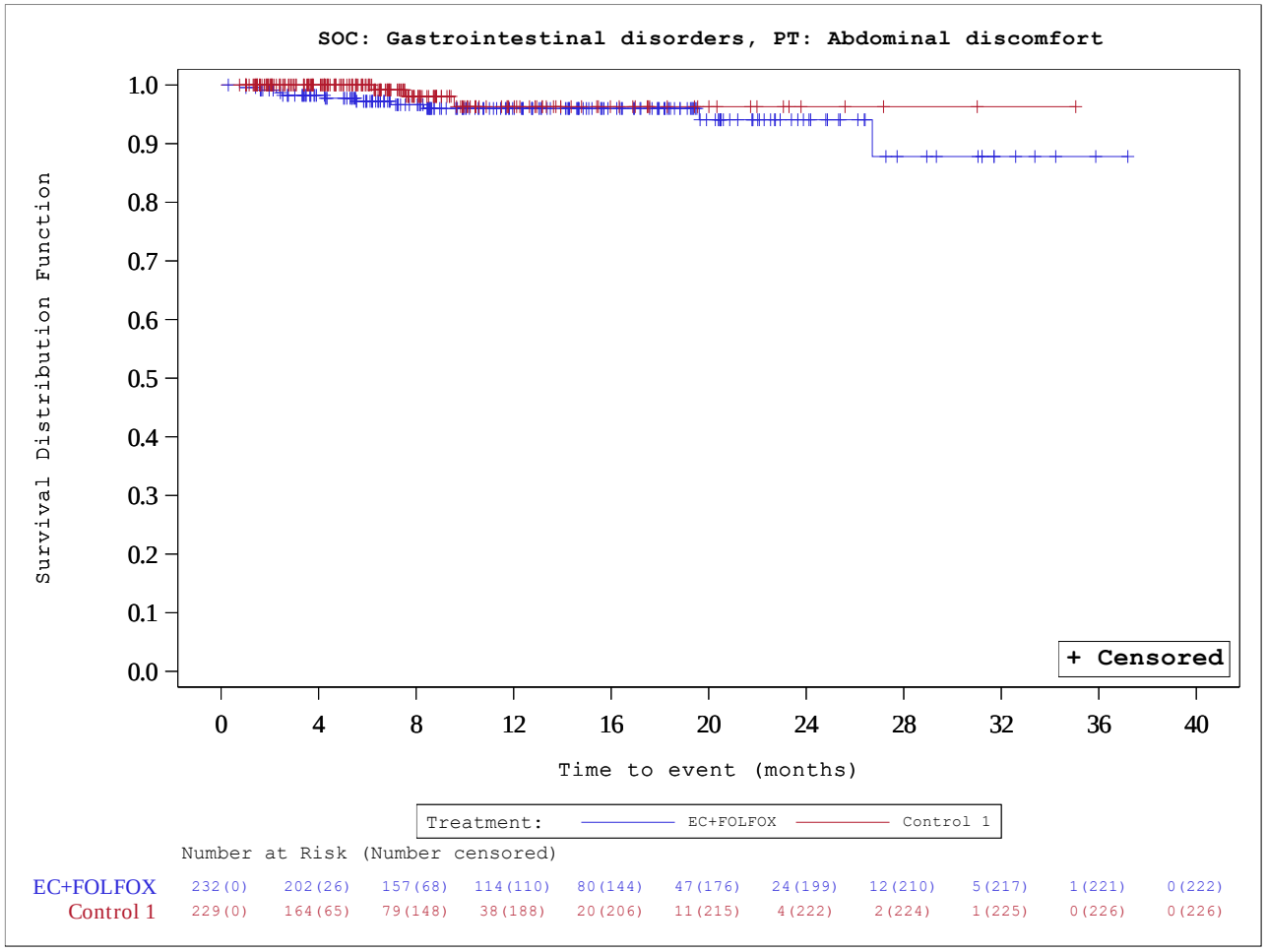

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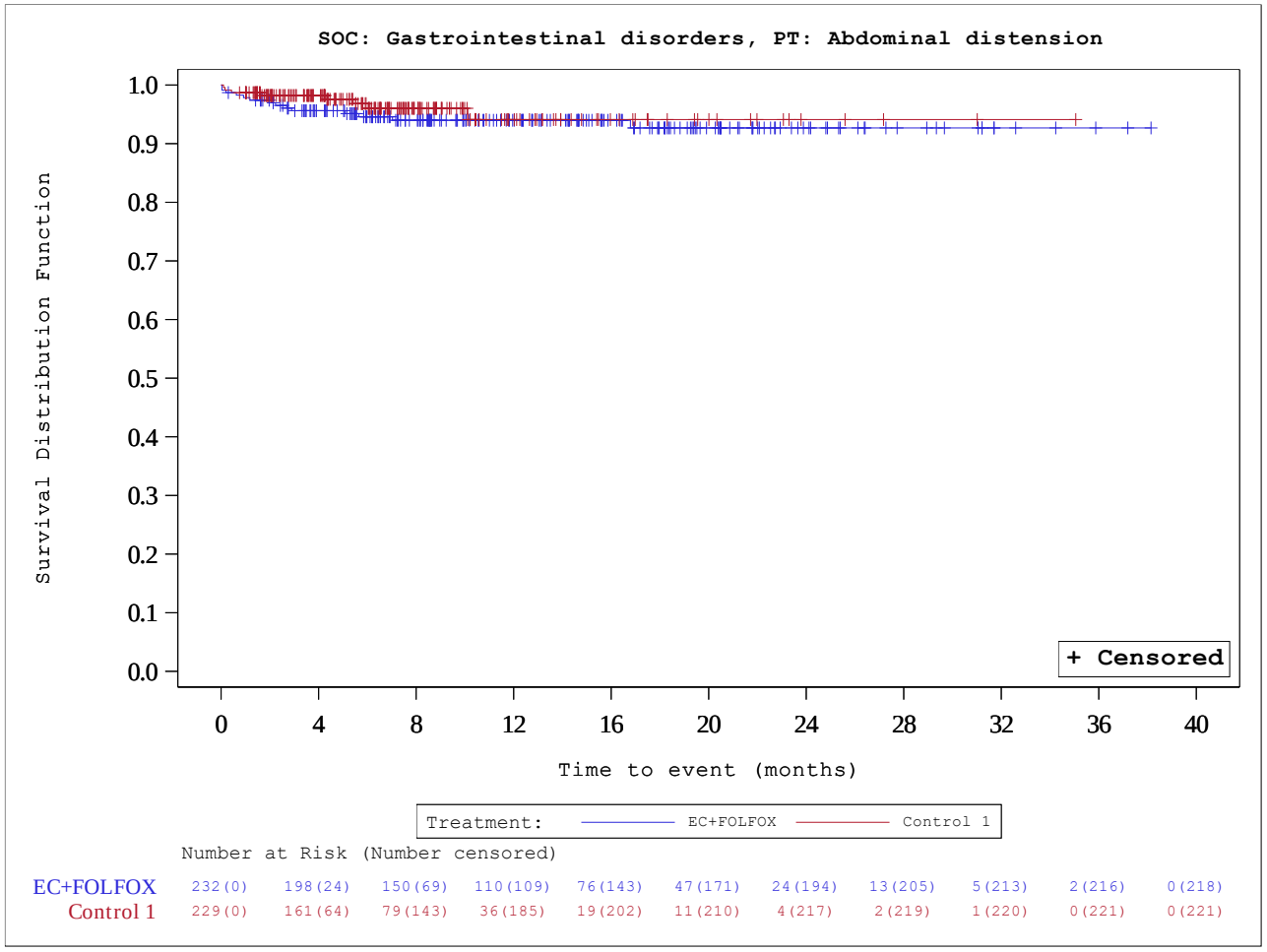

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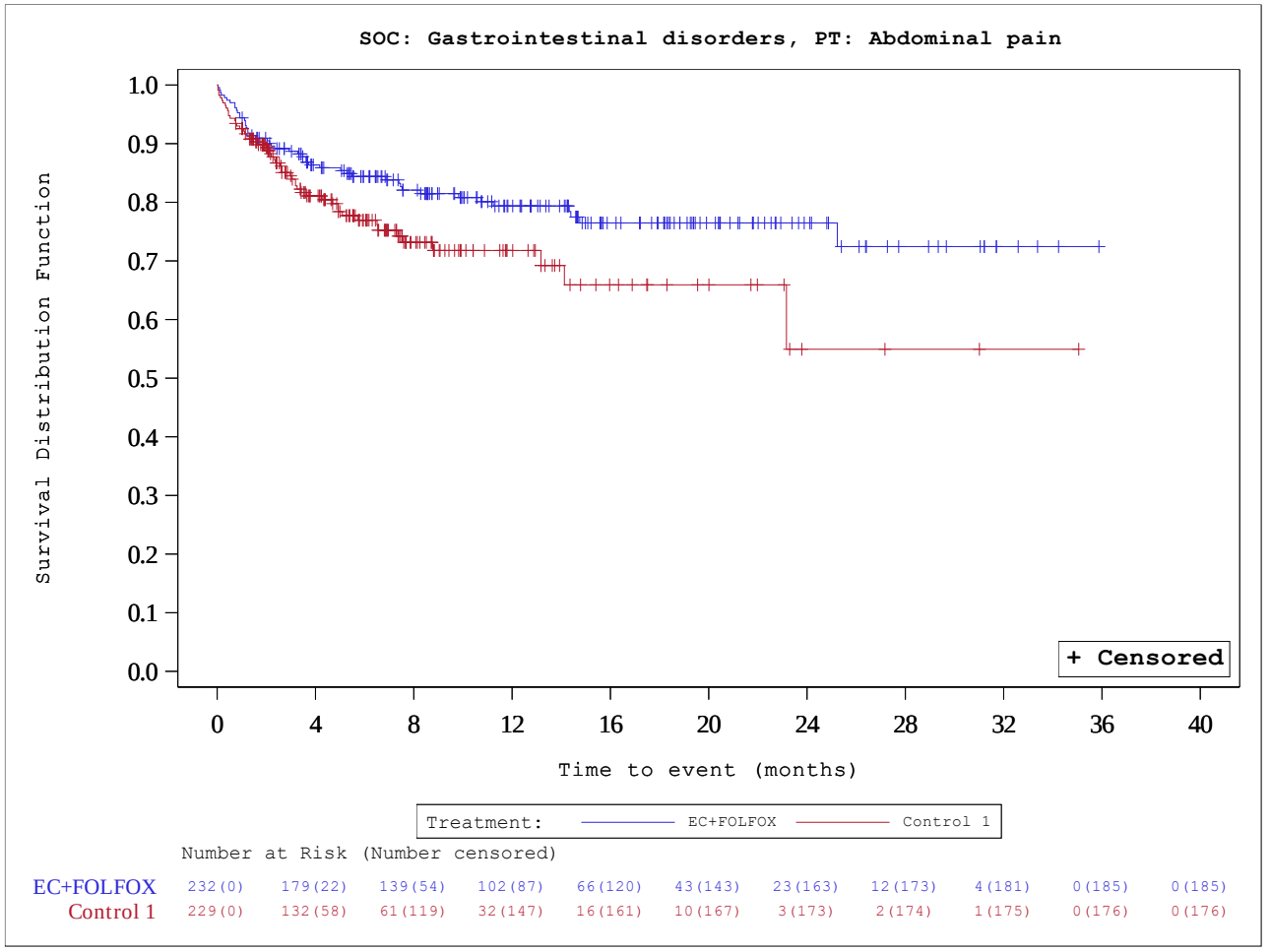

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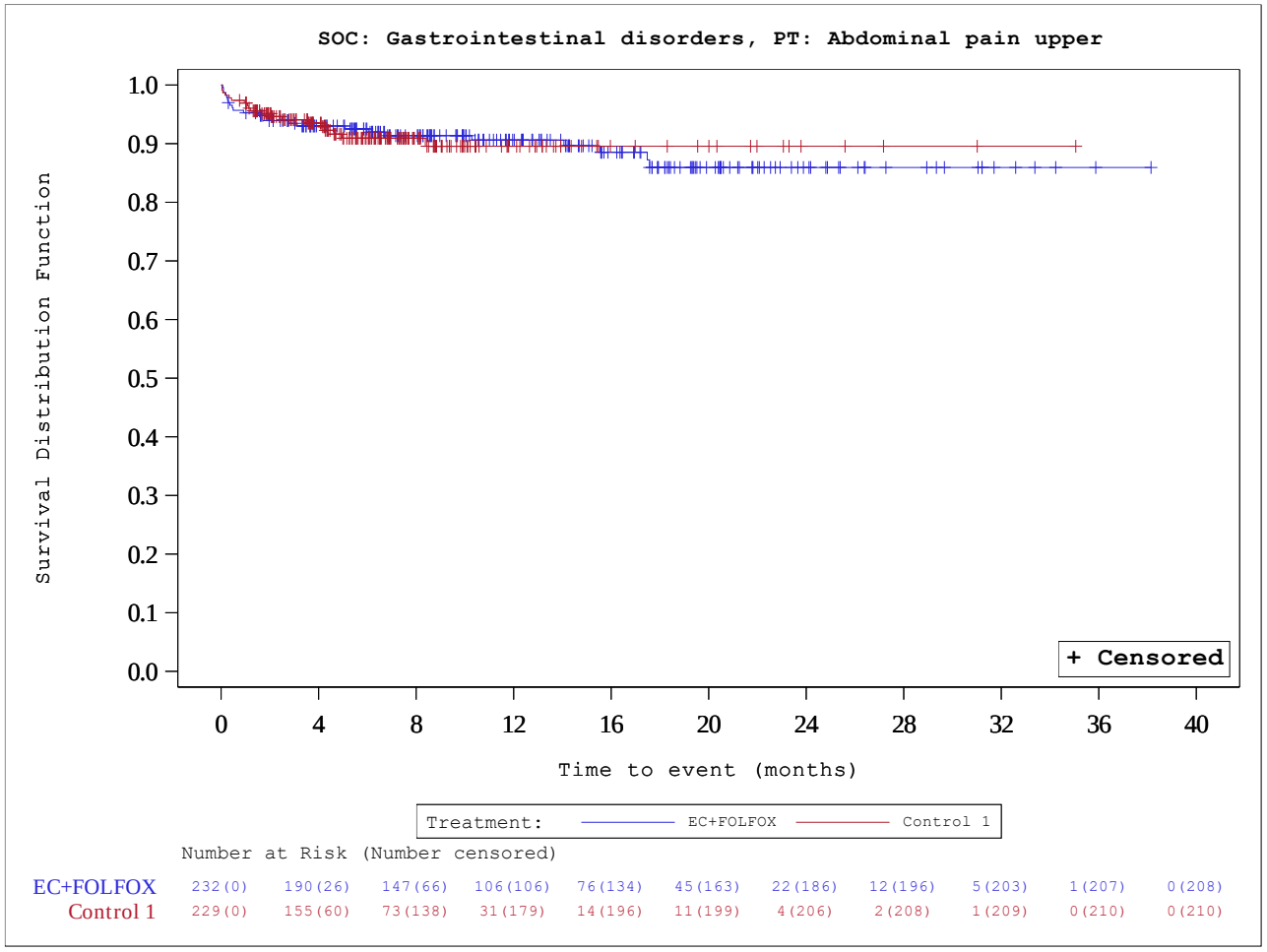

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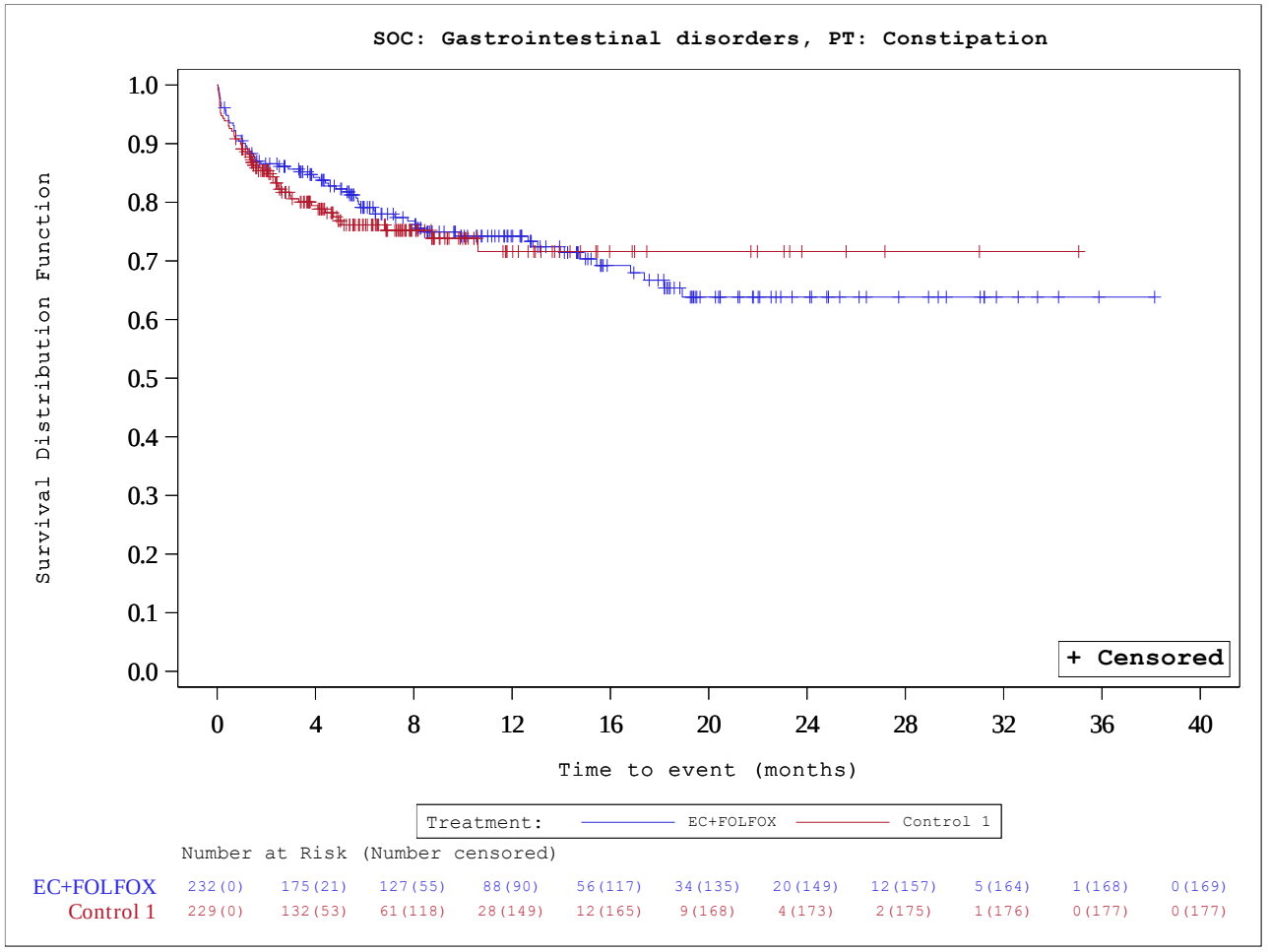

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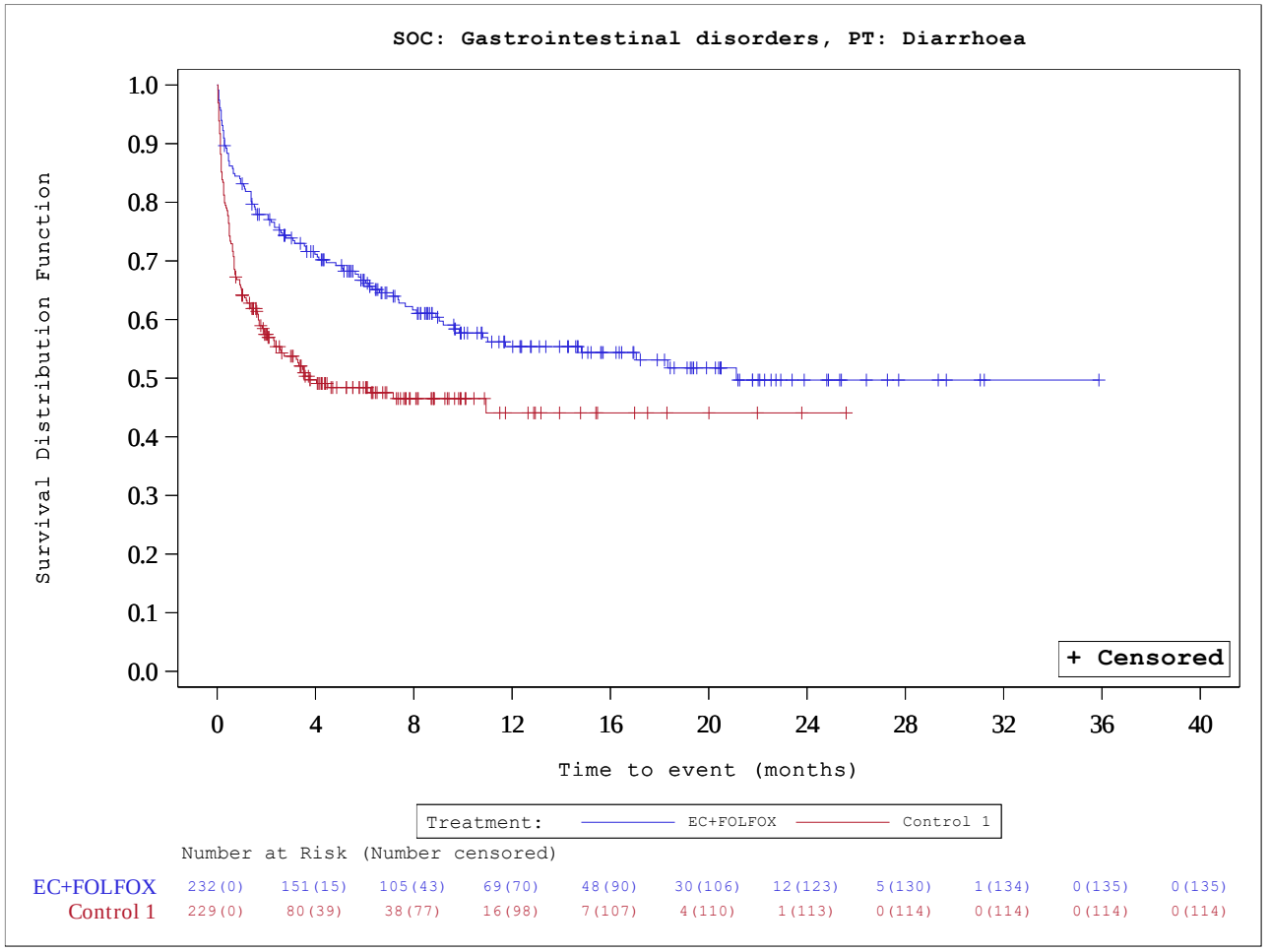

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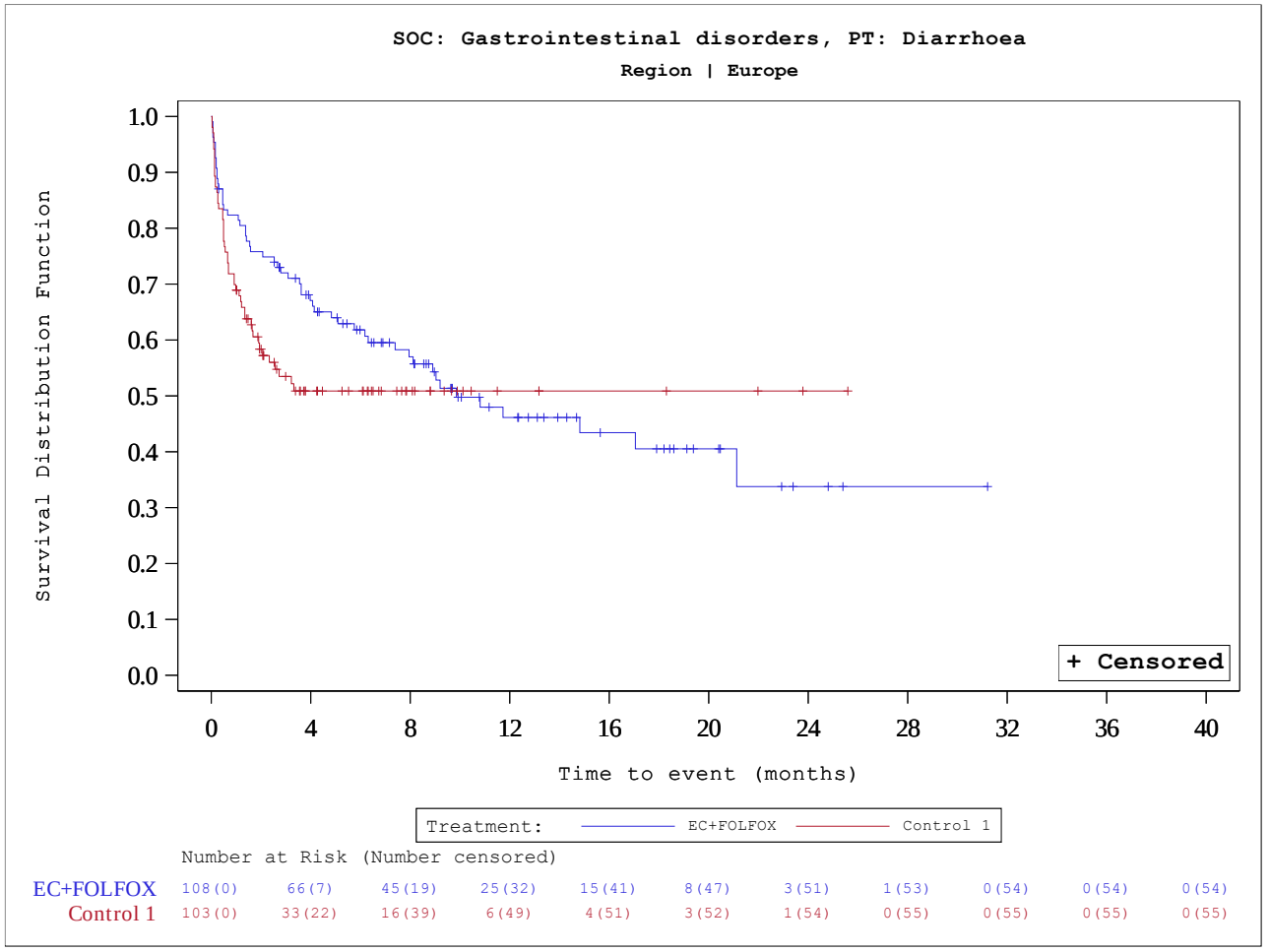

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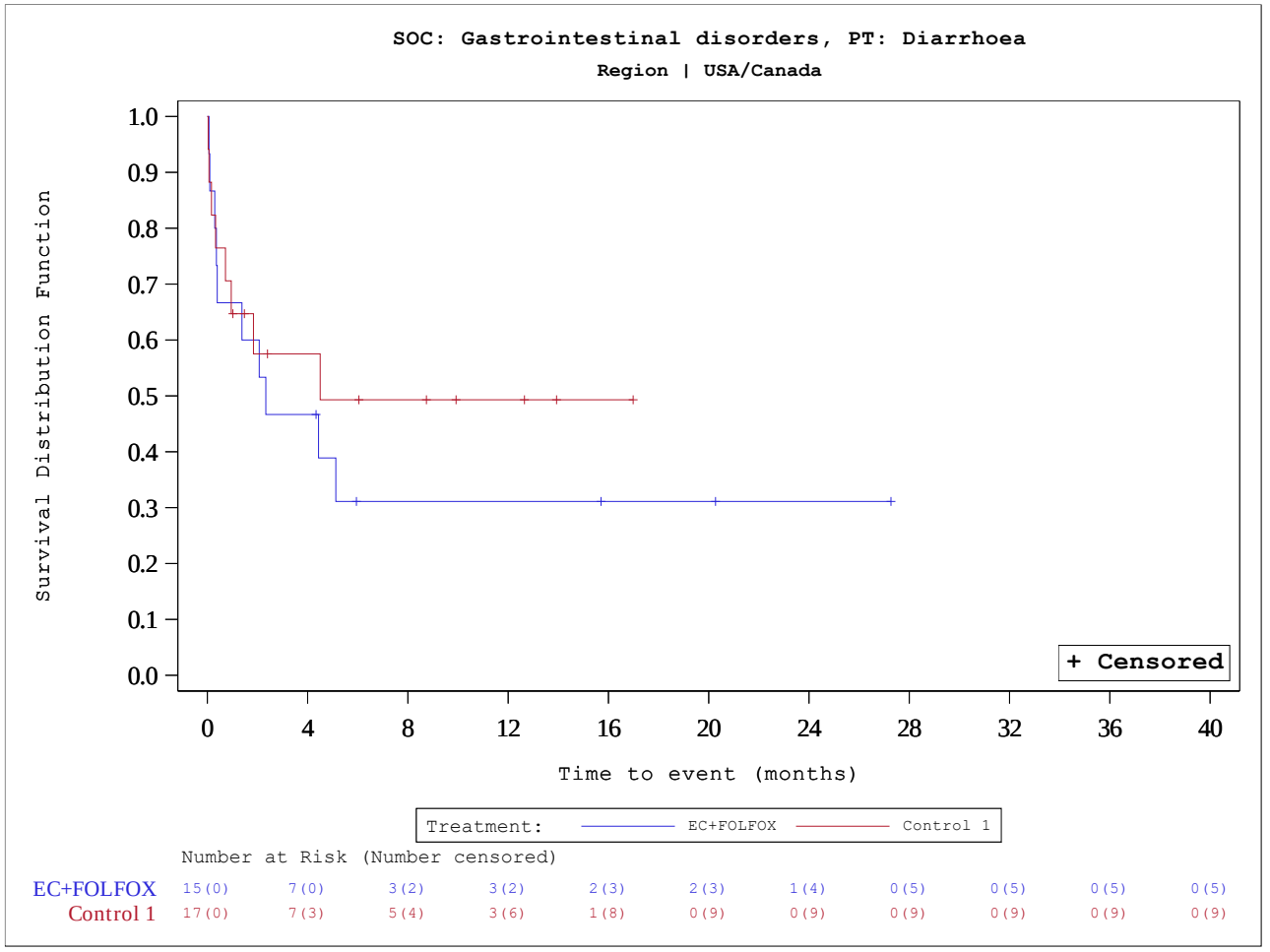

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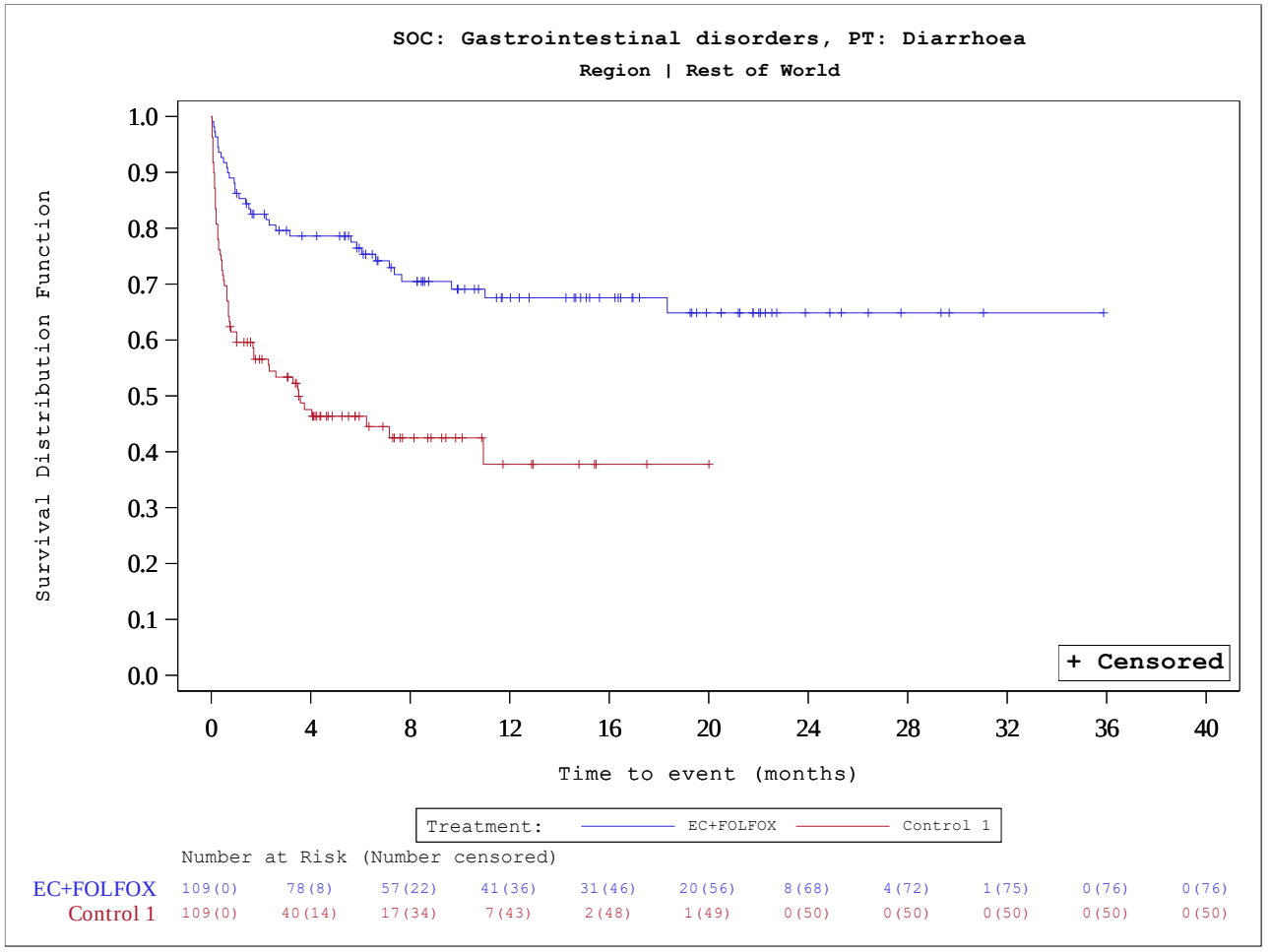

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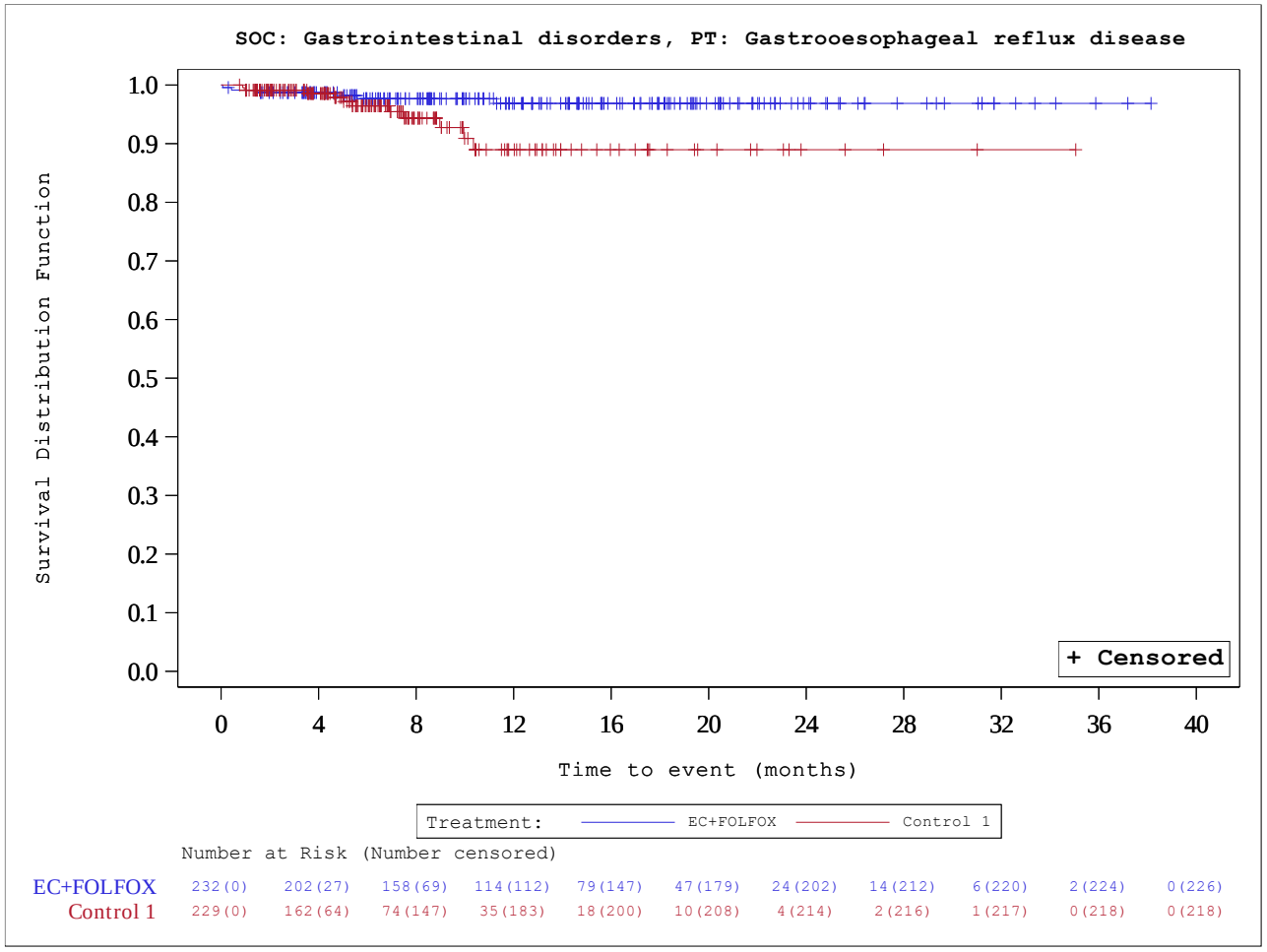

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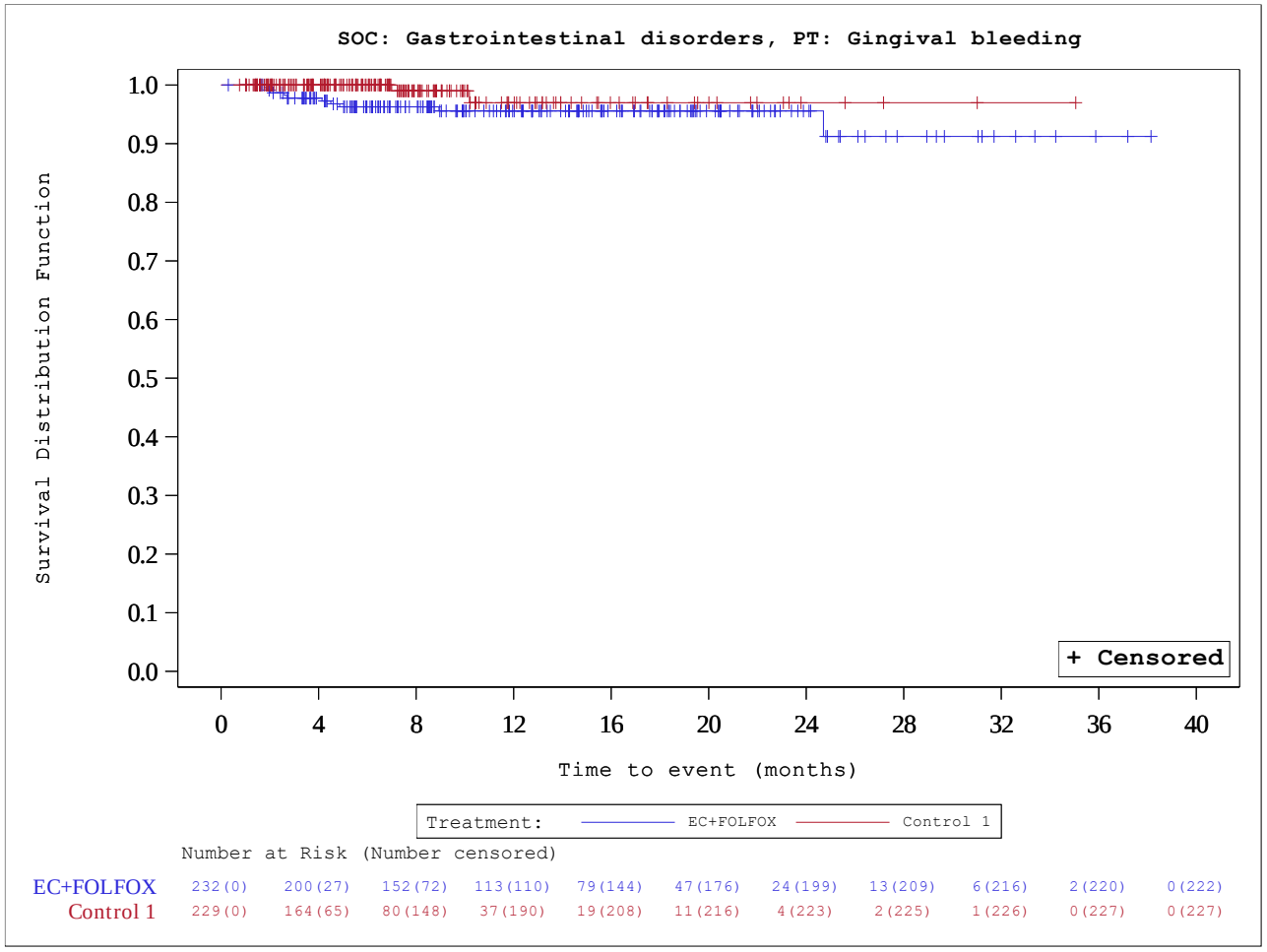

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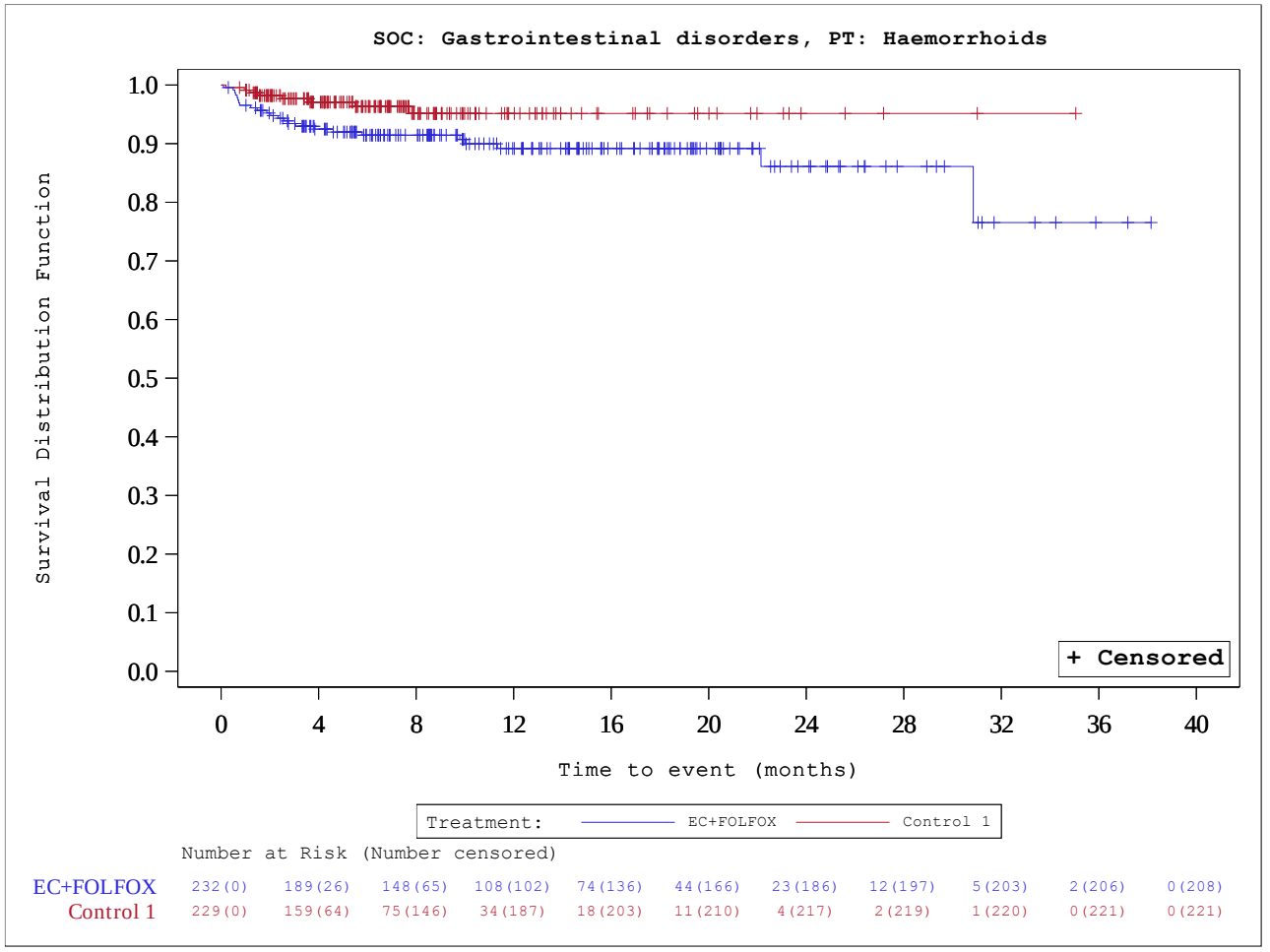

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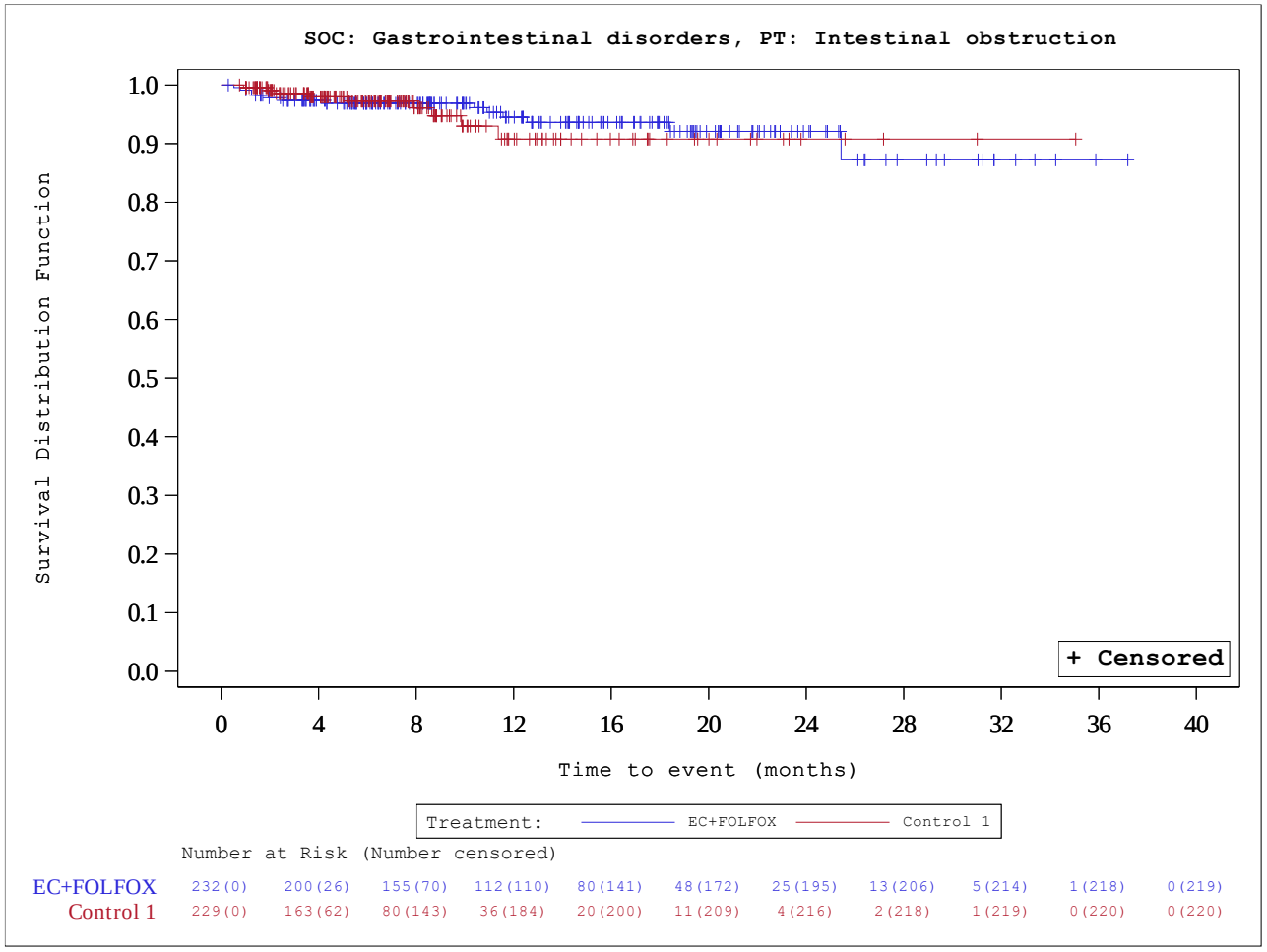

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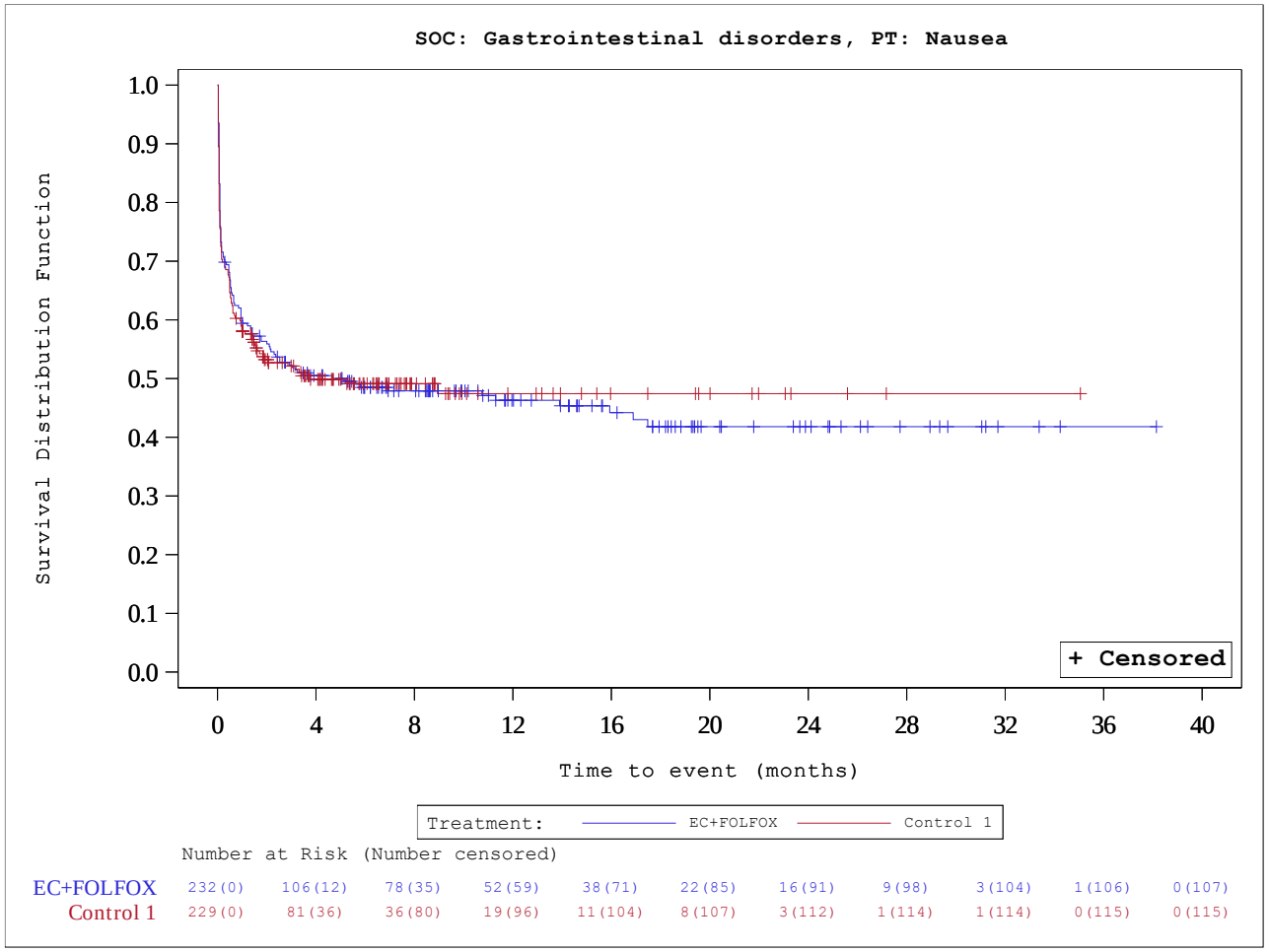

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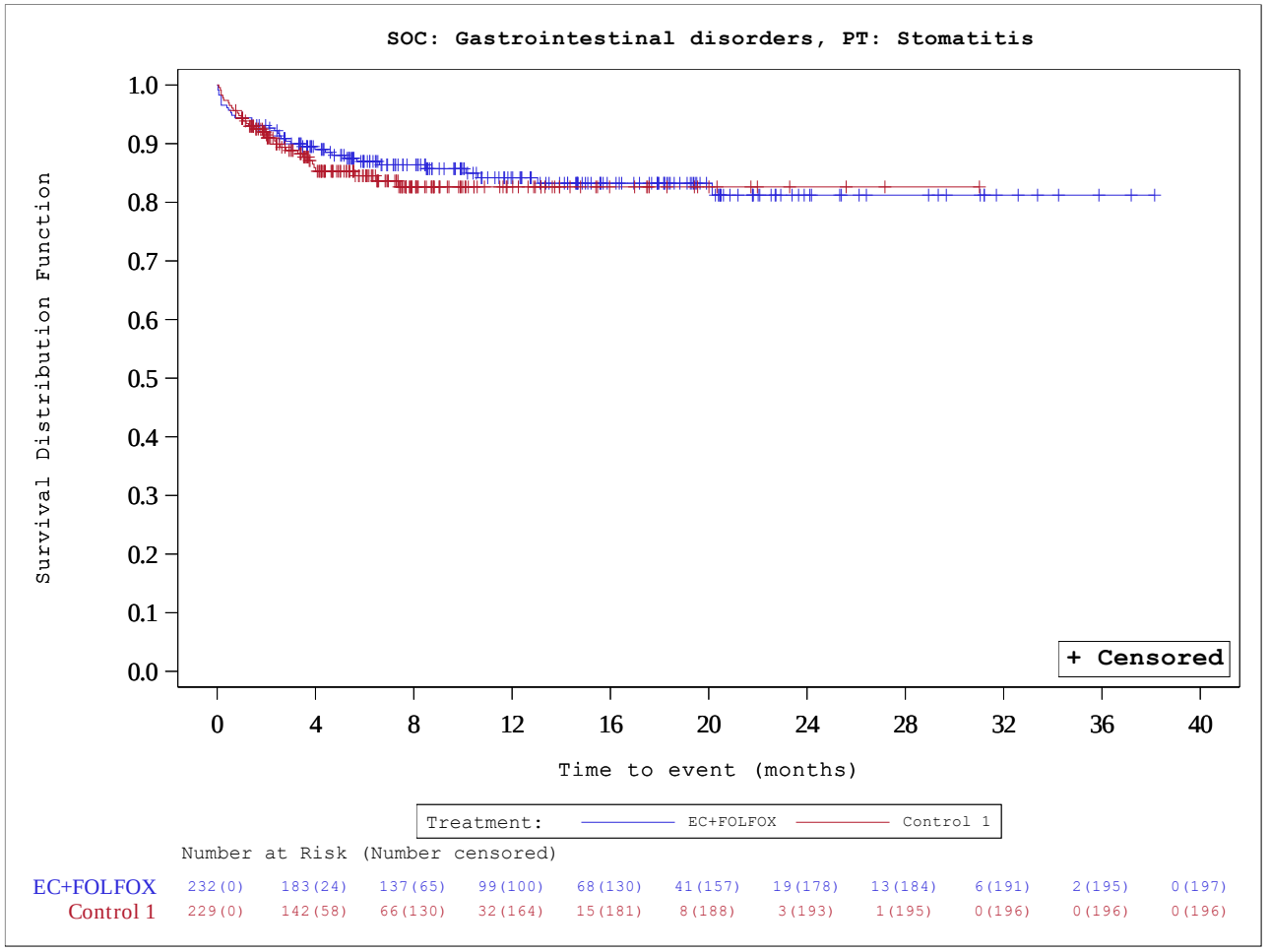

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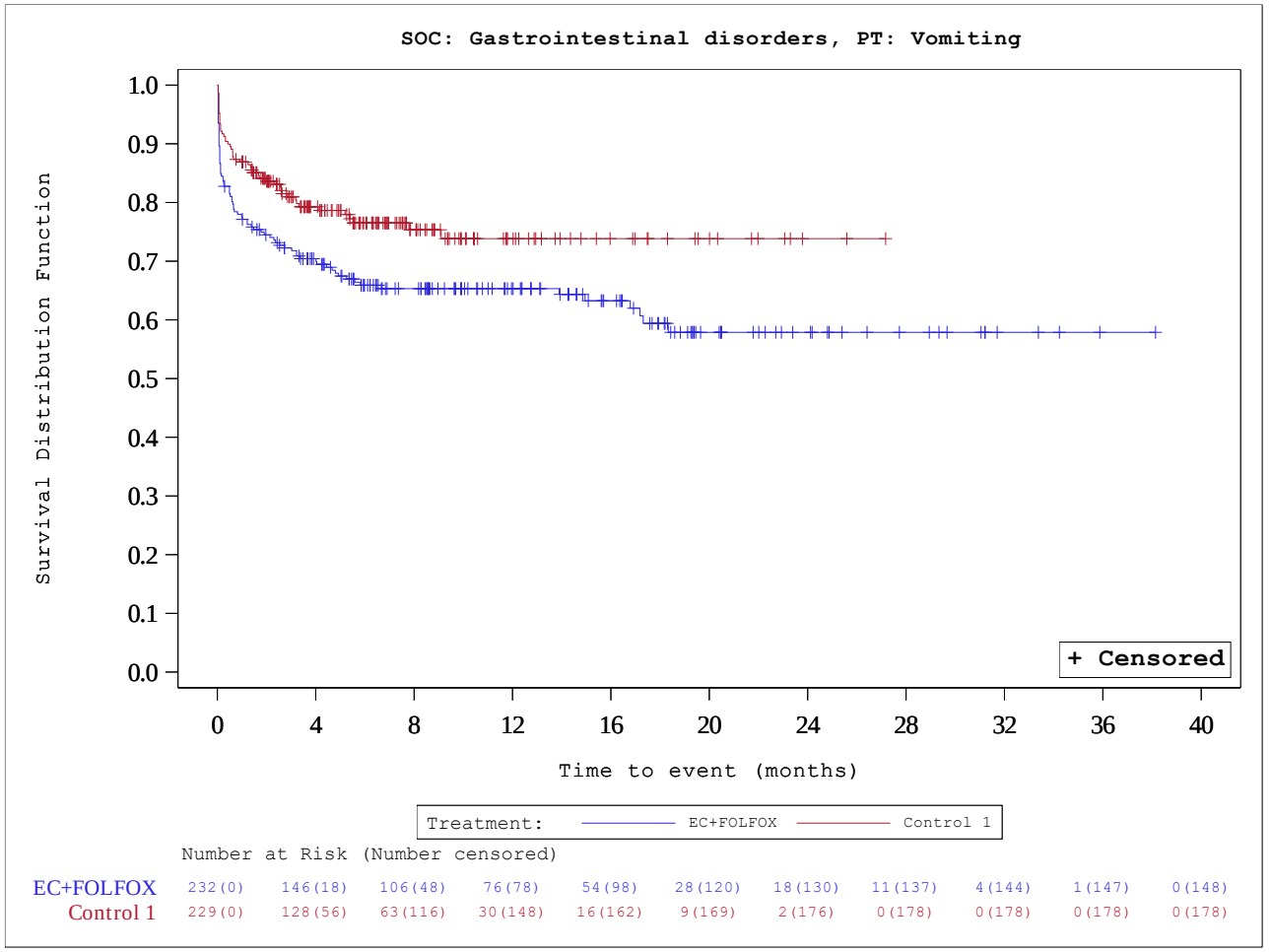

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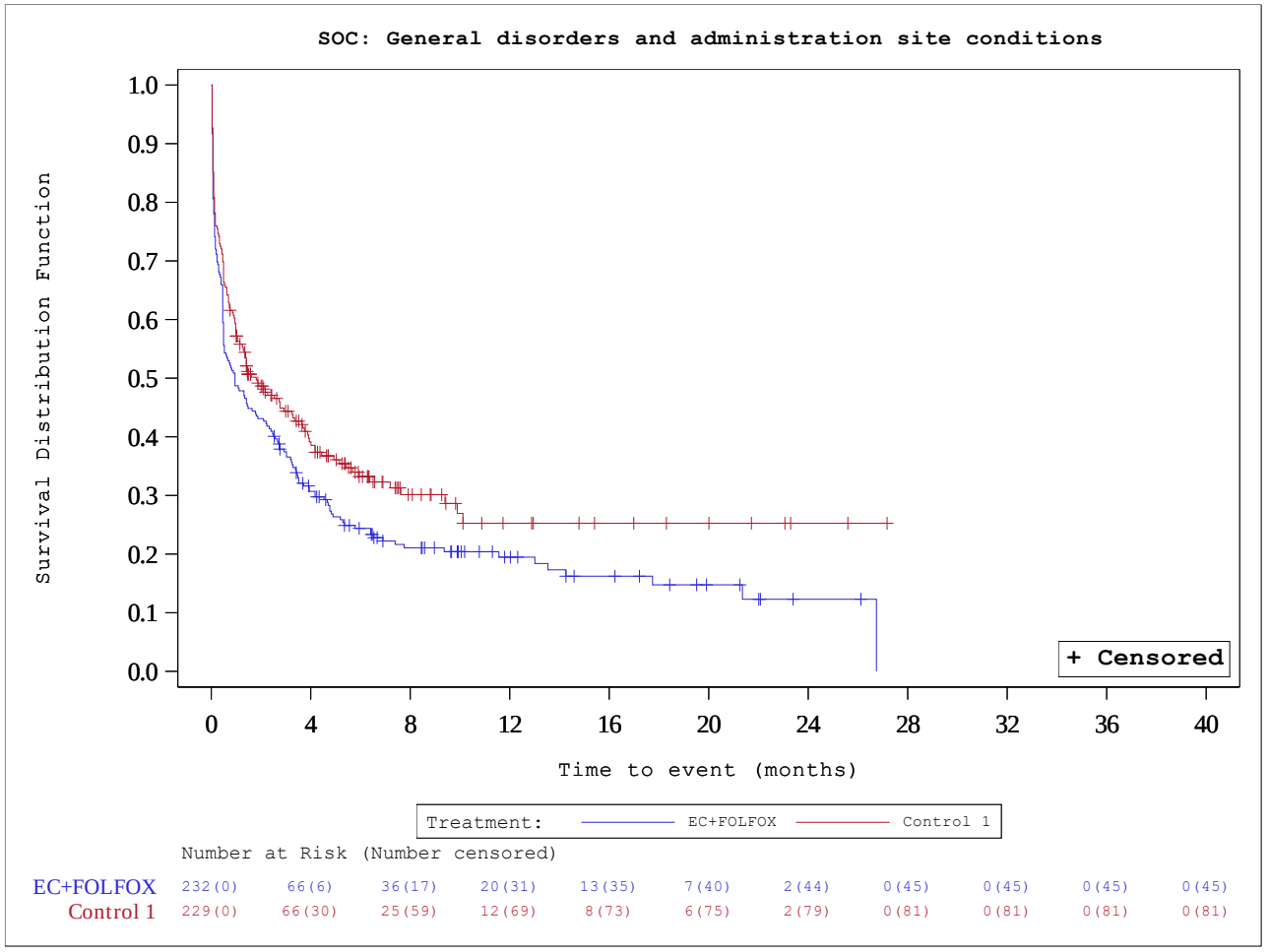

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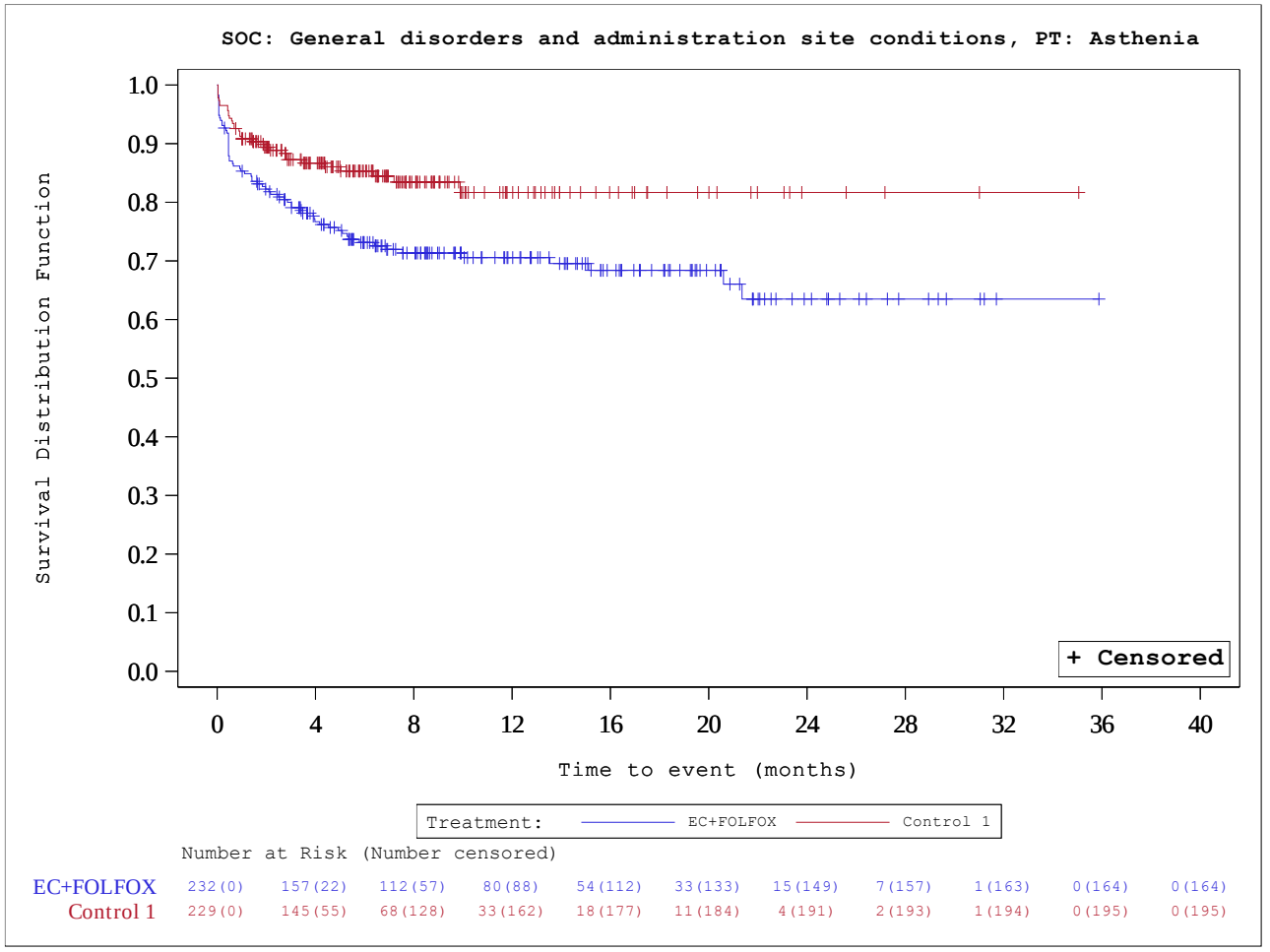

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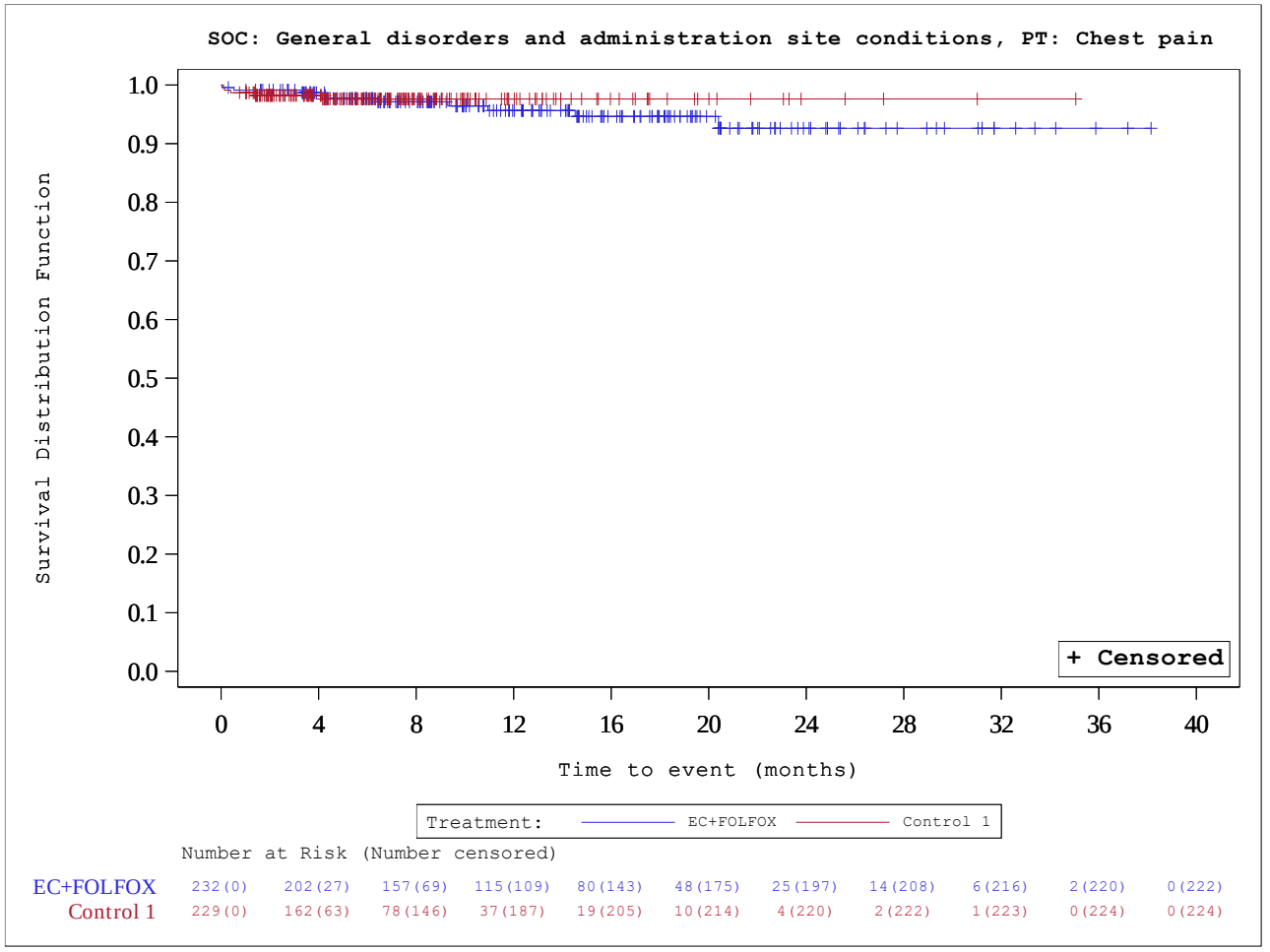

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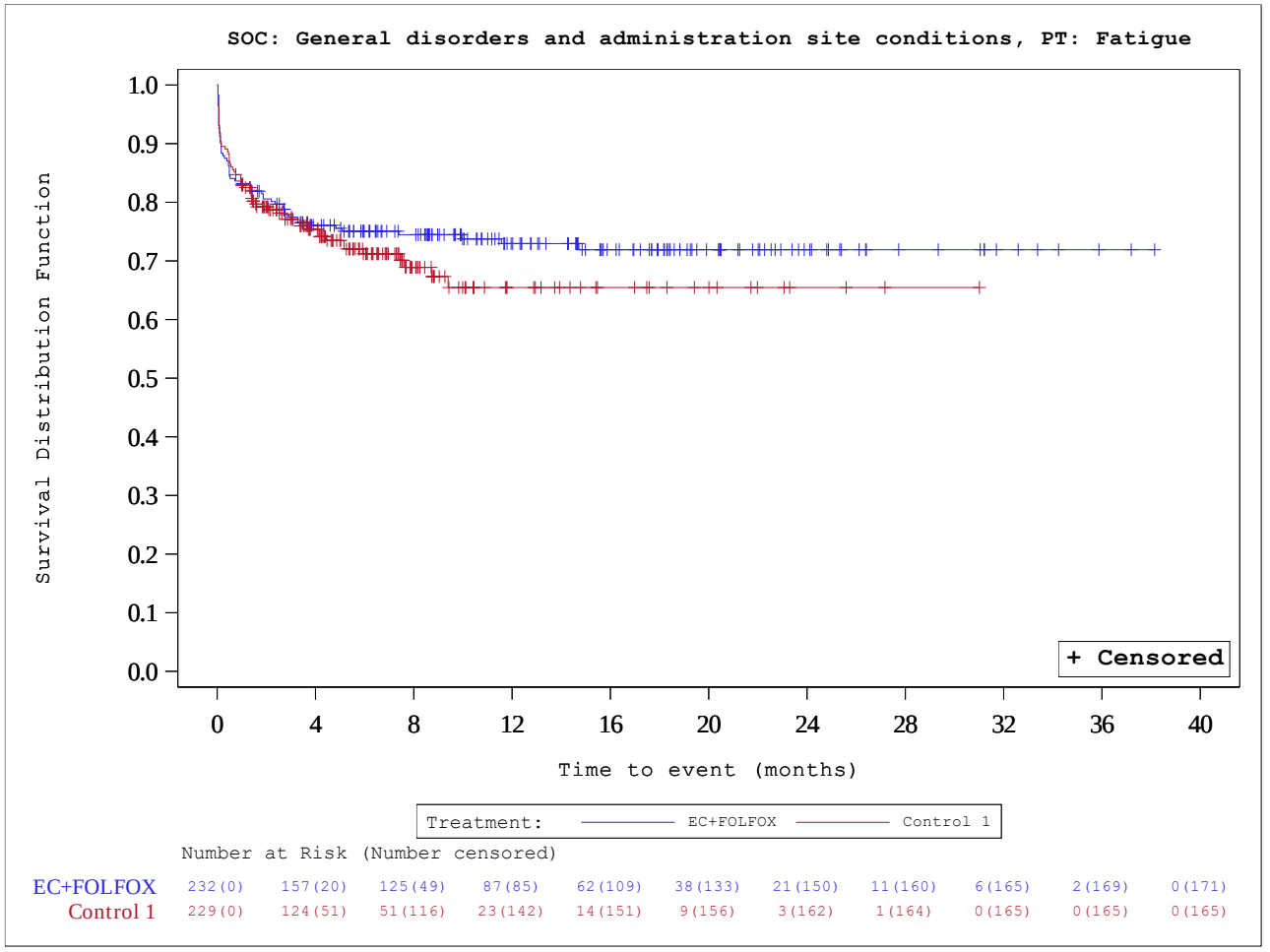

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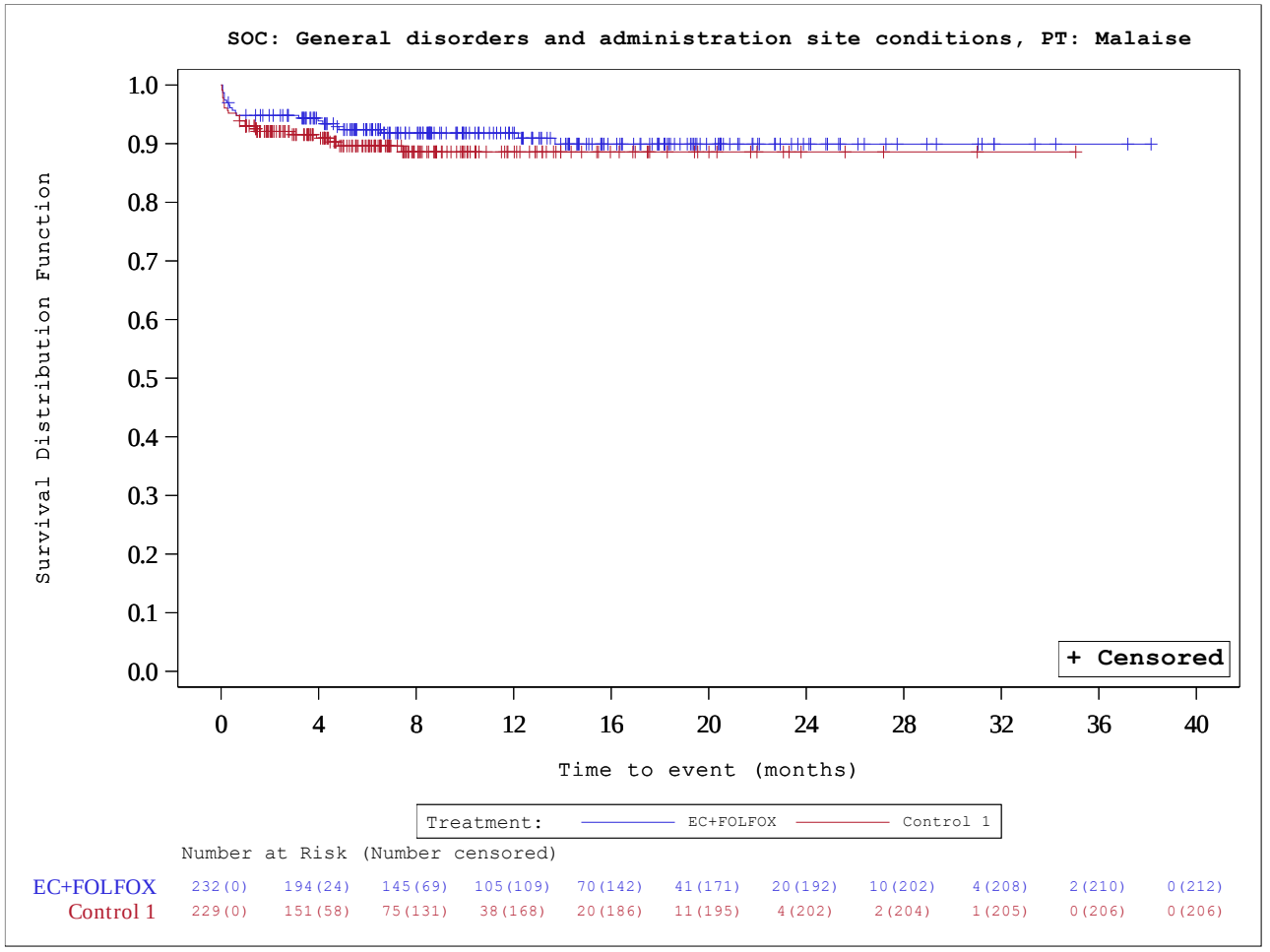

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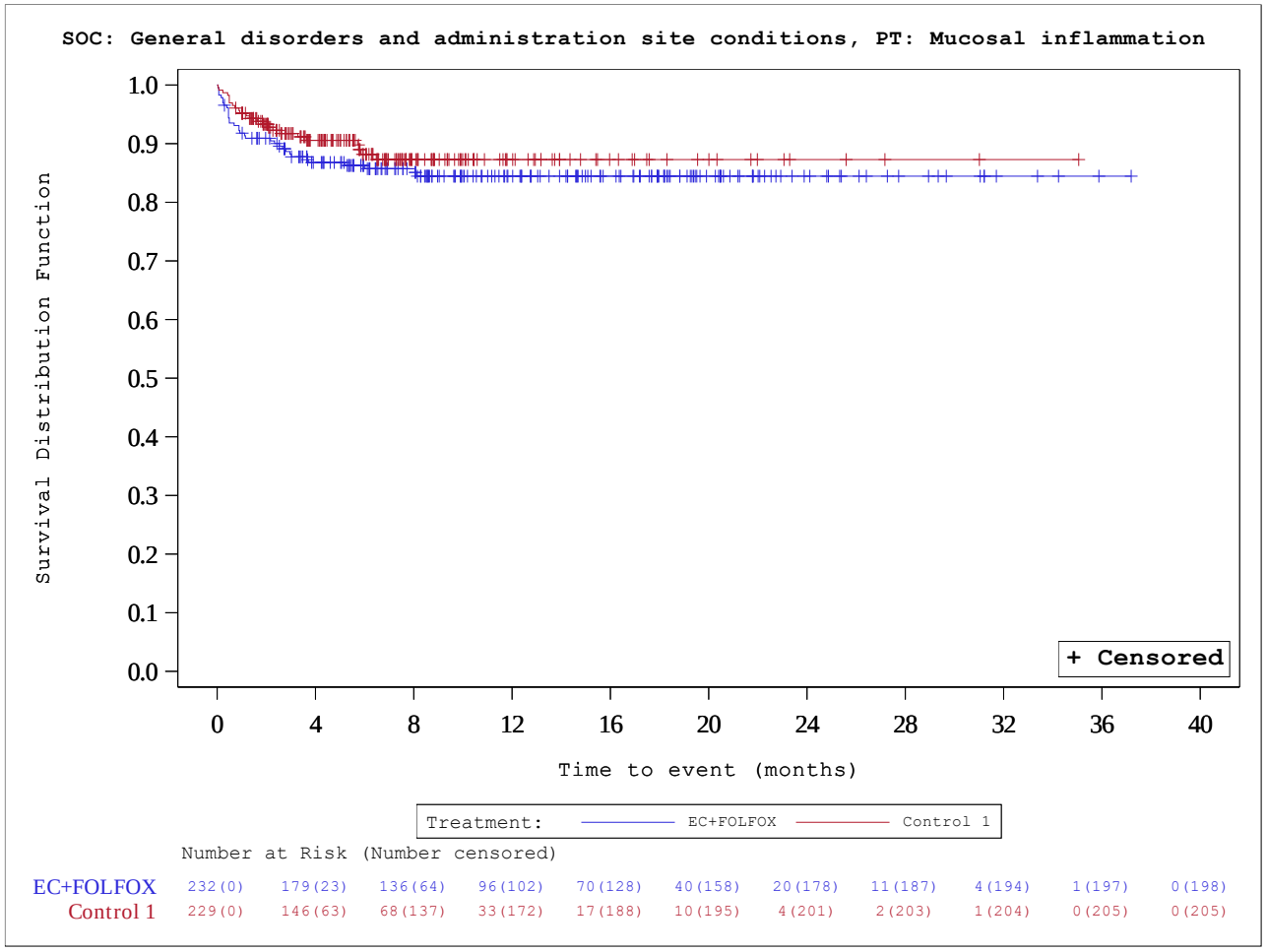

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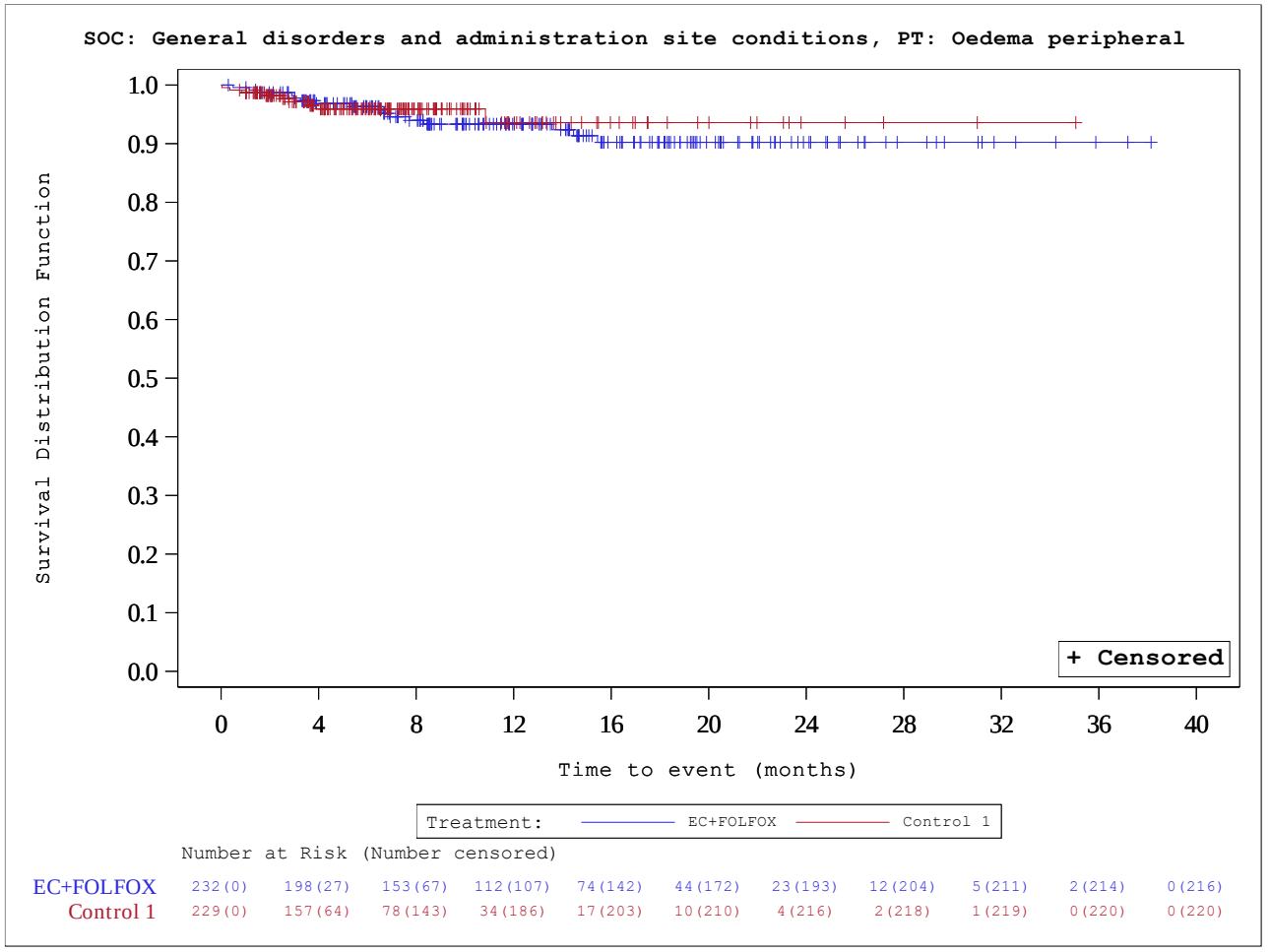

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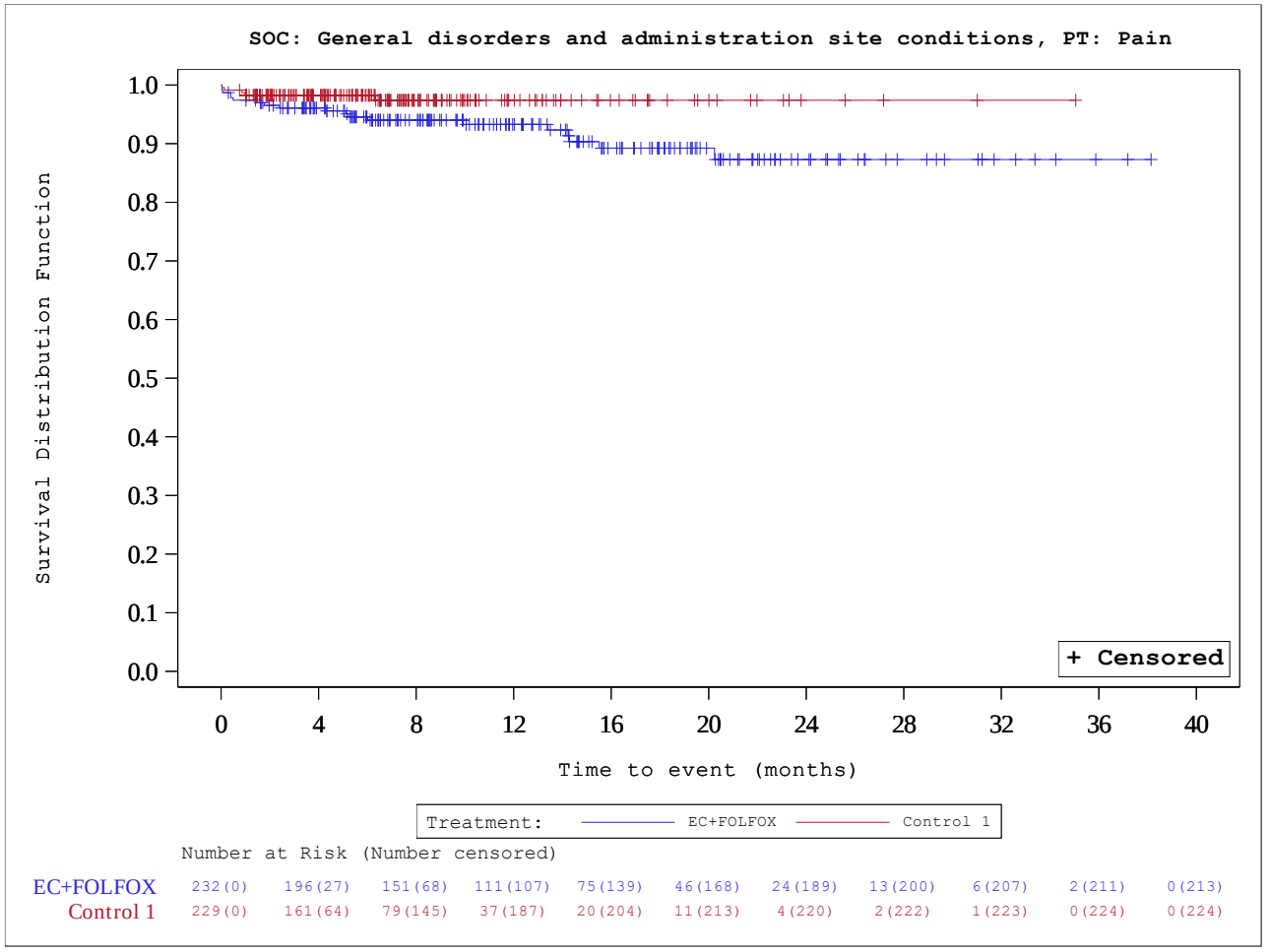

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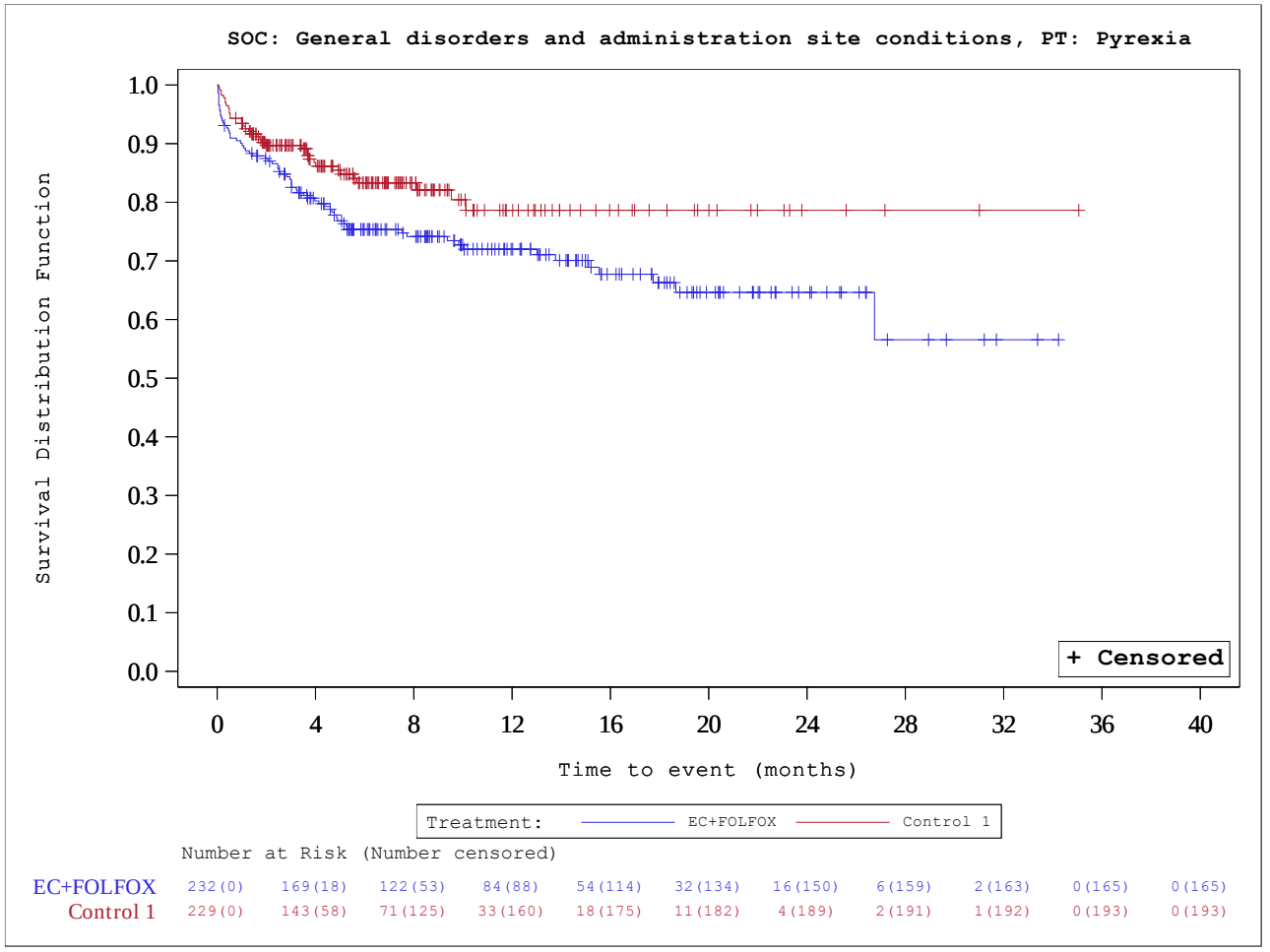

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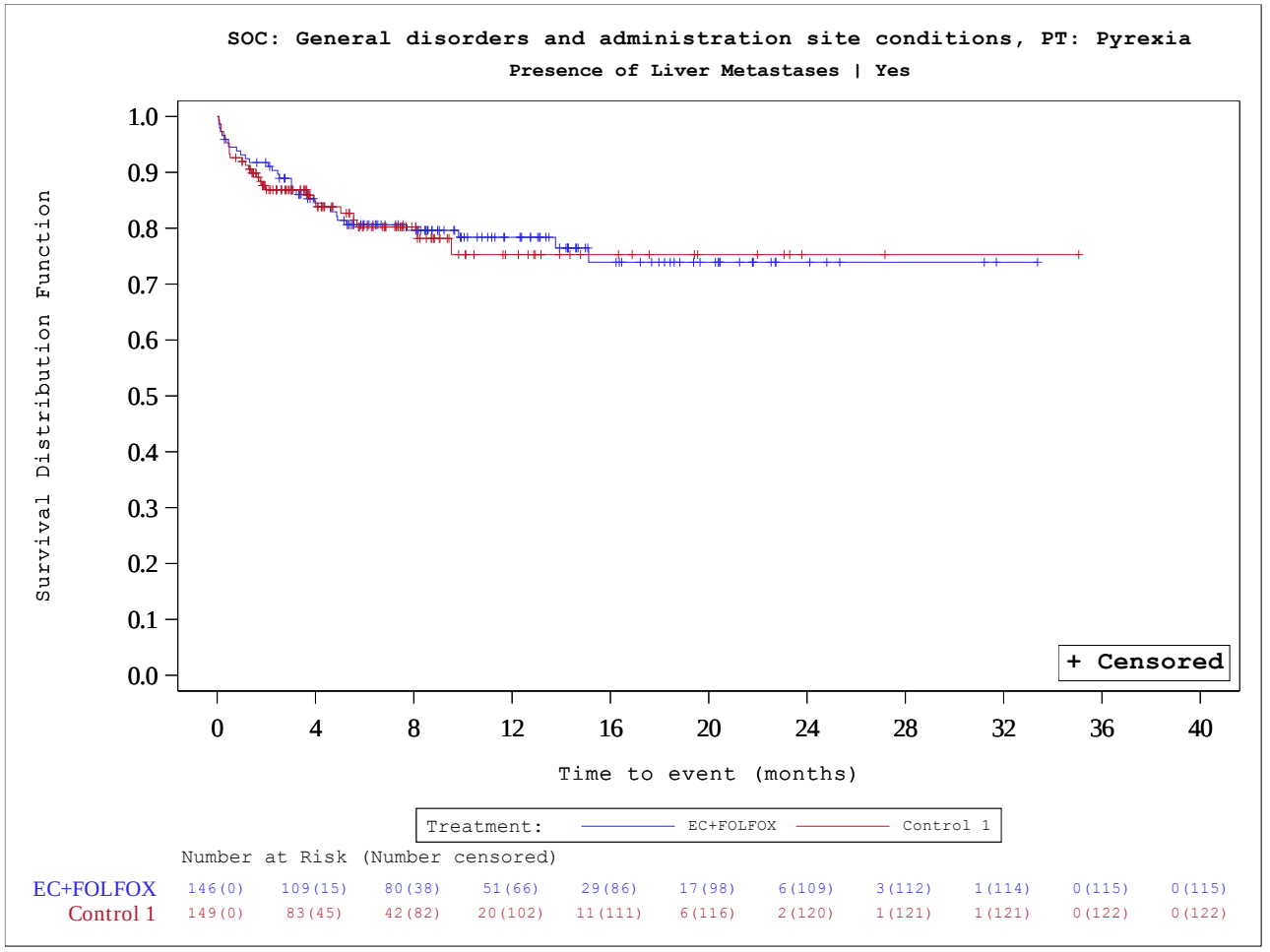

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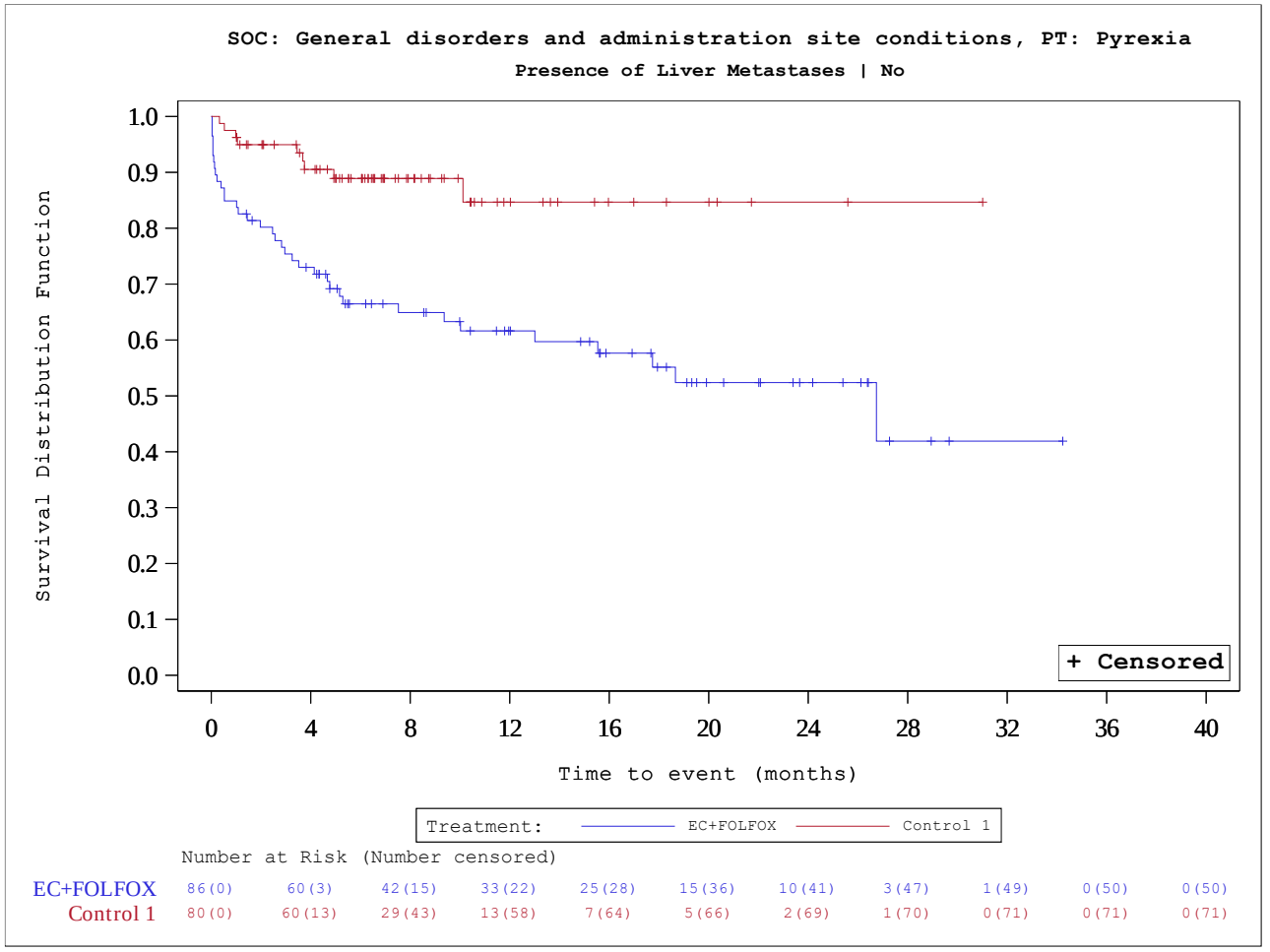

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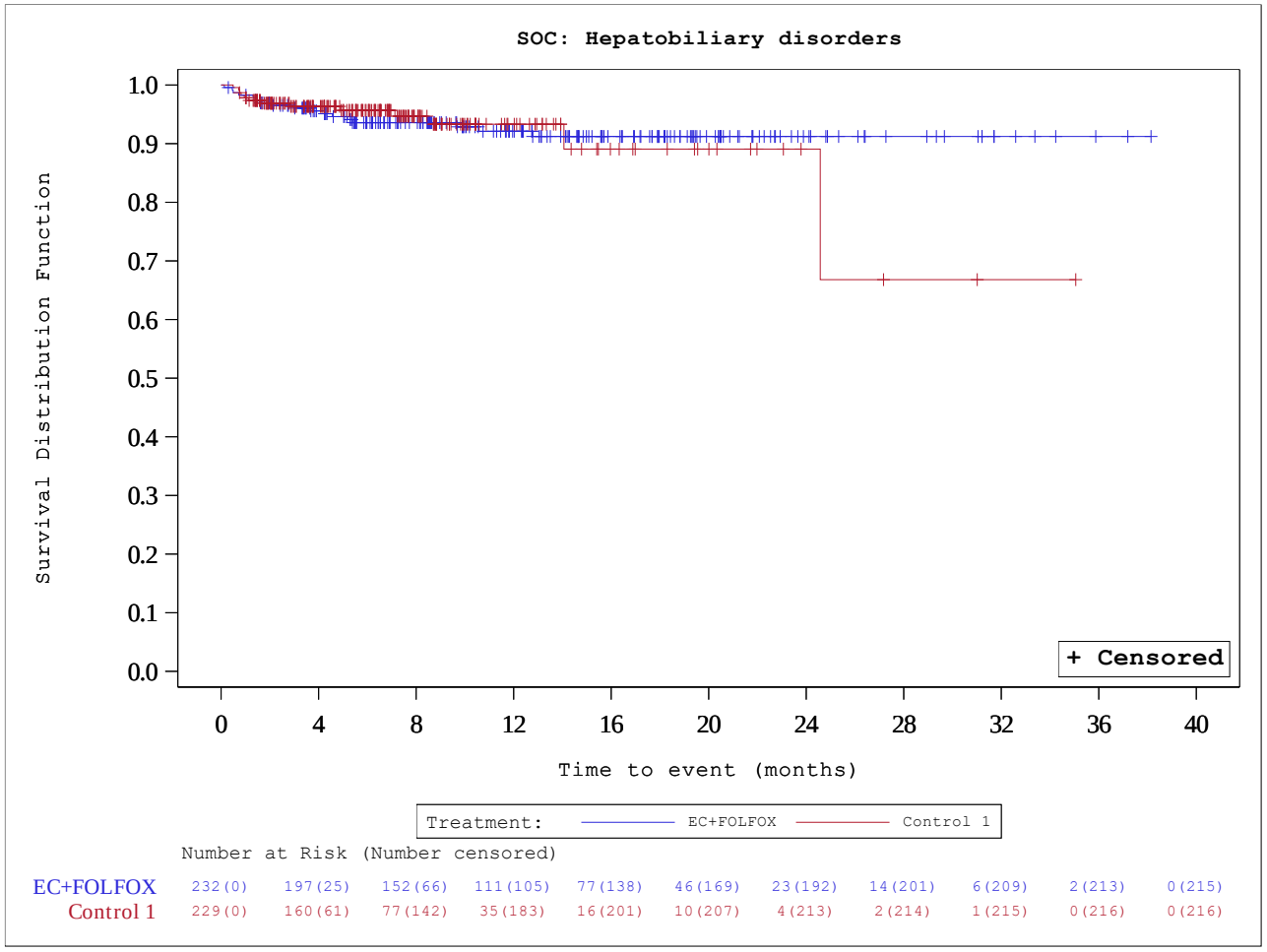

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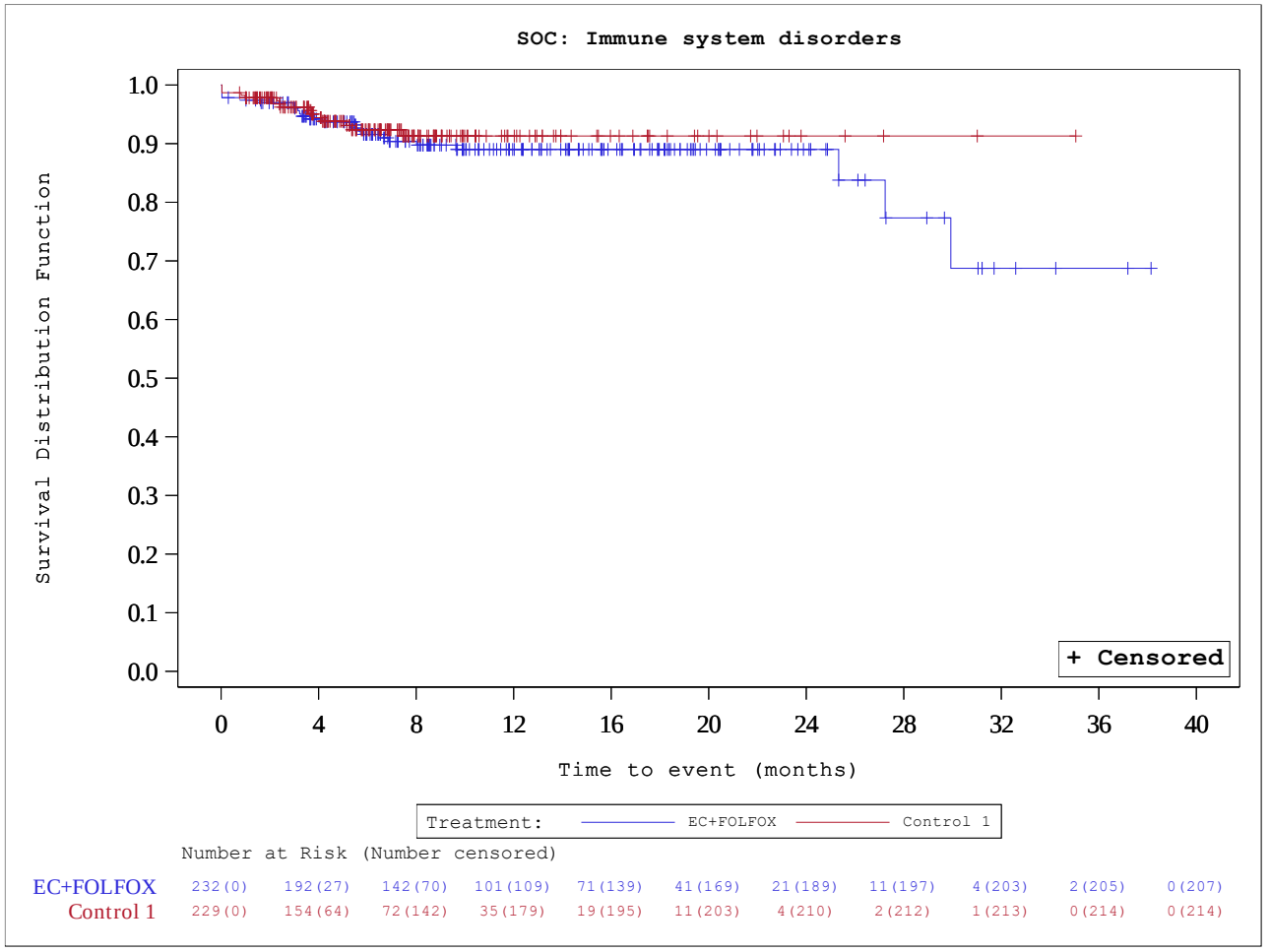

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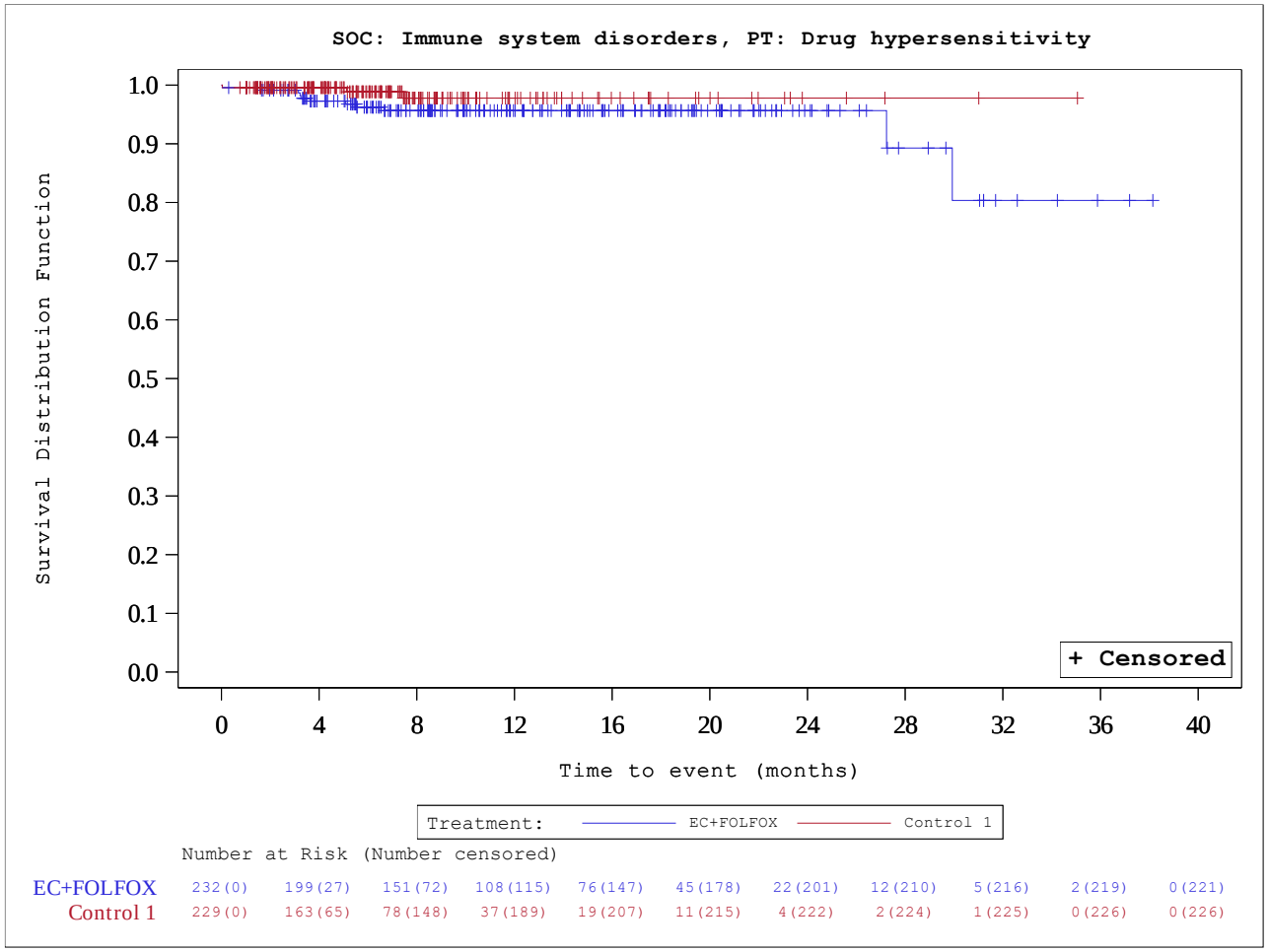

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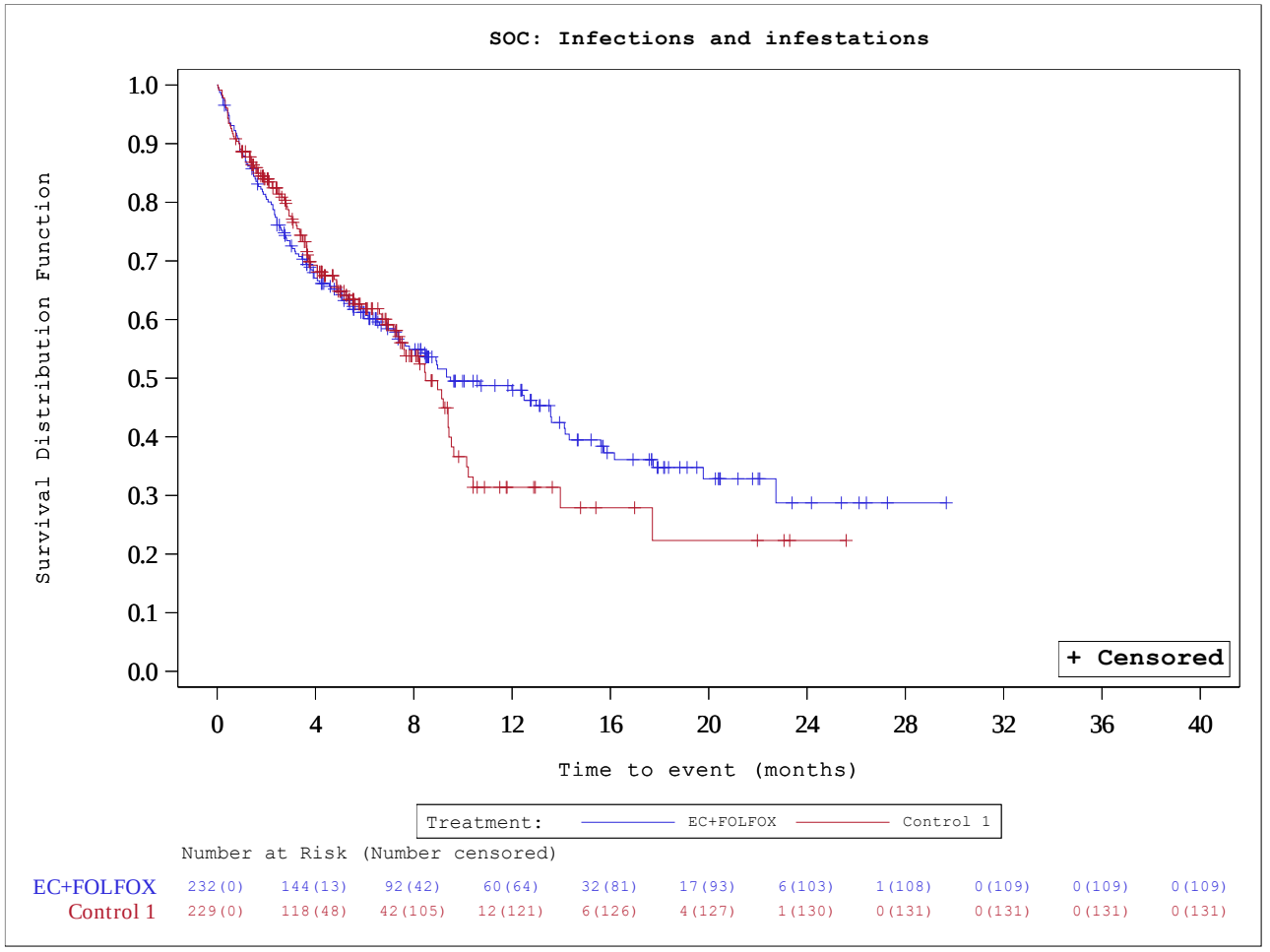

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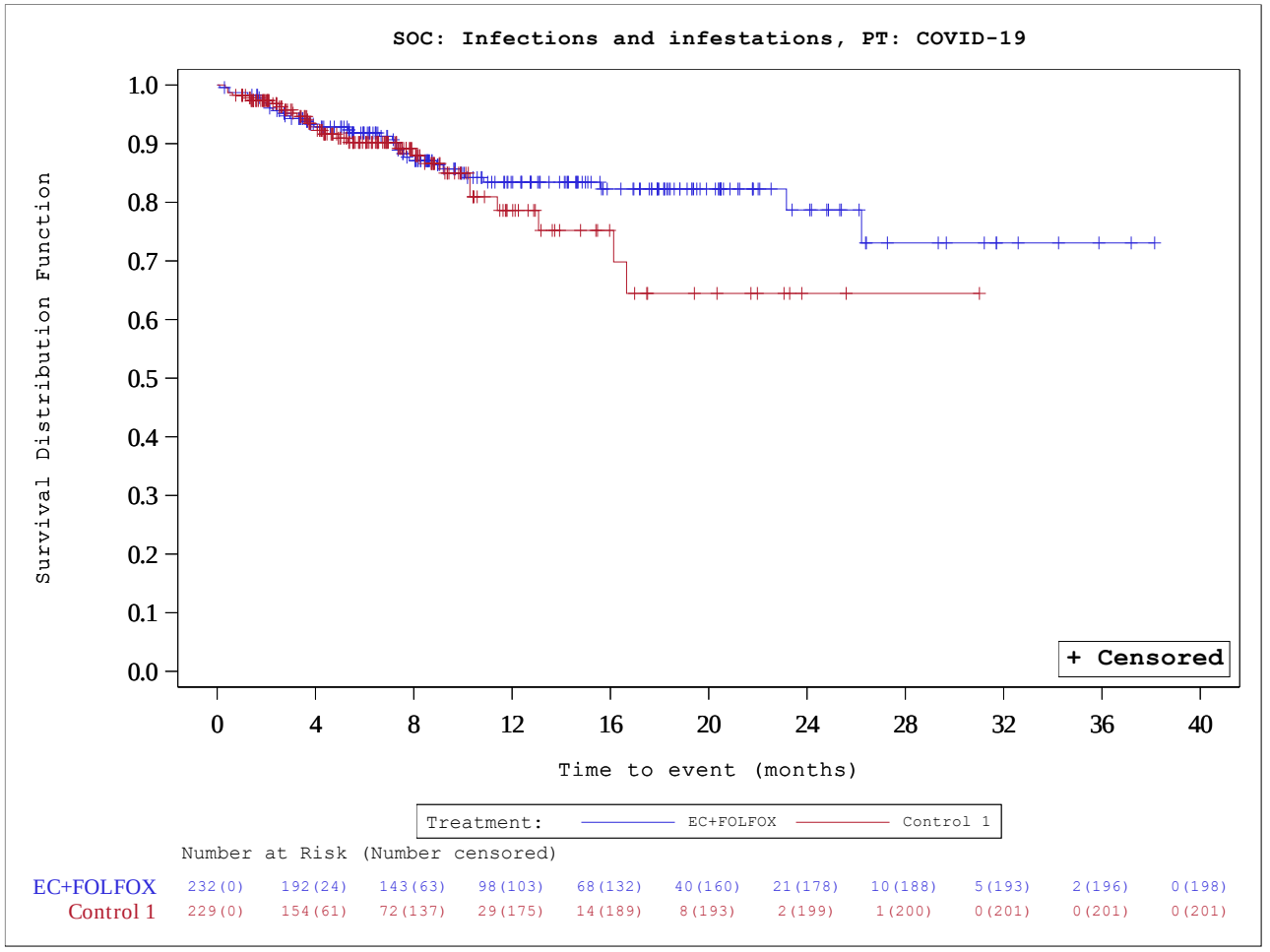

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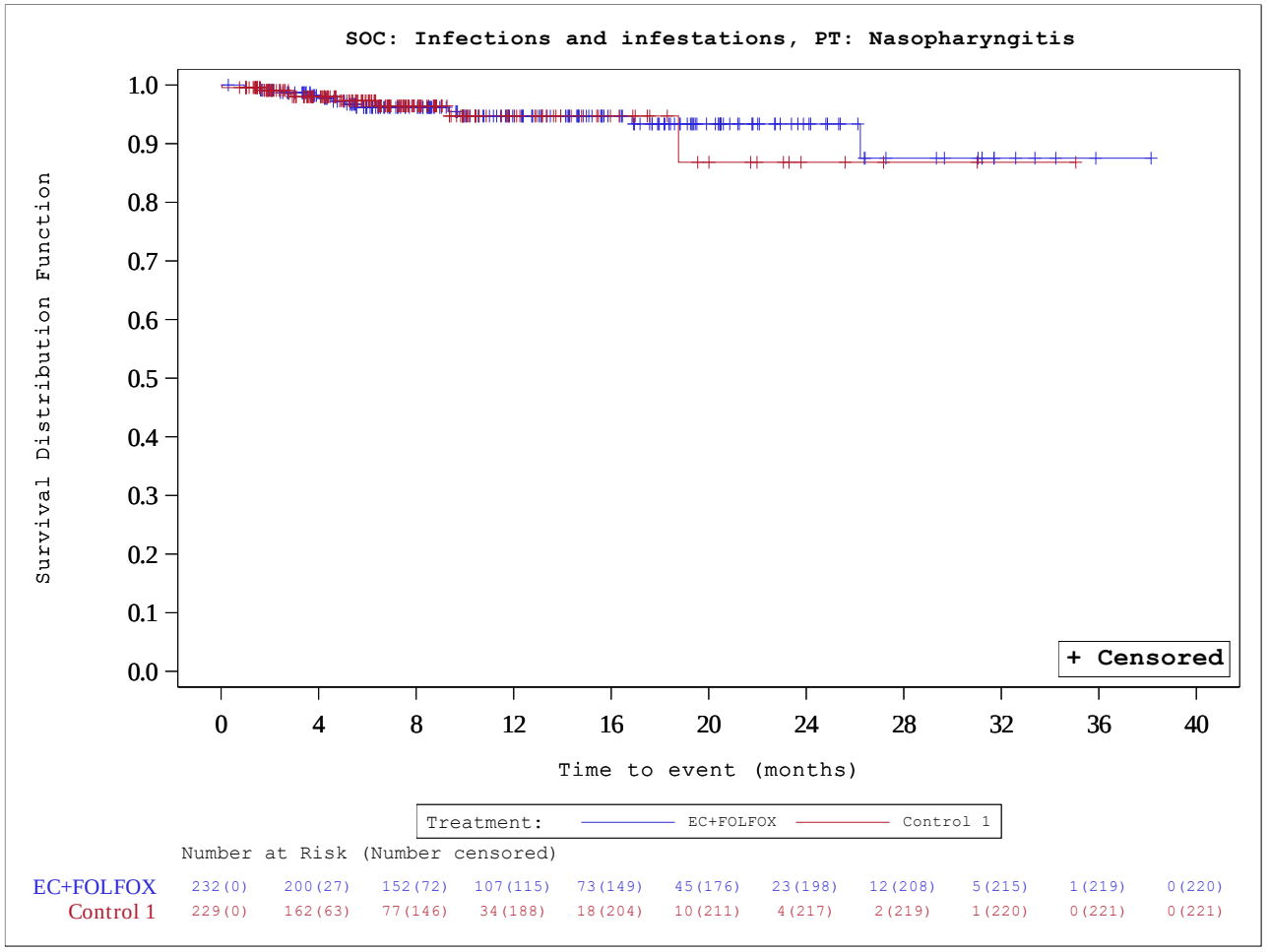

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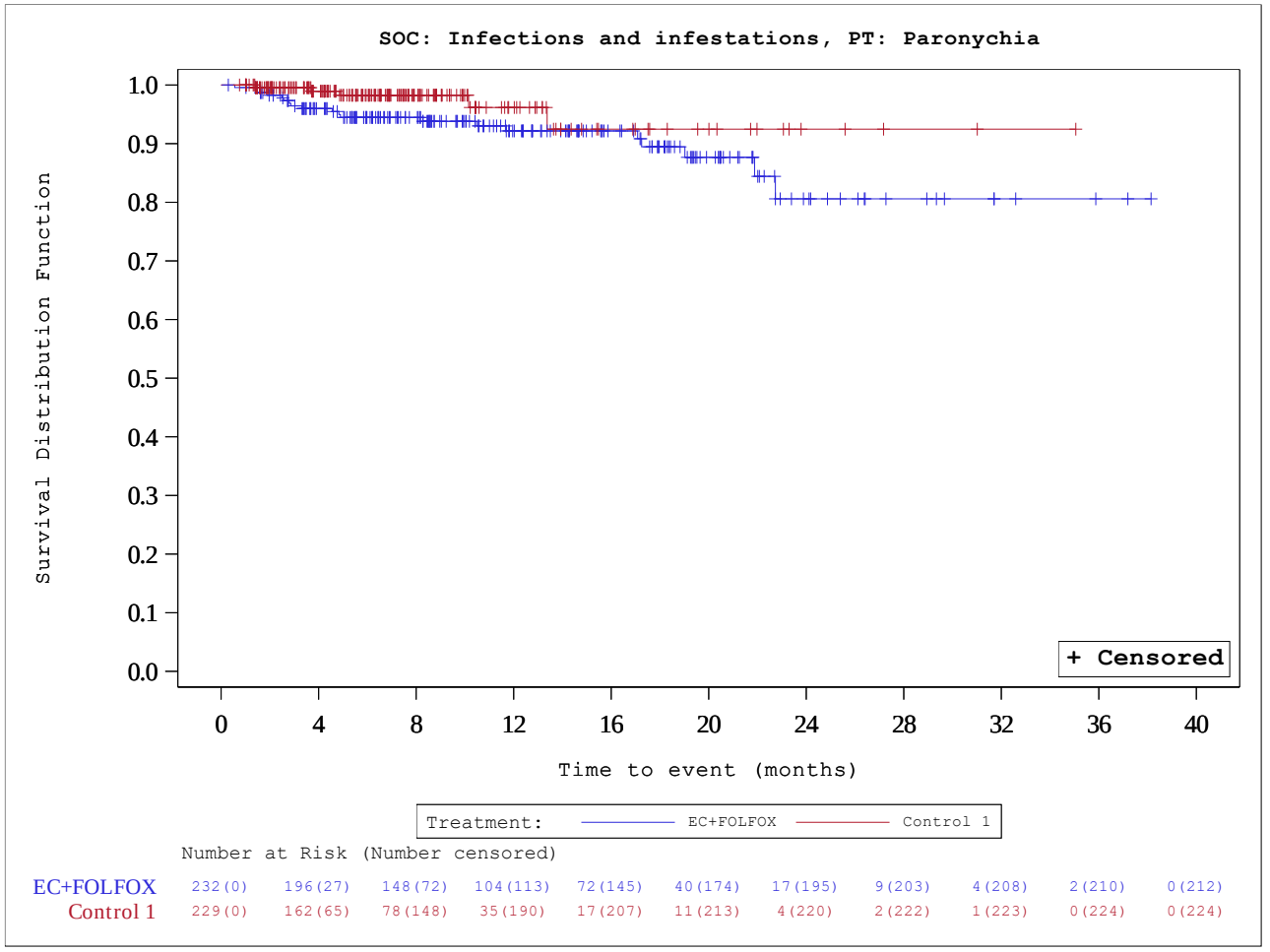

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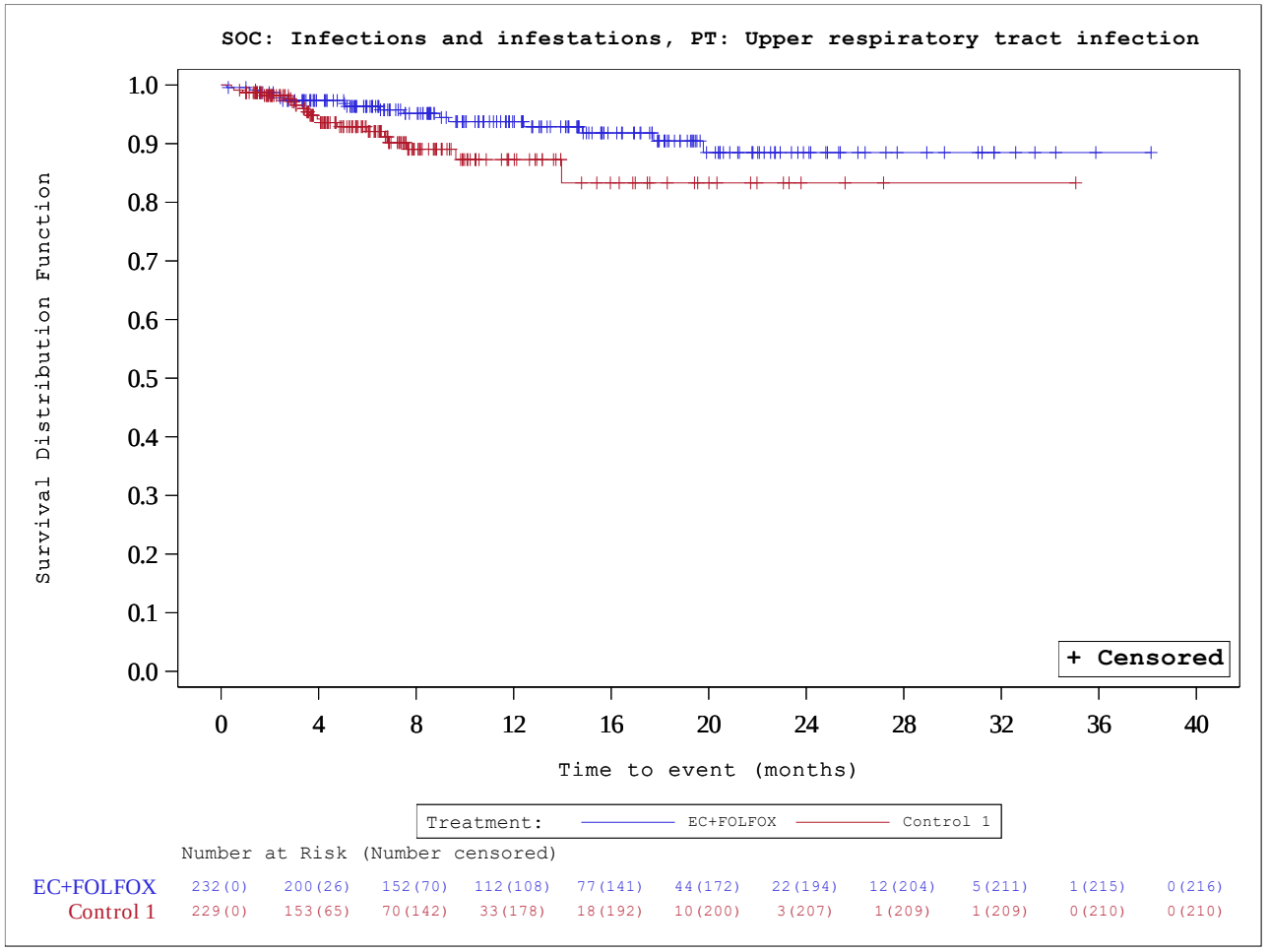

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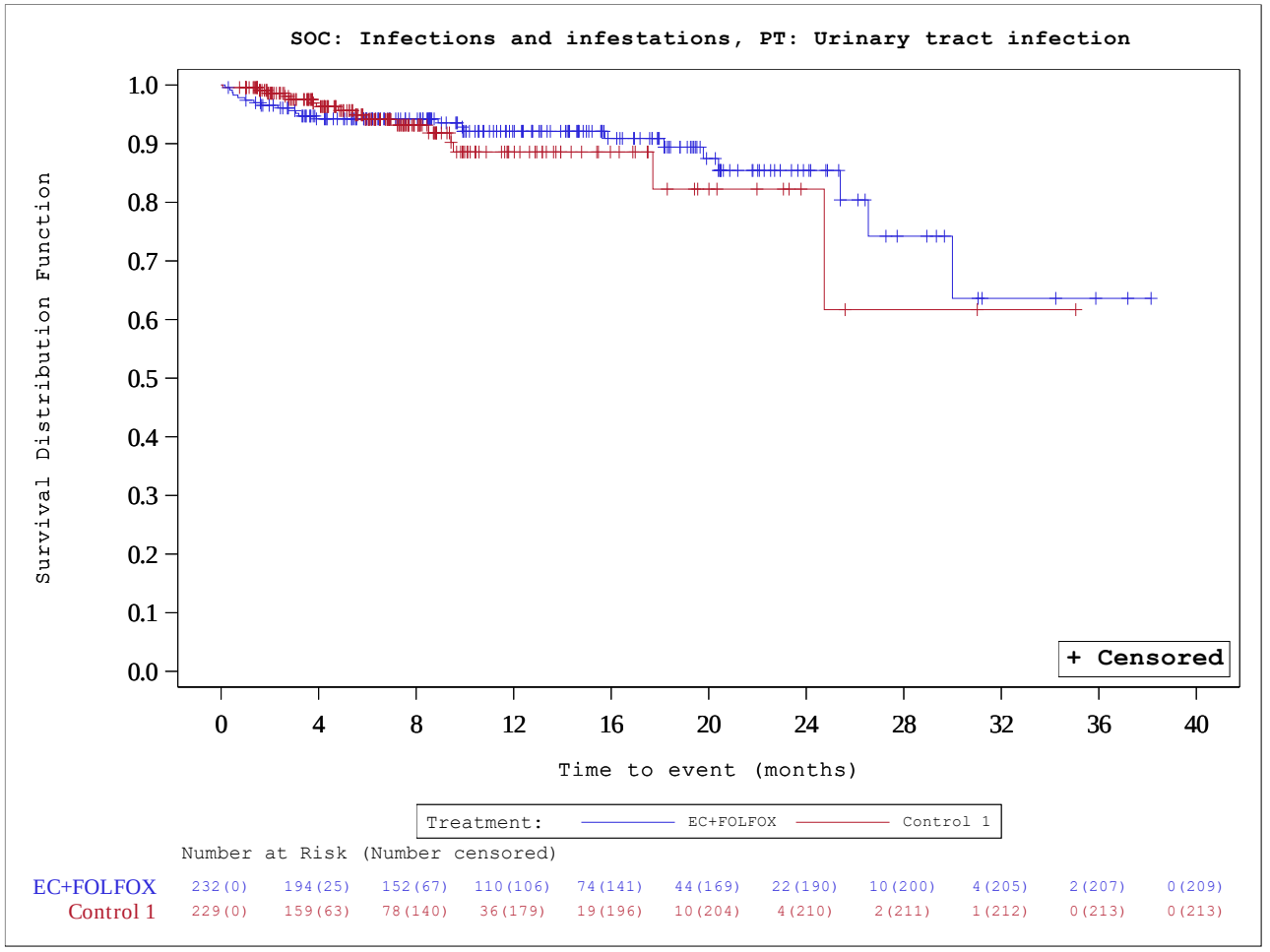

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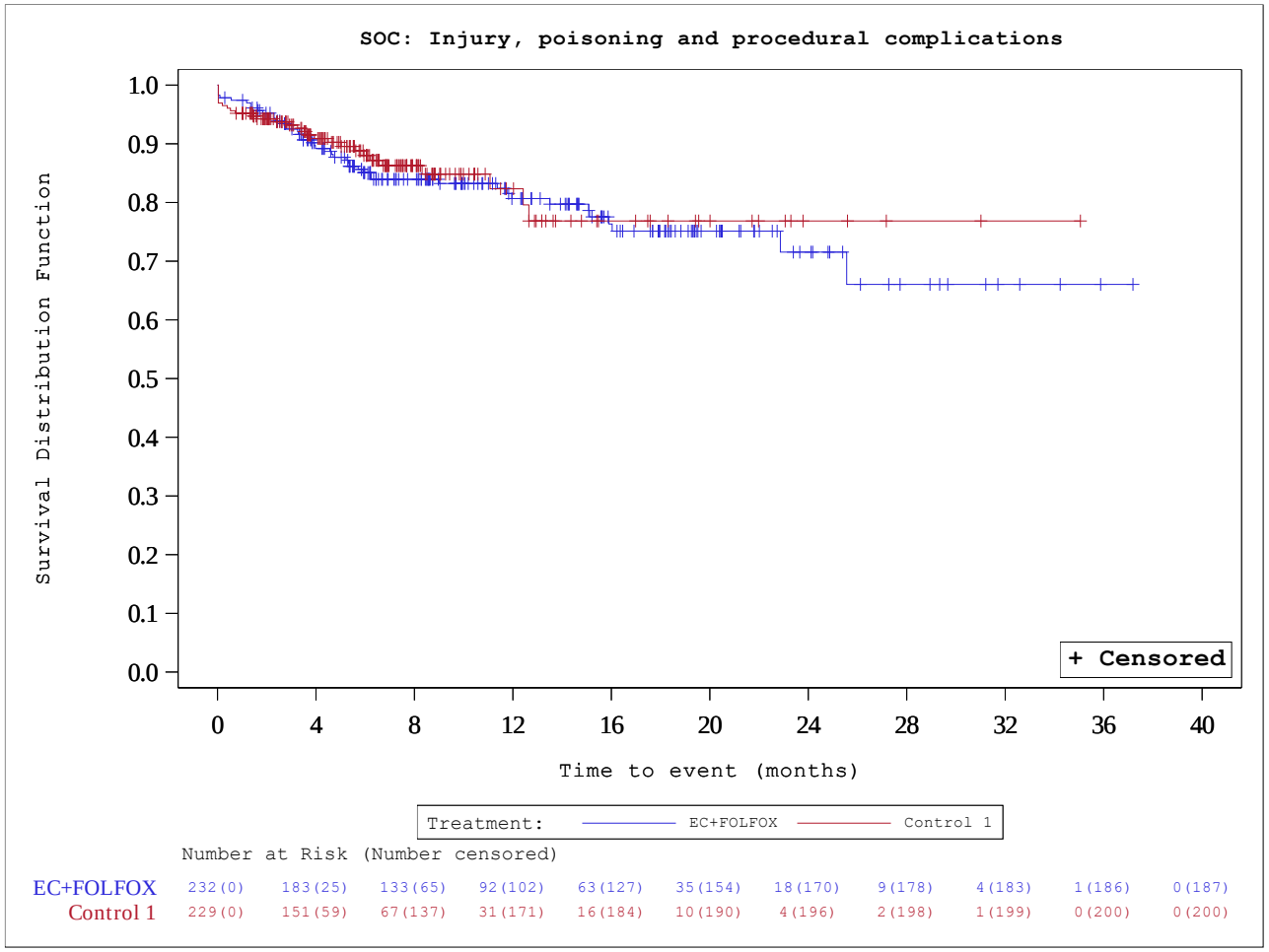

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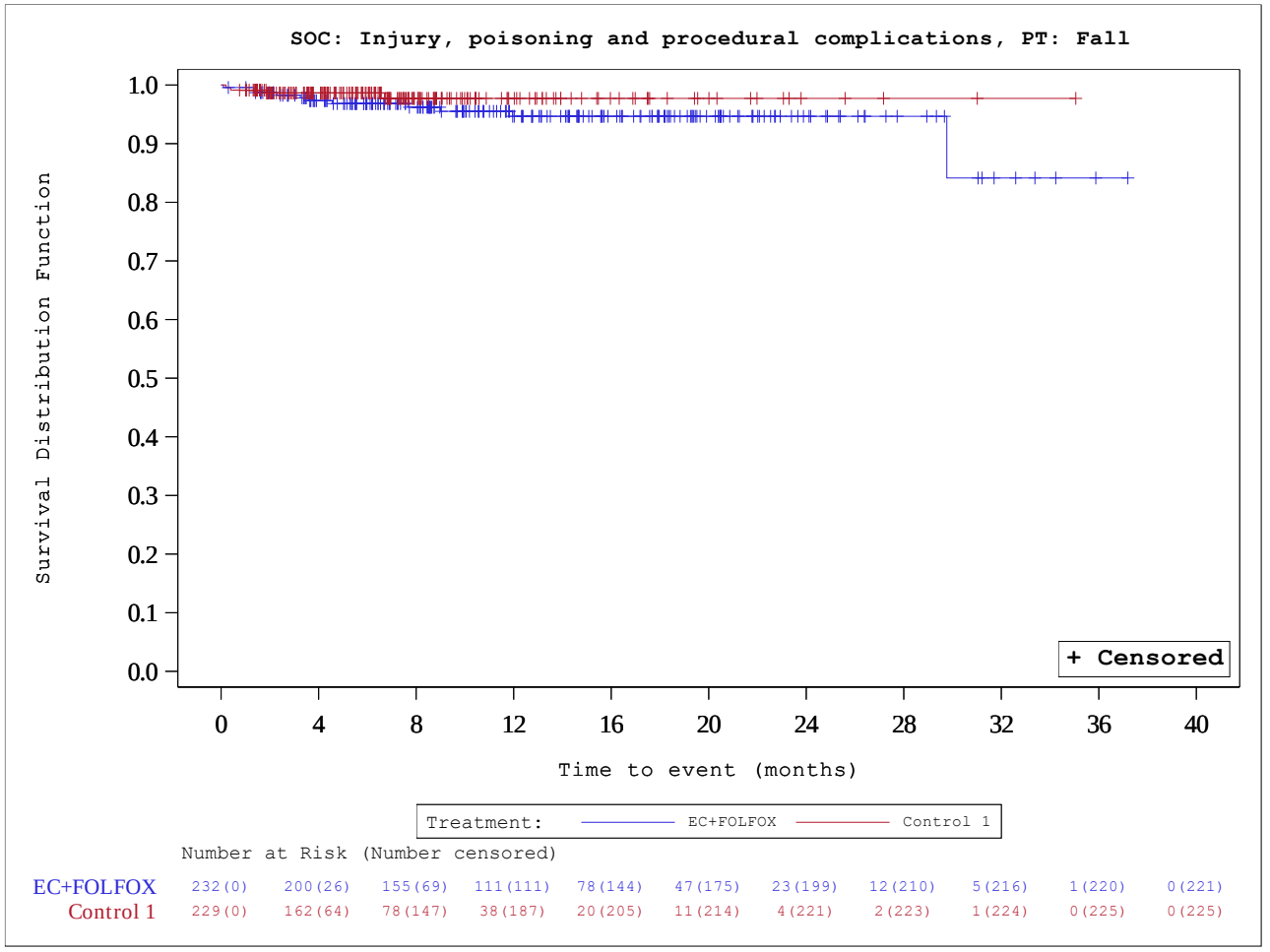

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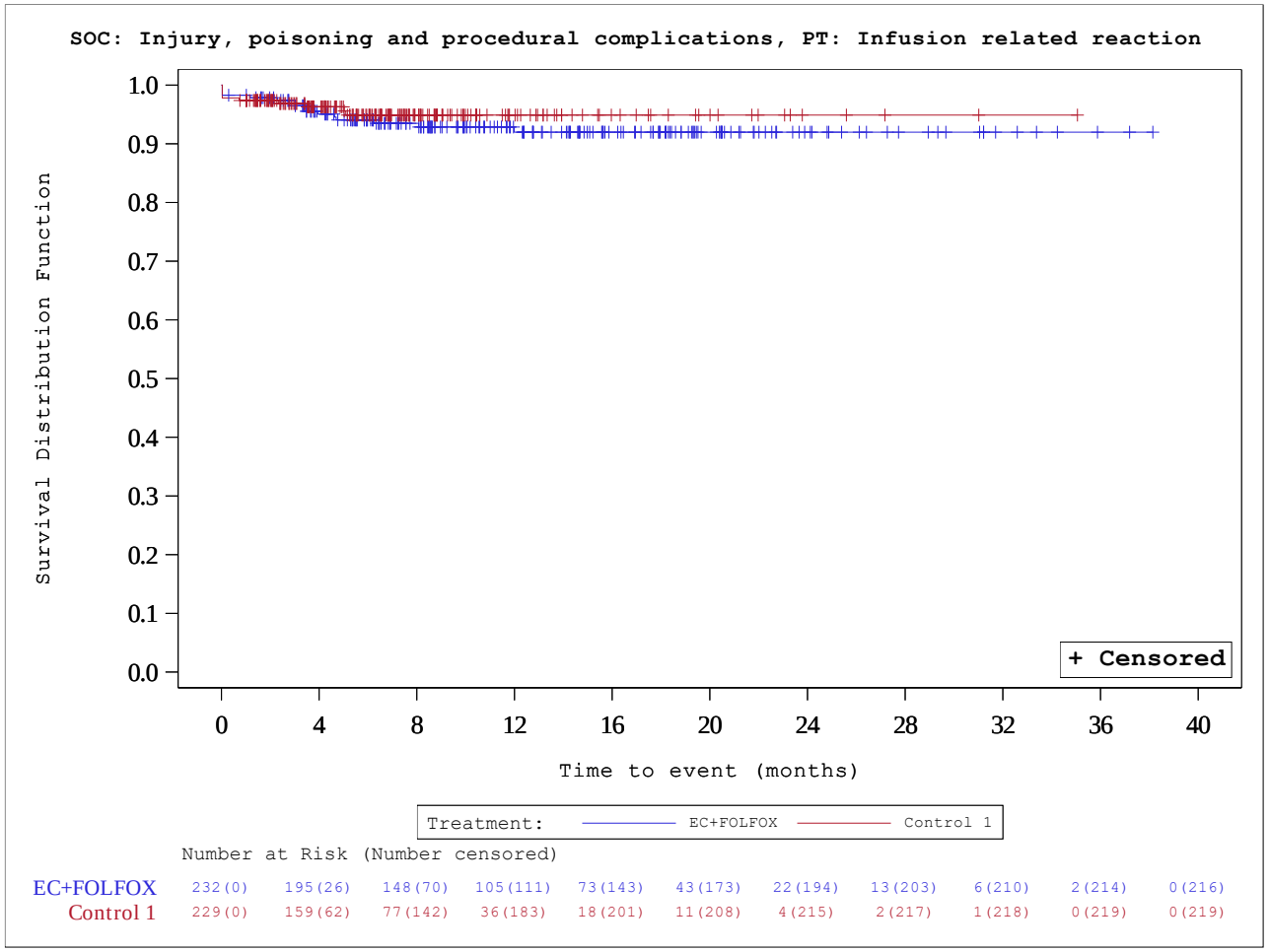

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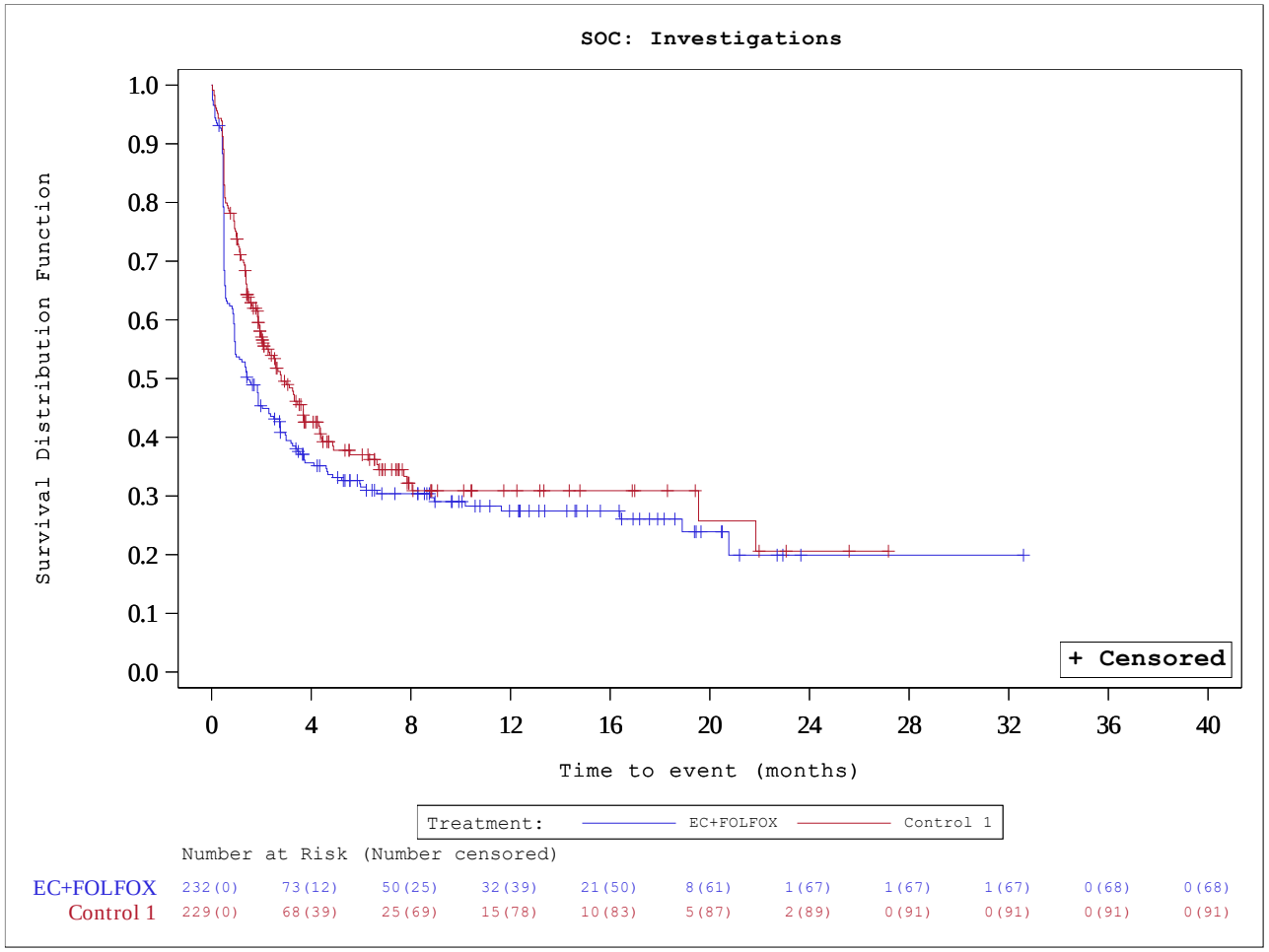

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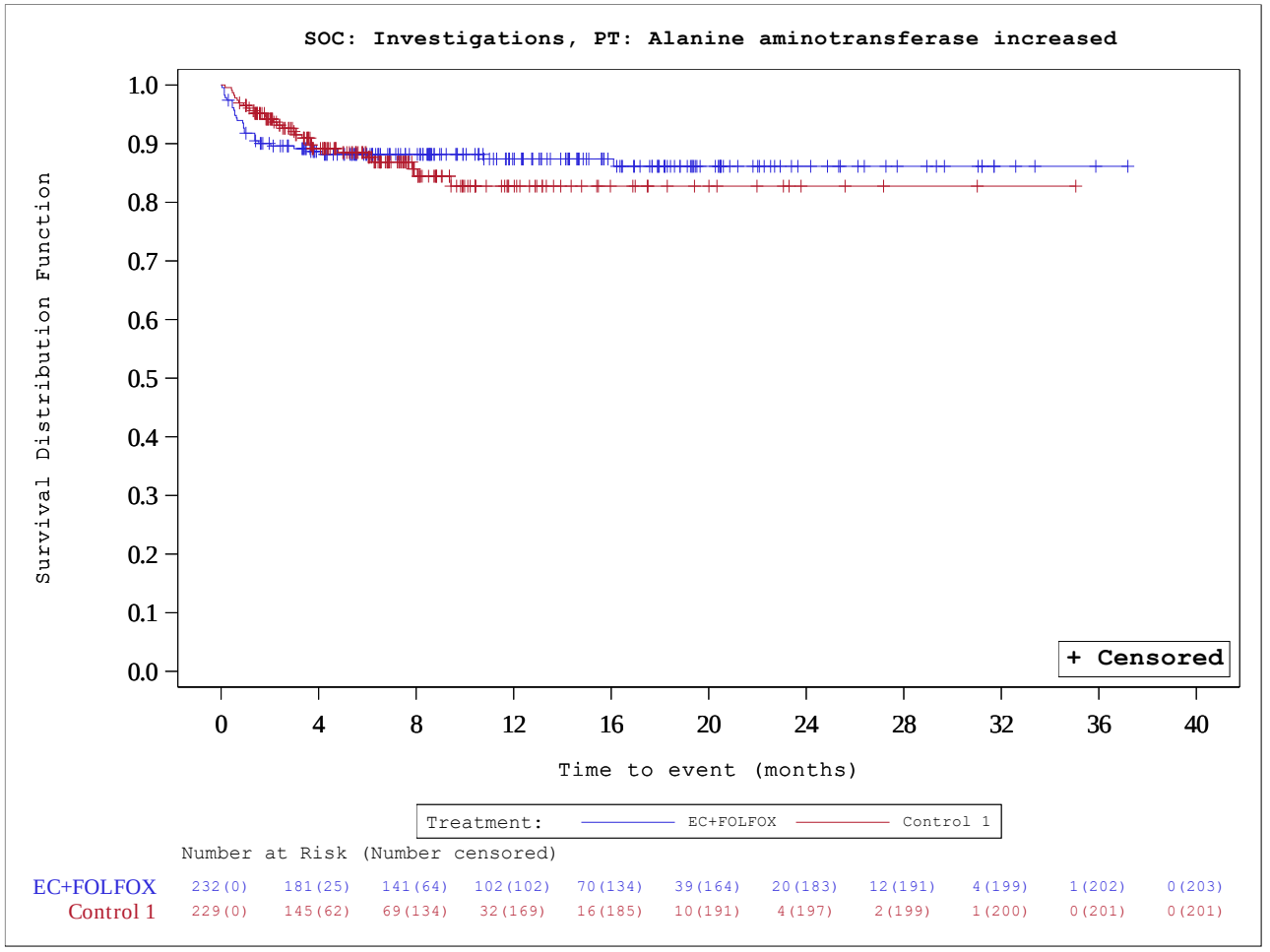

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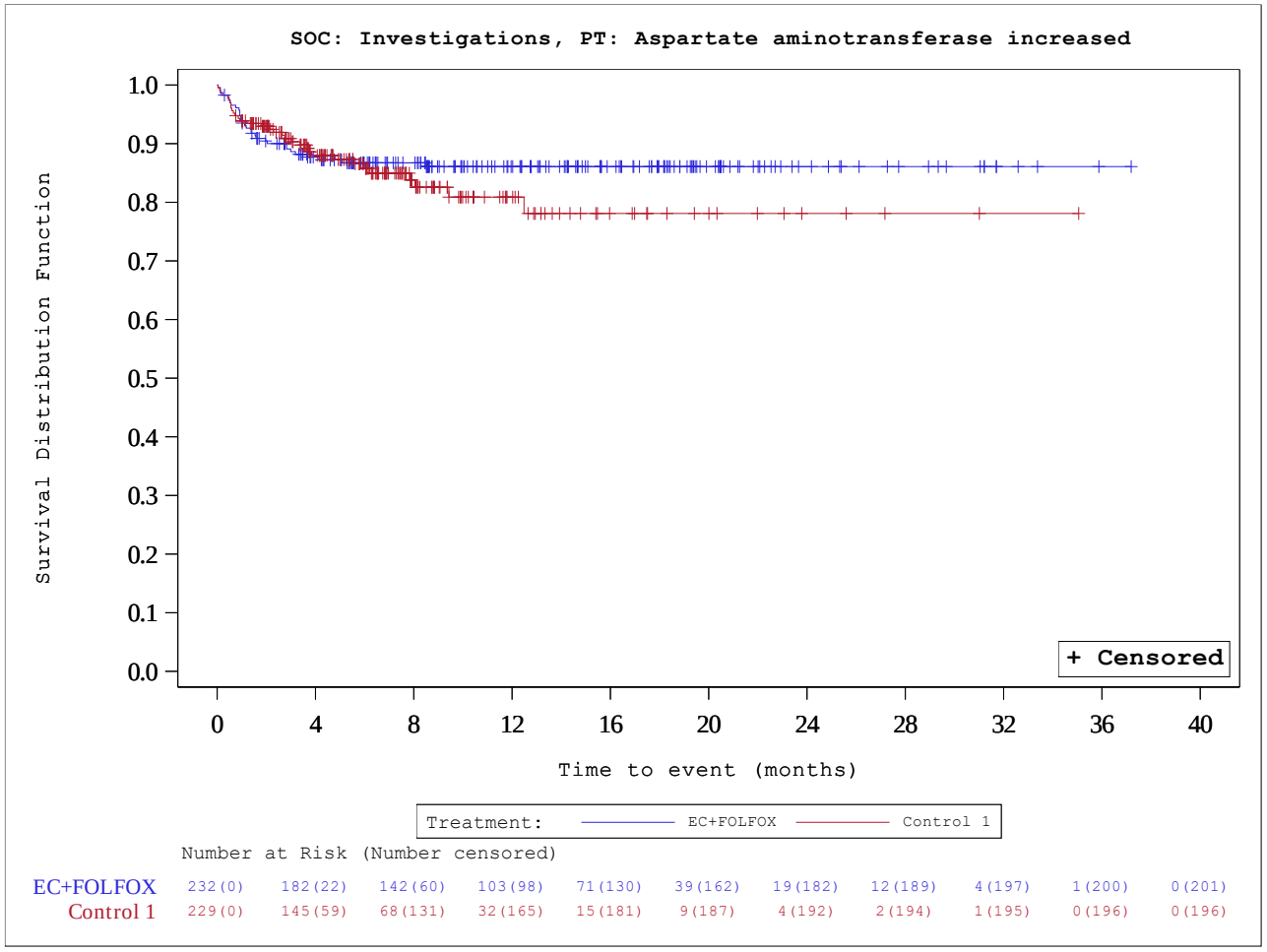

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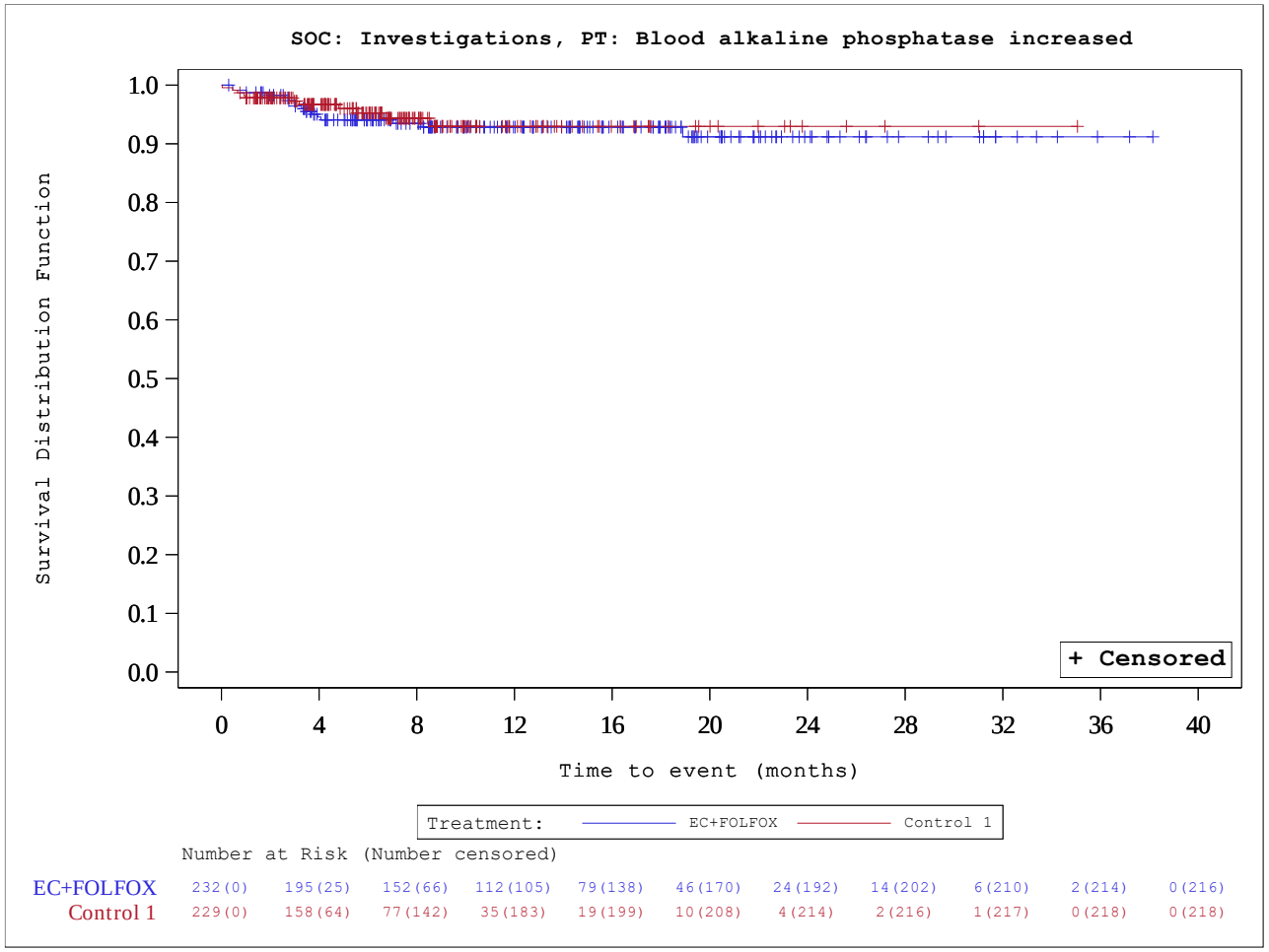

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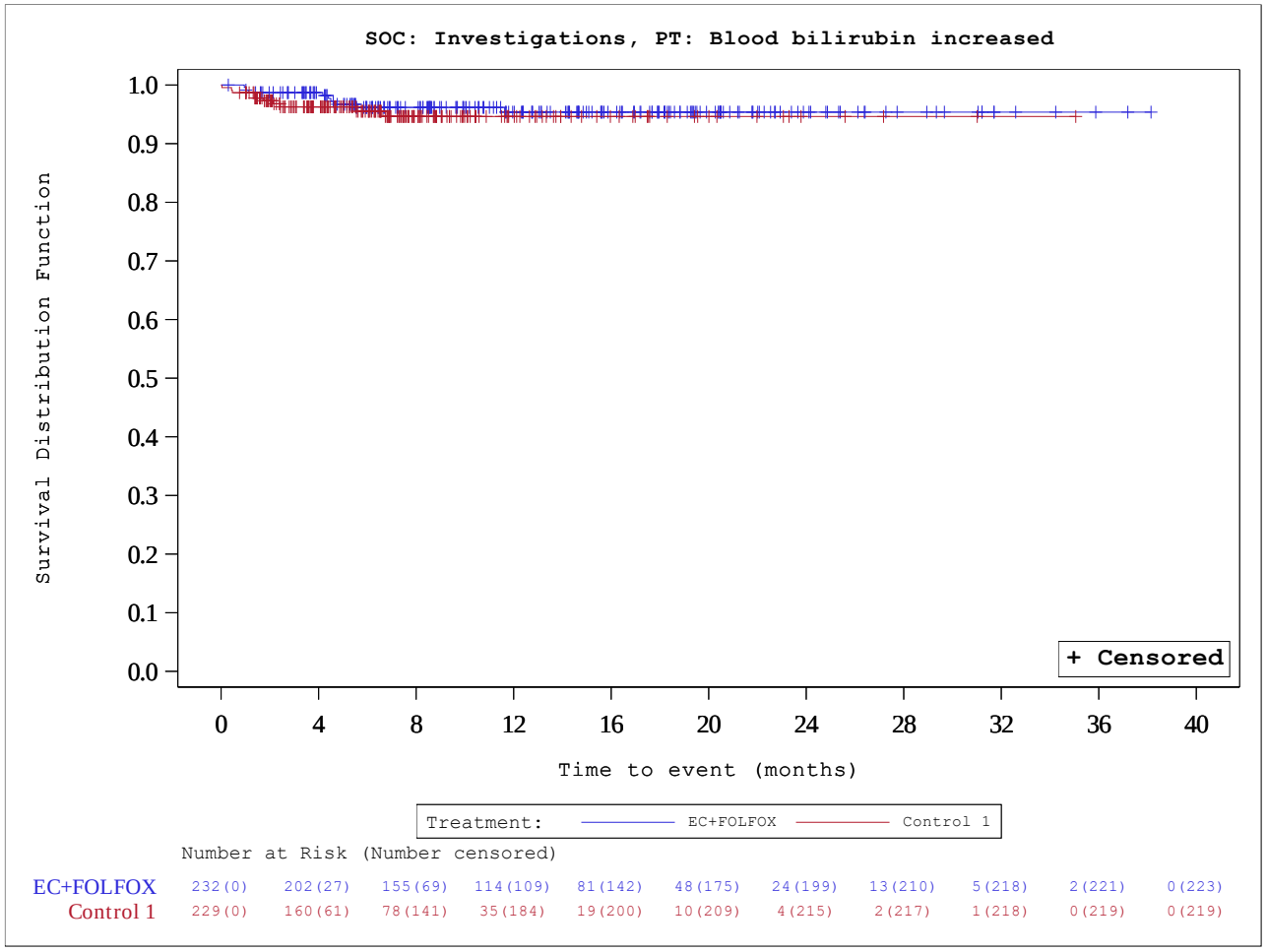

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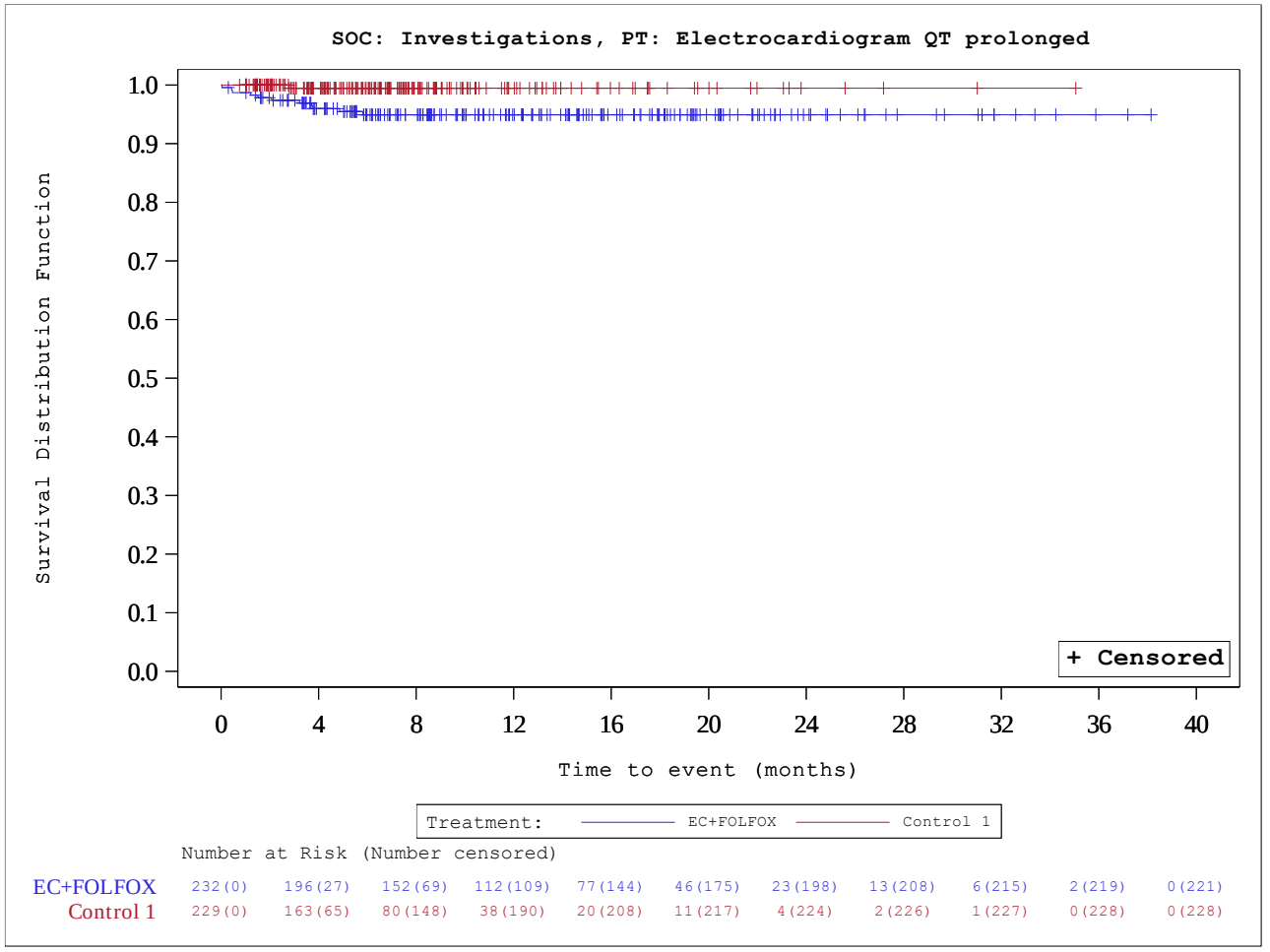

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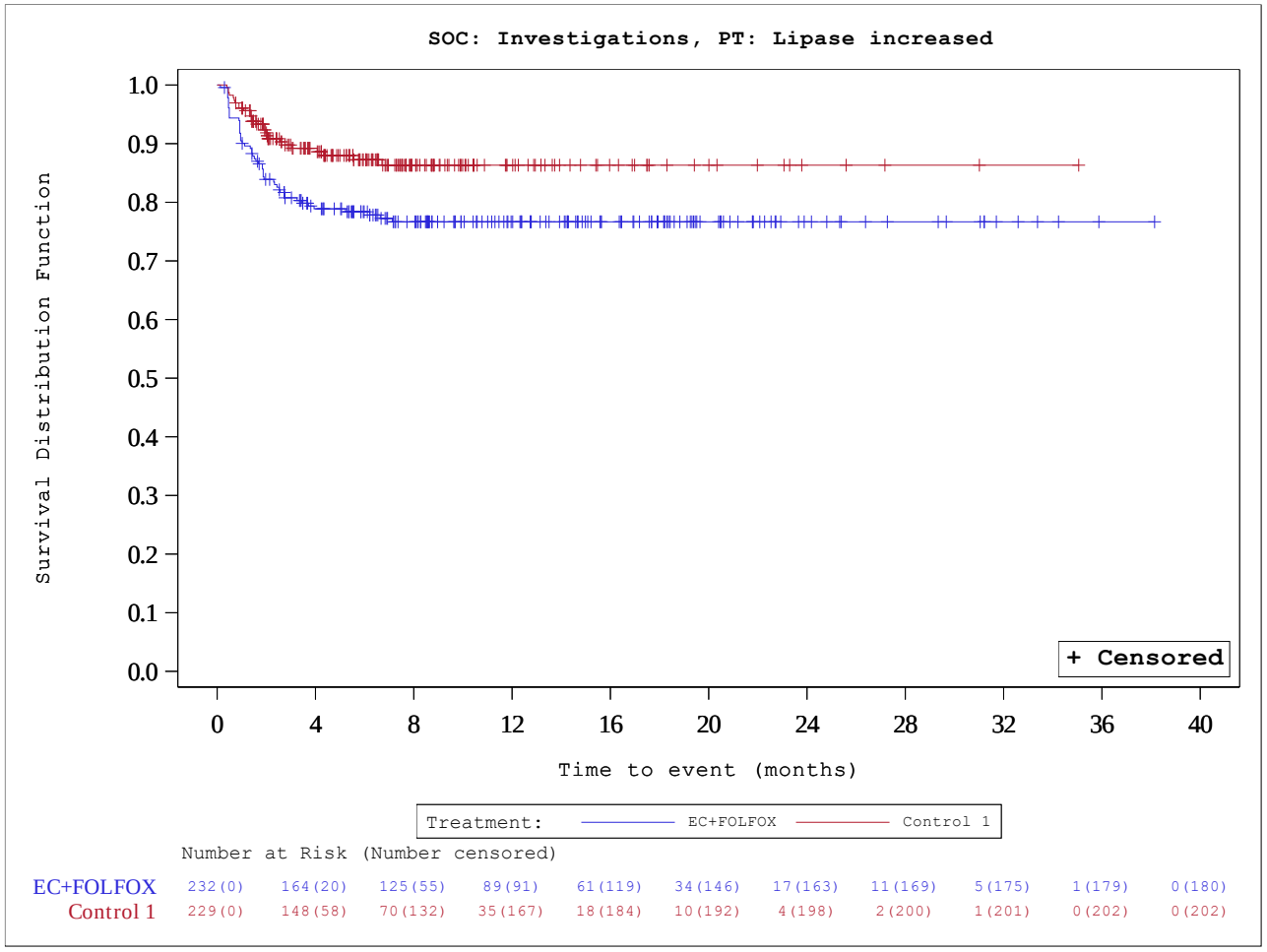

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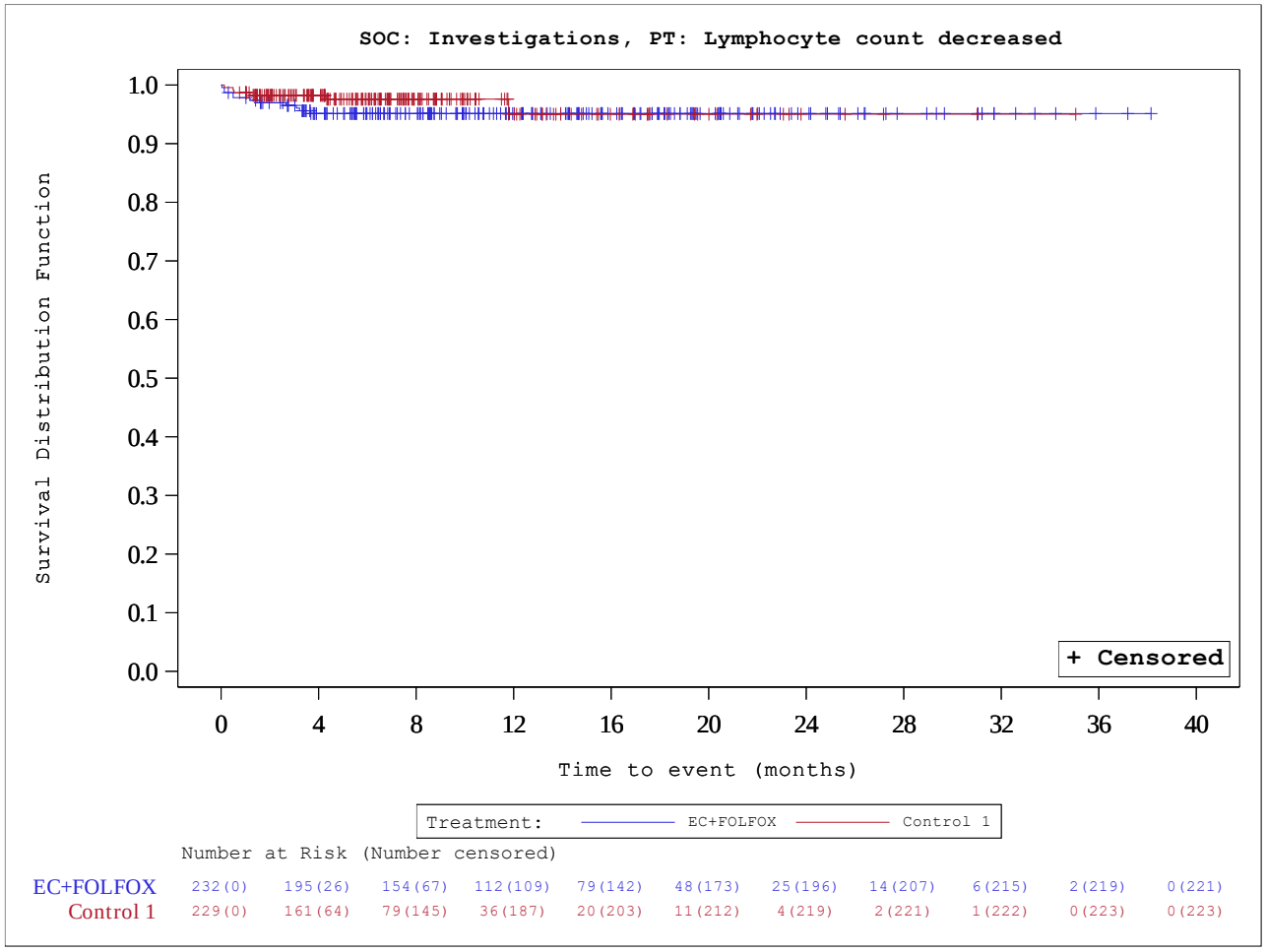

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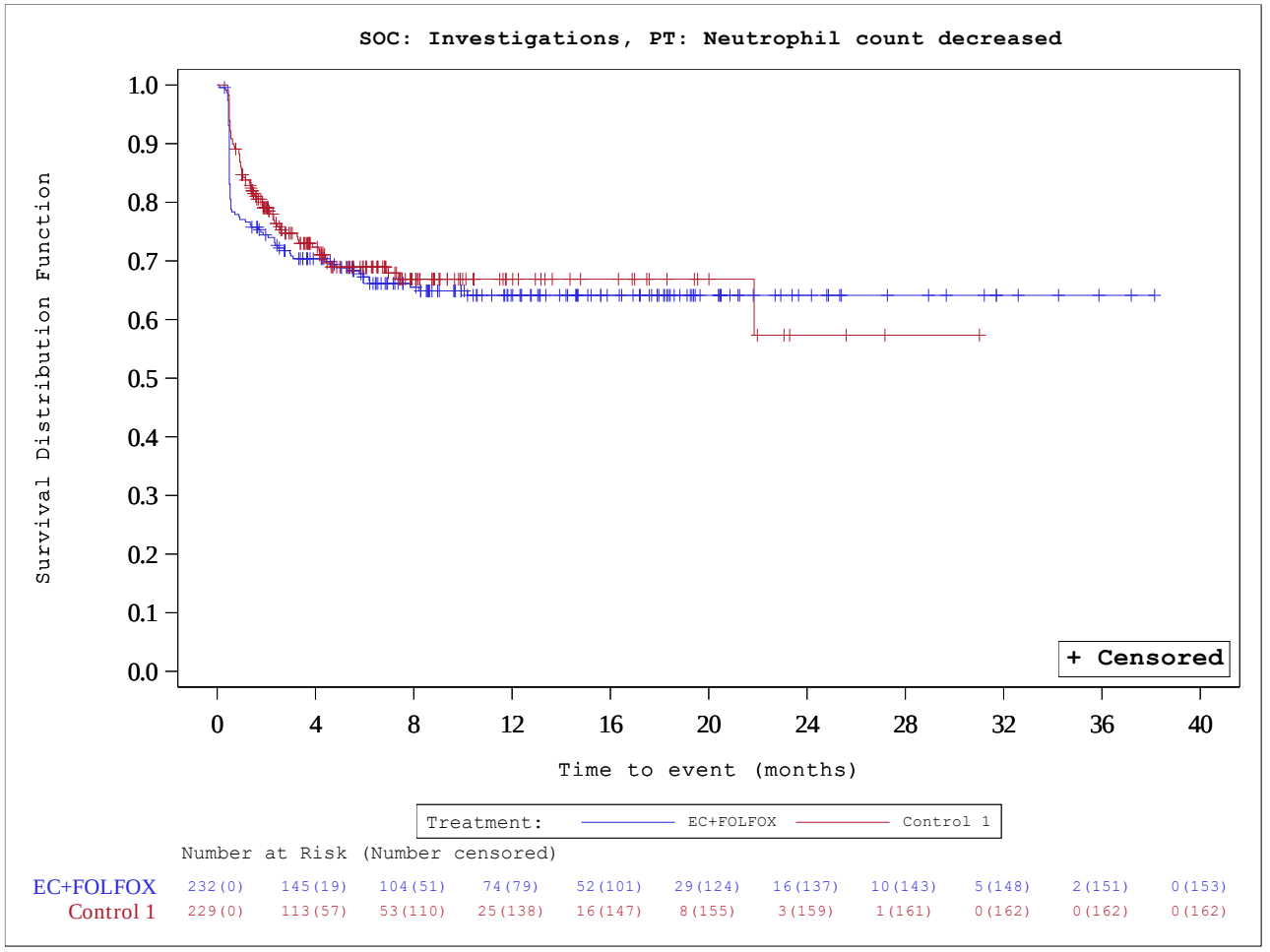

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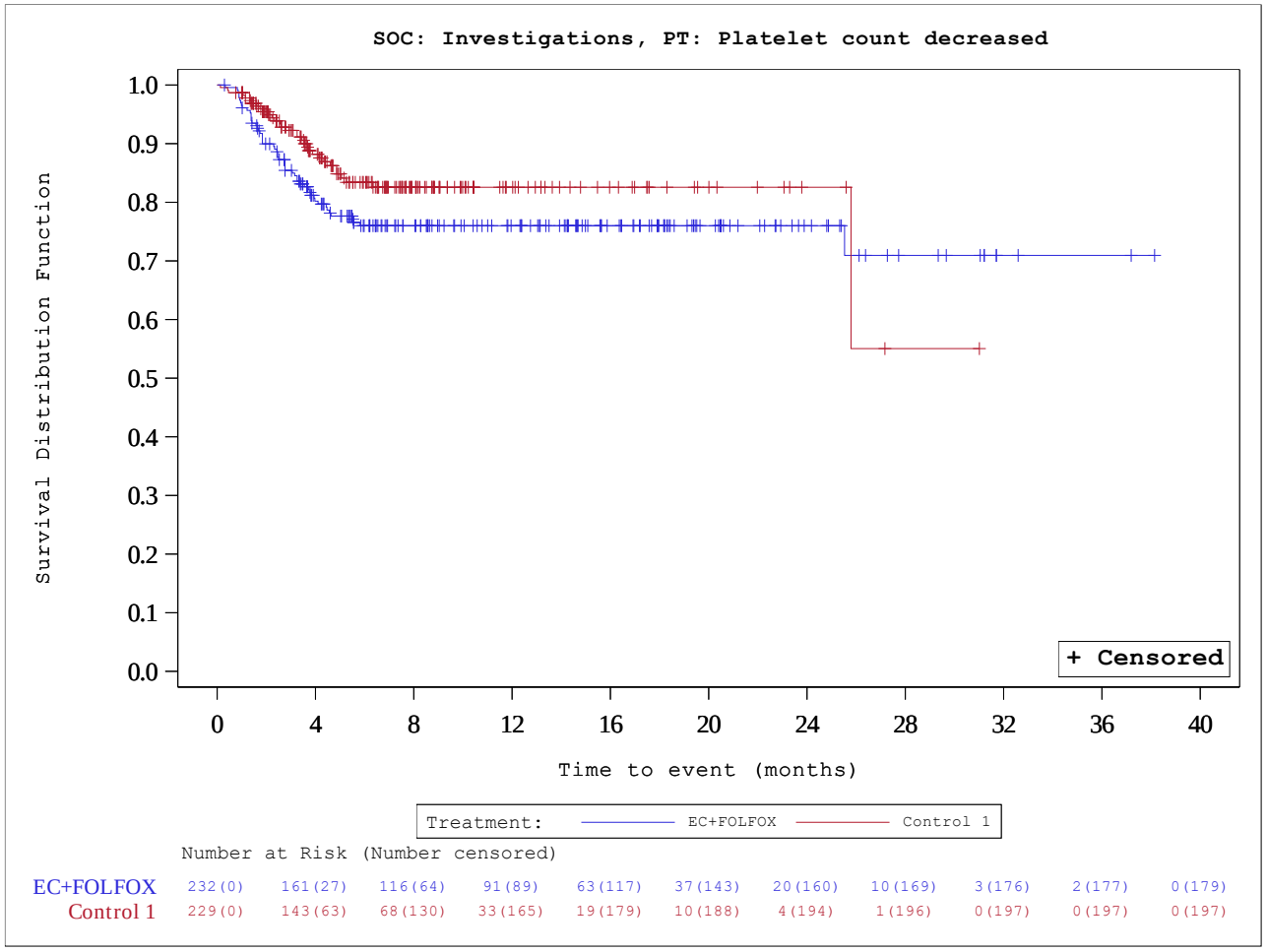

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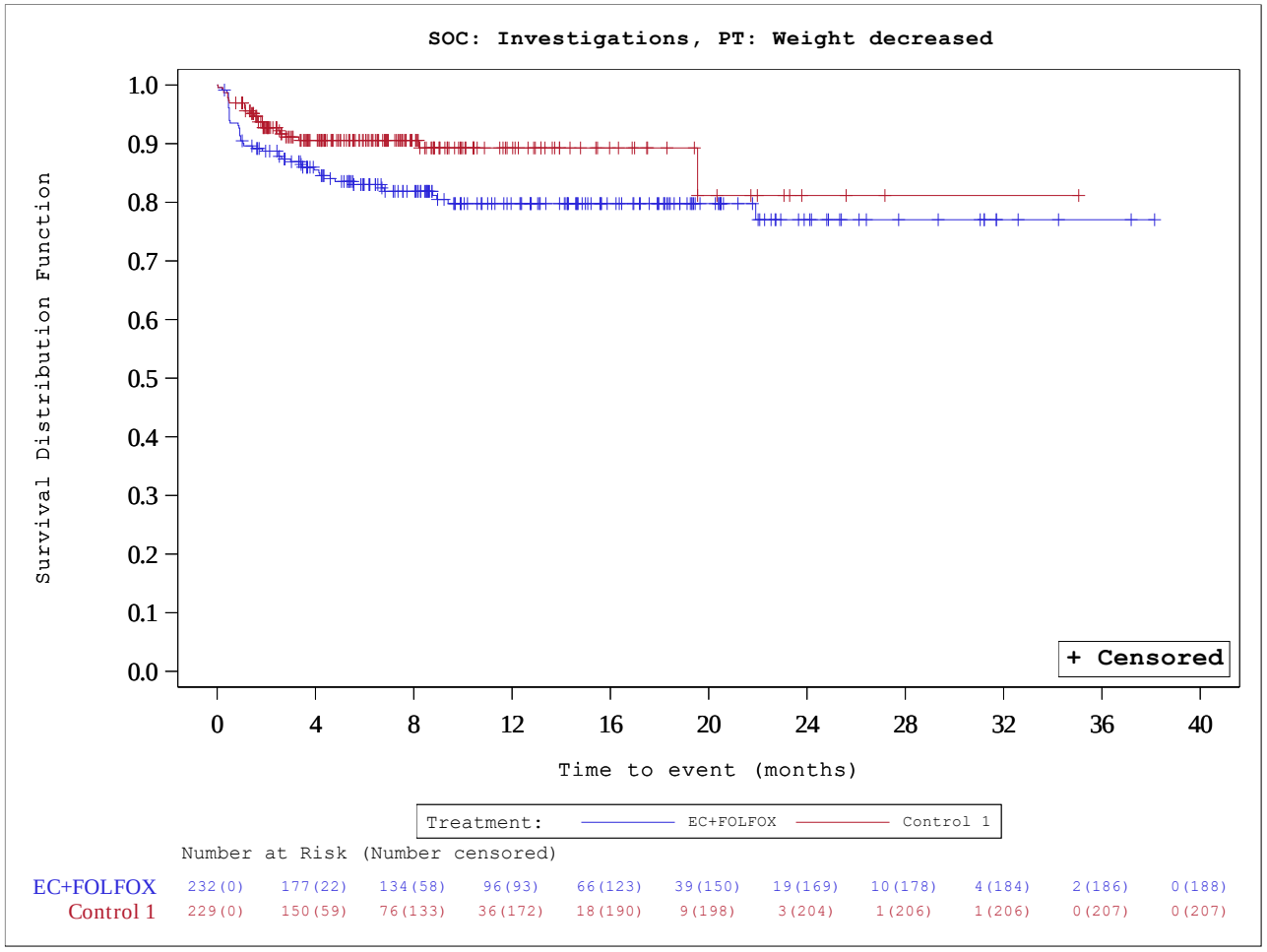

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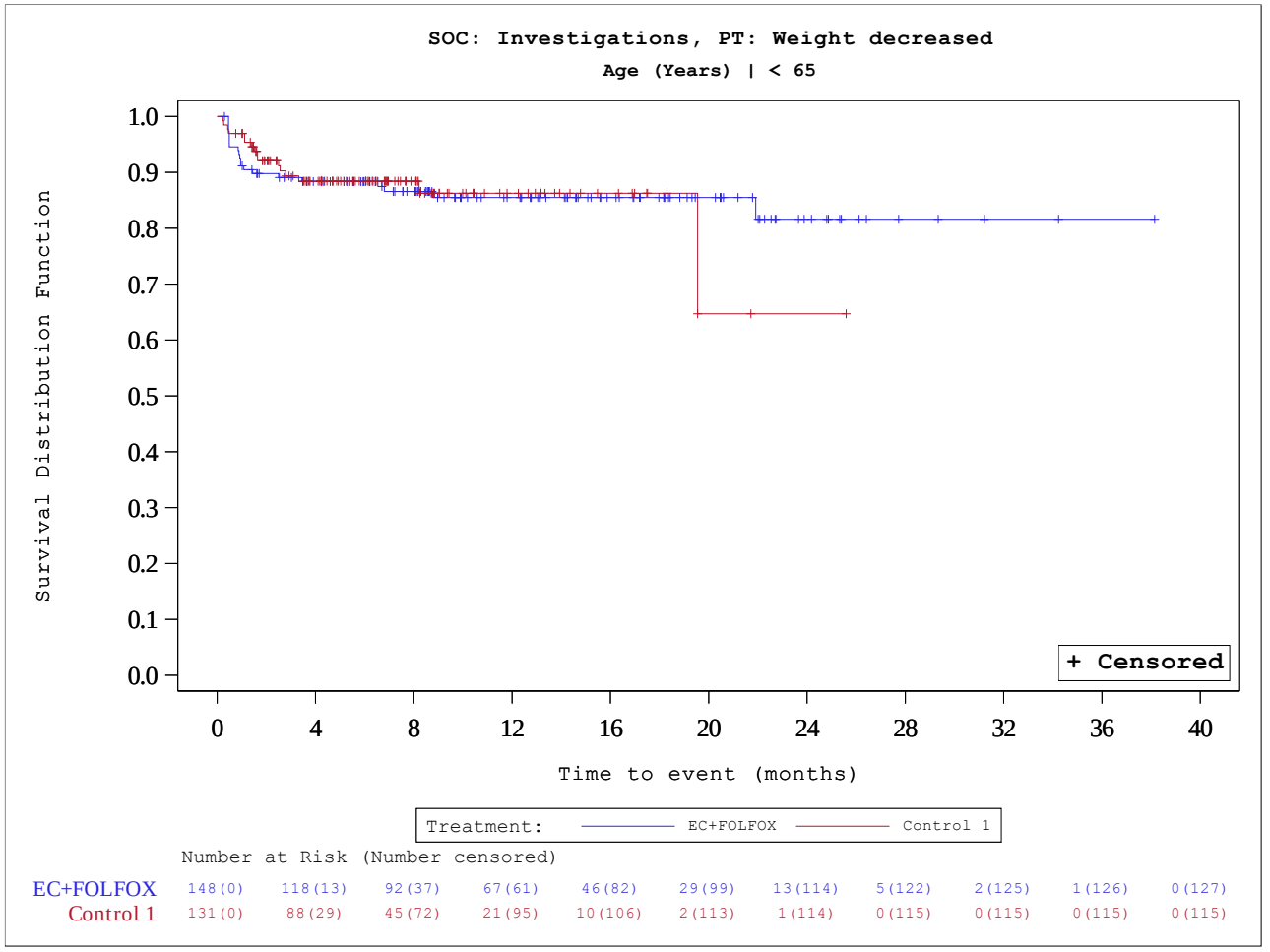

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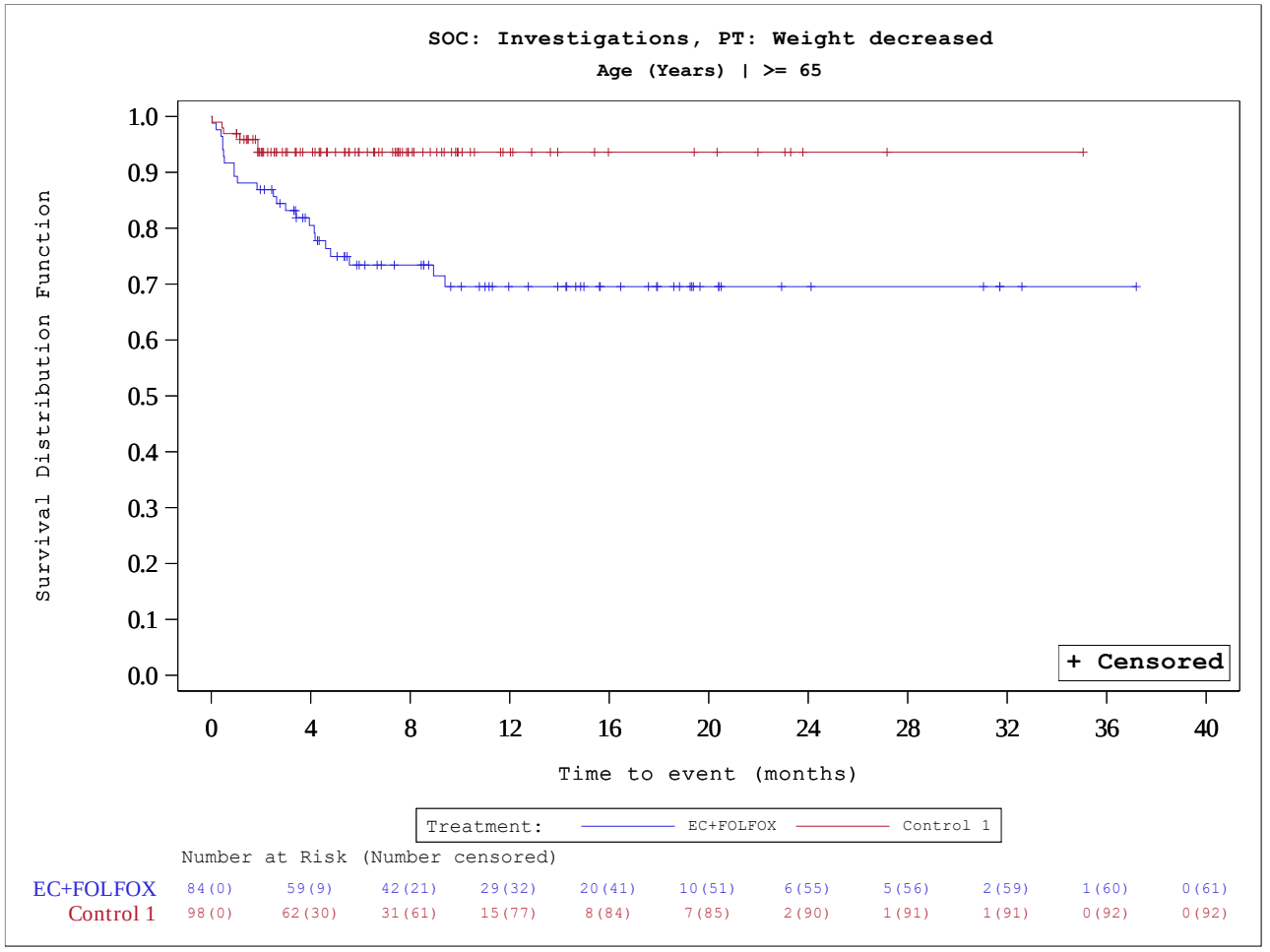

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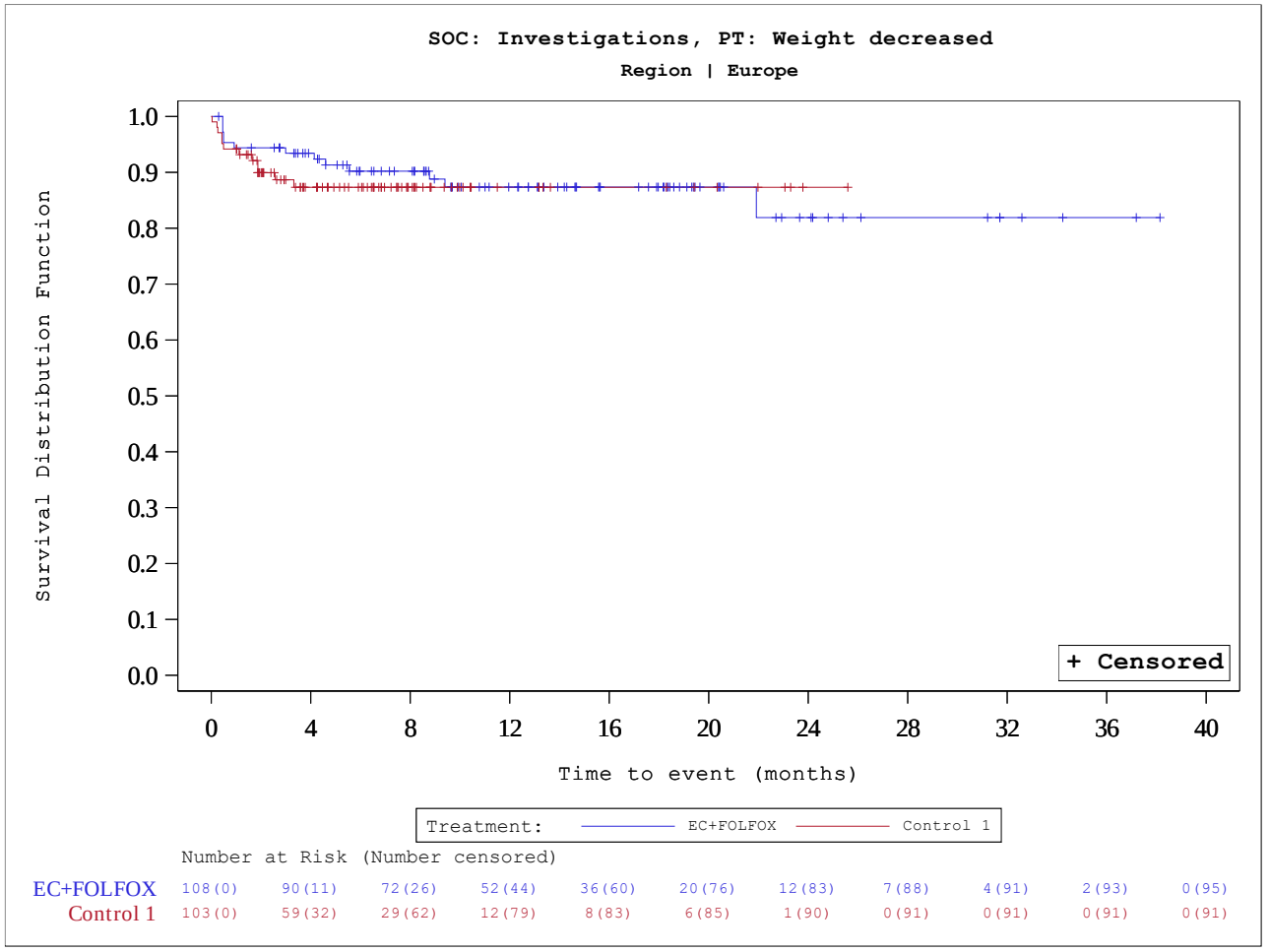

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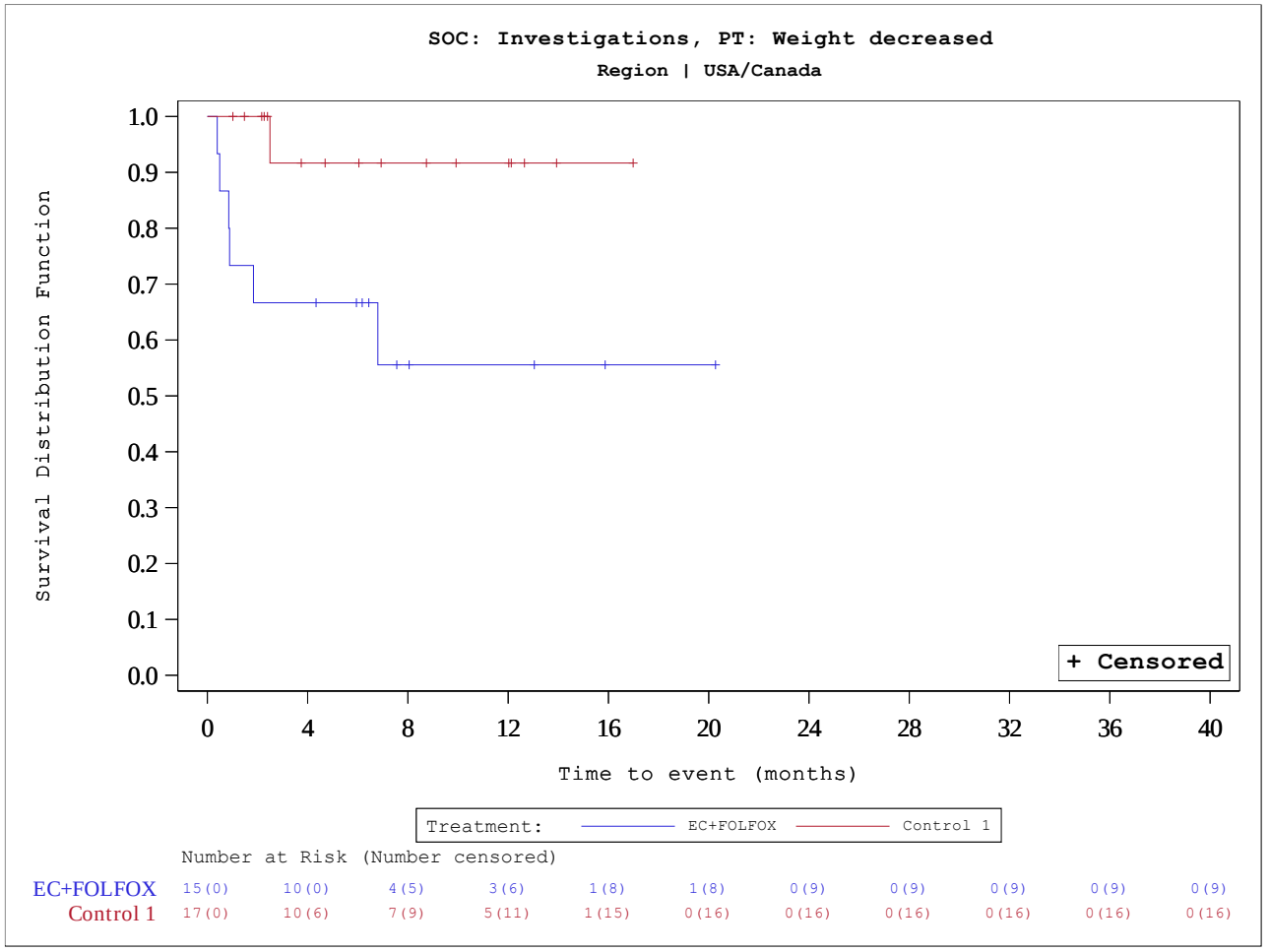

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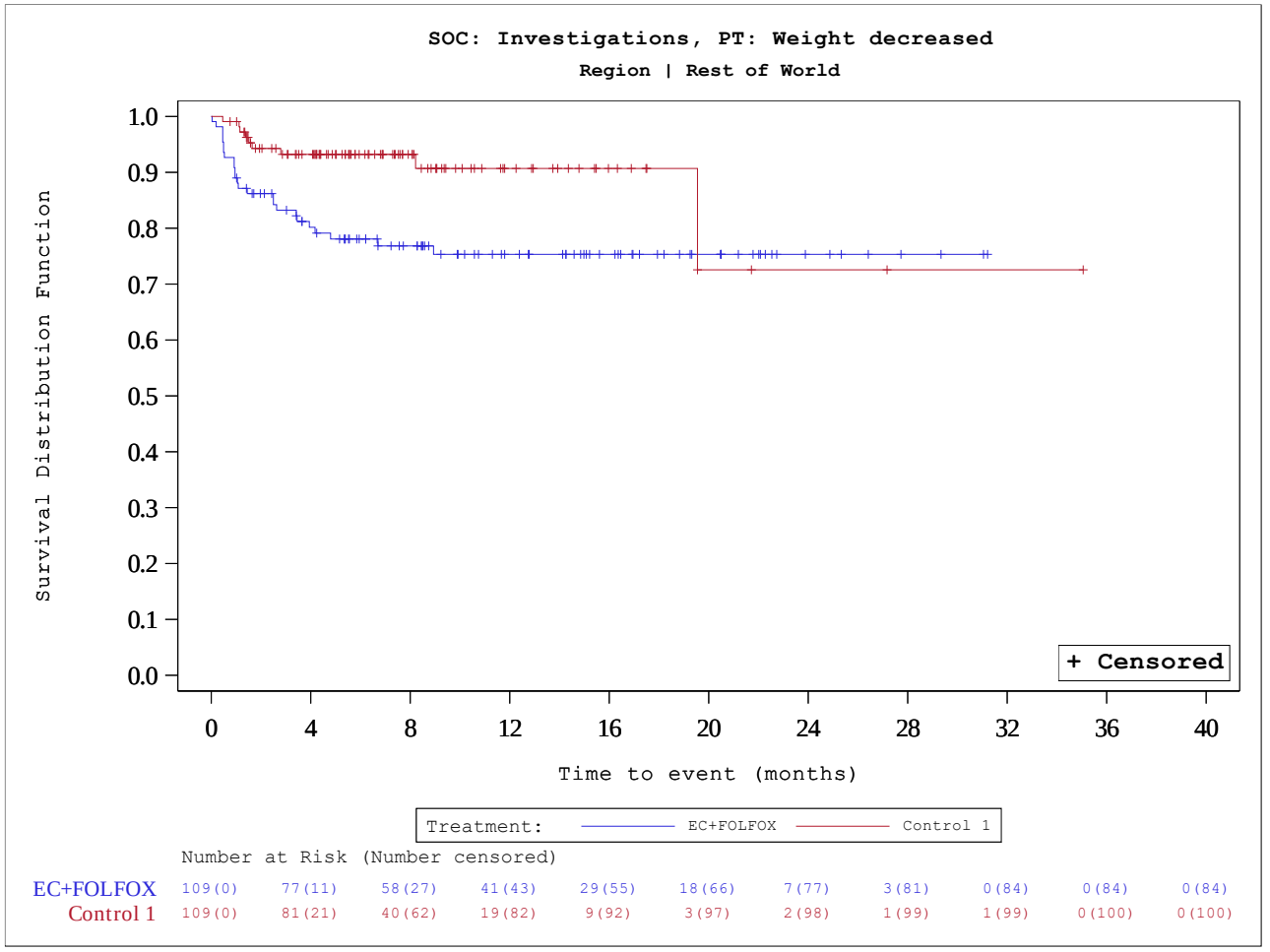

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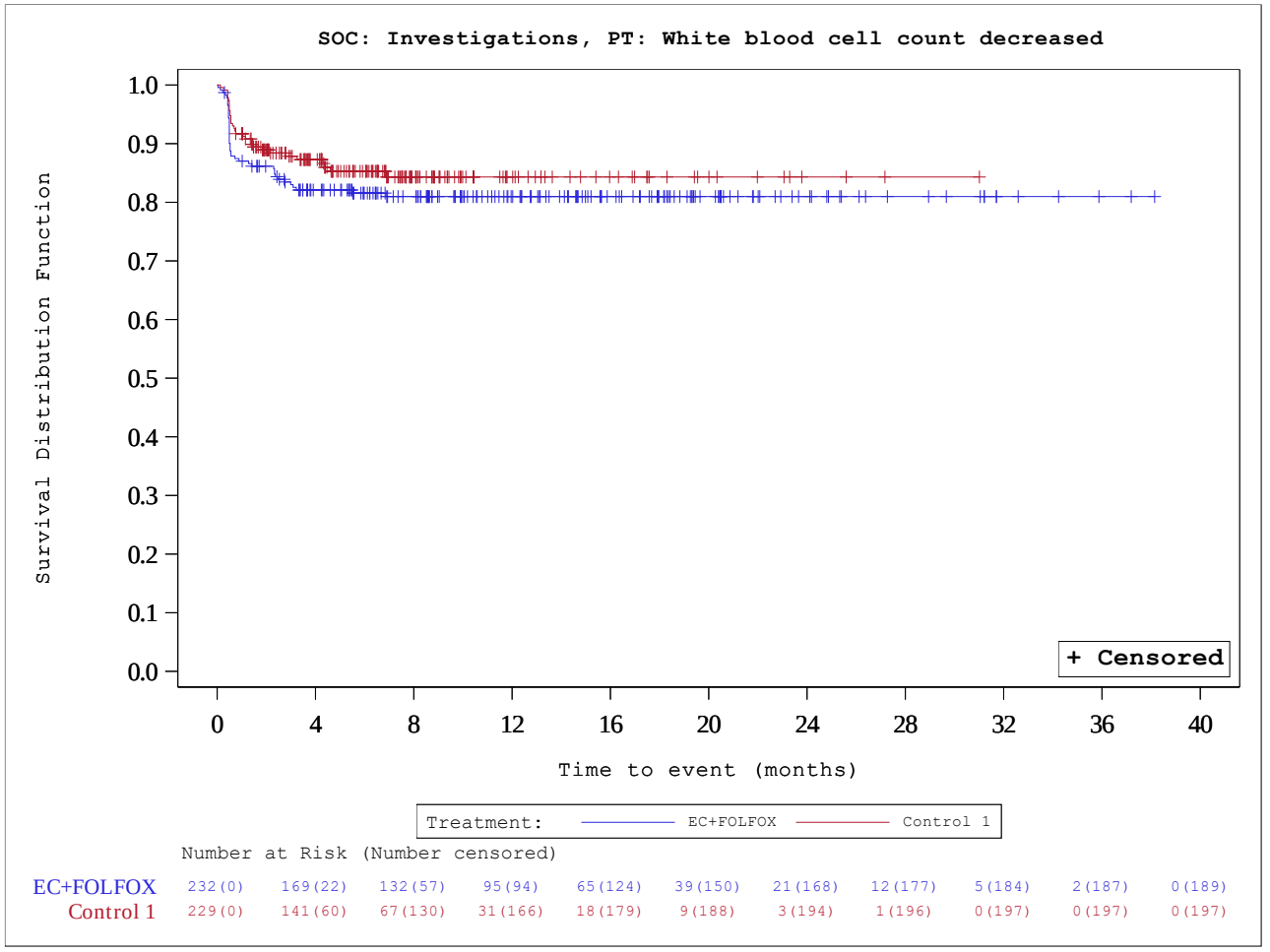

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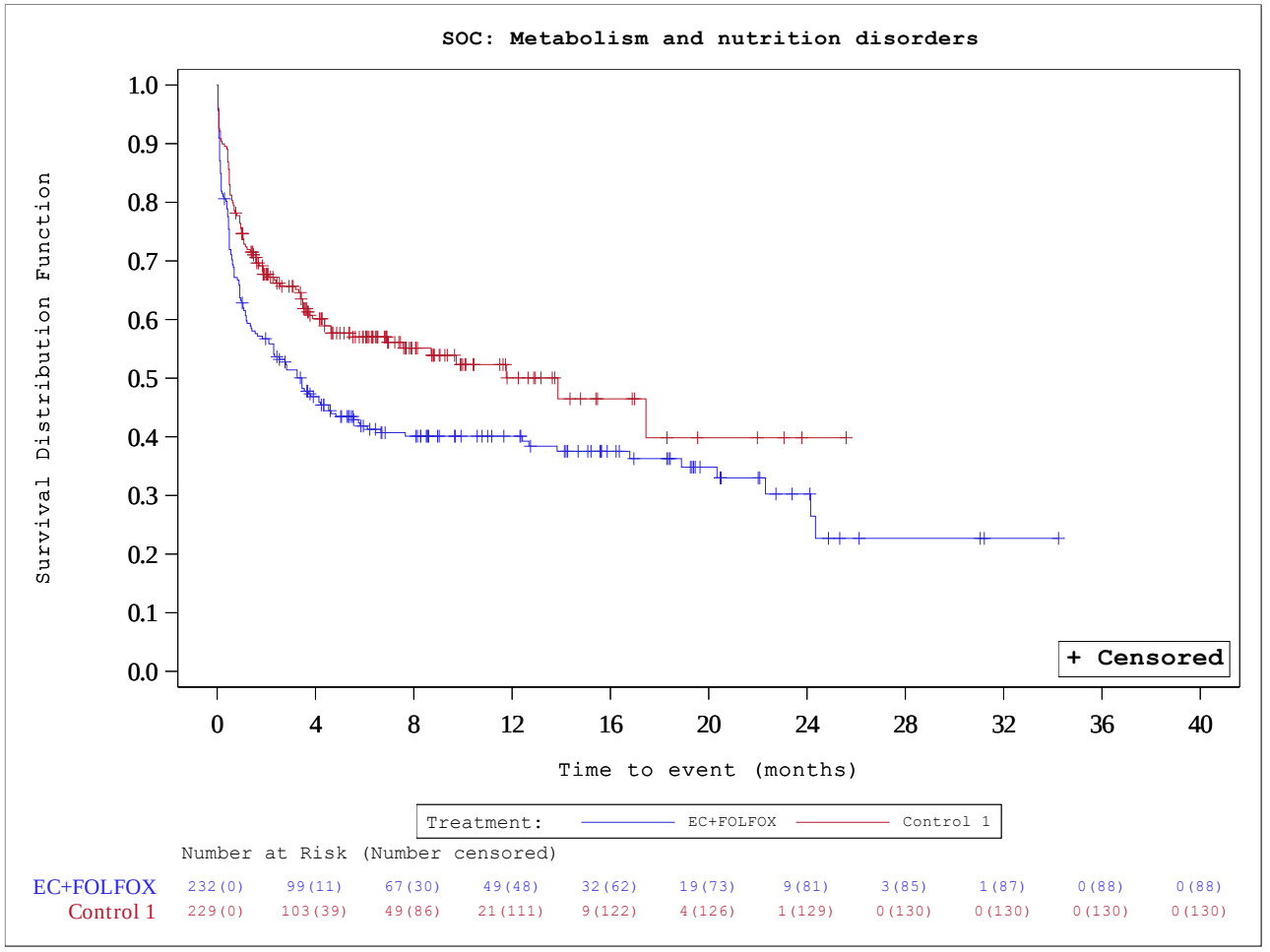

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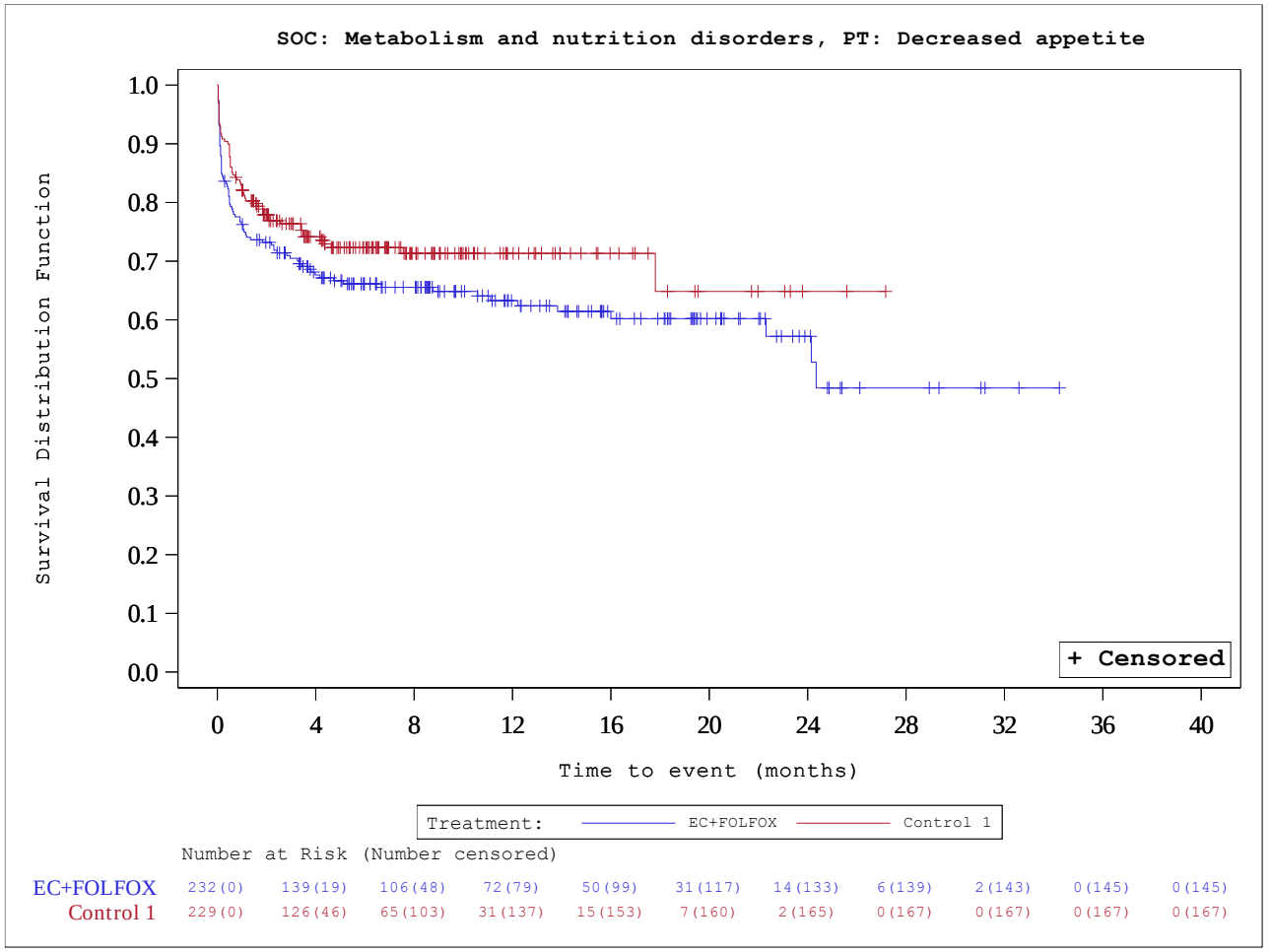

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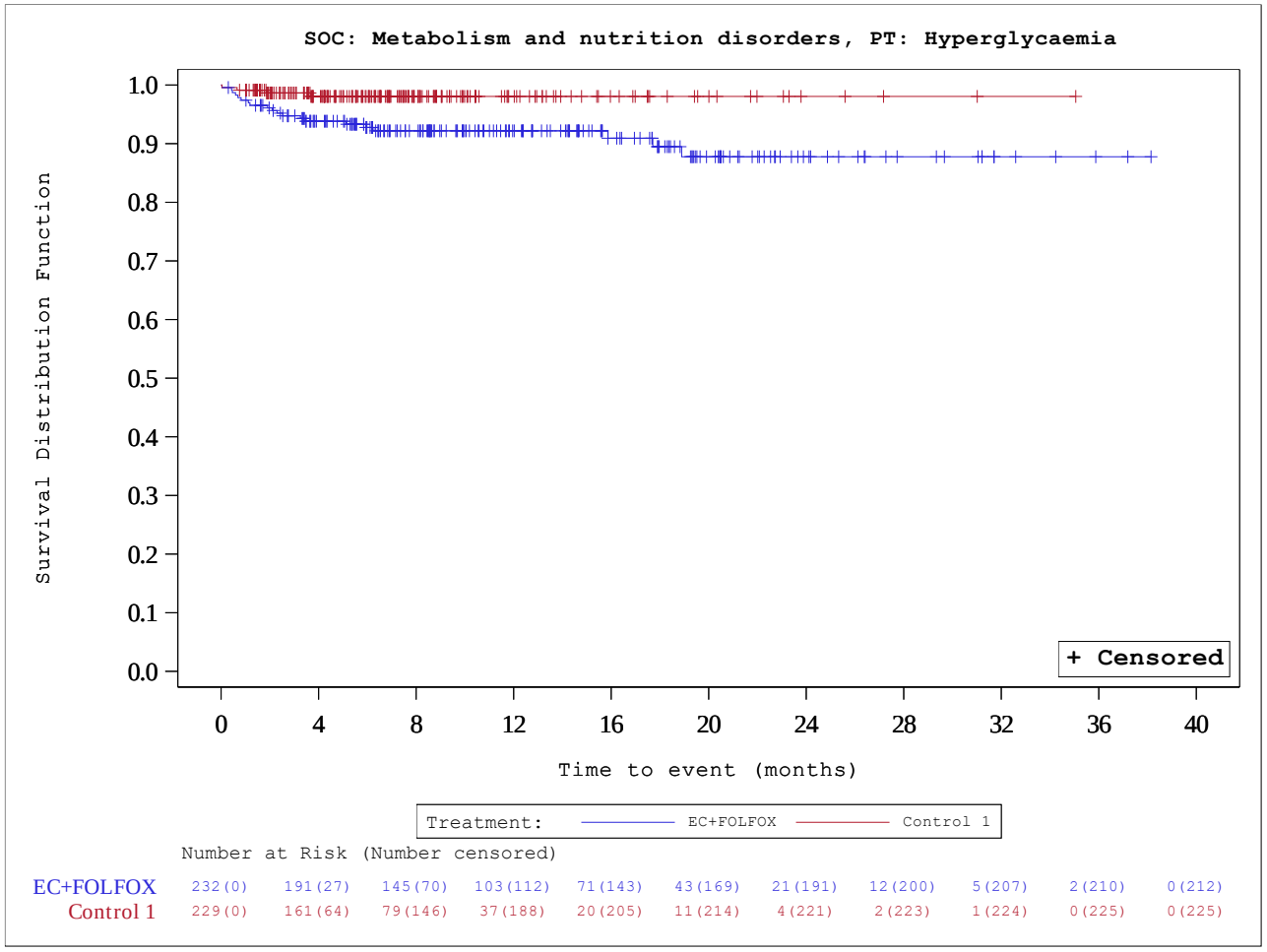

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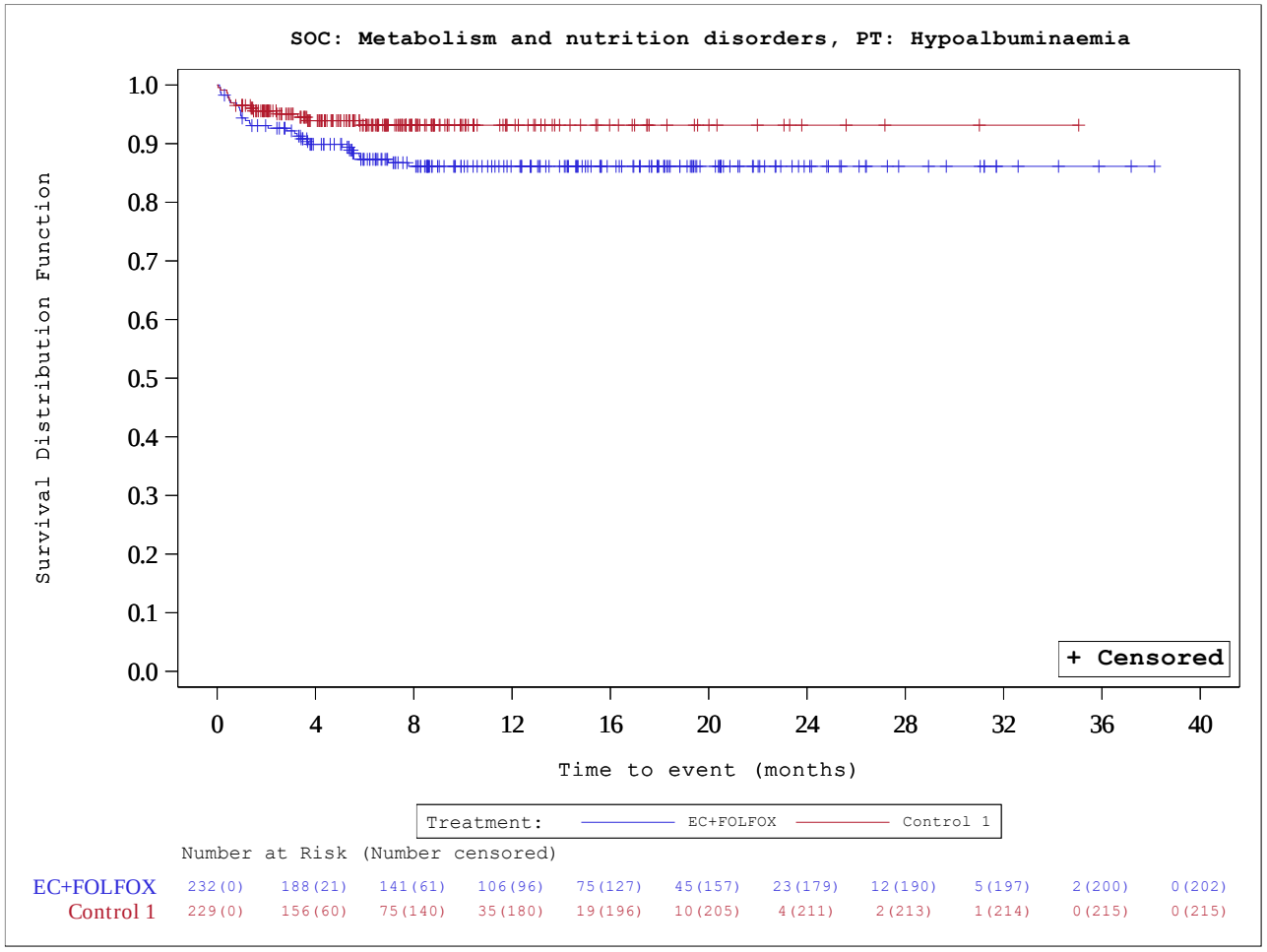

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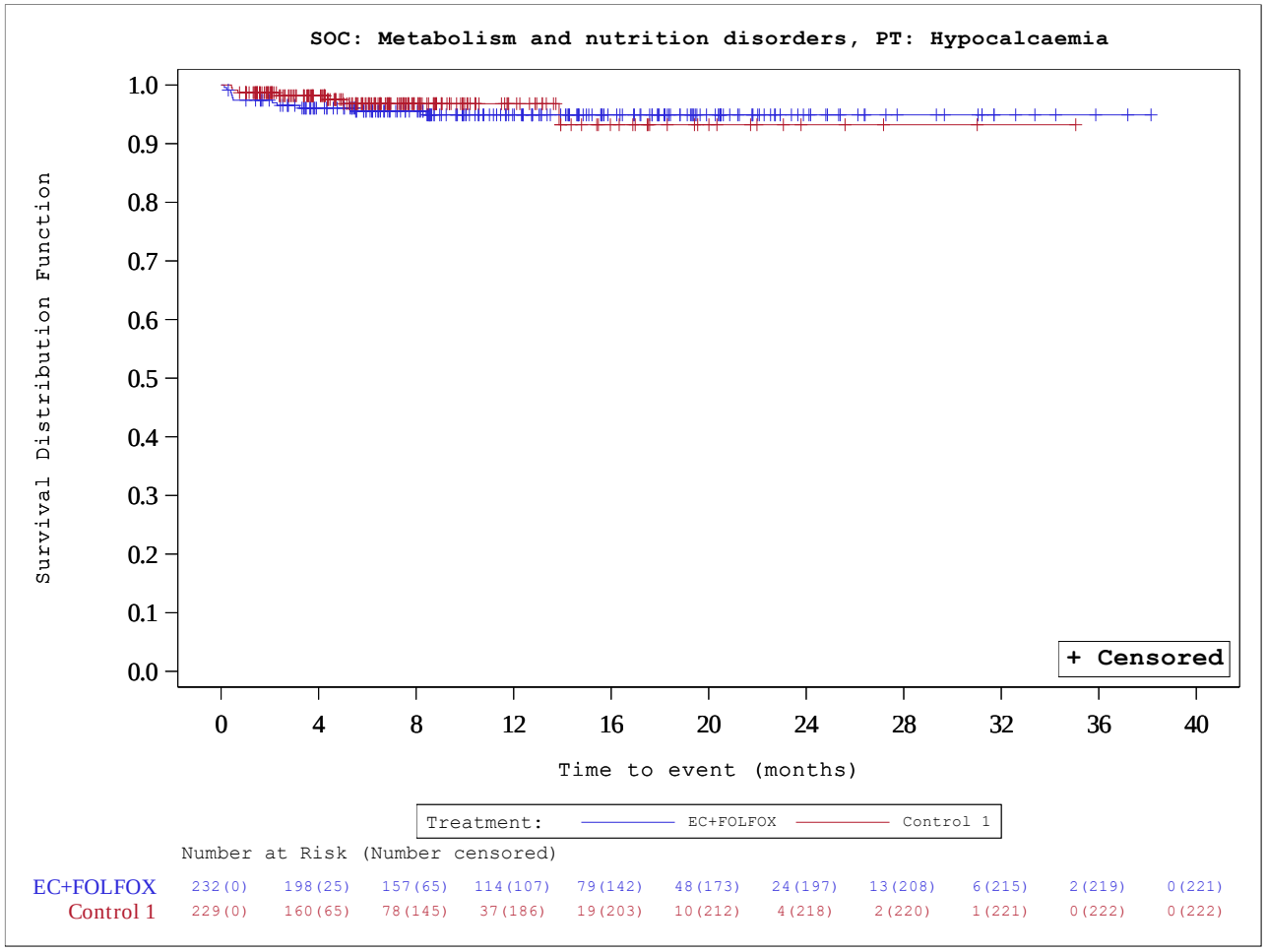

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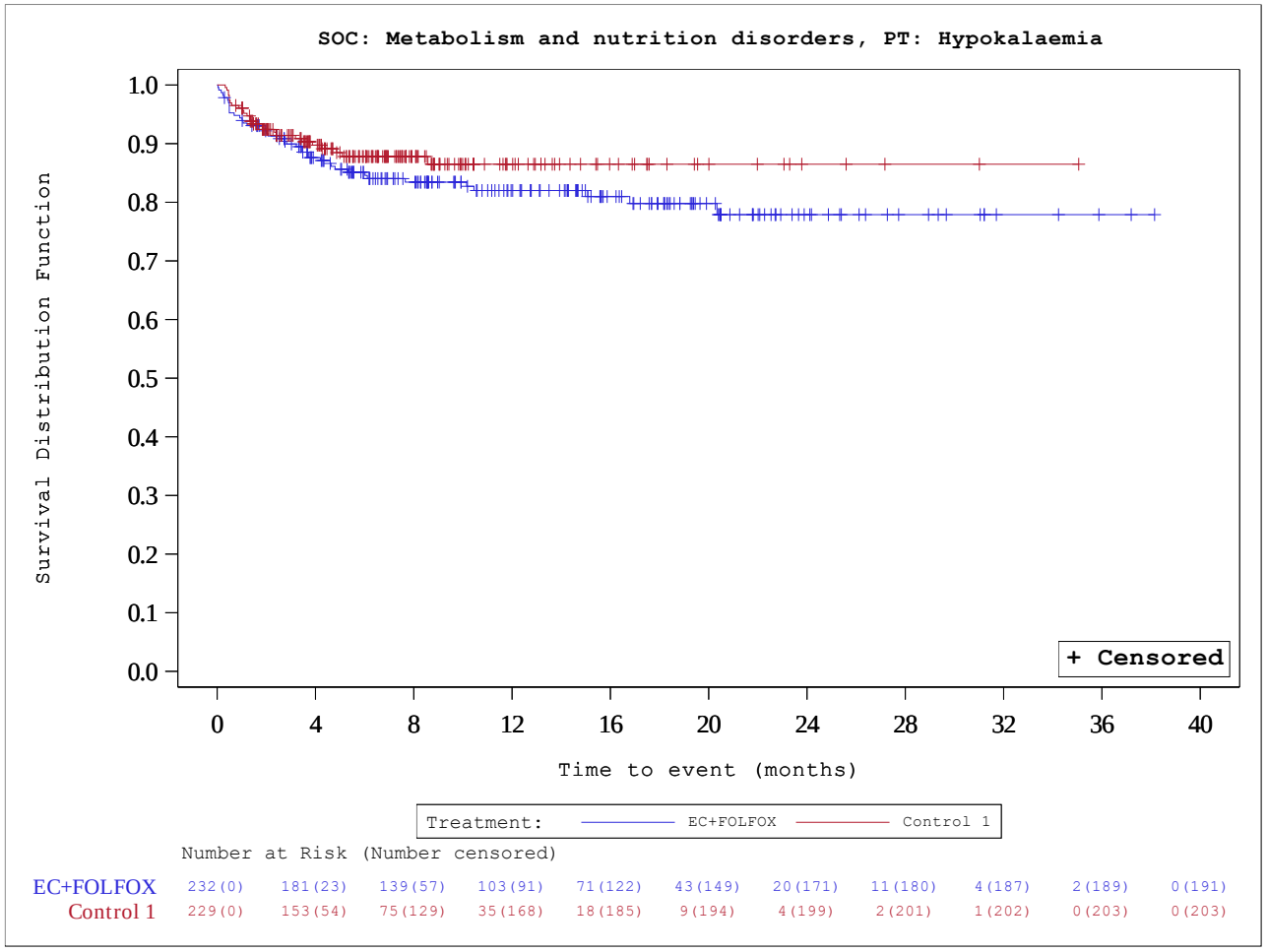

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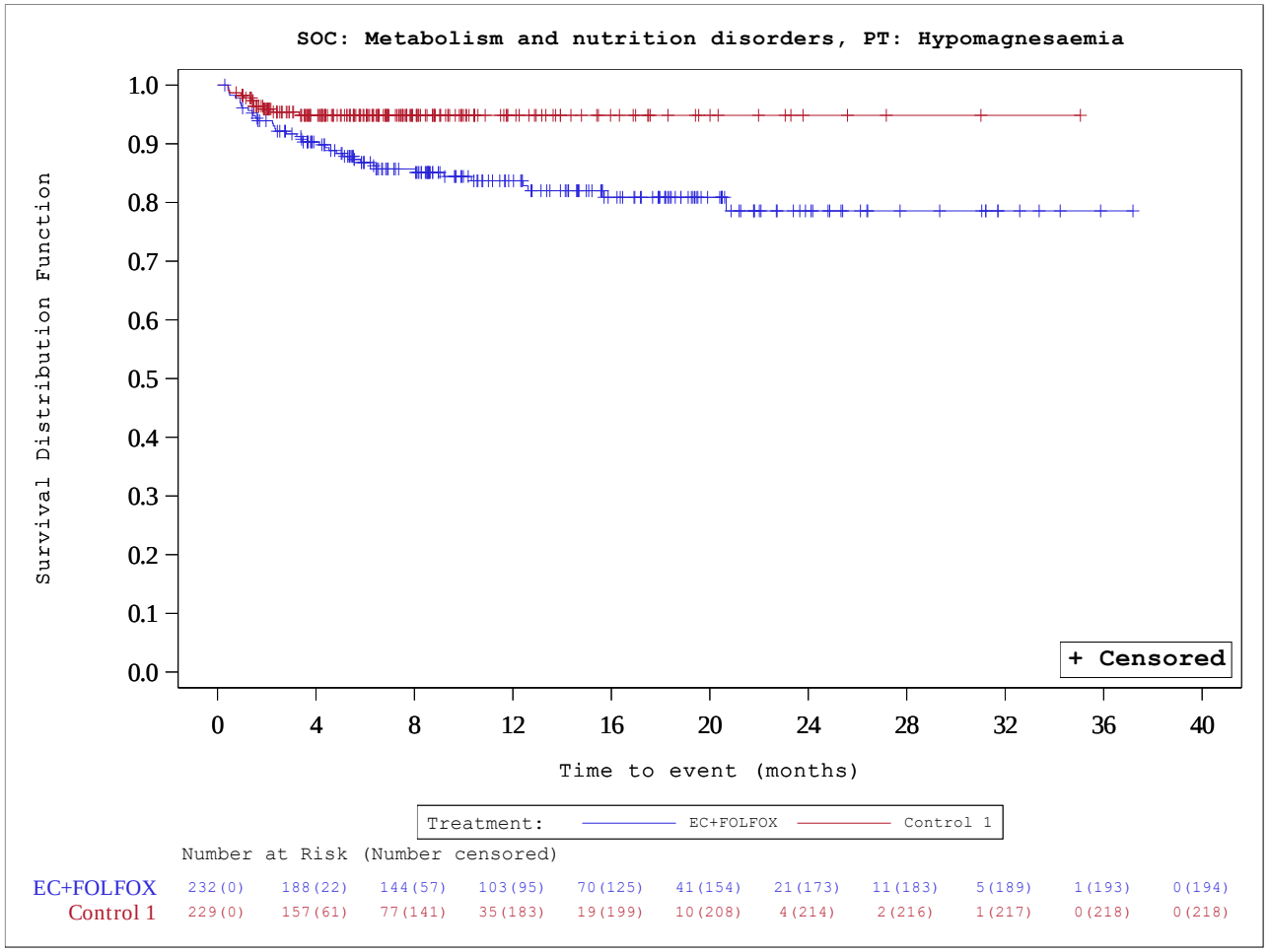

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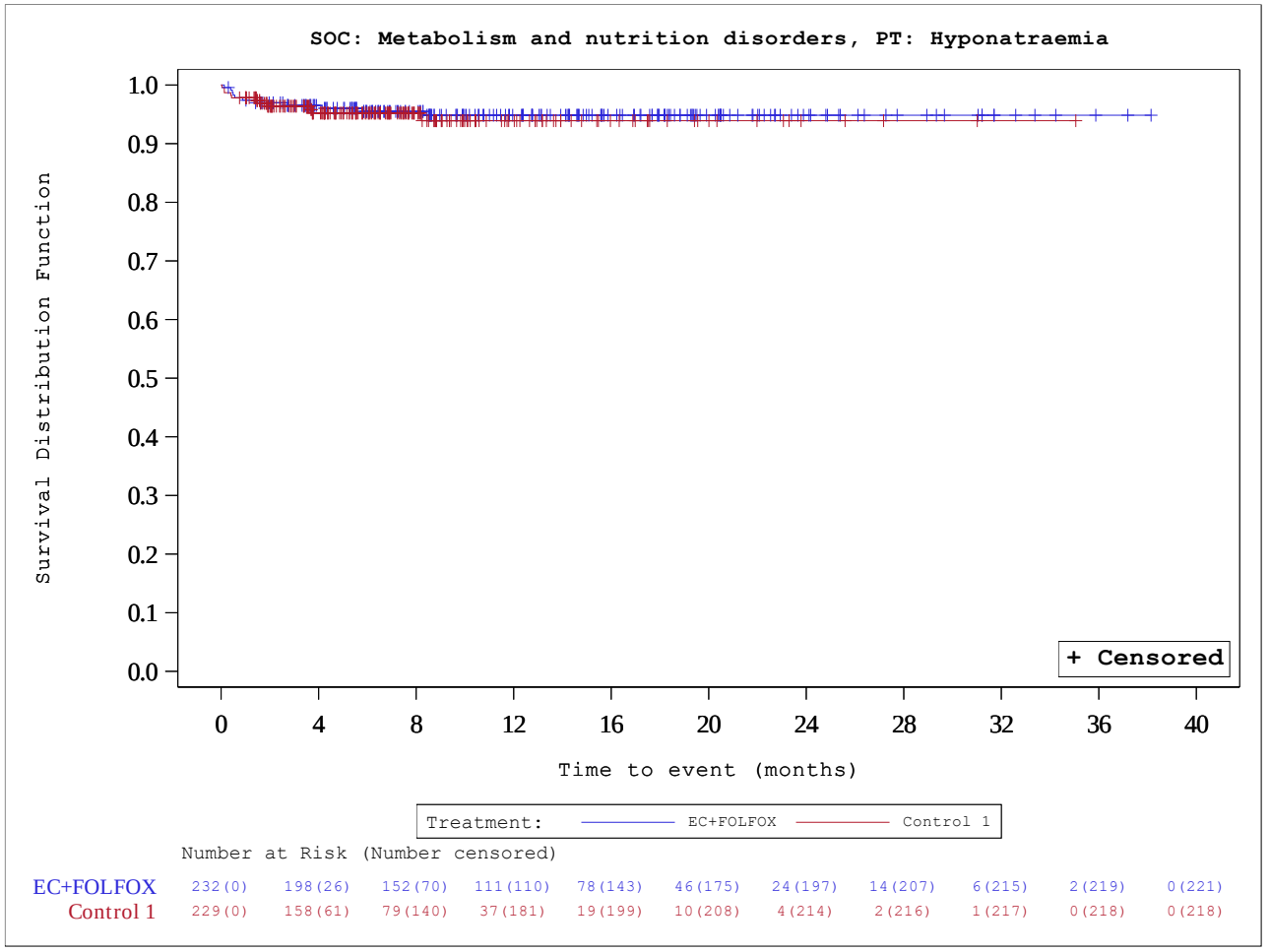

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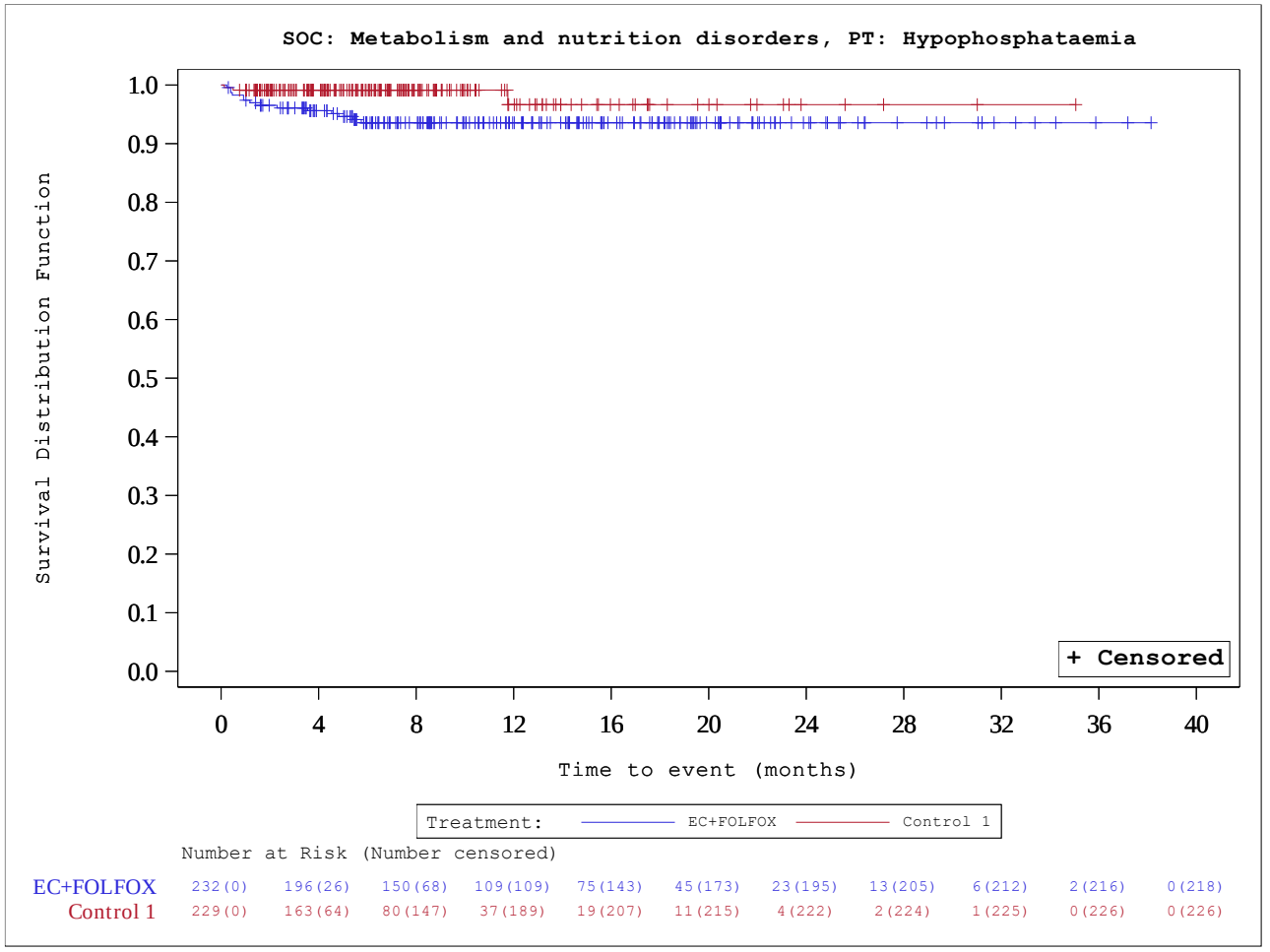

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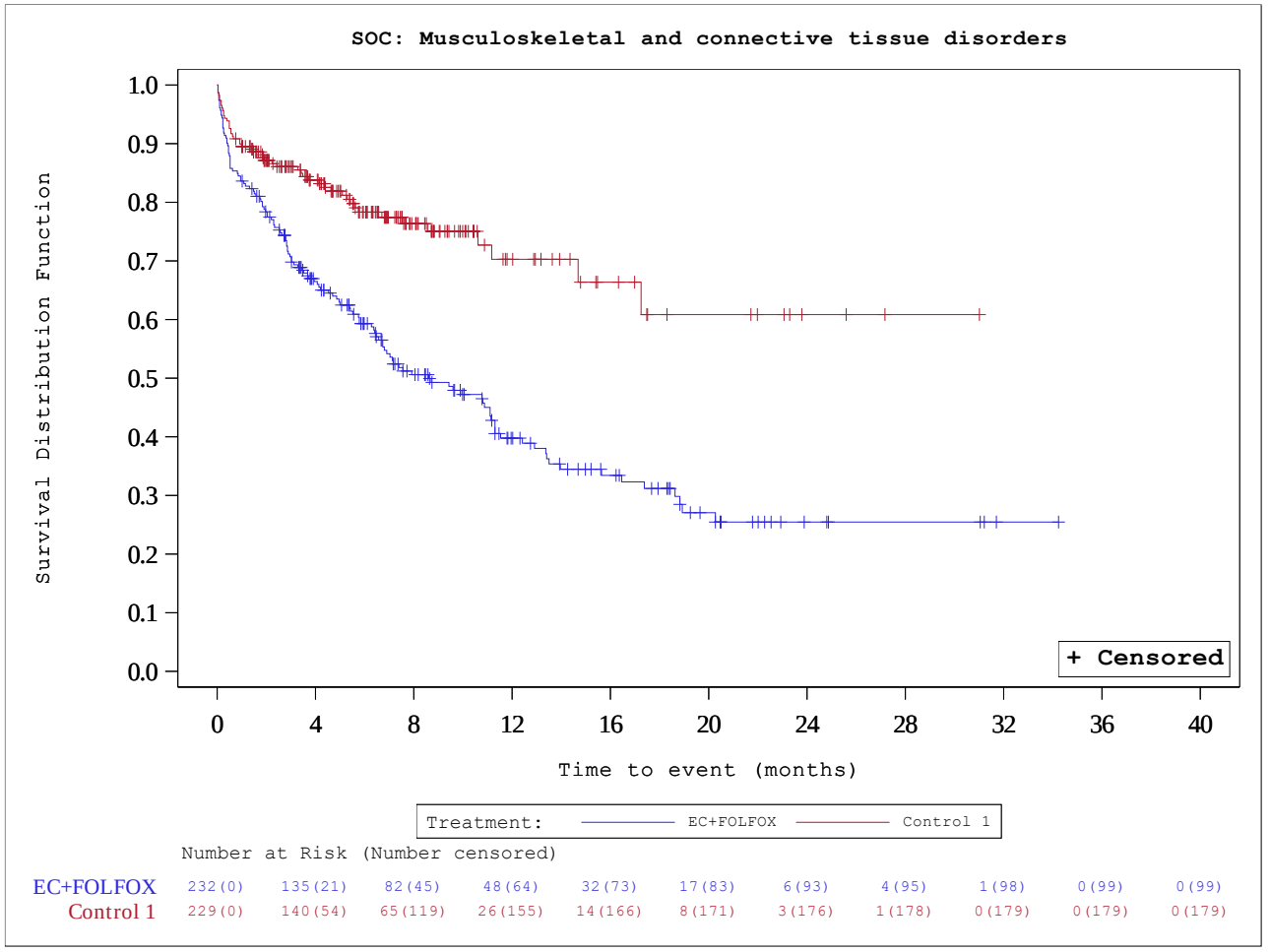

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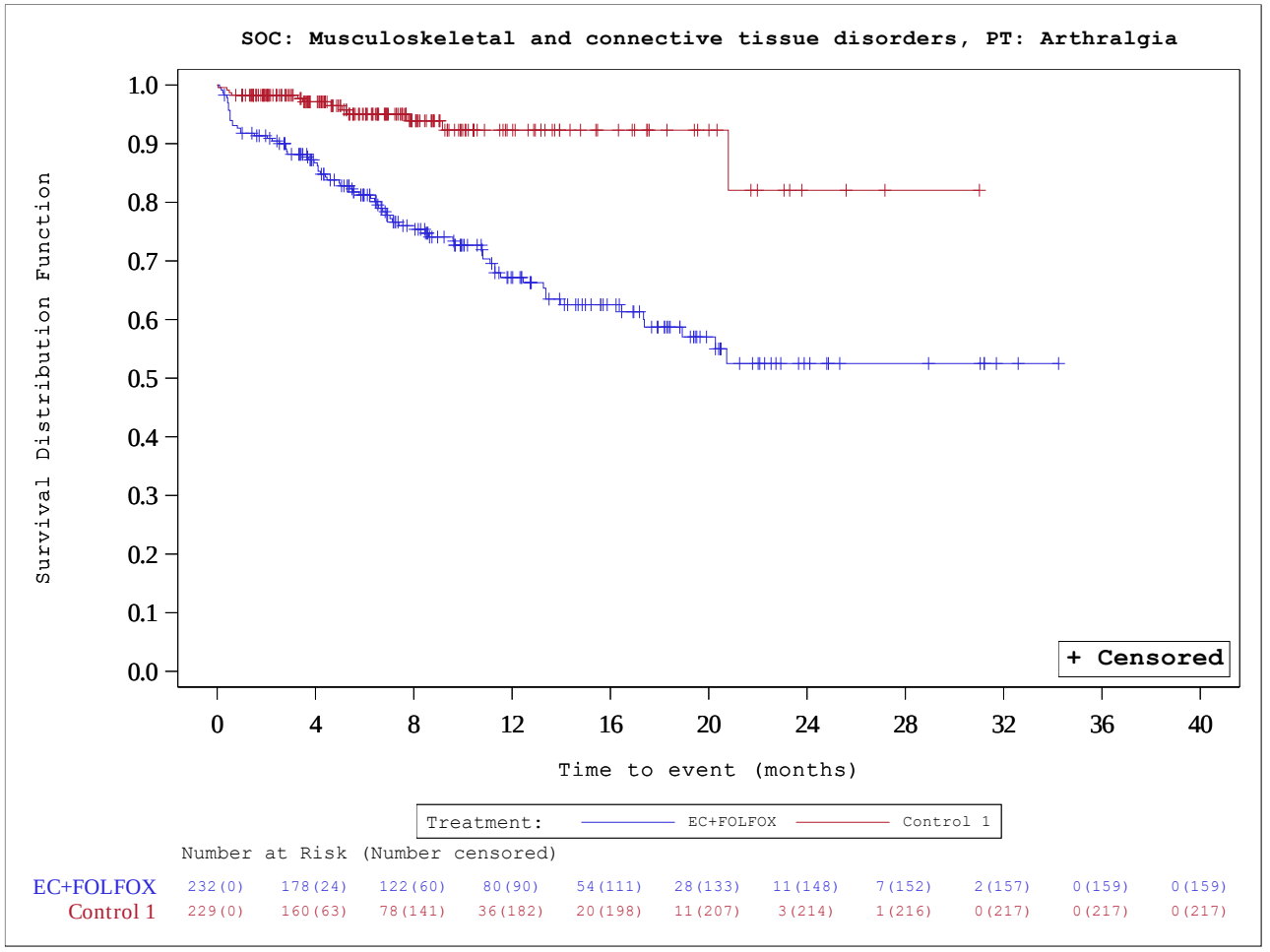

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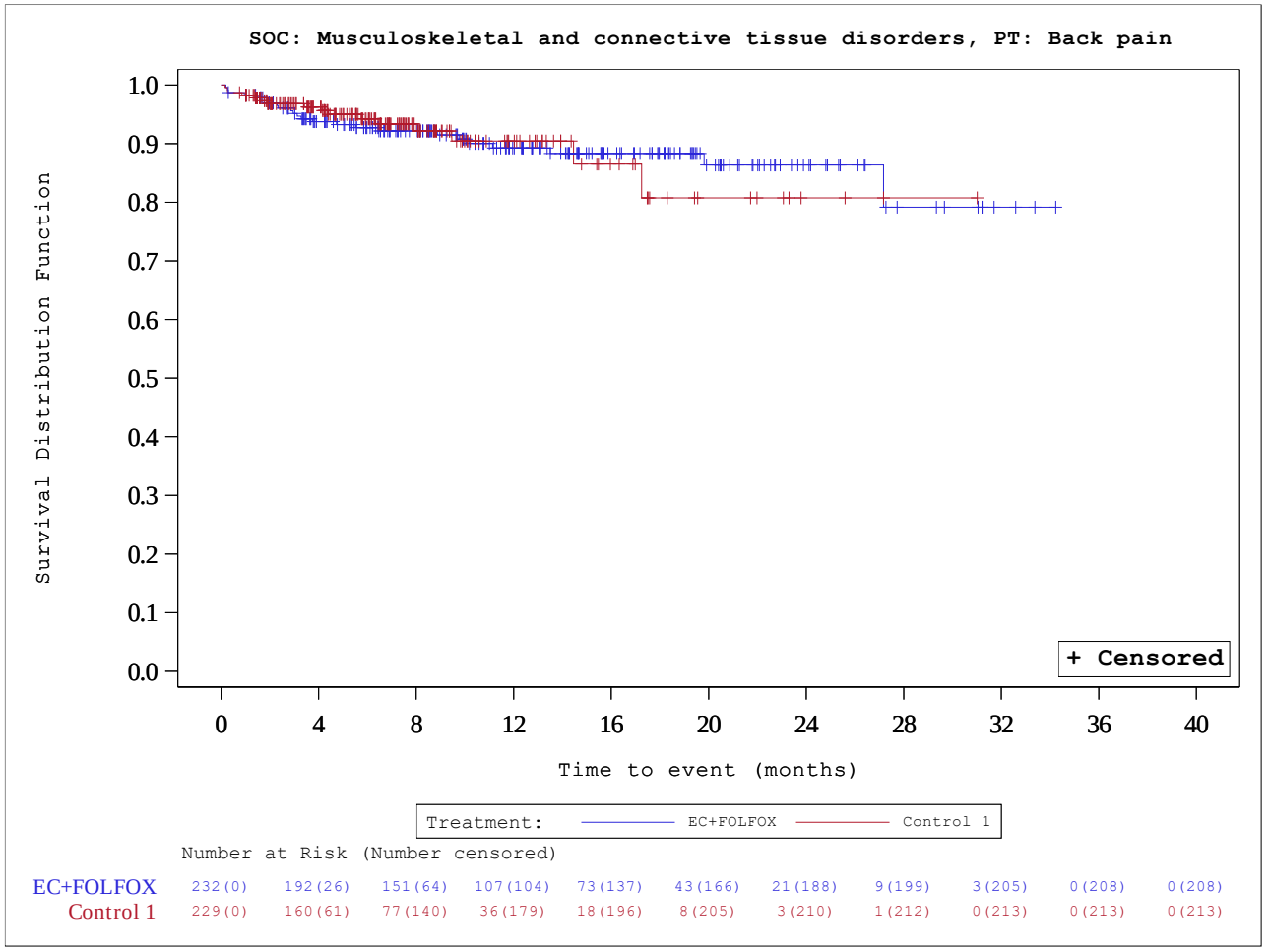

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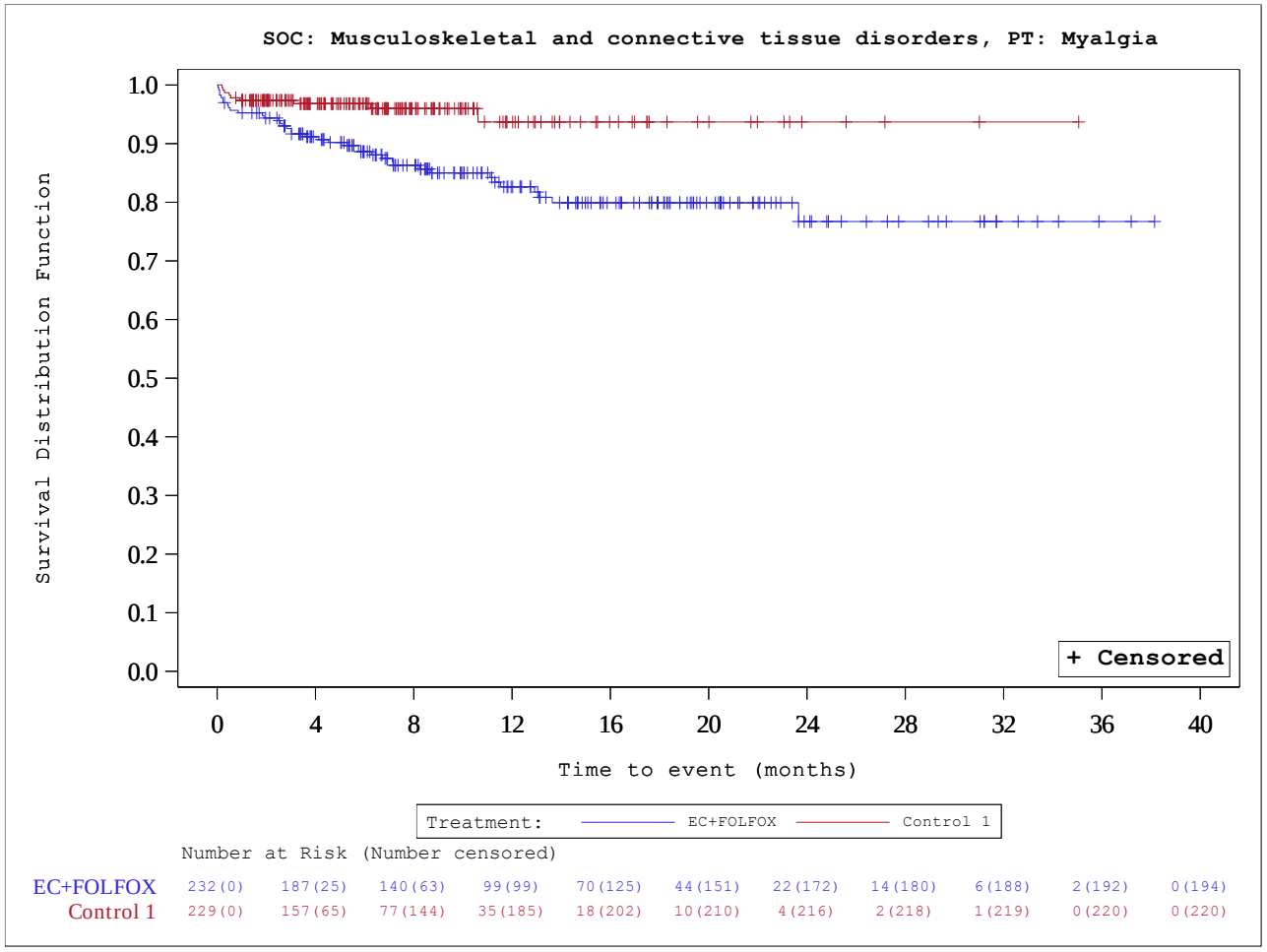

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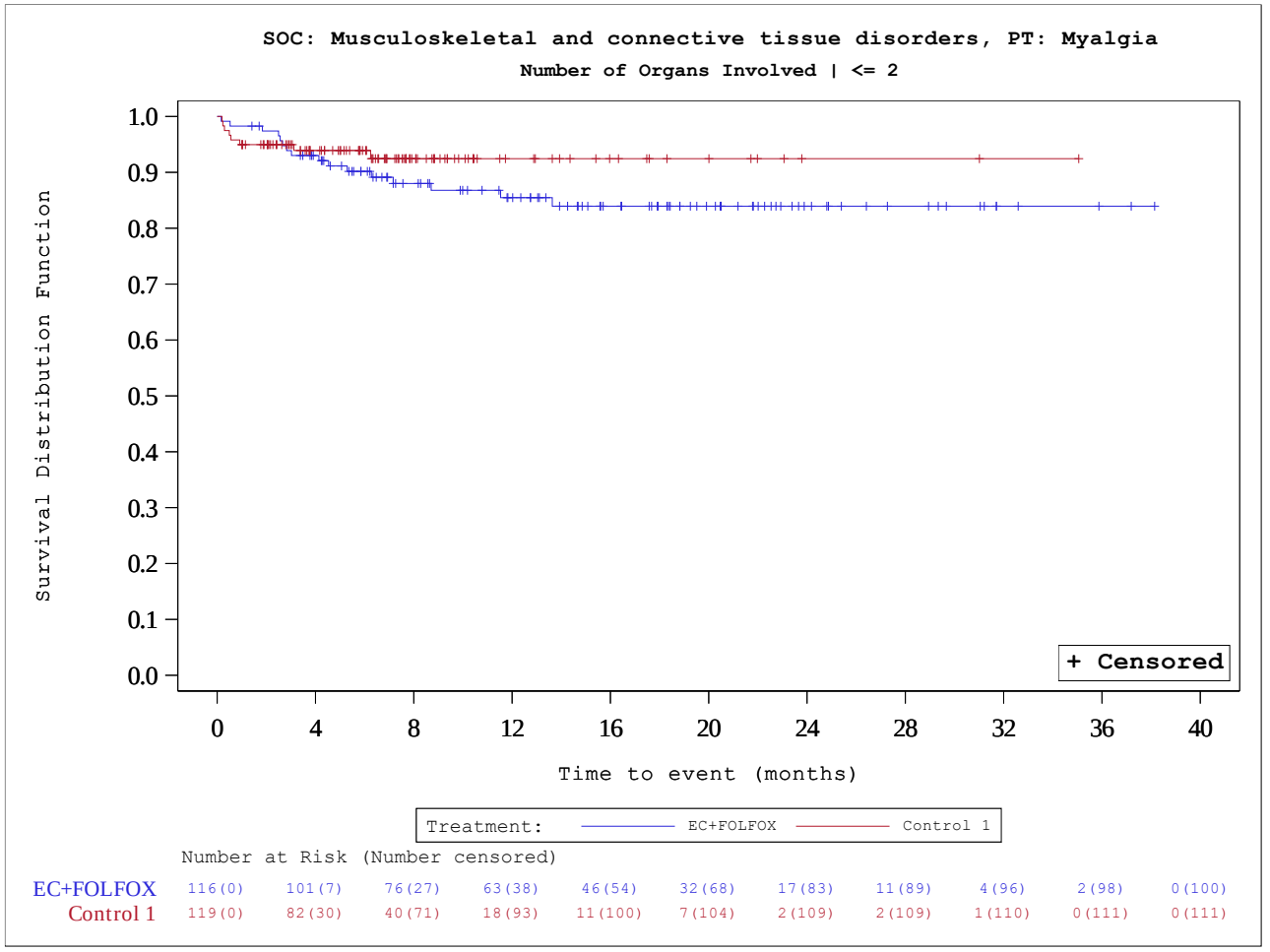

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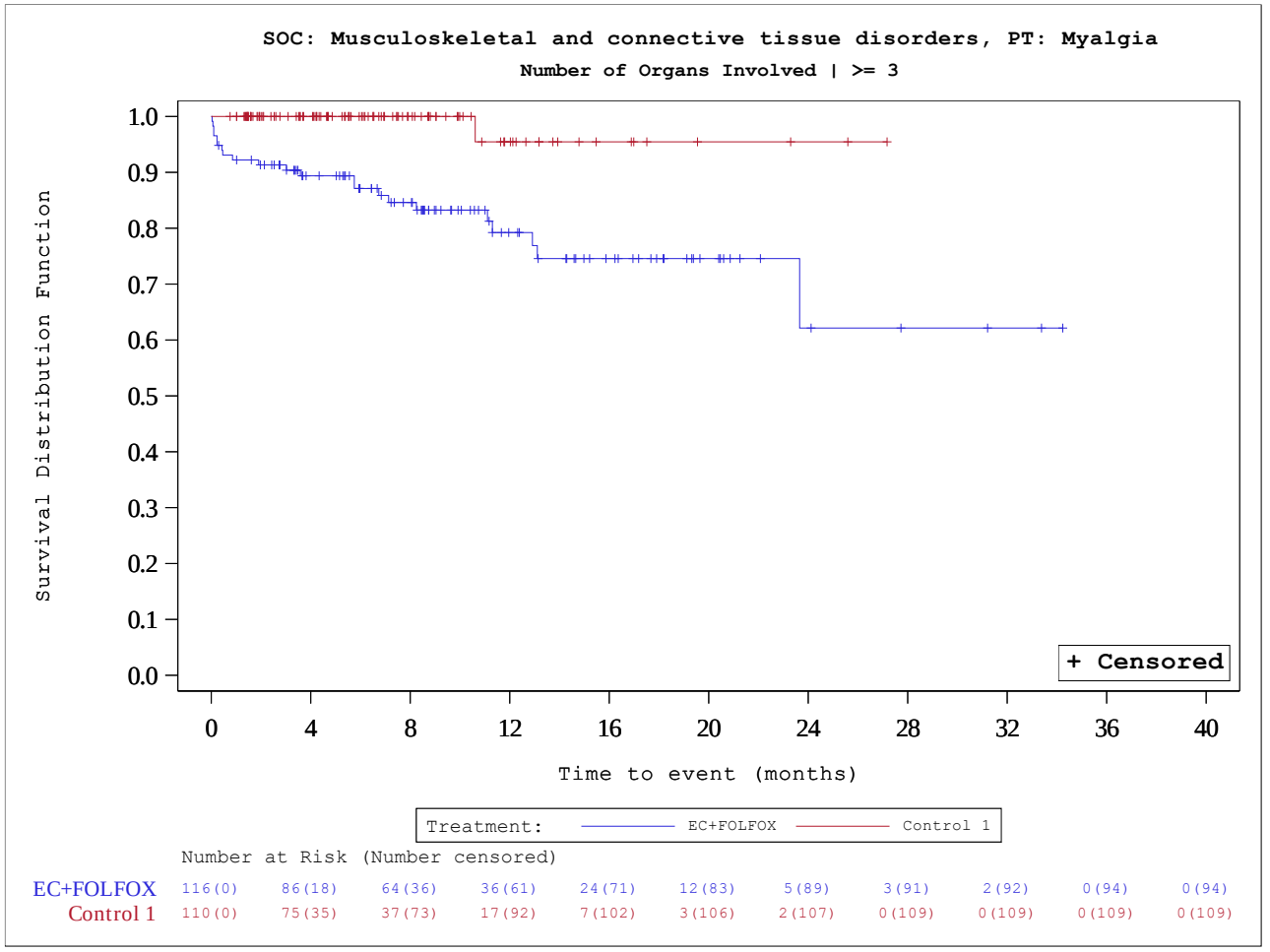

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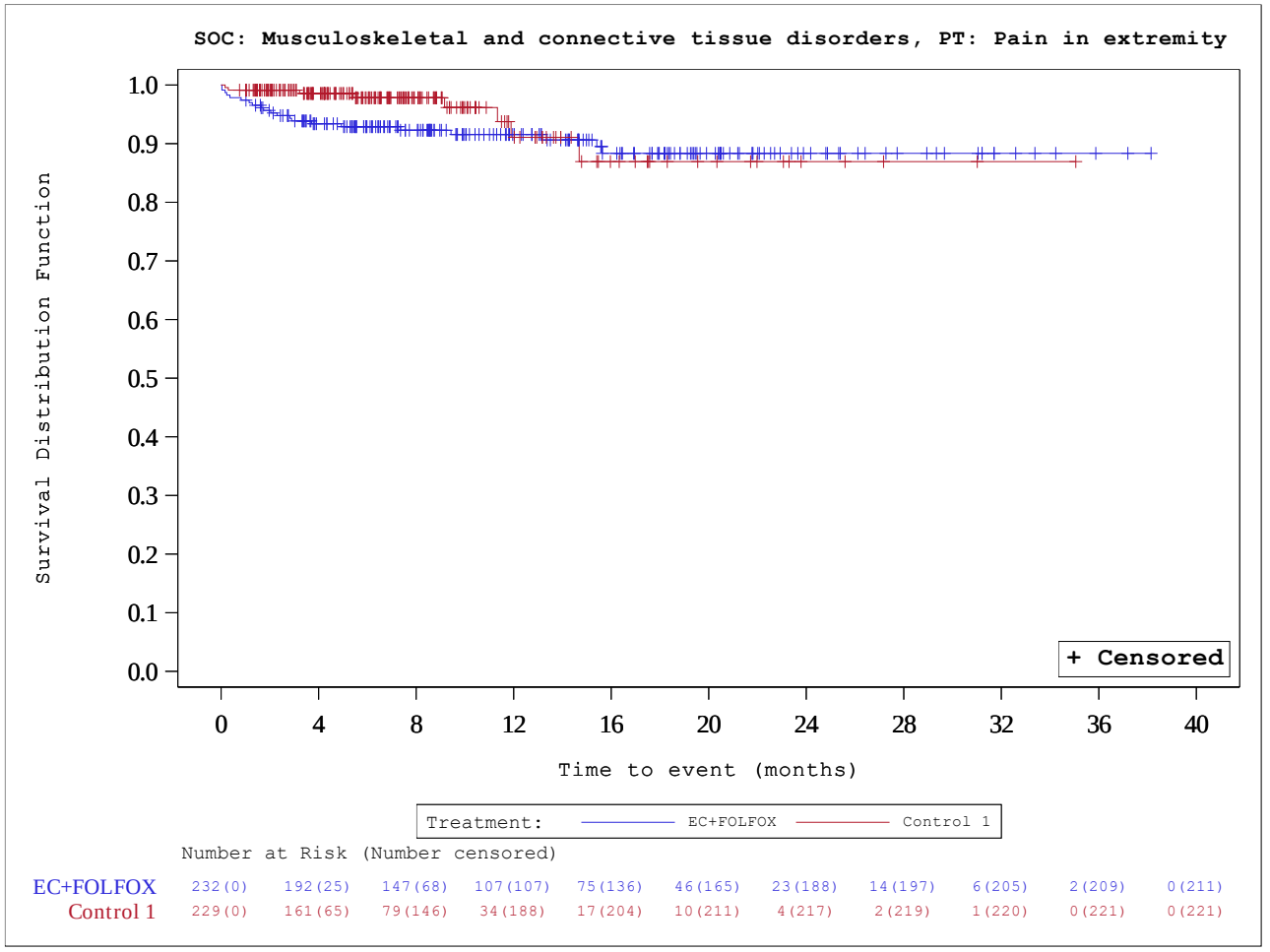

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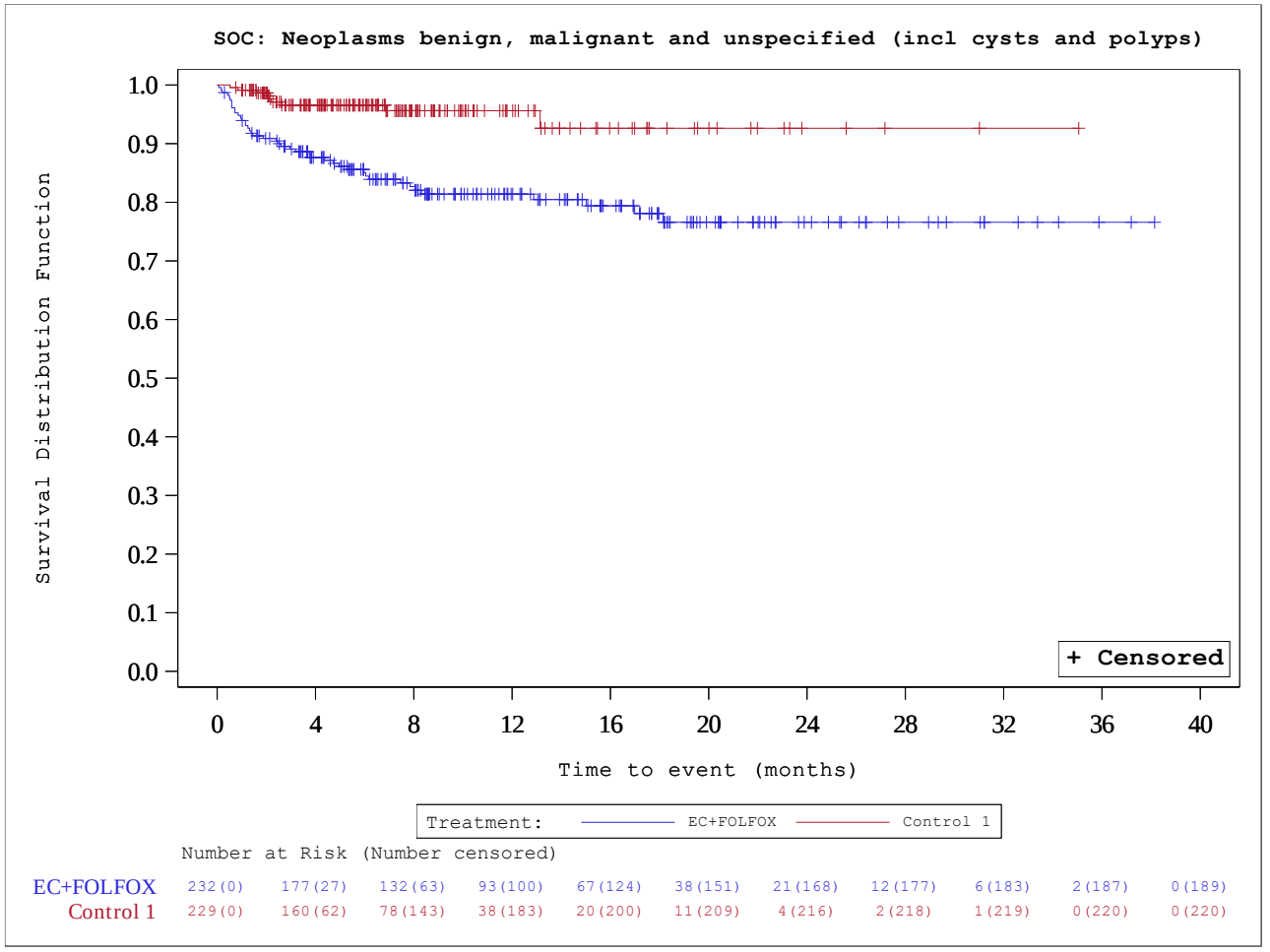

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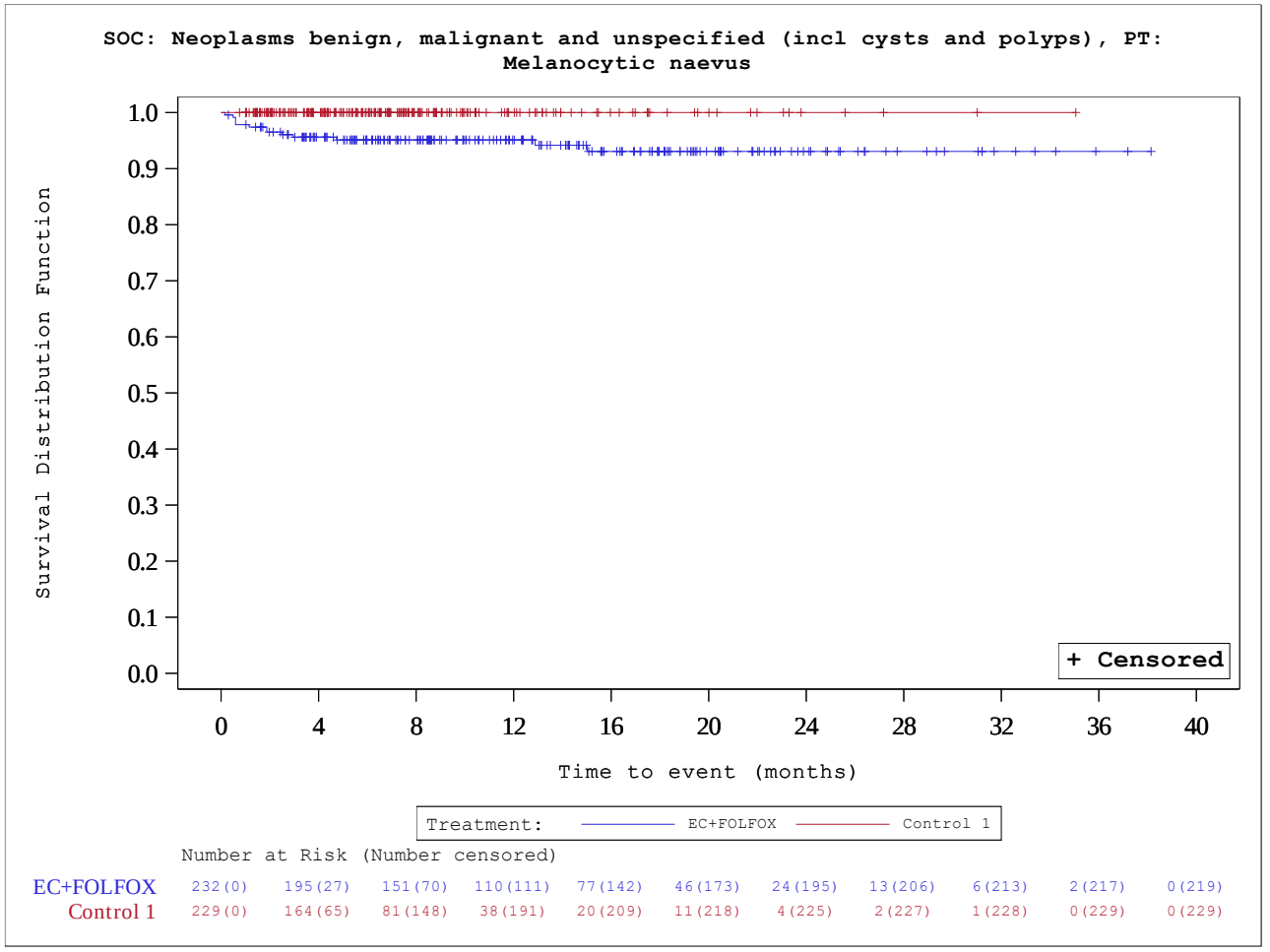

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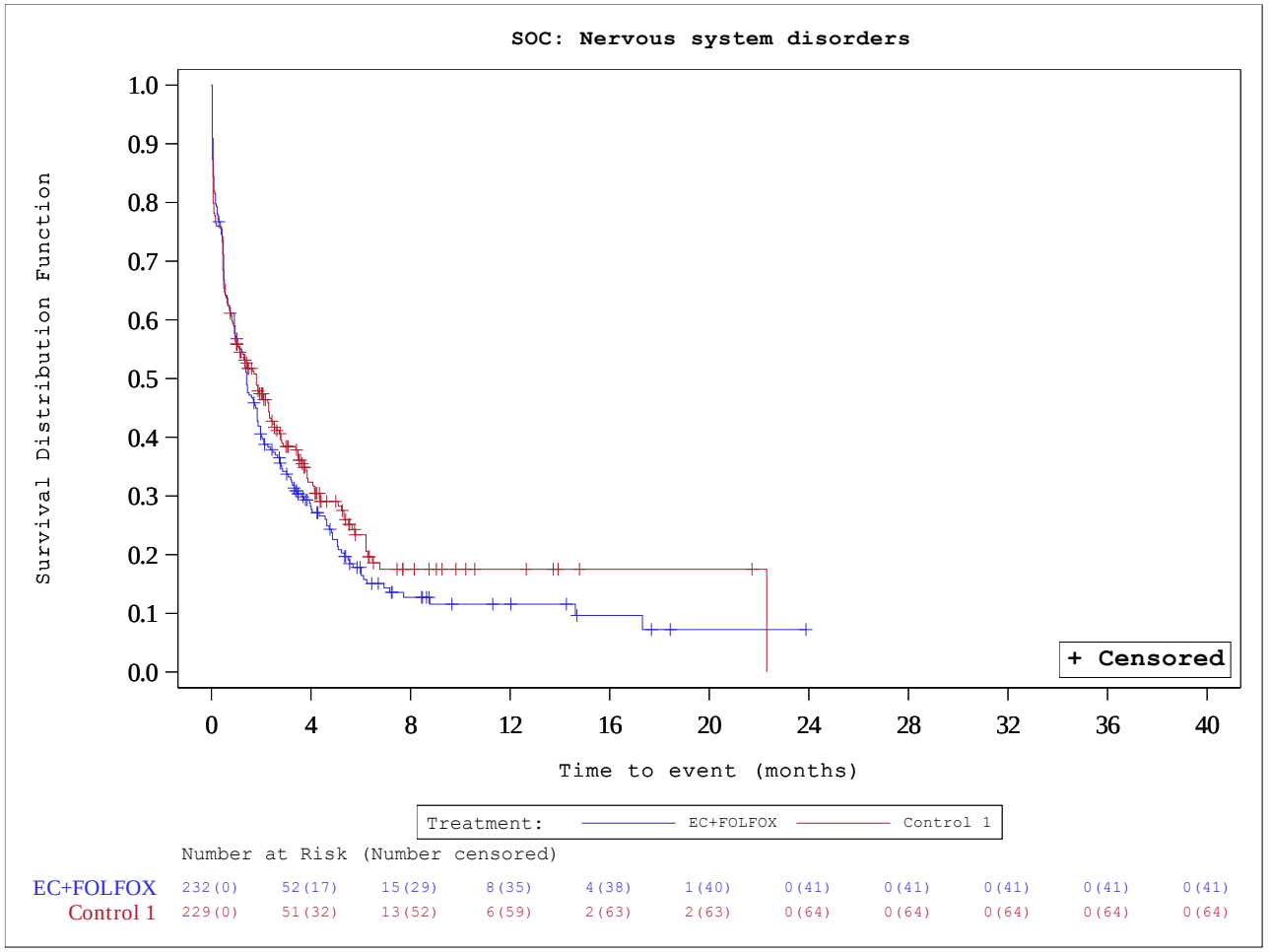

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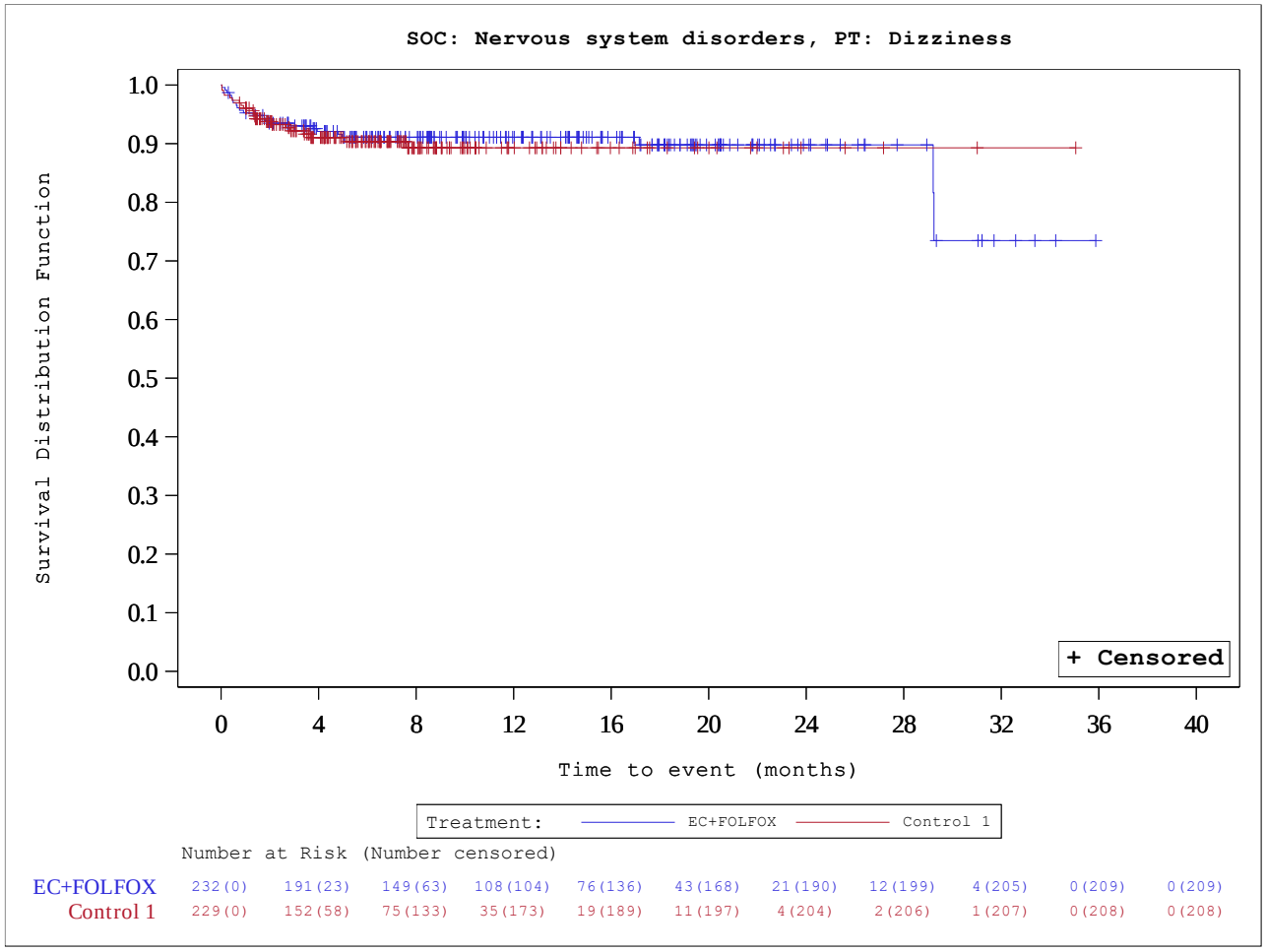

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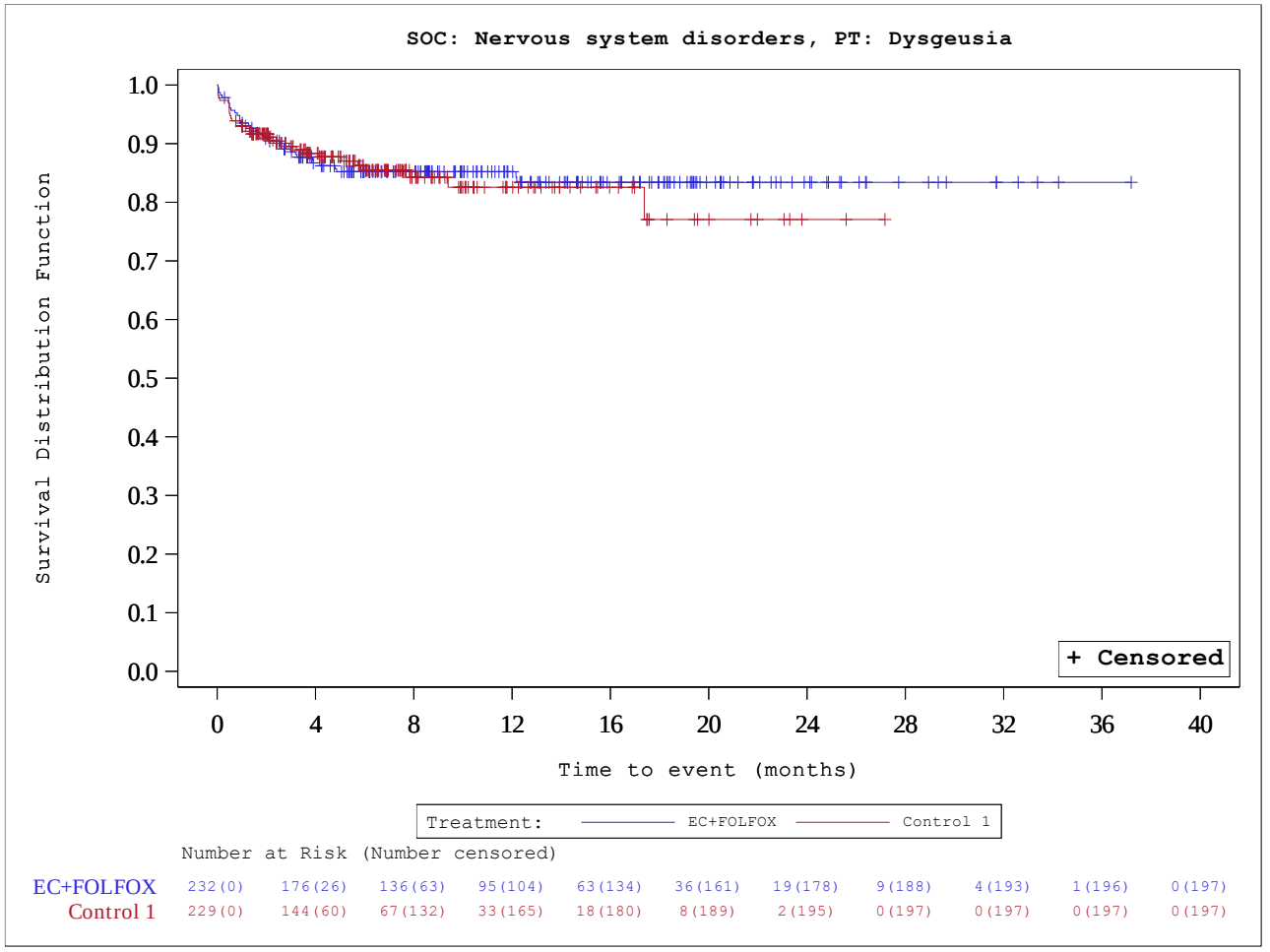

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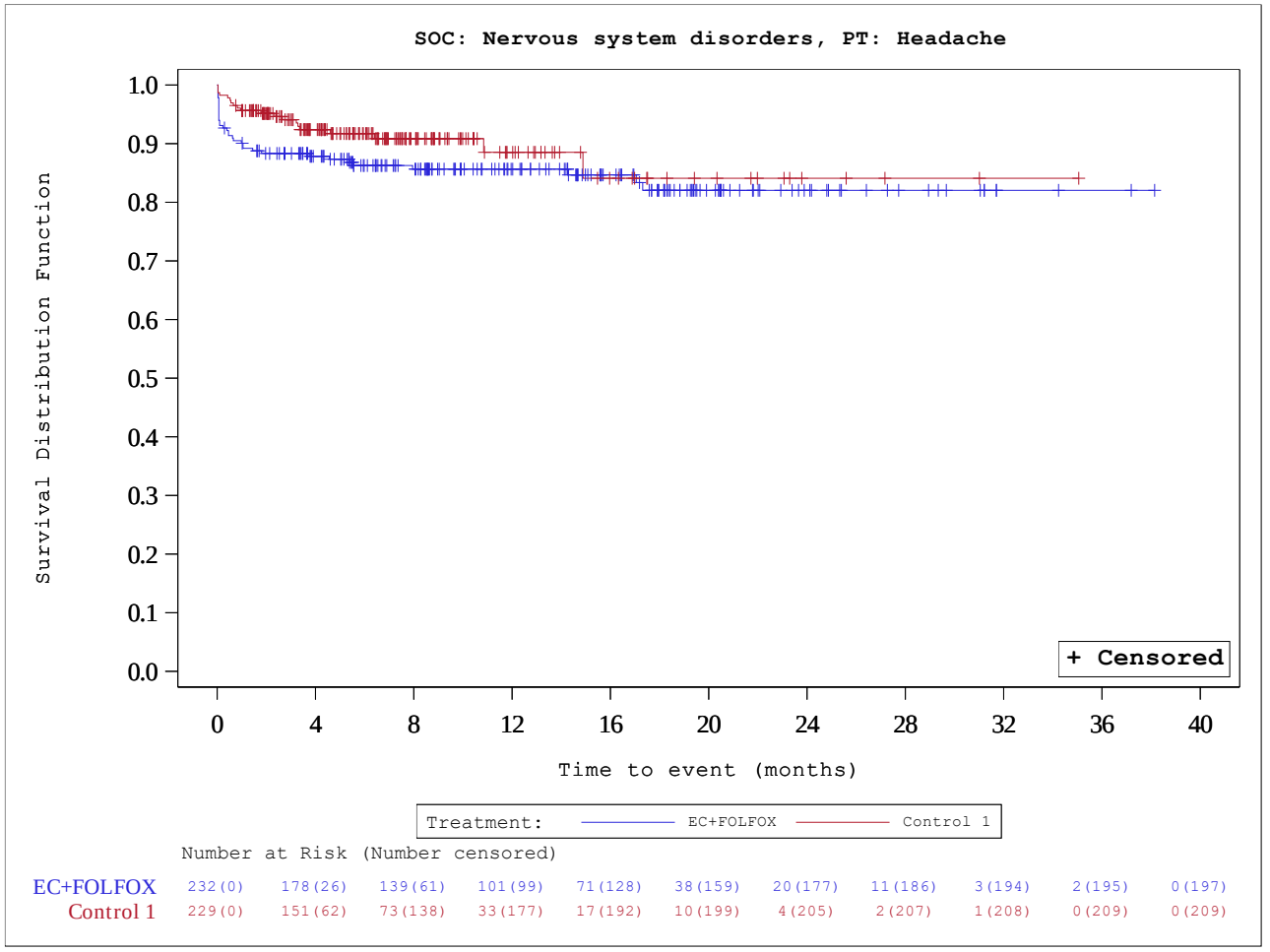

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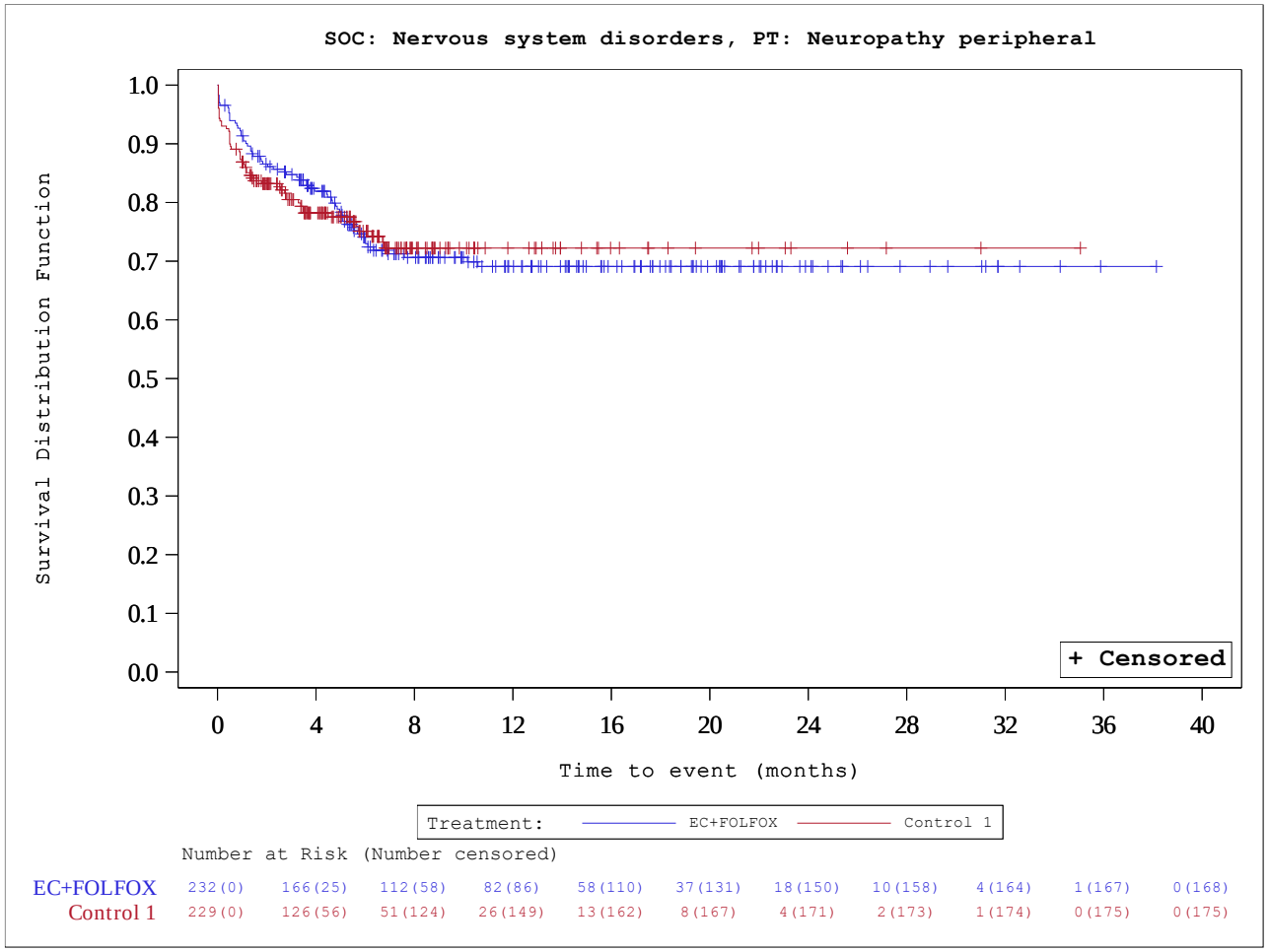

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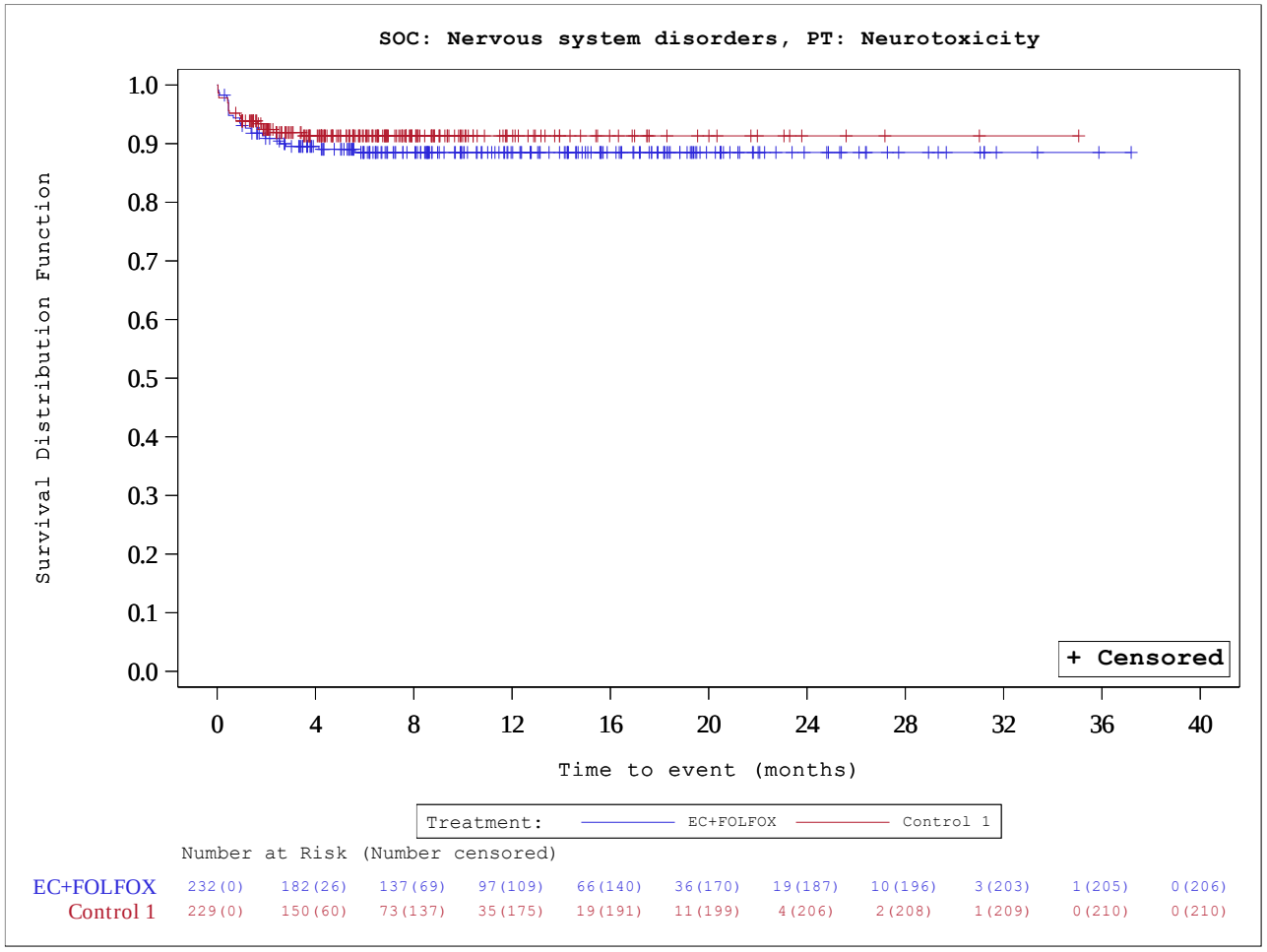

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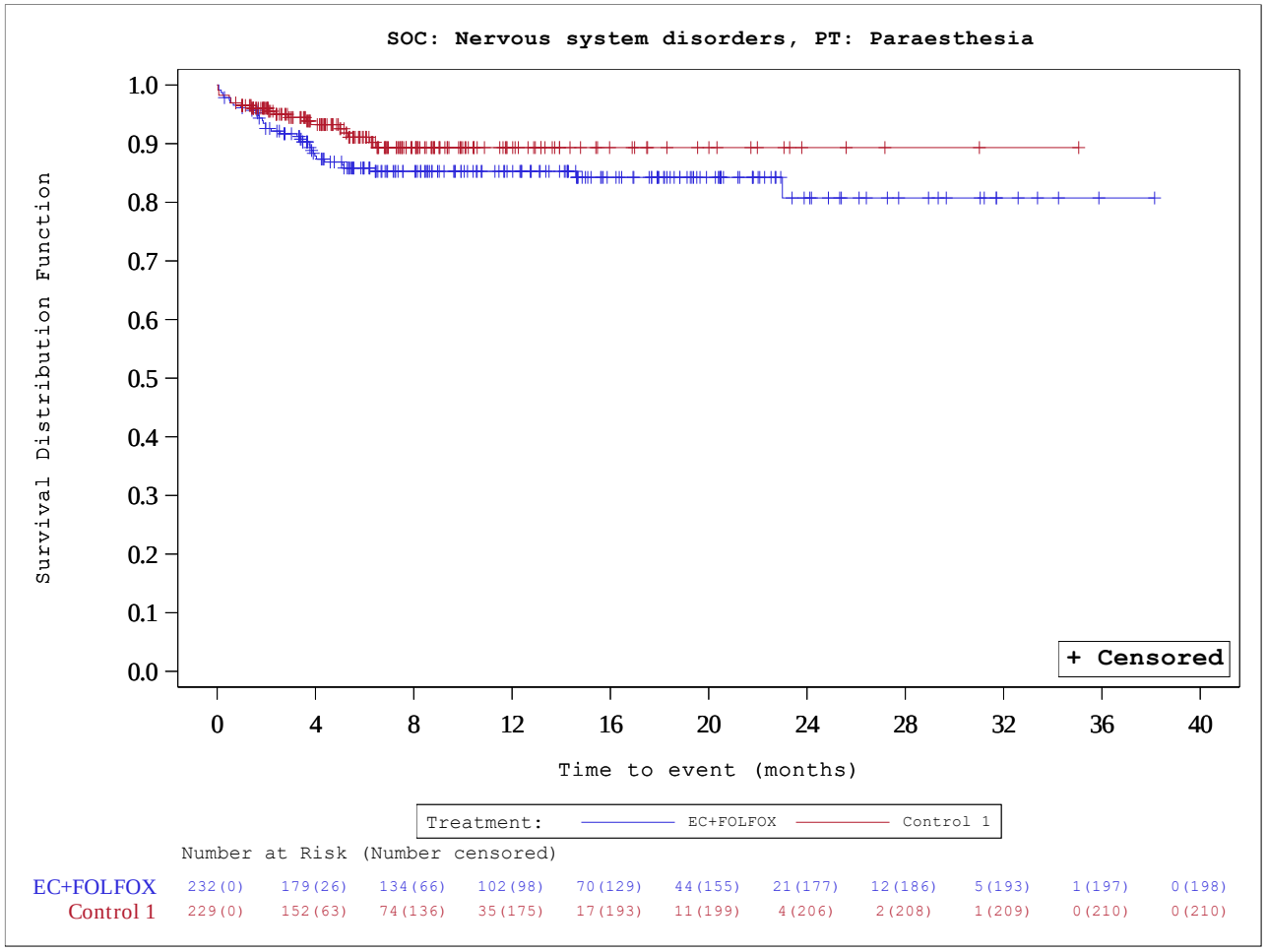

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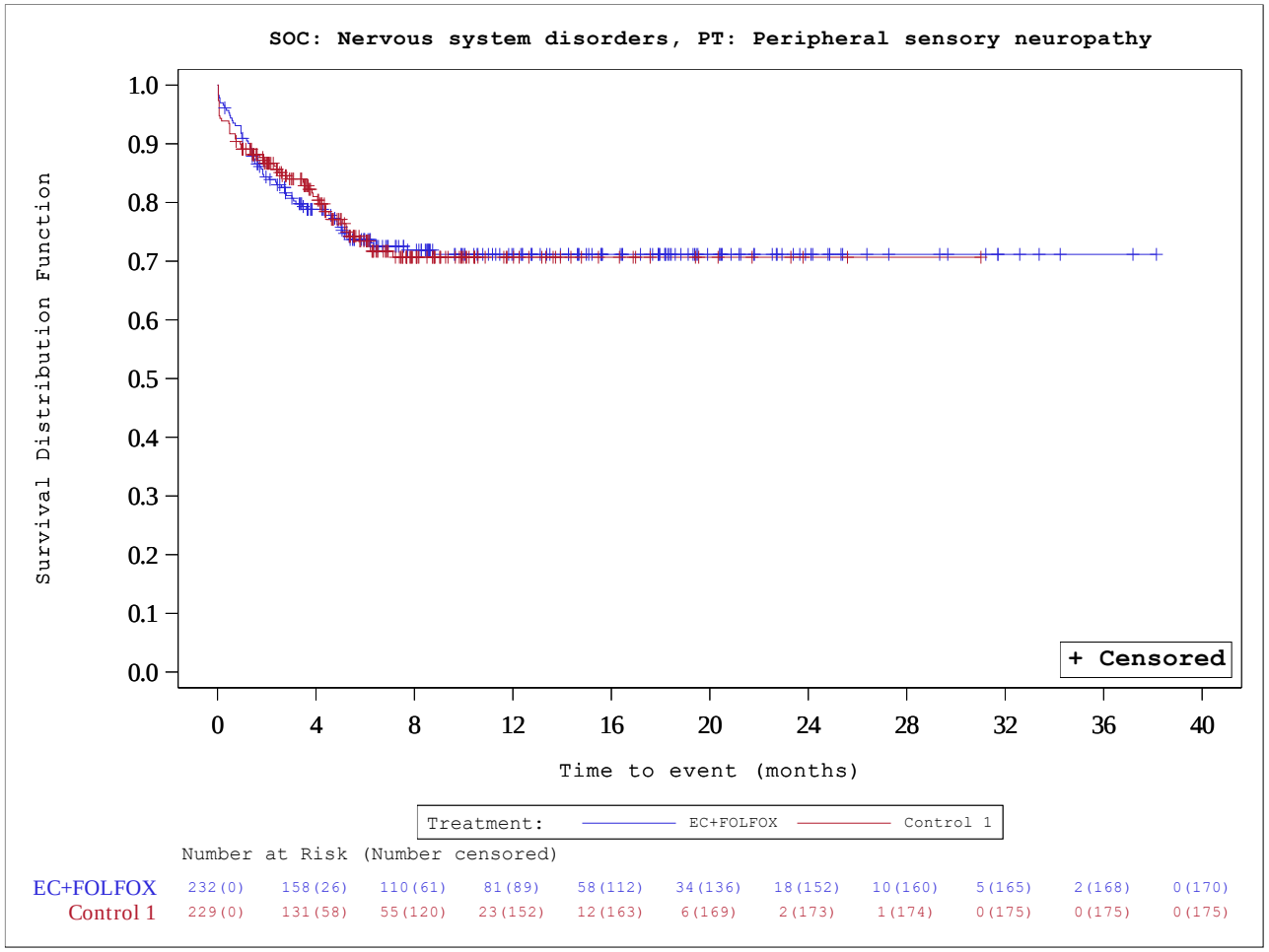

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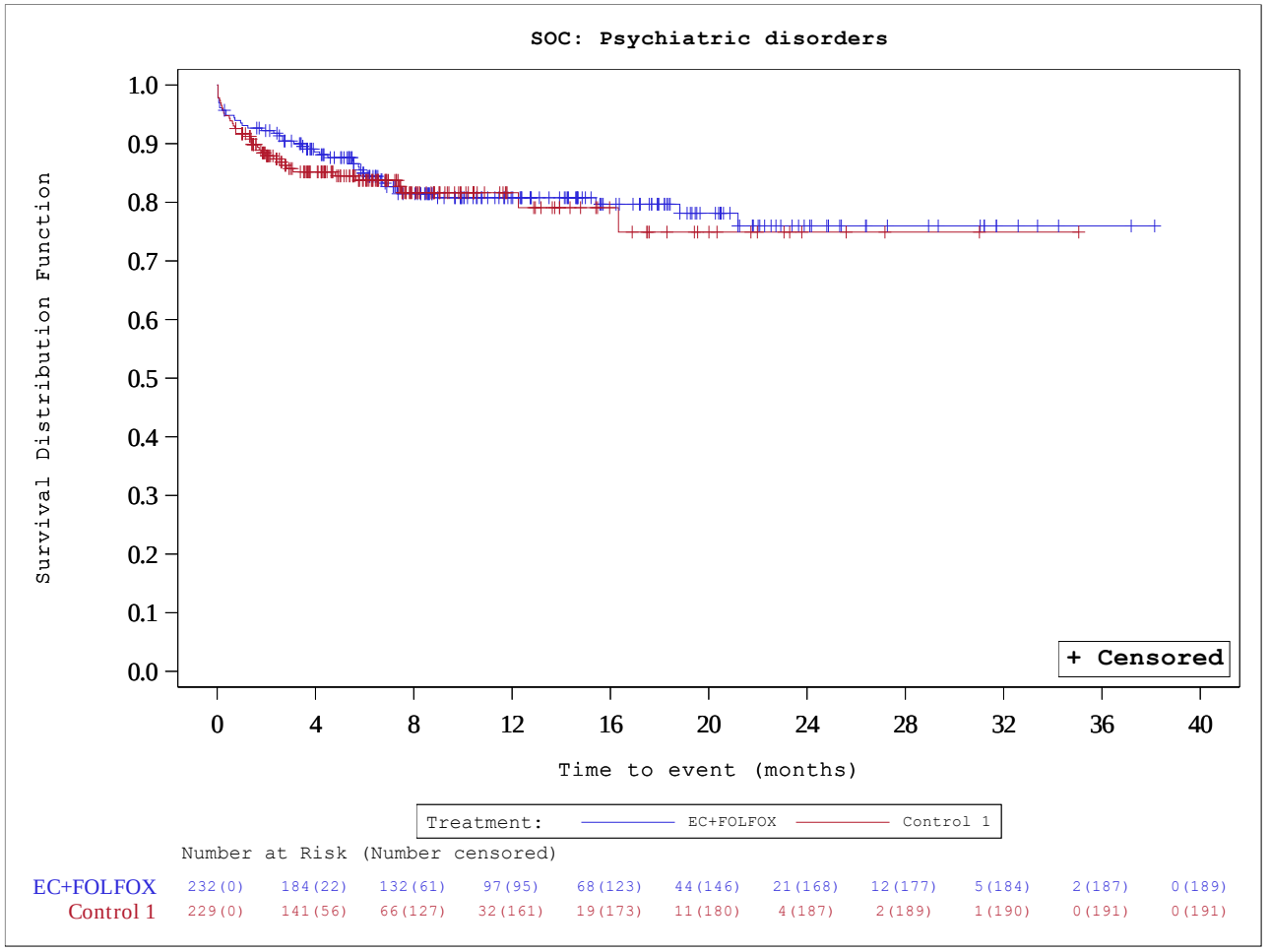

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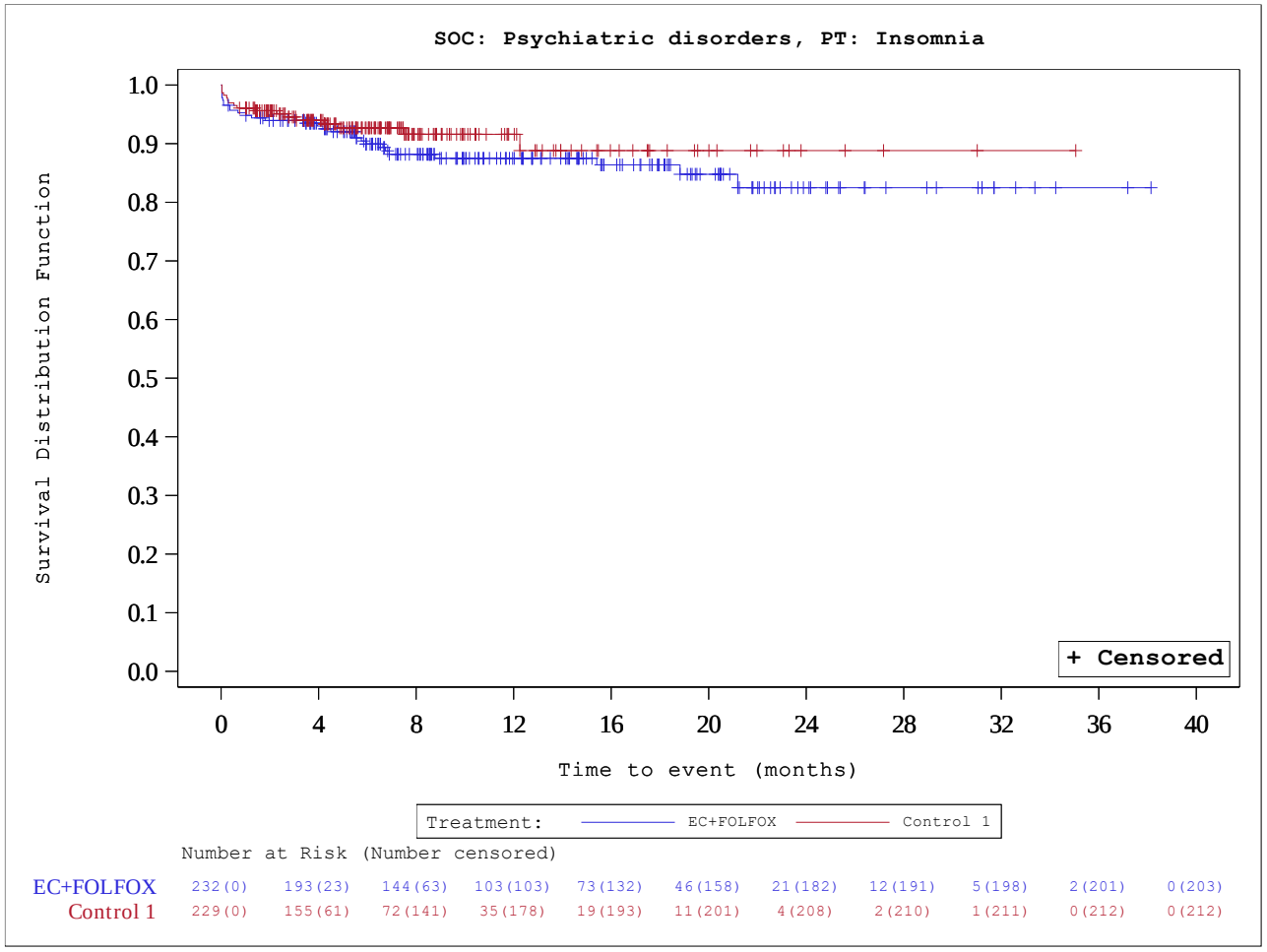

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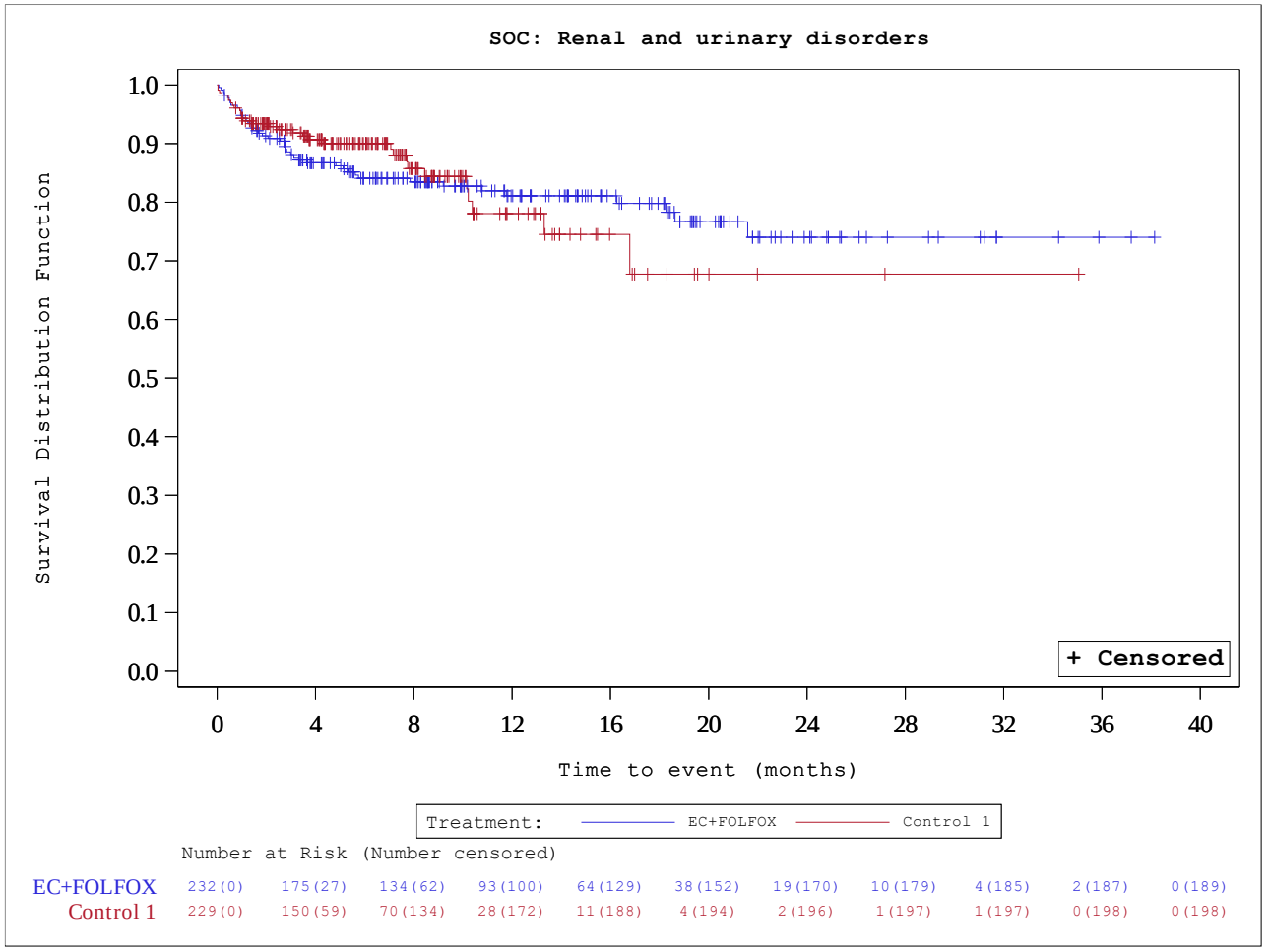

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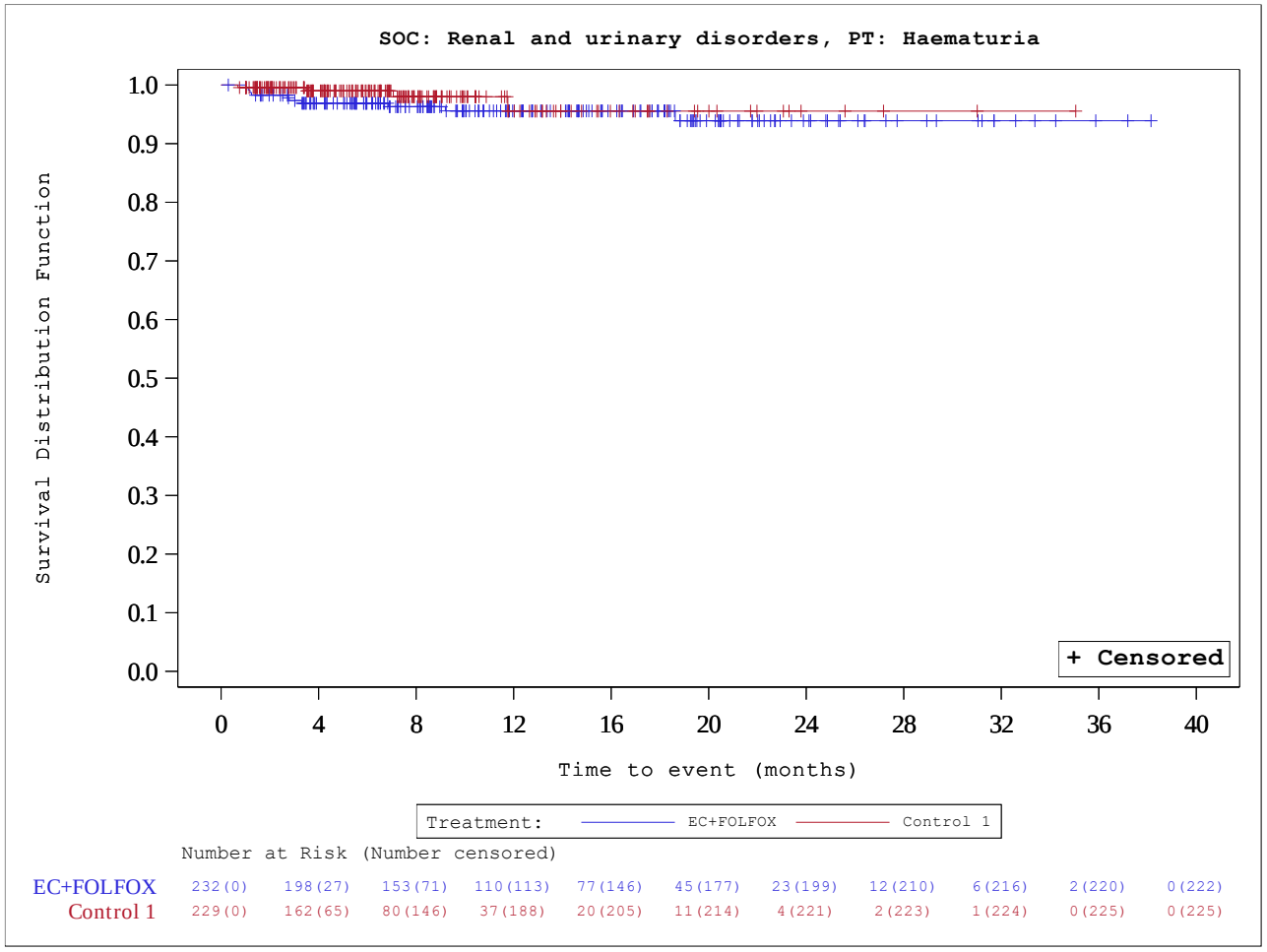

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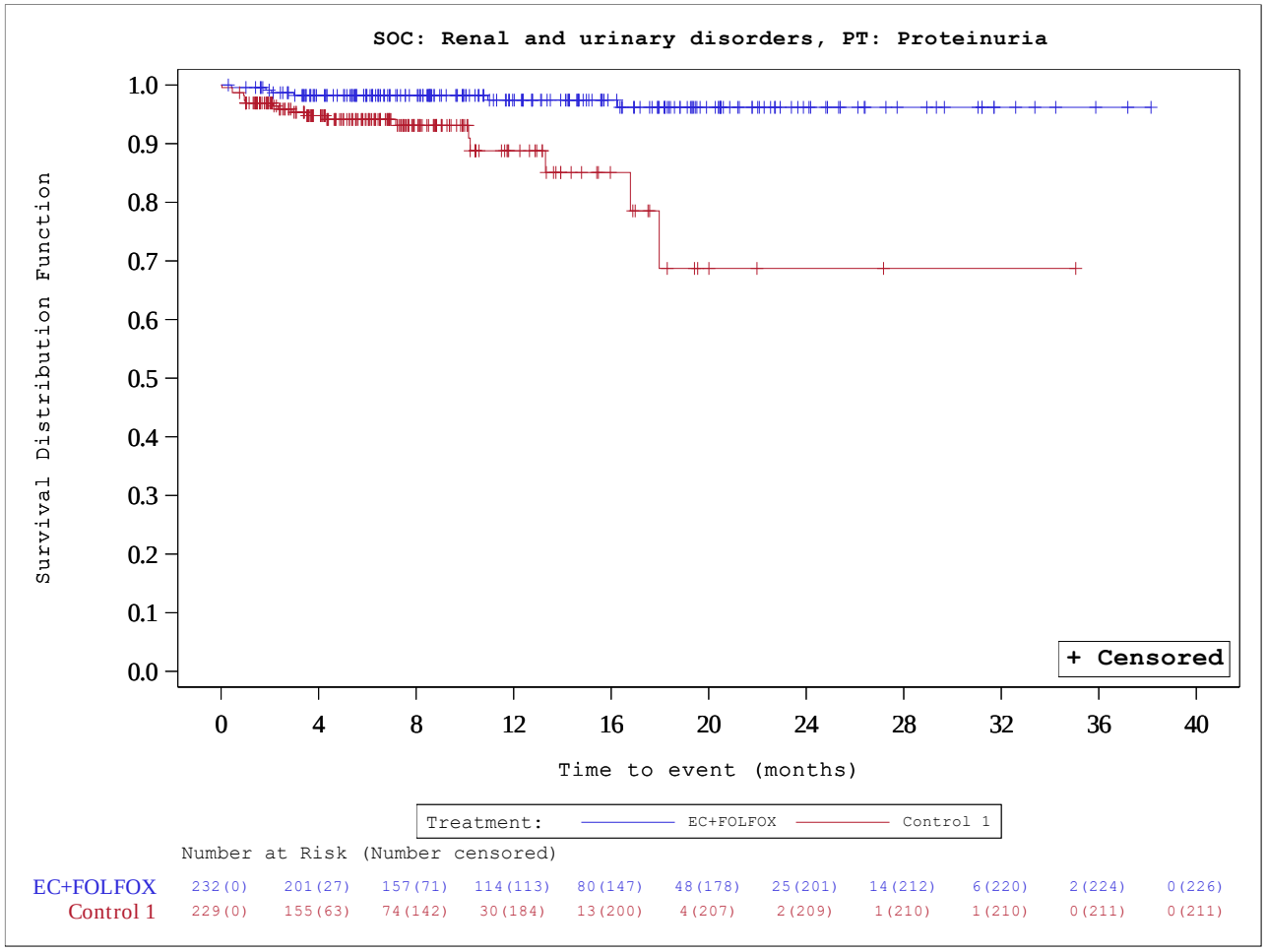

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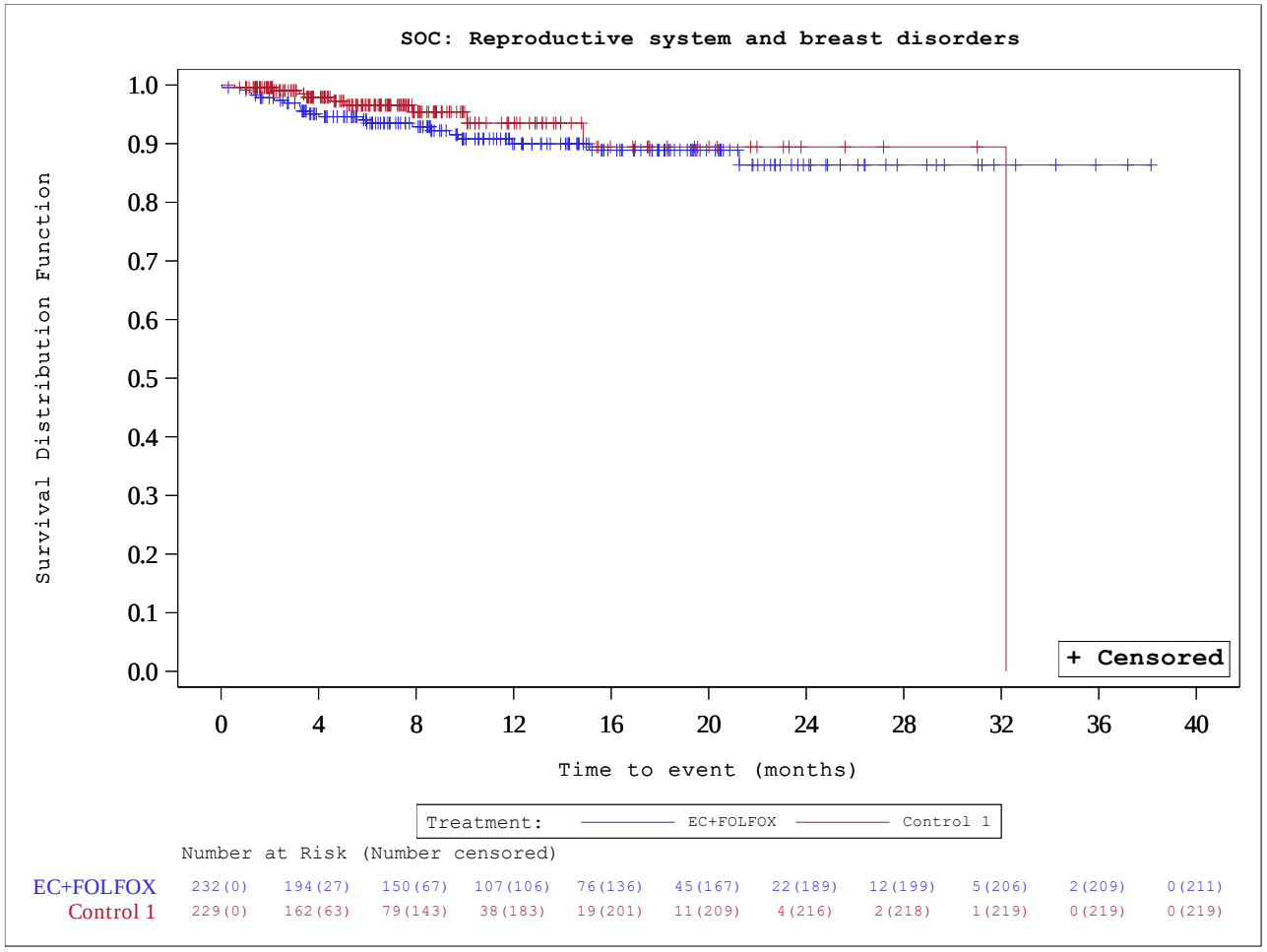

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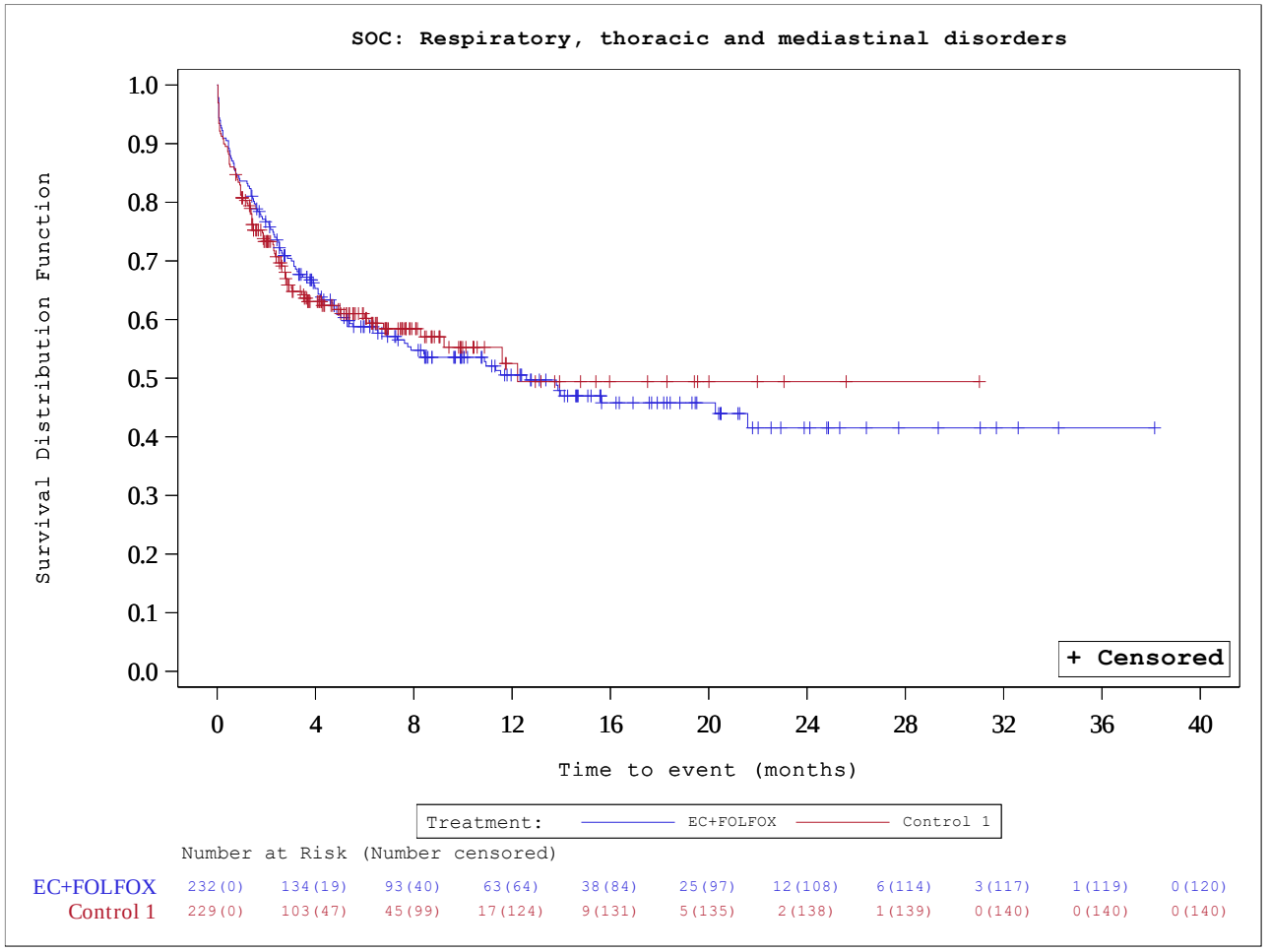

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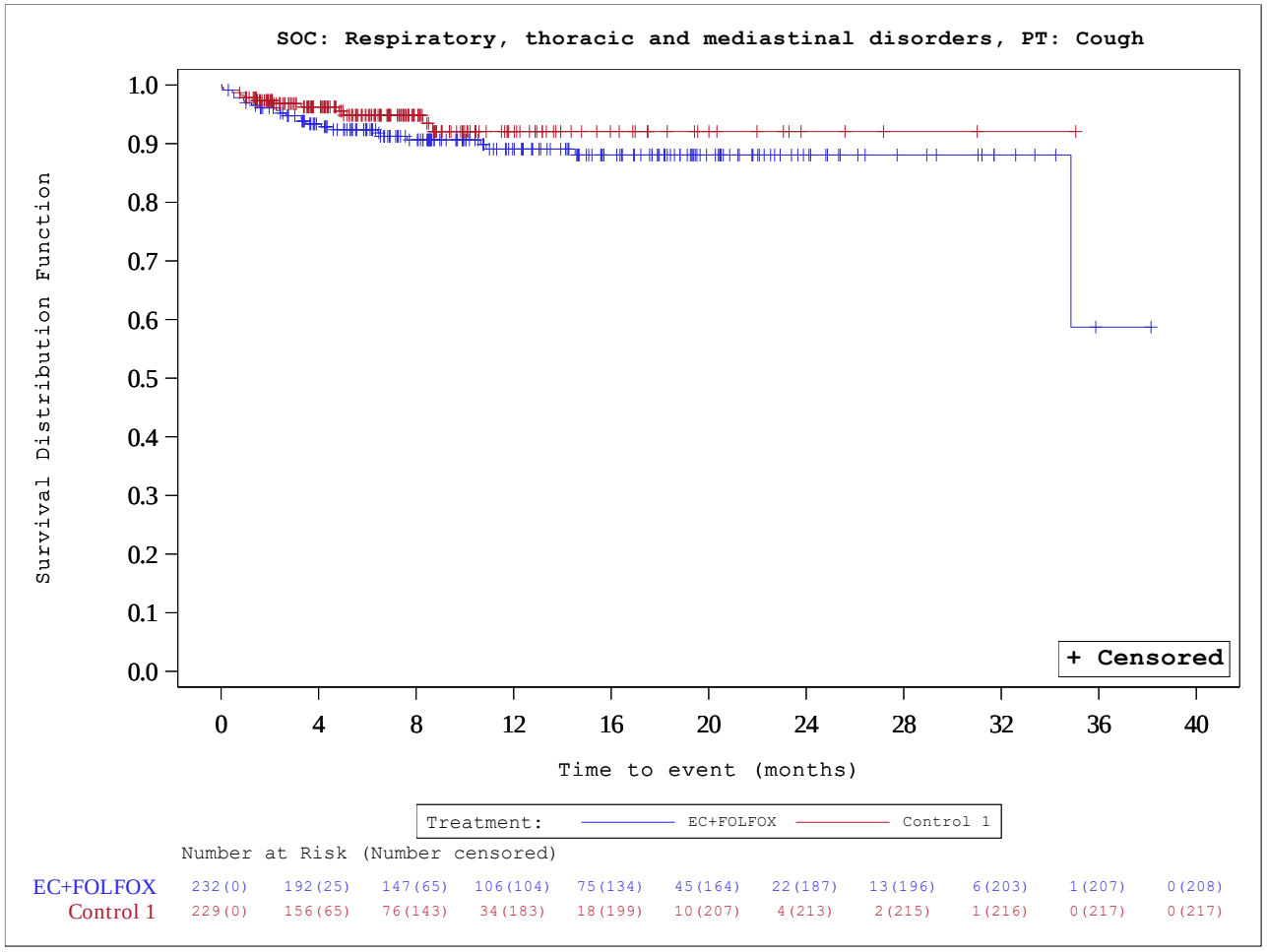

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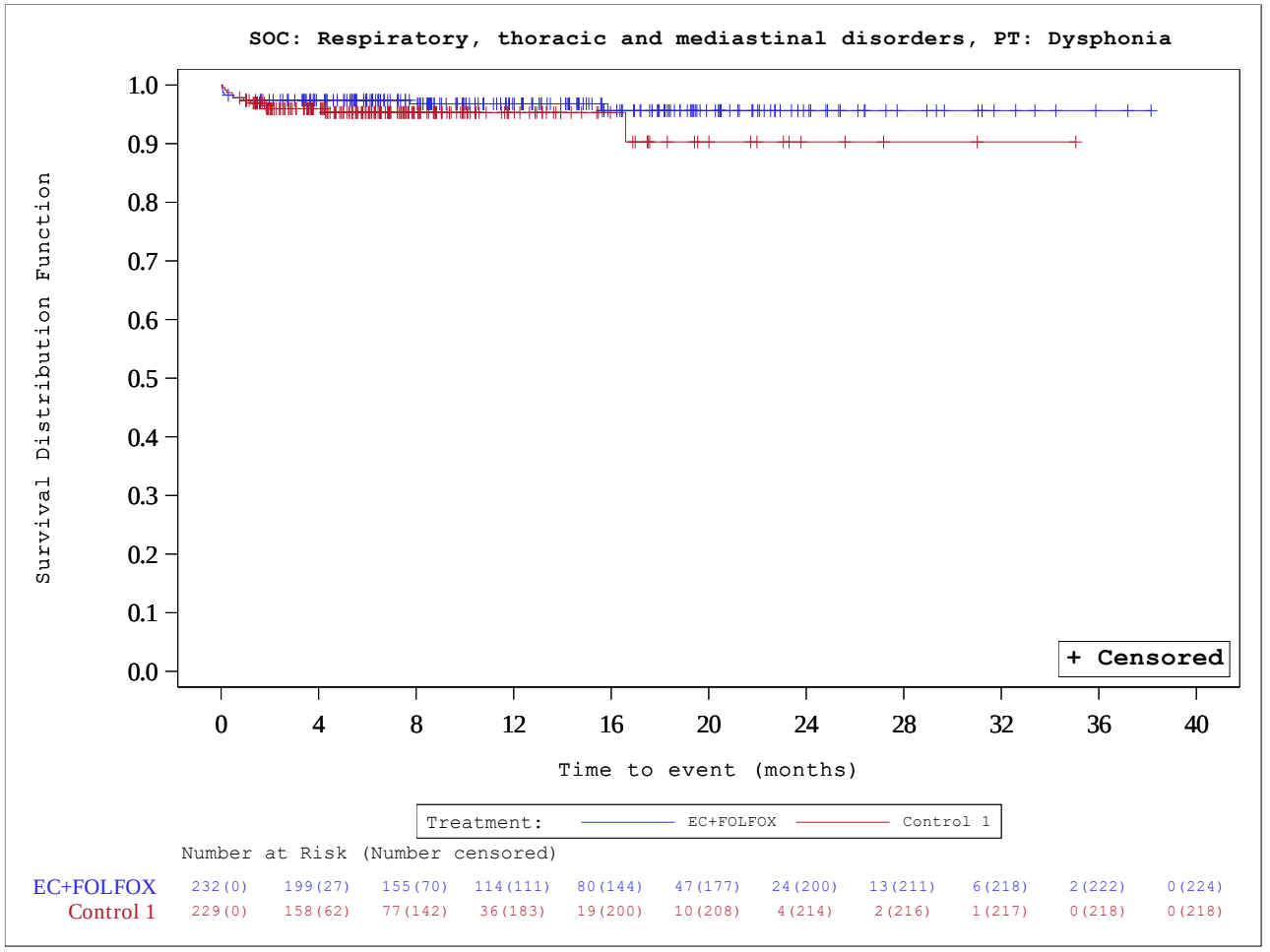

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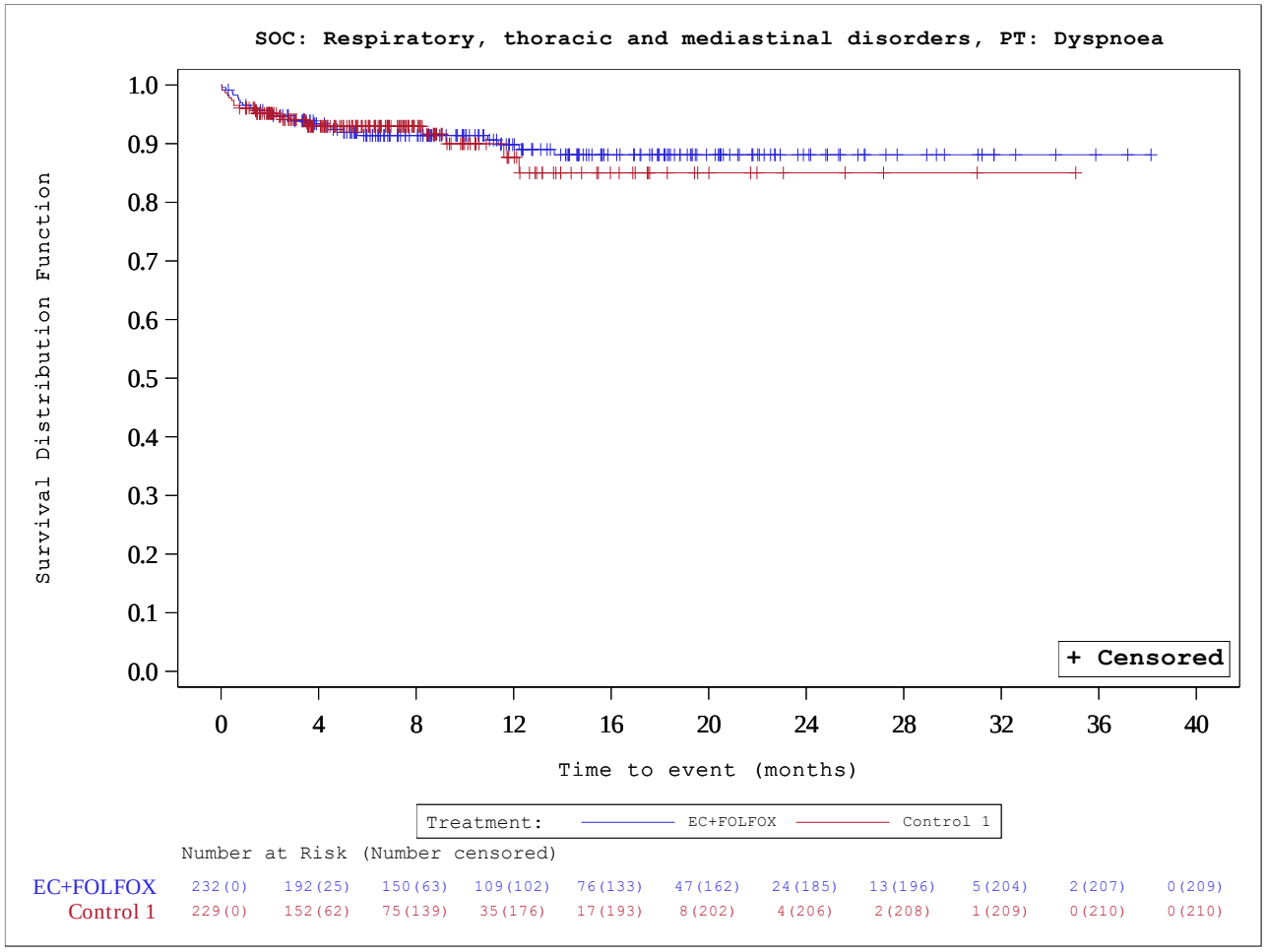

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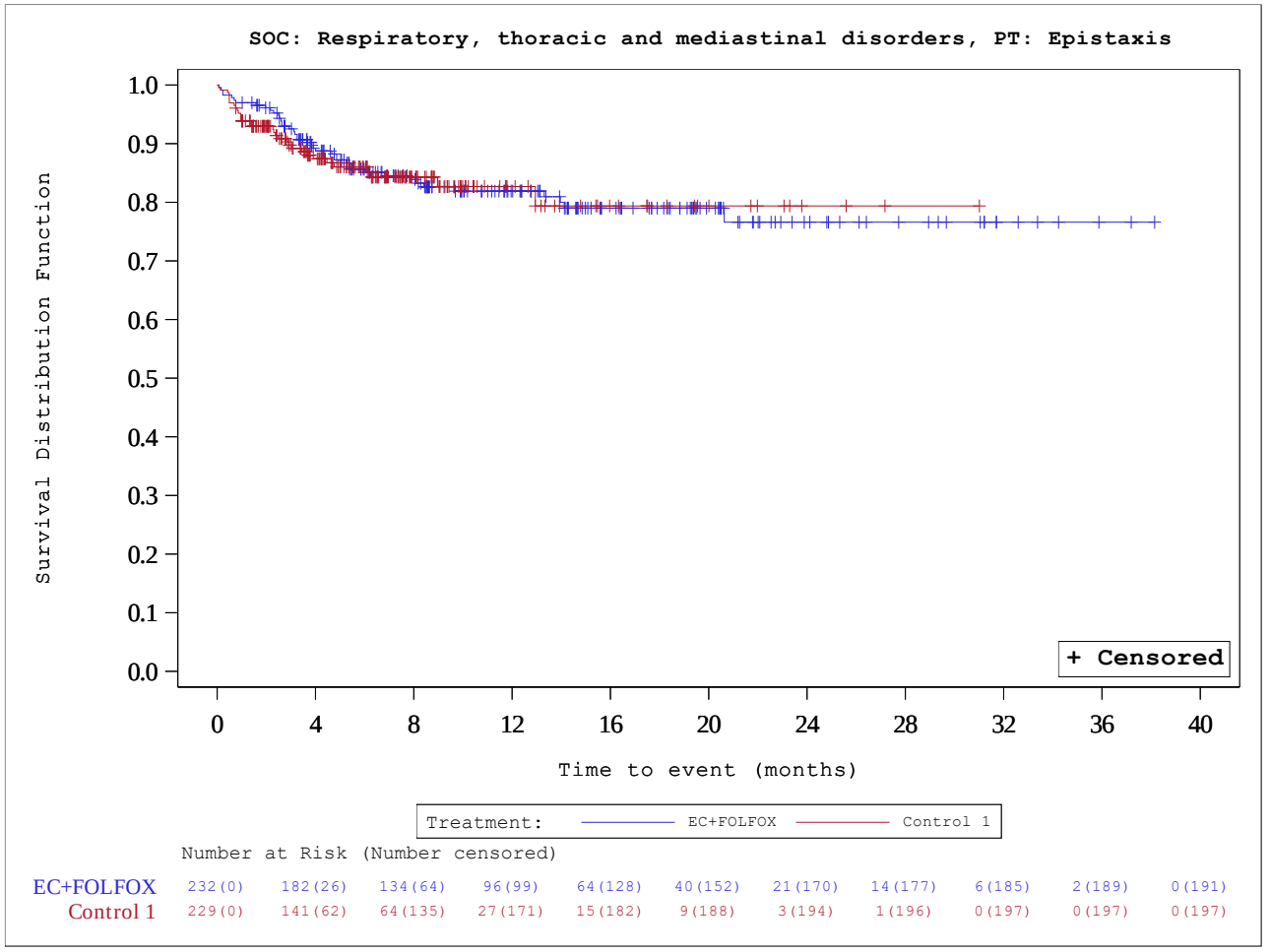

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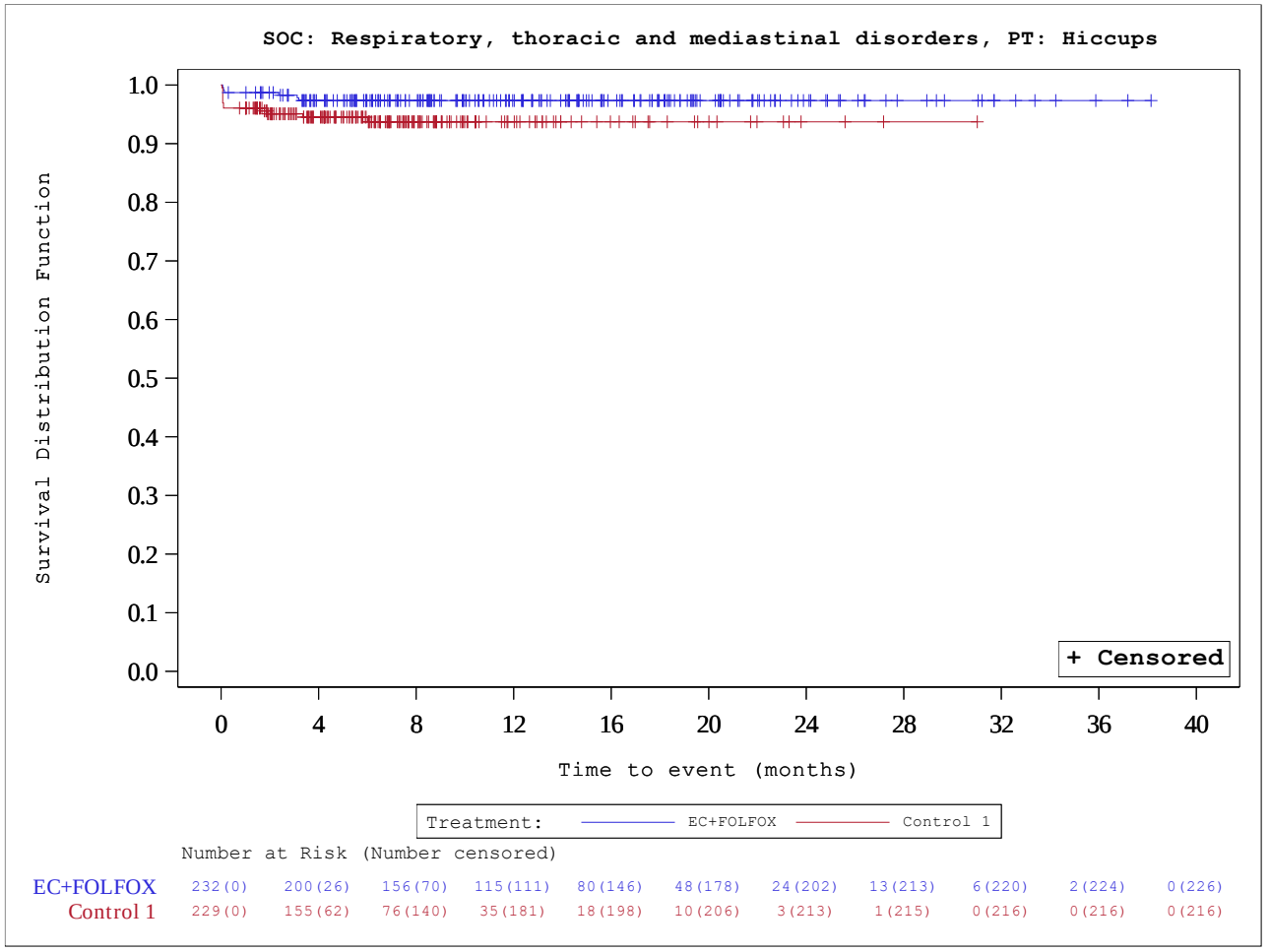

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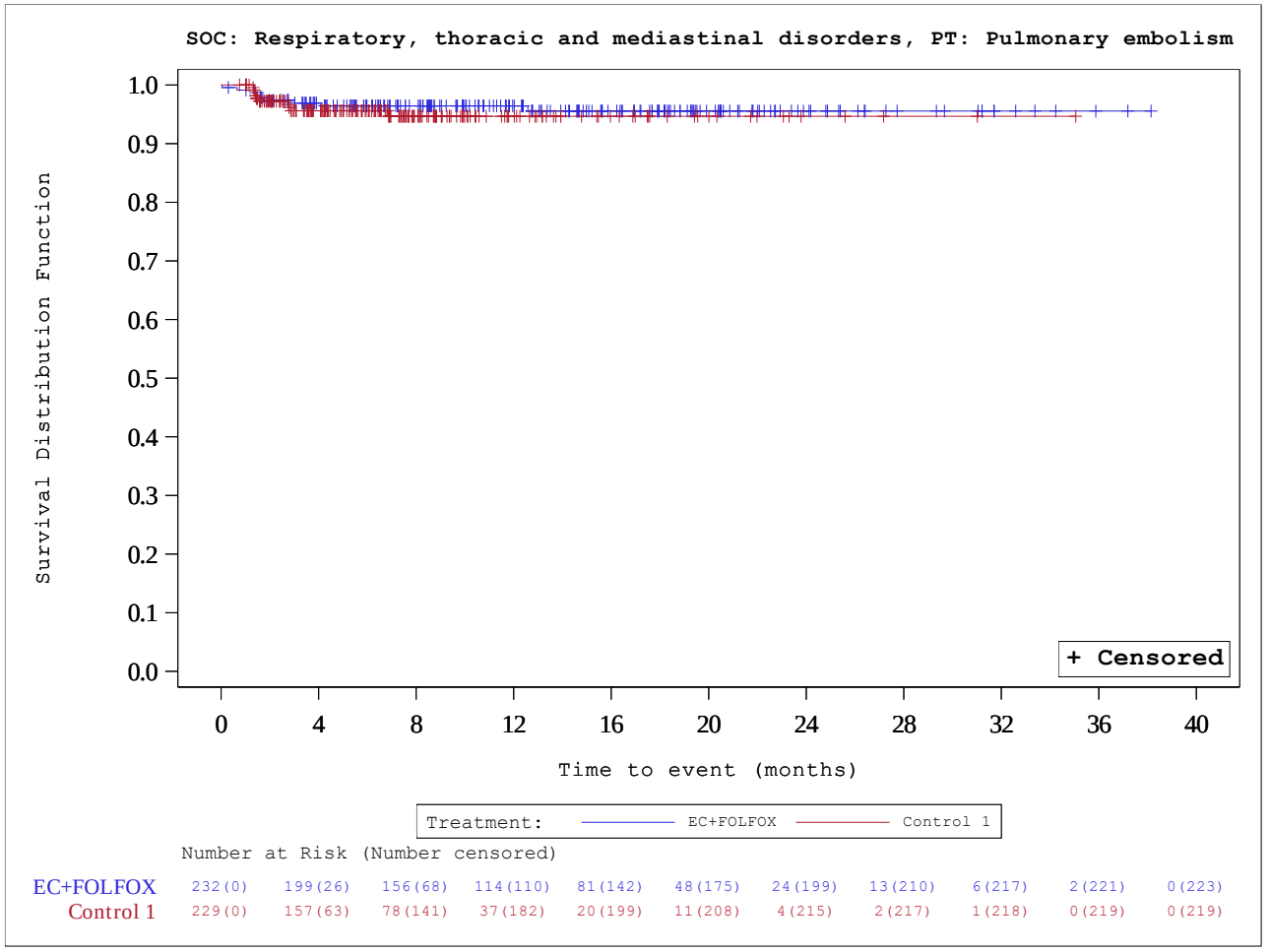

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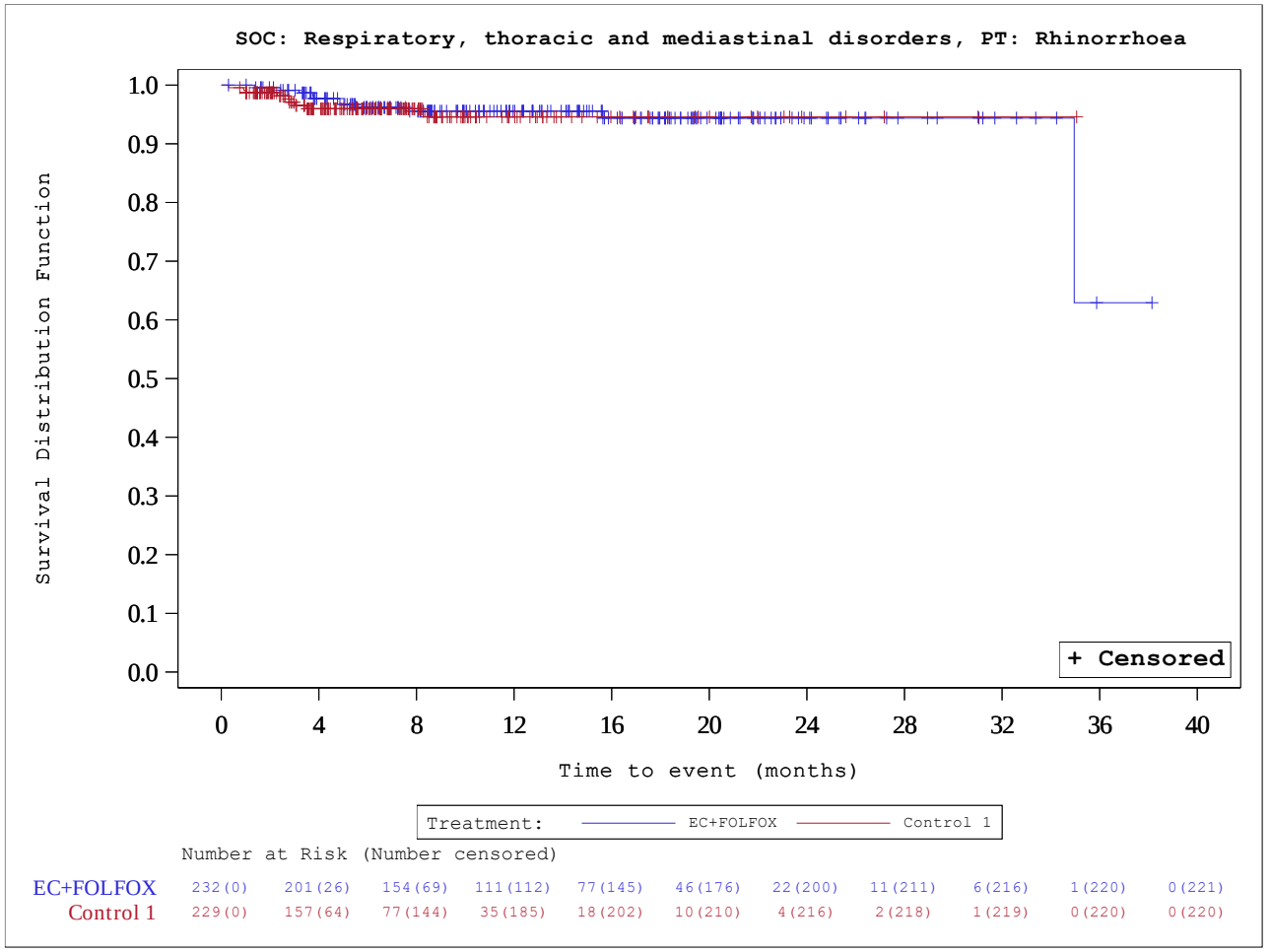

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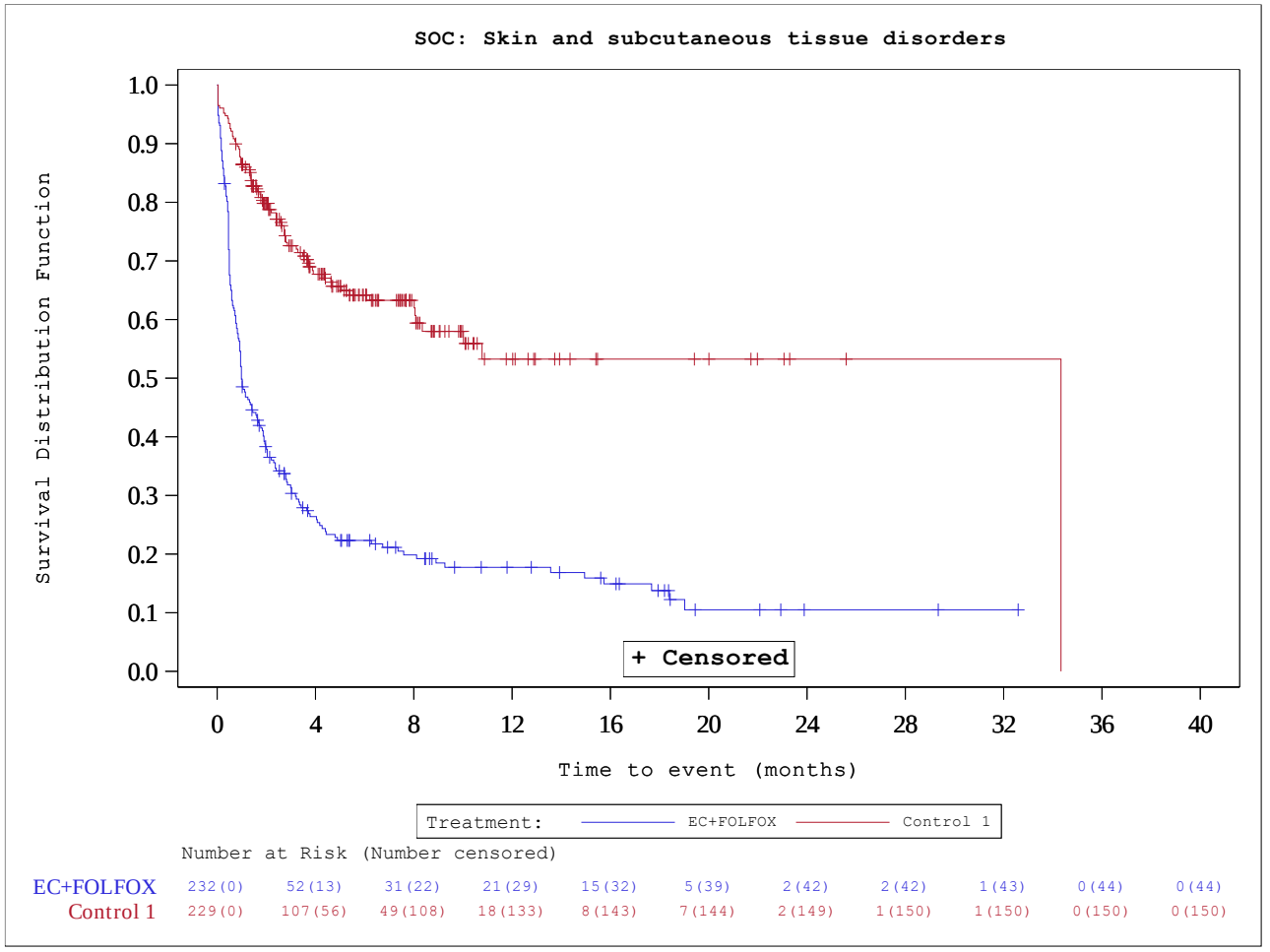

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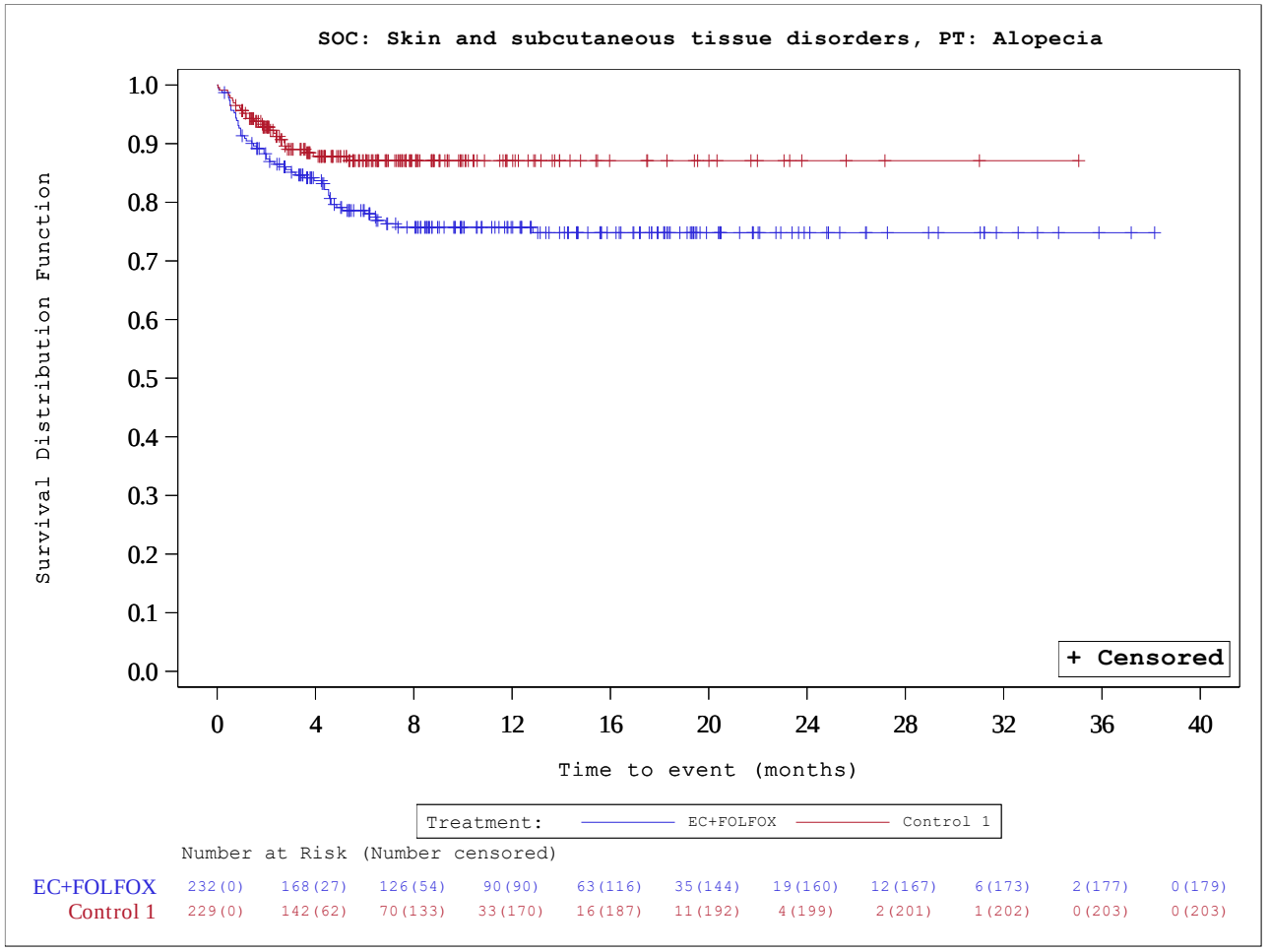

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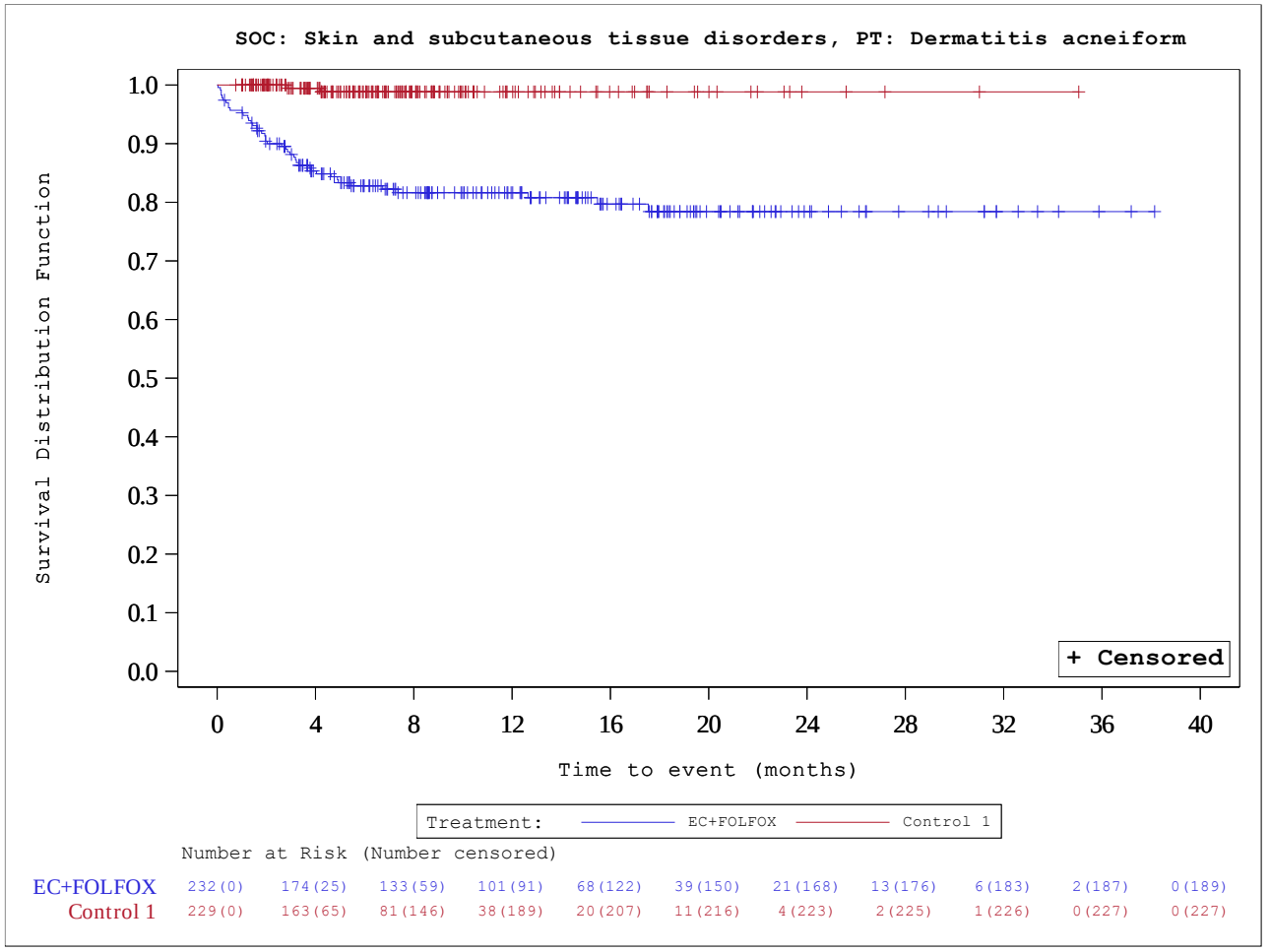

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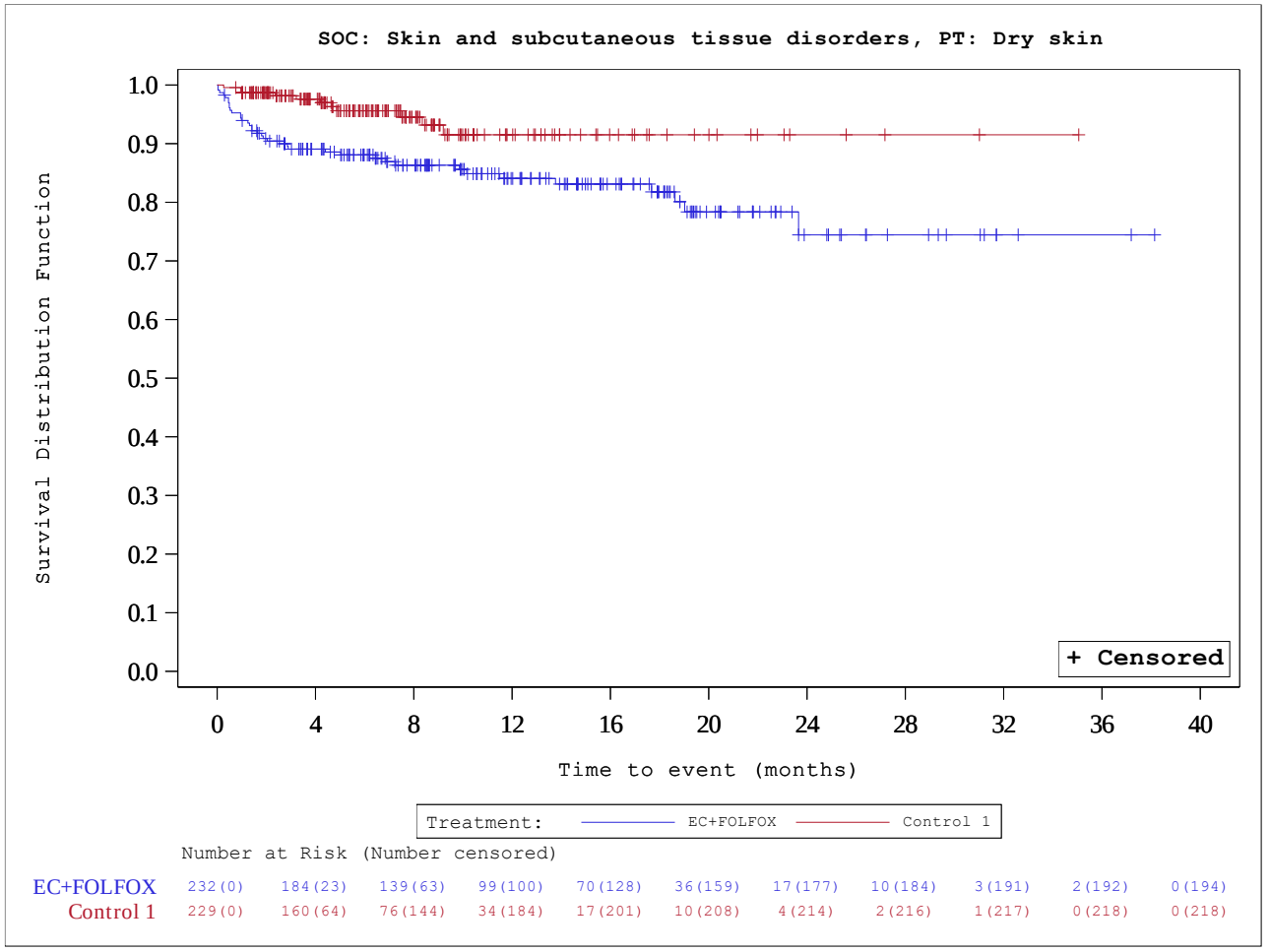

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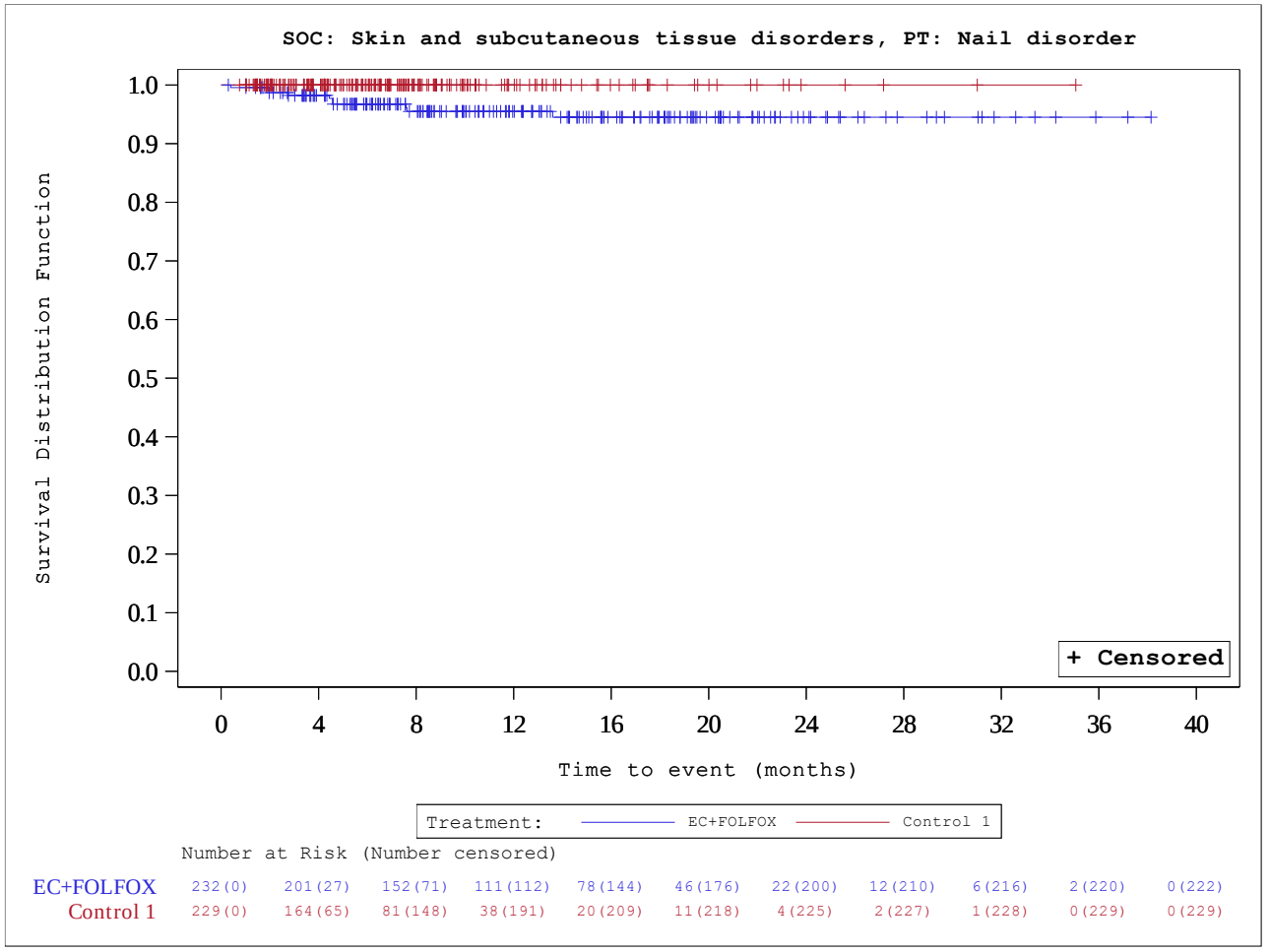

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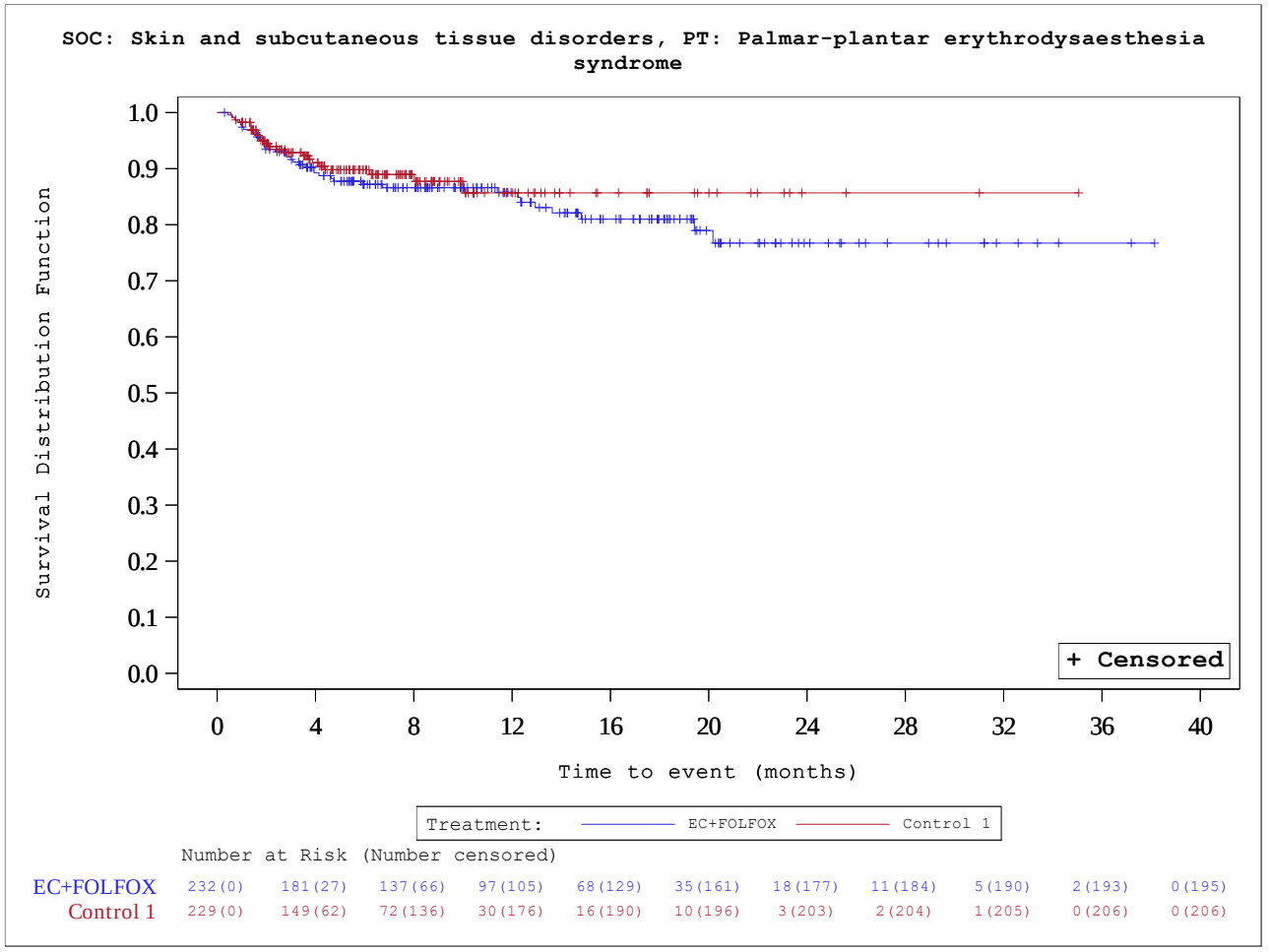

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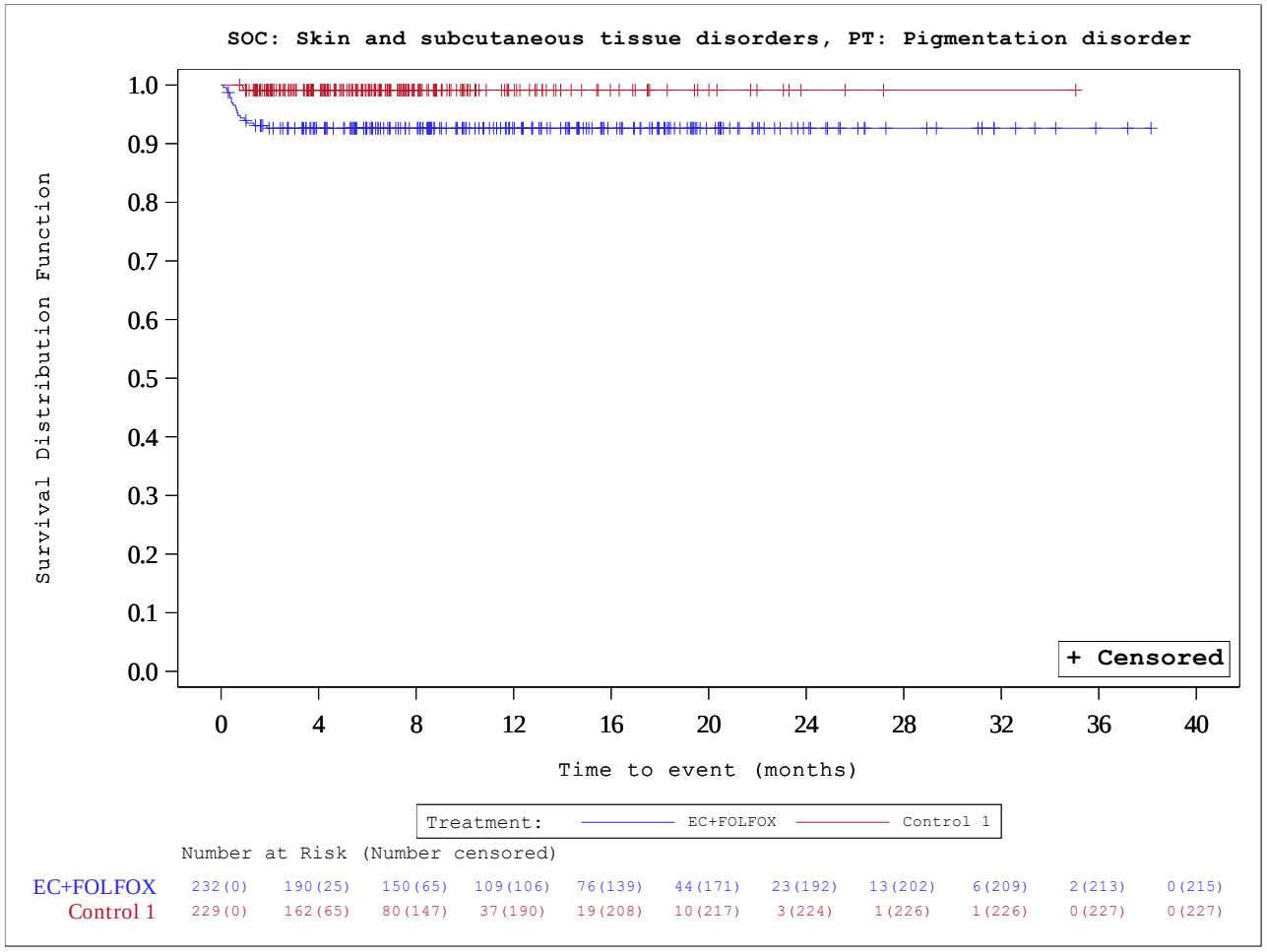

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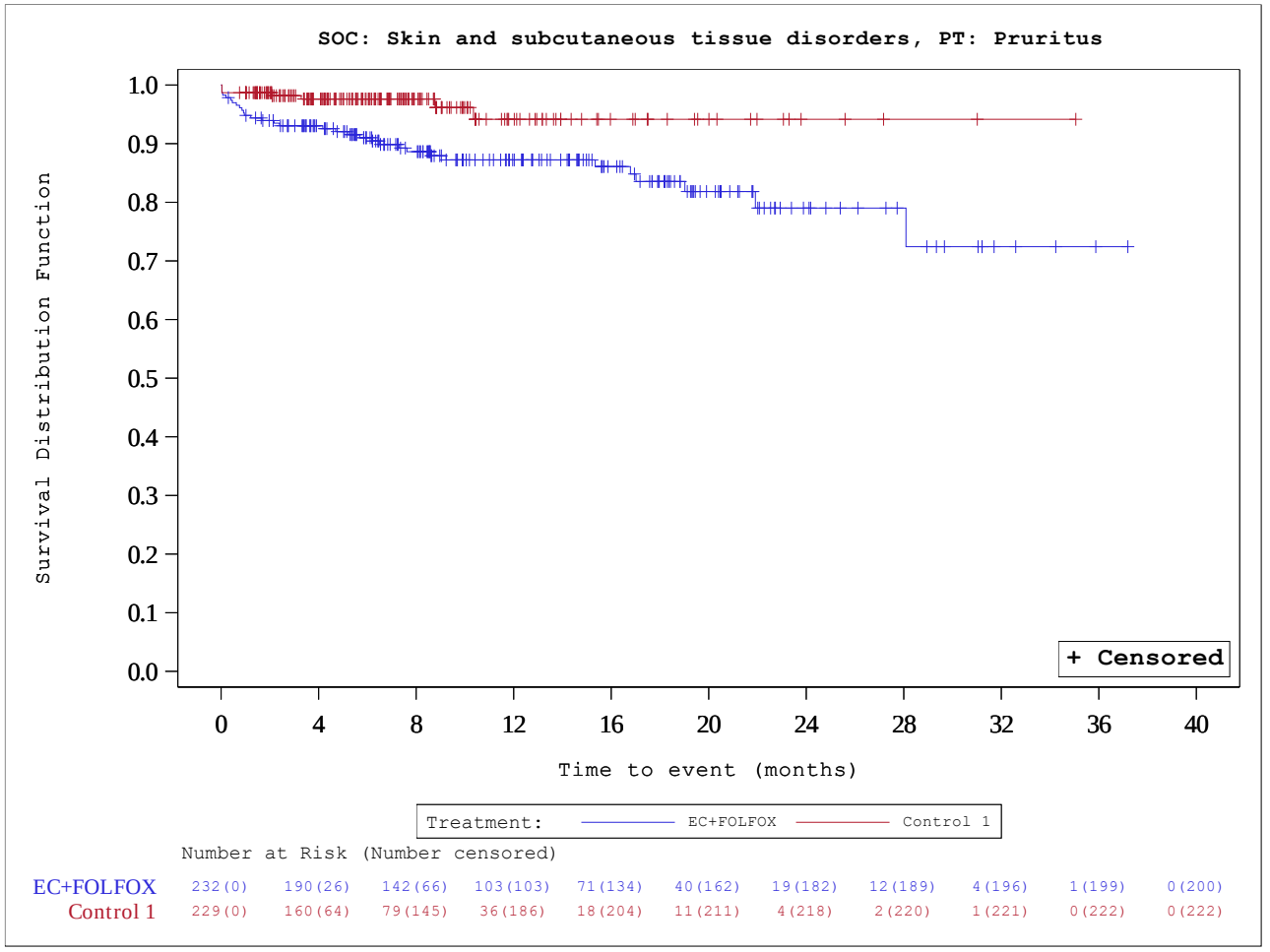

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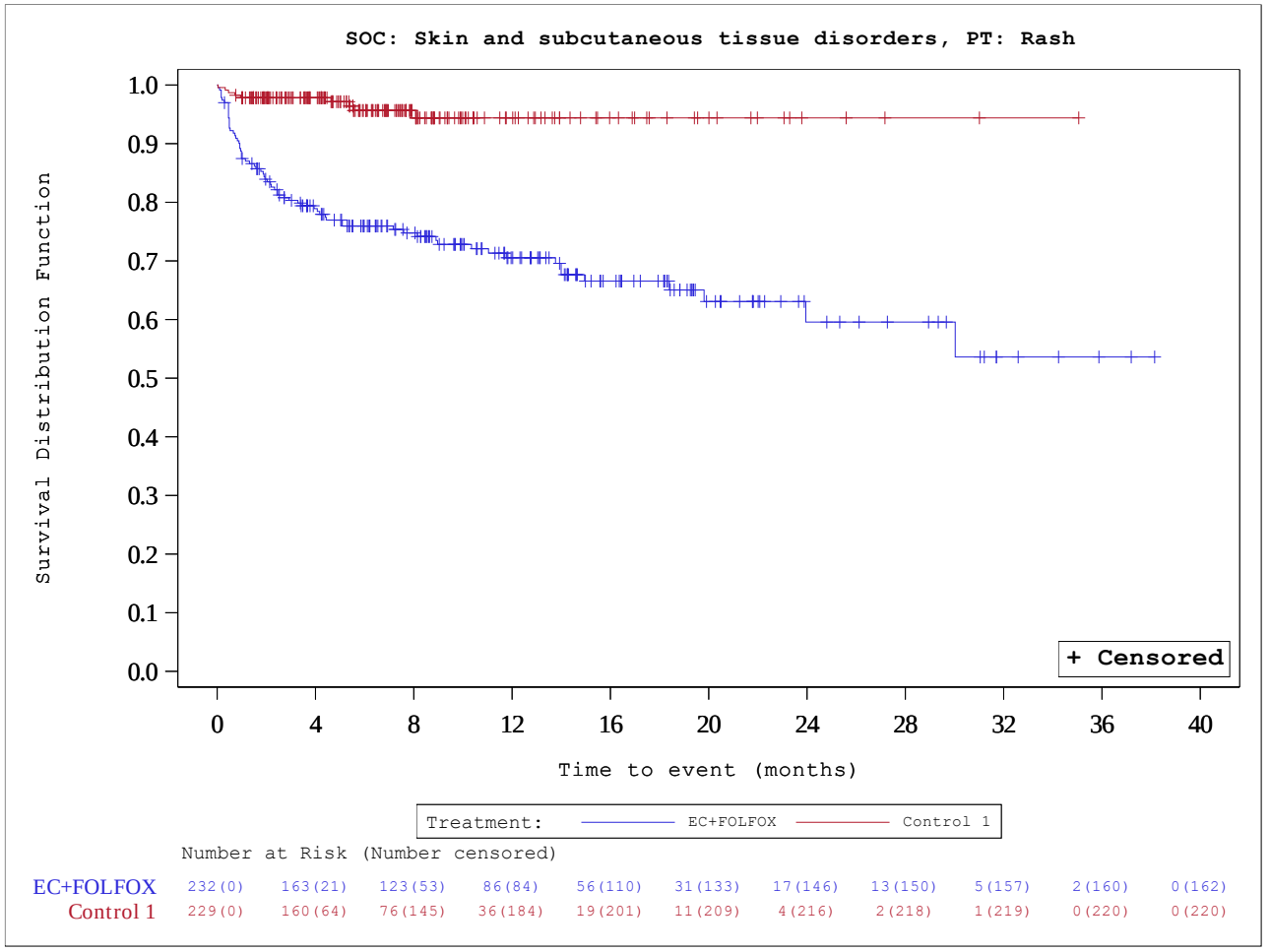

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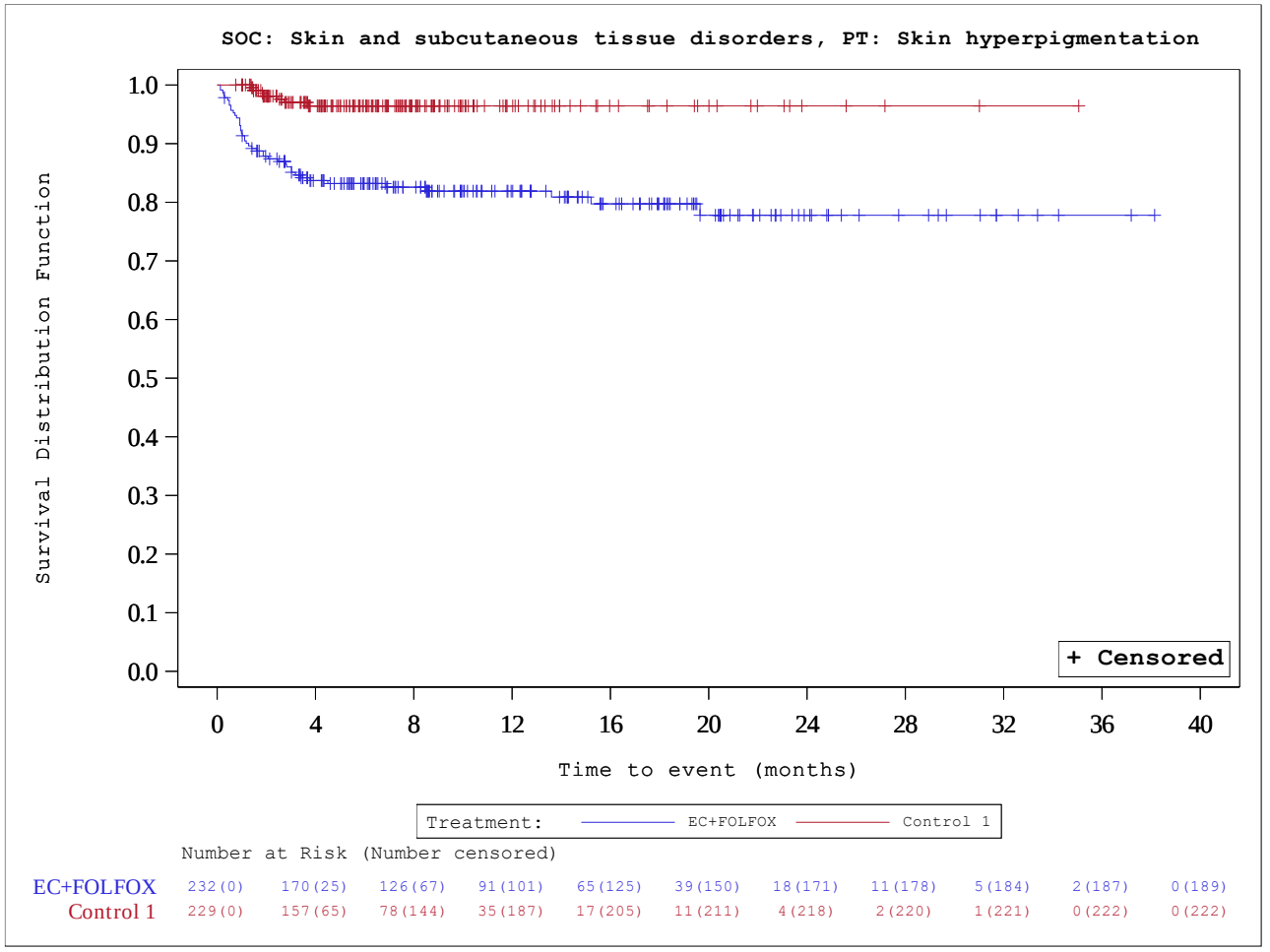

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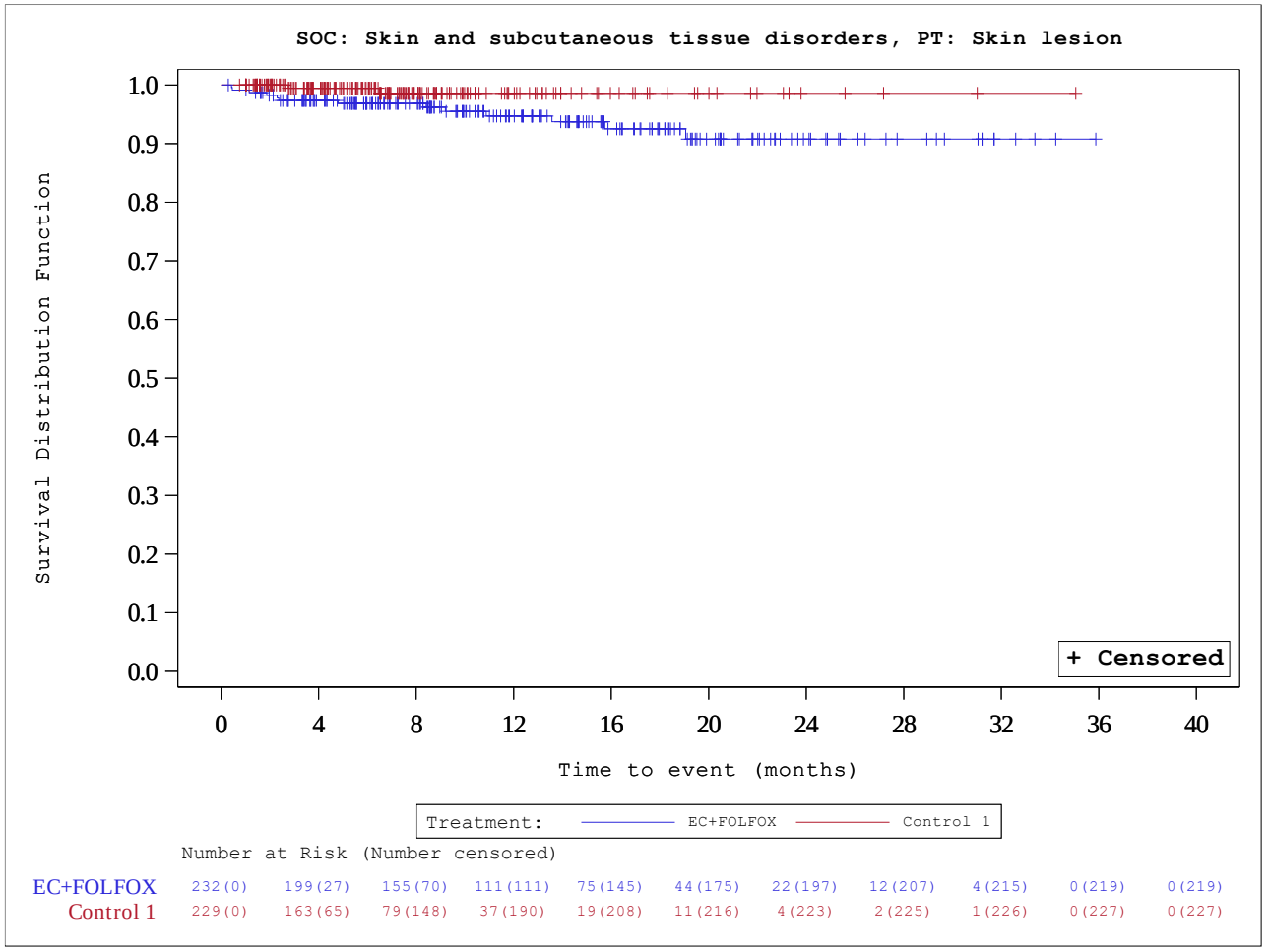

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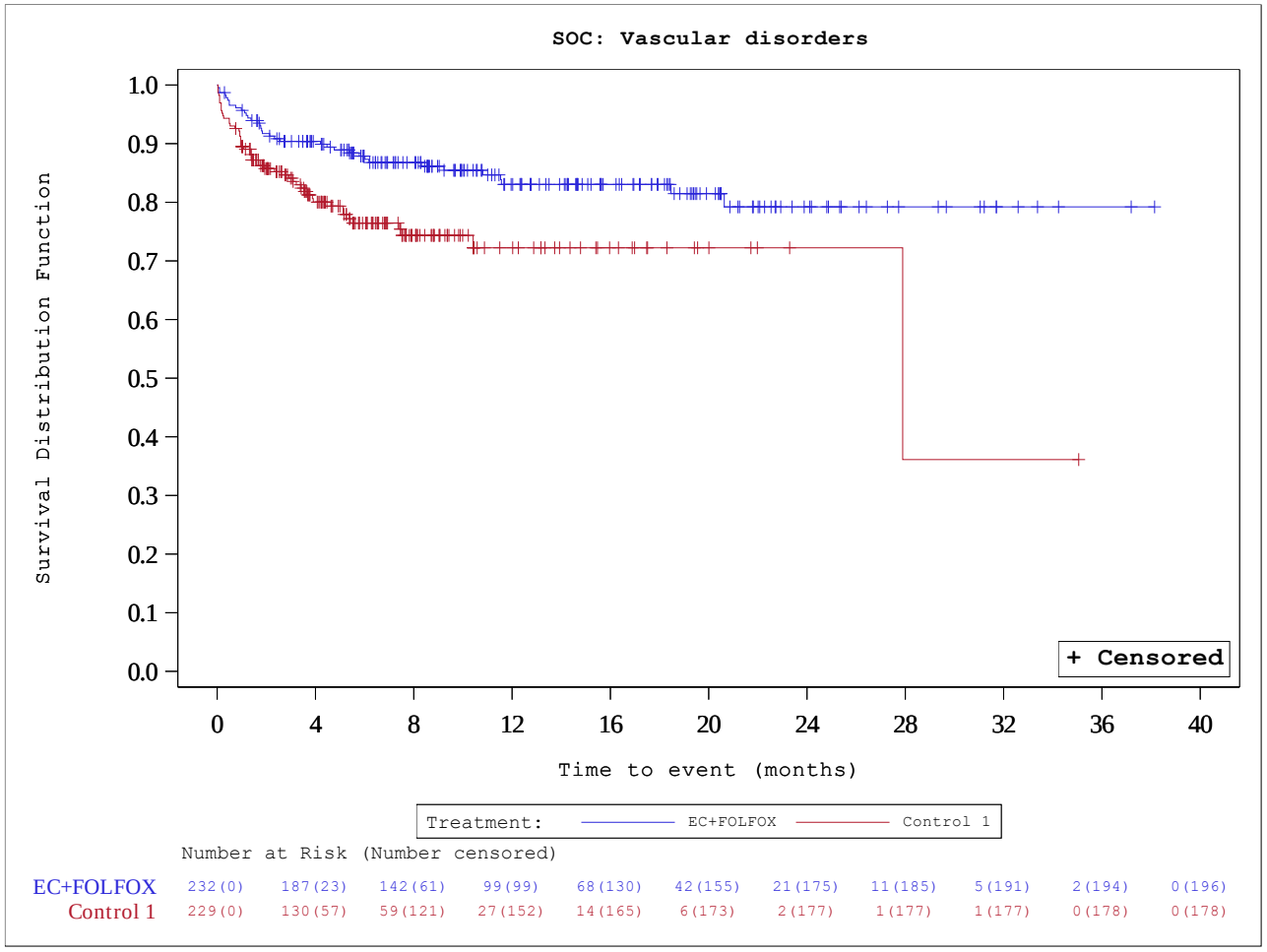
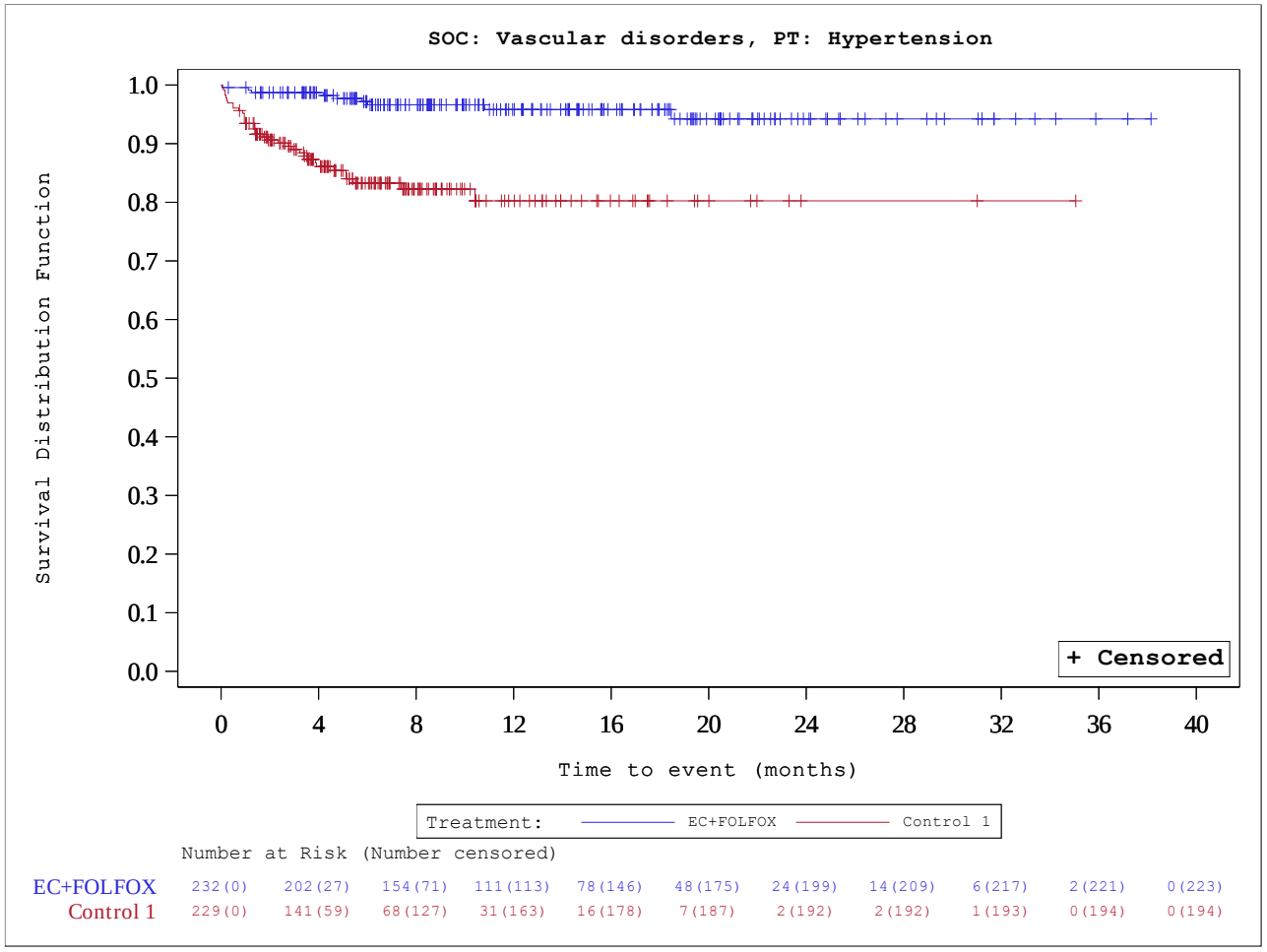
Kaplan Meier Plot of frequent Frequent AE by SOC, PT (incidence >= 10% or >=10 patients and incidence >= 1%)
Safety Analysis Set



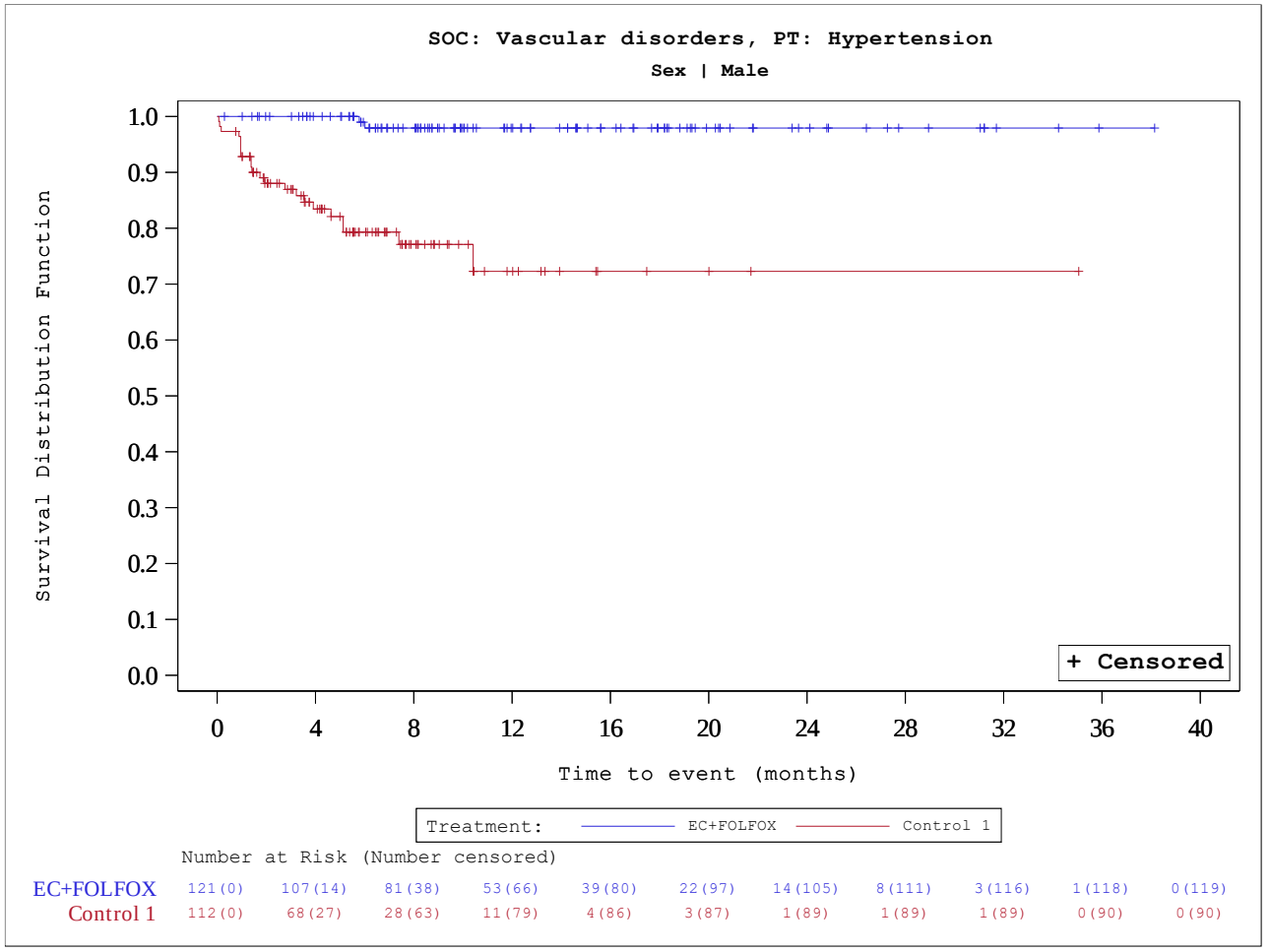
Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
Subgroup analysis was done for SOCs / PTs with significant overall treatment effect (significant log-rank).
Kaplan-Meier Plots for subgroups only created if p-value for interaction < 0.05.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Kaplan Meier Plot of frequent Frequent AE by SOC, PT (incidence >= 10% or >=10 patients and incidence >= 1%)
Safety Analysis Set



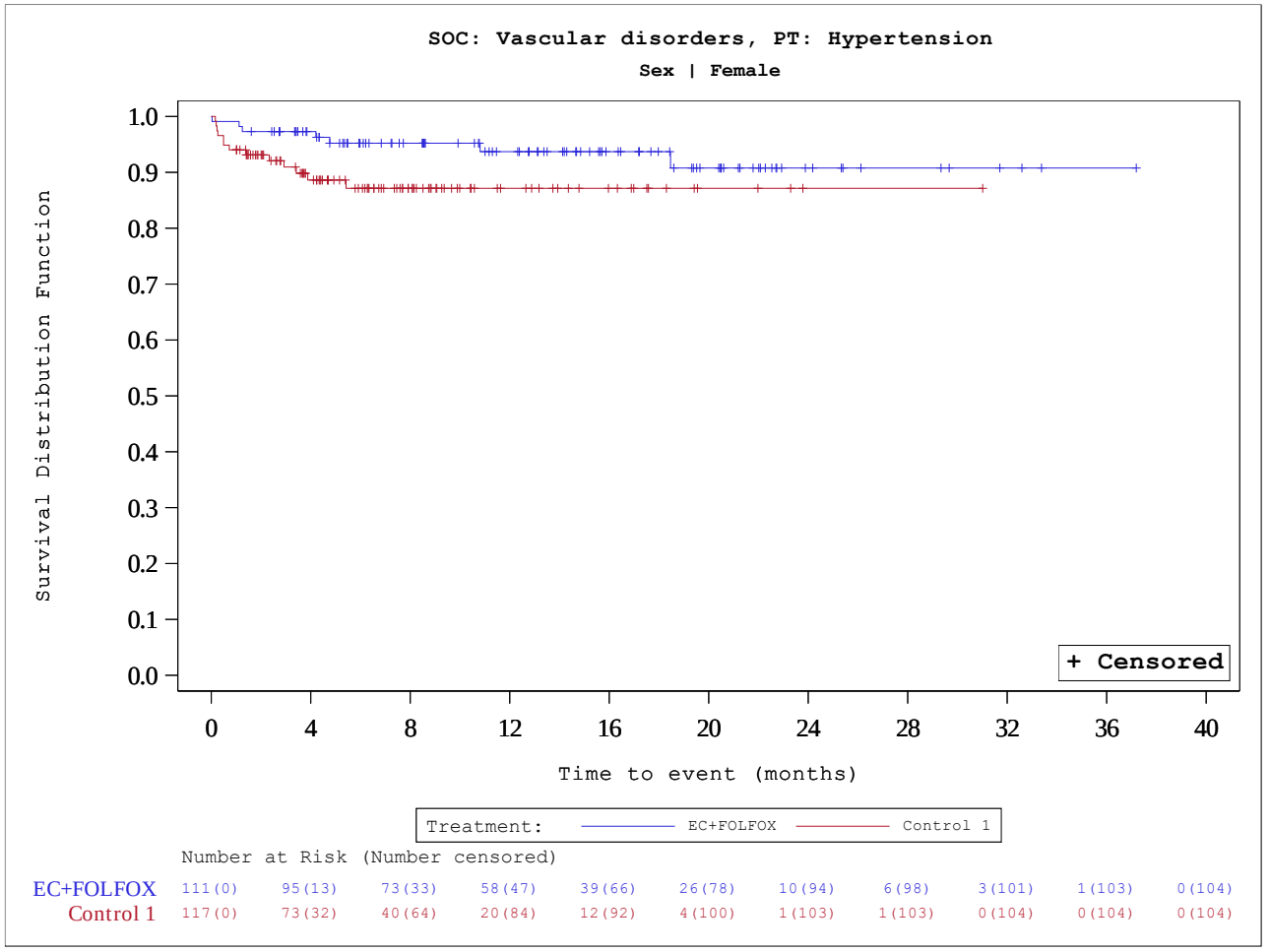
Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
Subgroup analysis was done for SOCs / PTs with significant overall treatment effect (significant log-rank).
Kaplan-Meier Plots for subgroups only created if p-value for interaction < 0.05.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Kaplan Meier Plot of frequent Frequent AE by SOC, PT (incidence >= 10% or >=10 patients and incidence >= 1%)
Safety Analysis Set



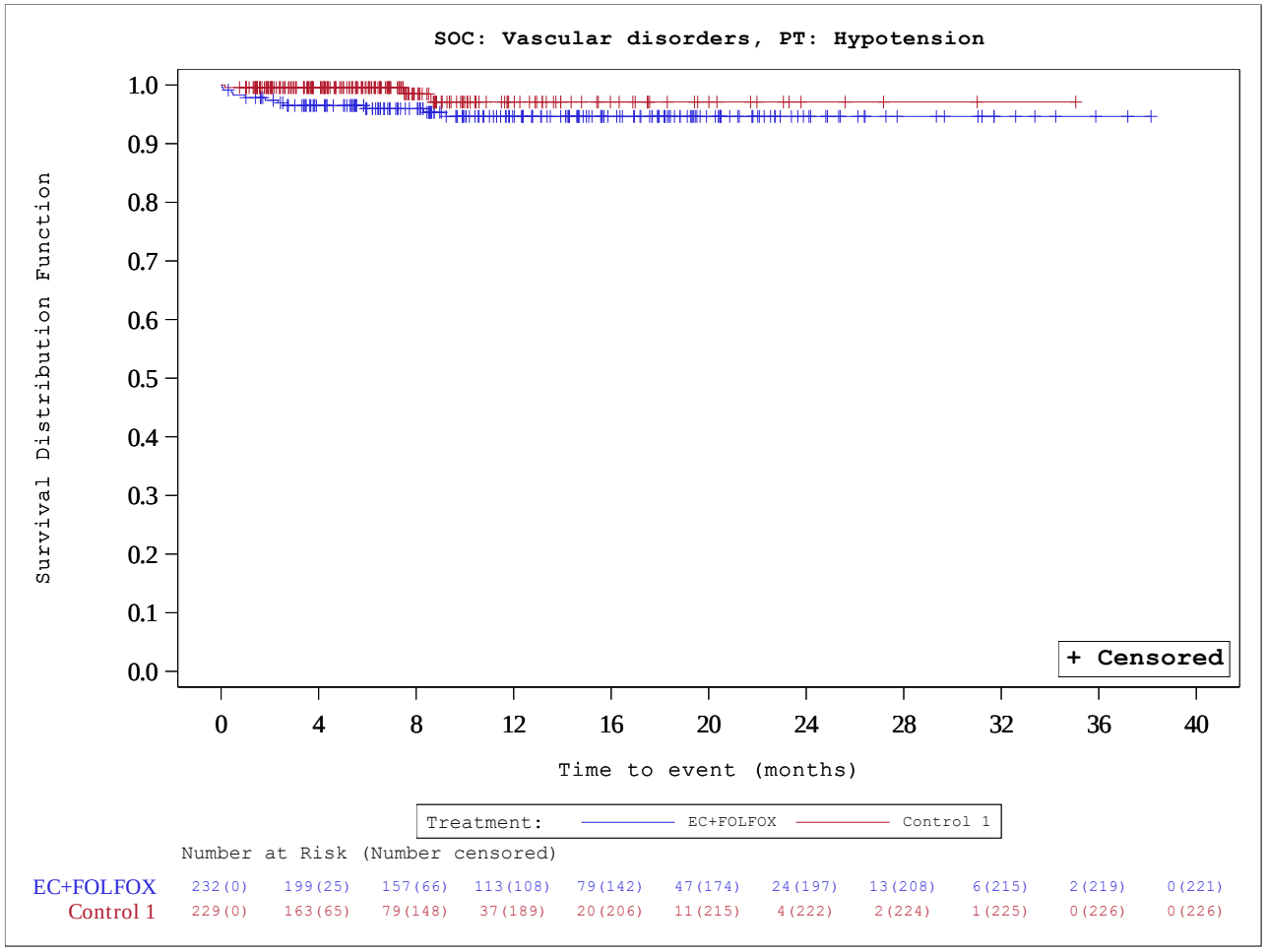
Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
Subgroup analysis was done for SOCs / PTs with significant overall treatment effect (significant log-rank).
Kaplan-Meier Plots for subgroups only created if p-value for interaction < 0.05.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Kaplan Meier Plot of frequent Frequent AE by SOC, PT (incidence >= 10% or >=10 patients and incidence >= 1%)
Safety Analysis Set



Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
Subgroup analysis was done for SOCs / PTs with significant overall treatment effect (significant log-rank).
Kaplan-Meier Plots for subgroups only created if p-value for interaction < 0.05.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Kaplan Meier Plot of frequent Frequent AE by SOC, PT (incidence >= 10% or >=10 patients and incidence >= 1%)
Safety Analysis Set



Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
Subgroup analysis was done for SOCs / PTs with significant overall treatment effect (significant log-rank).
Kaplan-Meier Plots for subgroups only created if p-value for interaction < 0.05.

		EC+FOLFOX (N=232)	Control 1 (N=229)
SOC: Blood and lymphatic system disorders	Number of subjects with events, n (%)	12 (5.2)	12 (5.2)
	Number of censored subjects, n (%)	220 (94.8)	217 (94.8)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Median (95% CI)	NE (NE, NE)	NE (NE, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	0.77 (0.34, 1.73)	
	p-value [3]	0.5238	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Frequent Serious AE by SOC, PT (incidence >= 5% or >=10 patients and incidence >= 1%)
Safety Analysis Set

		EC+FOLFOX (N=232)	Control 1 (N=229)
SOC: Gastrointestinal disorders	Number of subjects with events, n (%)	40 (17.2)	39 (17.0)
	Number of censored subjects, n (%)	192 (82.8)	190 (83.0)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	25.4 (14.4, NE)	12.5 (8.6, NE)
	Median (95% CI)	NE (NE, NE)	NE (NE, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	0.74 (0.47, 1.16)	
	p-value [3]	0.1831	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Frequent Serious AE by SOC, PT (incidence >= 5% or >=10 patients and incidence >= 1%)
Safety Analysis Set

		EC+FOLFOX (N=232)	Control 1 (N=229)
SOC: Gastrointestinal disorders, PT: Intestinal obstruction	Number of subjects with events, n (%)	11 (4.7)	5 (2.2)
	Number of censored subjects, n (%)	221 (95.3)	224 (97.8)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Median (95% CI)	NE (NE, NE)	NE (NE, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	1.47 (0.50, 4.33)	
	p-value [3]	0.4800	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Frequent Serious AE by SOC, PT (incidence >= 5% or >=10 patients and incidence >= 1%)
Safety Analysis Set

		EC+FOLFOX (N=232)	Control 1 (N=229)
SOC: General disorders and administration site conditions	Number of subjects with events, n (%)	23 (9.9)	8 (3.5)
	Number of censored subjects, n (%)	209 (90.1)	221 (96.5)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Median (95% CI)	NE (NE, NE)	NE (NE, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	2.15 (0.95, 4.85)	
	p-value [3]	0.0591	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Frequent Serious AE by SOC, PT (incidence >= 5% or >=10 patients and incidence >= 1%)
Safety Analysis Set

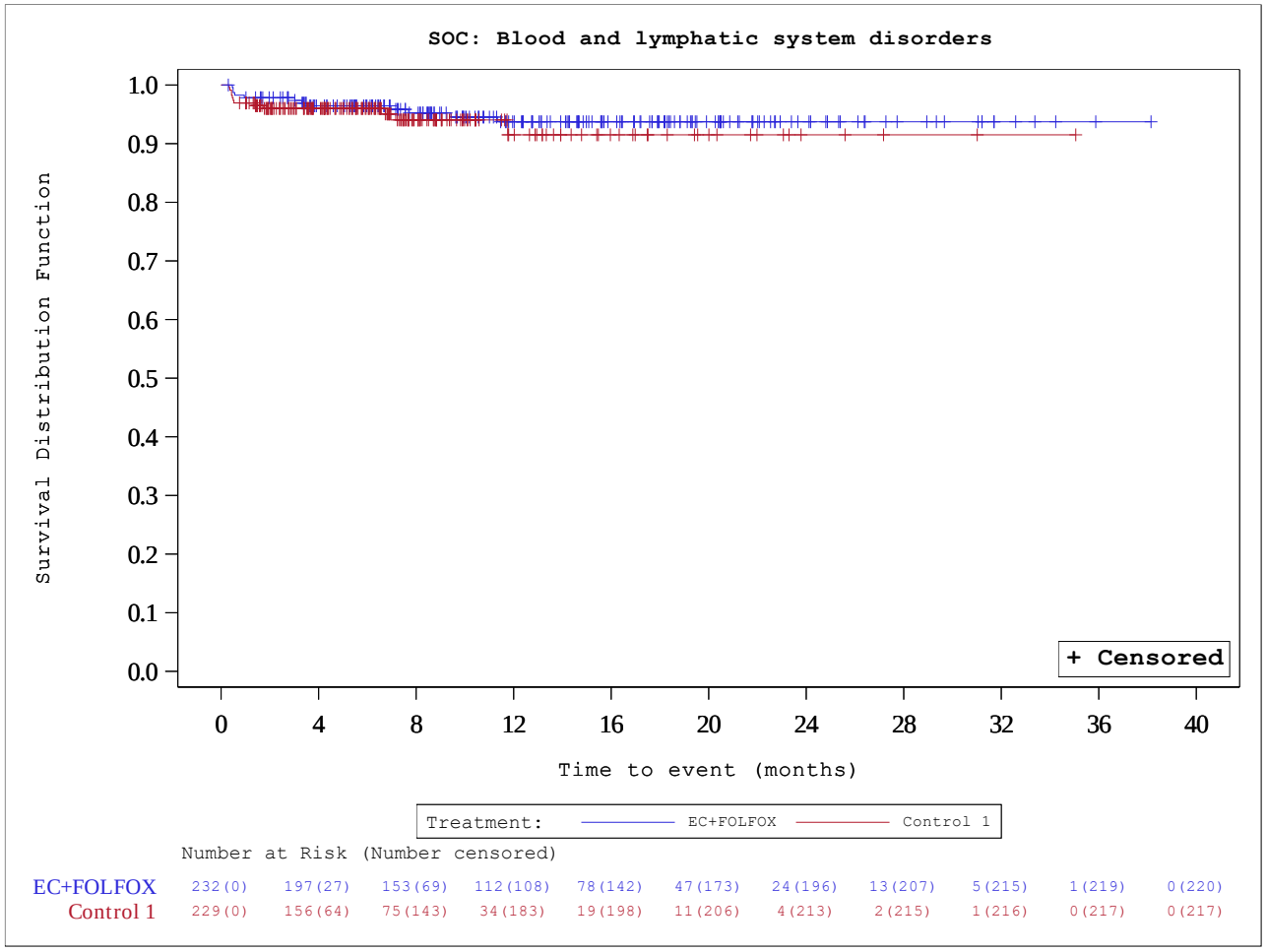
		EC+FOLFOX (N=232)	Control 1 (N=229)
SOC: Infections and infestations	Number of subjects with events, n (%)	22 (9.5)	24 (10.5)
	Number of censored subjects, n (%)	210 (90.5)	205 (89.5)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	NE (NE, NE)	NE (14.5, NE)
	Median (95% CI)	NE (NE, NE)	NE (NE, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	0.67 (0.37, 1.21)	
	p-value [3]	0.1825	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.

- NO OBSERVATIONS FOR THIS REPORT -

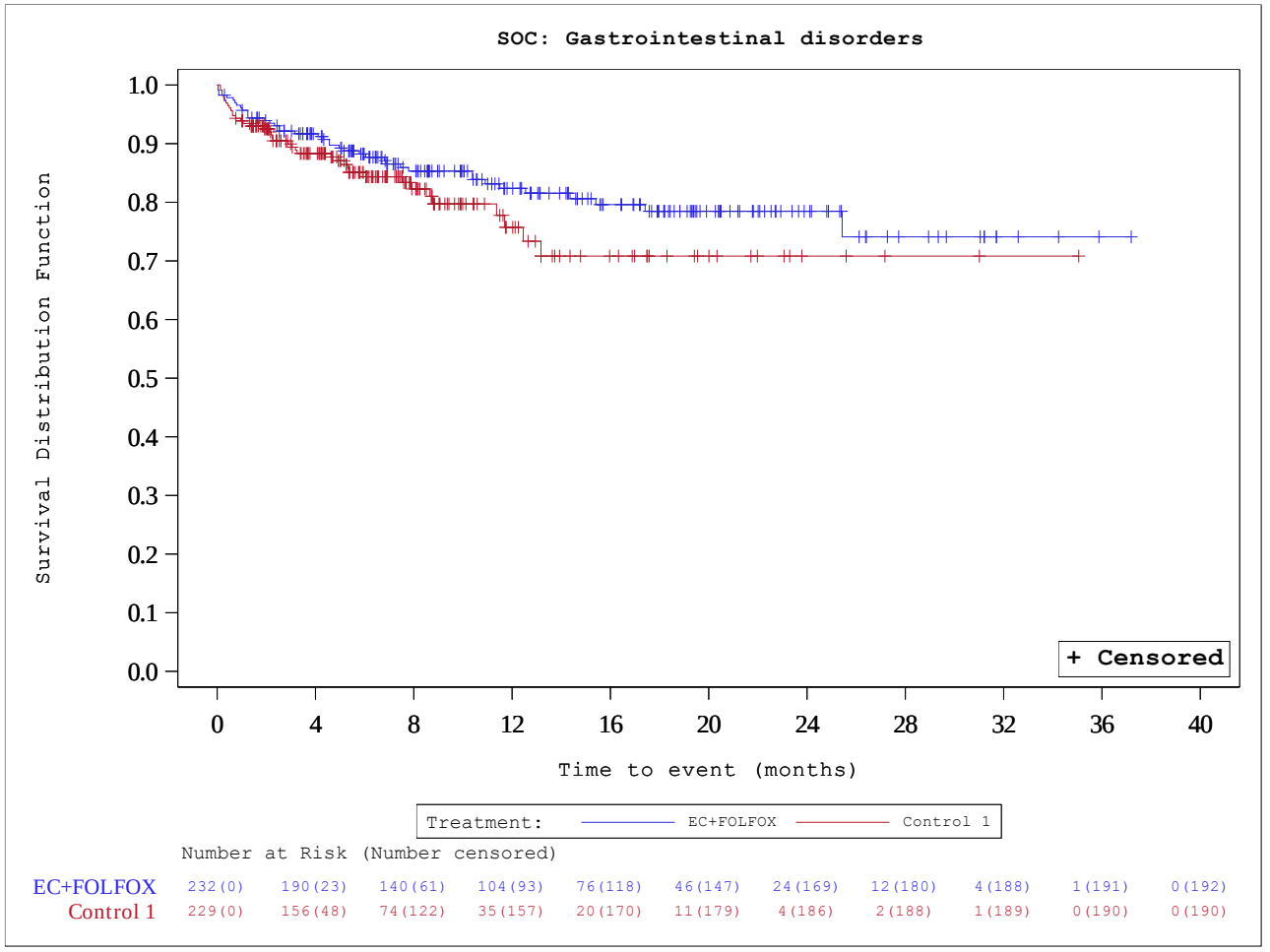
Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
Subgroup analysis was done for SOCs / PTs with significant overall treatment effect (significant log-rank).
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.
[4] P-Value for interaction from Cox proportional hazards model using ties=exact option with treatment, subgroup and treatment*subgroup interaction as covariates.
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Kaplan Meier Plot of frequent Frequent Serious AE by SOC, PT (incidence >= 5% or >=10 patients and incidence >= 1%)
Safety Analysis Set



Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
Subgroup analysis was done for SOCs / PTs with significant overall treatment effect (significant log-rank).
Kaplan-Meier Plots for subgroups only created if p-value for interaction < 0.05.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Kaplan Meier Plot of frequent Frequent Serious AE by SOC, PT (incidence >= 5% or >=10 patients and incidence >= 1%)
Safety Analysis Set



Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
Subgroup analysis was done for SOCs / PTs with significant overall treatment effect (significant log-rank).
Kaplan-Meier Plots for subgroups only created if p-value for interaction < 0.05.

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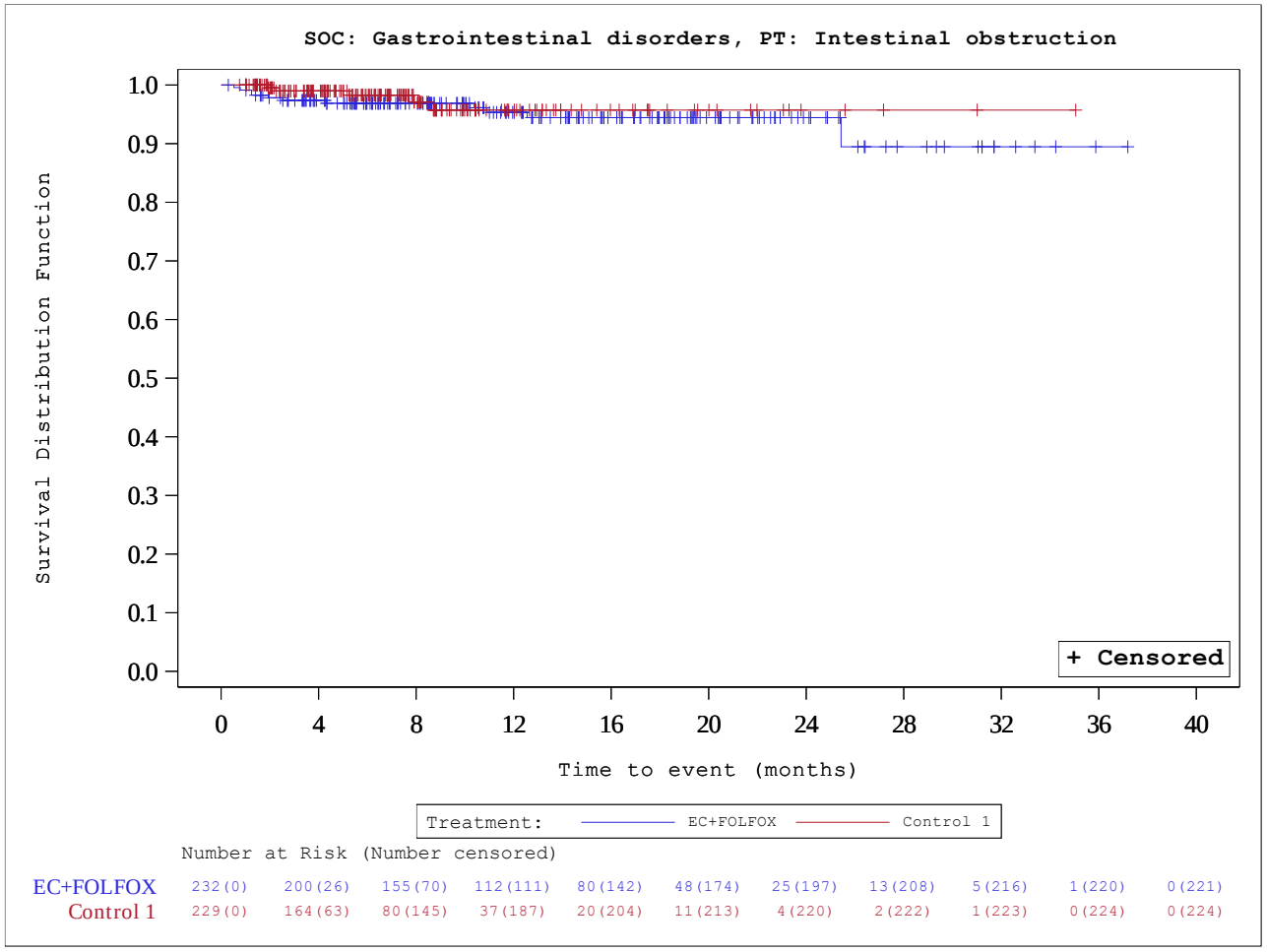
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Kaplan Meier Plot of frequent Frequent Serious AE by SOC, PT (incidence >= 5% or >=10 patients and incidence >= 1%)
Safety Analysis Set



Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
Subgroup analysis was done for SOCs / PTs with significant overall treatment effect (significant log-rank).
Kaplan-Meier Plots for subgroups only created if p-value for interaction < 0.05.

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Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
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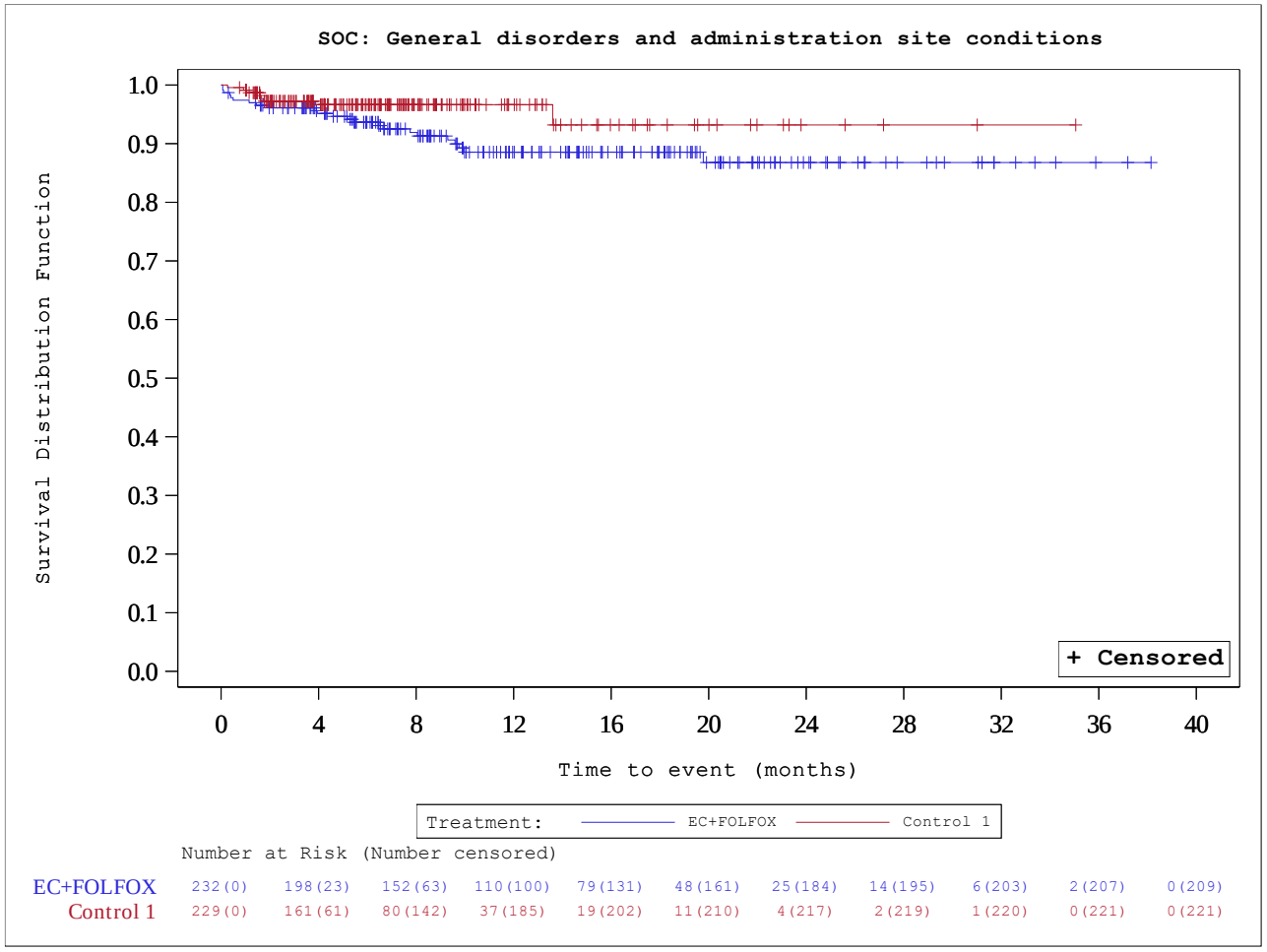
Kaplan Meier Plot of frequent Frequent Serious AE by SOC, PT (incidence >= 5% or >=10 patients and incidence >= 1%)
Safety Analysis Set



Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
Subgroup analysis was done for SOCs / PTs with significant overall treatment effect (significant log-rank).
Kaplan-Meier Plots for subgroups only created if p-value for interaction < 0.05.

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Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
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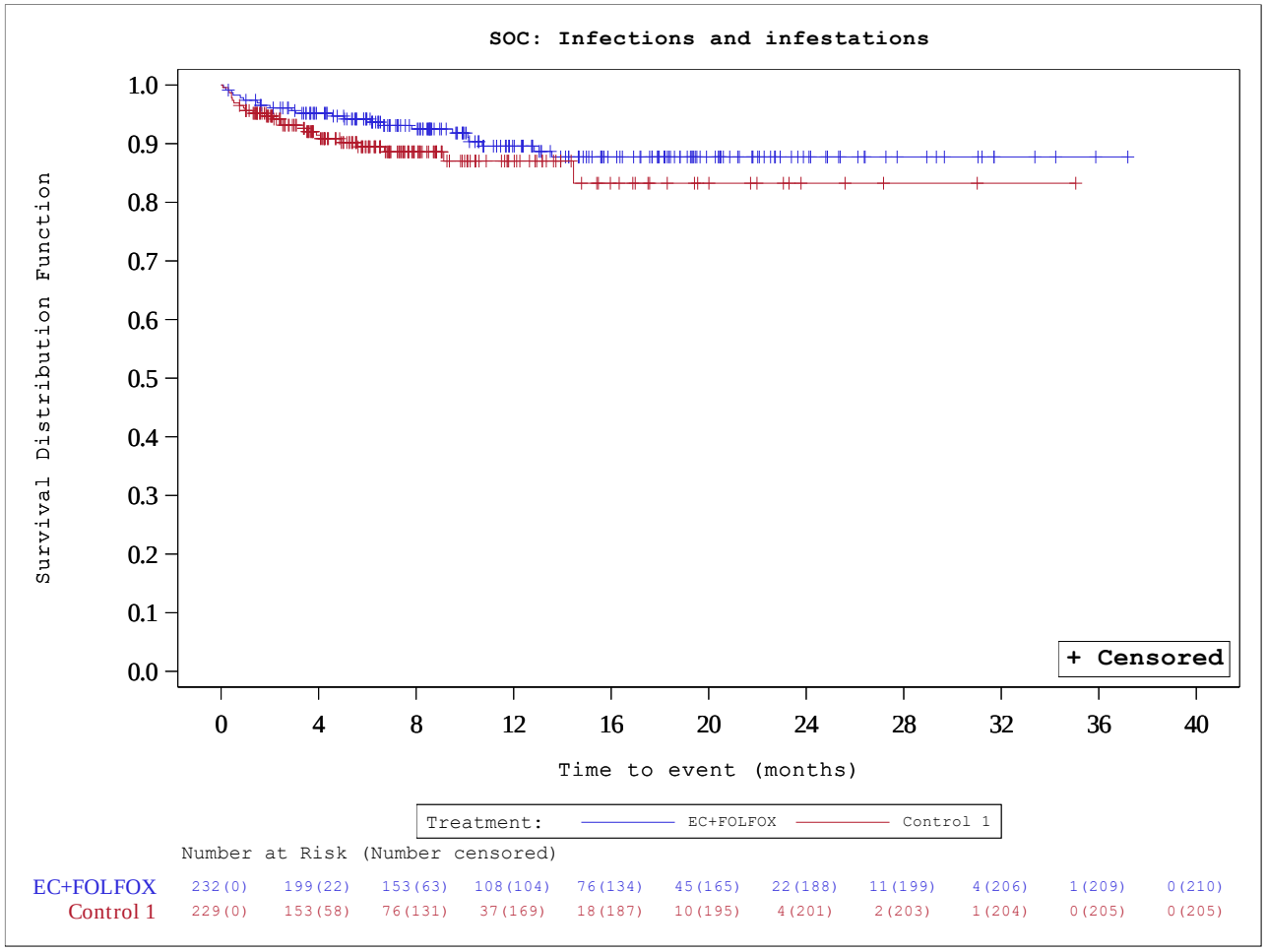
Kaplan Meier Plot of frequent Frequent Serious AE by SOC, PT (incidence >= 5% or >=10 patients and incidence >= 1%)
Safety Analysis Set



Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
Subgroup analysis was done for SOCs / PTs with significant overall treatment effect (significant log-rank).
Kaplan-Meier Plots for subgroups only created if p-value for interaction < 0.05.

		EC+FOLFOX (N=232)	Control 1 (N=229)
SOC: Blood and lymphatic system disorders	Number of subjects with events, n (%)	67 (28.9)	43 (18.8)
	Number of censored subjects, n (%)	165 (71.1)	186 (81.2)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	6.2 (3.6, 13.8)	13.4 (7.2, NE)
	Median (95% CI)	NE (NE, NE)	NE (15.9, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	1.31 (0.89, 1.92)	
	p-value [3]	0.1783	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.

		EC+FOLFOX (N=232)	Control 1 (N=229)
SOC: Blood and lymphatic system disorders, PT: Anaemia	Number of subjects with events, n (%)	35 (15.1)	9 (3.9)
	Number of censored subjects, n (%)	197 (84.9)	220 (96.1)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	NE (14.3, NE)	NE (NE, NE)
	Median (95% CI)	NE (NE, NE)	NE (NE, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	2.70 (1.29, 5.67)	
	p-value [3]	0.0063	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.

		EC+FOLFOX (N=232)	Control 1 (N=229)
SOC: Blood and lymphatic system disorders, PT: Febrile neutropenia	Number of subjects with events, n (%)	5 (2.2)	11 (4.8)
	Number of censored subjects, n (%)	227 (97.8)	218 (95.2)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Median (95% CI)	NE (NE, NE)	NE (NE, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	0.43 (0.15, 1.23)	
	p-value [3]	0.1035	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.

		EC+FOLFOX (N=232)	Control 1 (N=229)
SOC: Blood and lymphatic system disorders, PT: Neutropenia	Number of subjects with events, n (%)	35 (15.1)	23 (10.0)
	Number of censored subjects, n (%)	197 (84.9)	206 (90.0)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	NE (NE, NE)	NE (15.9, NE)
	Median (95% CI)	NE (NE, NE)	NE (NE, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	1.39 (0.82, 2.36)	
	p-value [3]	0.2252	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Frequent Severe AE by SOC, PT (incidence >= 5% or >=10 patients and incidence >= 1%)
Safety Analysis Set

		EC+FOLFOX (N=232)	Control 1 (N=229)
SOC: Gastrointestinal disorders	Number of subjects with events, n (%)	53 (22.8)	46 (20.1)
	Number of censored subjects, n (%)	179 (77.2)	183 (79.9)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	17.4 (10.4, NE)	11.4 (6.0, NE)
	Median (95% CI)	NE (NE, NE)	NE (NE, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	0.87 (0.58, 1.31)	
	p-value [3]	0.5100	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.

		EC+FOLFOX (N=232)	Control 1 (N=229)
SOC: Gastrointestinal disorders, PT: Abdominal pain	Number of subjects with events, n (%)	11 (4.7)	3 (1.3)
	Number of censored subjects, n (%)	221 (95.3)	226 (98.7)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Median (95% CI)	NE (NE, NE)	NE (NE, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	2.48 (0.68, 9.05)	
	p-value [3]	0.1547	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.

		EC+FOLFOX (N=232)	Control 1 (N=229)
SOC: Gastrointestinal disorders, PT: Diarrhoea	Number of subjects with events, n (%)	3 (1.3)	11 (4.8)
	Number of censored subjects, n (%)	229 (98.7)	218 (95.2)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Median (95% CI)	NE (NE, NE)	NE (NE, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	0.22 (0.06, 0.78)	
	p-value [3]	0.0108	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.

		EC+FOLFOX (N=232)	Control 1 (N=229)
SOC: Gastrointestinal disorders, PT: Intestinal obstruction	Number of subjects with events, n (%)	12 (5.2)	6 (2.6)
	Number of censored subjects, n (%)	220 (94.8)	223 (97.4)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Median (95% CI)	NE (NE, NE)	NE (NE, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	1.20 (0.44, 3.30)	
	p-value [3]	0.7240	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.

Pierre Fabre Pharma GmbH: Final
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Population: arm B vs. arm C
Datacut: 06JAN2025
Frequent Severe AE by SOC, PT (incidence >= 5% or >=10 patients and incidence >= 1%)
Safety Analysis Set

		EC+FOLFOX (N=232)	Control 1 (N=229)
SOC: General disorders and administration site conditions	Number of subjects with events, n (%)	36 (15.5)	20 (8.7)
	Number of censored subjects, n (%)	196 (84.5)	209 (91.3)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	NE (19.7, NE)	NE (13.6, NE)
	Median (95% CI)	NE (NE, NE)	NE (NE, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	1.28 (0.74, 2.24)	
	p-value [3]	0.3768	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Frequent Severe AE by SOC, PT (incidence >= 5% or >=10 patients and incidence >= 1%)
Safety Analysis Set

		EC+FOLFOX (N=232)	Control 1 (N=229)
SOC: General disorders and administration site conditions, PT: Asthenia	Number of subjects with events, n (%)	12 (5.2)	3 (1.3)
	Number of censored subjects, n (%)	220 (94.8)	226 (98.7)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Median (95% CI)	NE (NE, NE)	NE (NE, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	2.88 (0.80, 10.38)	
	p-value [3]	0.0916	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Frequent Severe AE by SOC, PT (incidence >= 5% or >=10 patients and incidence >= 1%)
Safety Analysis Set

		EC+FOLFOX (N=232)	Control 1 (N=229)
SOC: Infections and infestations	Number of subjects with events, n (%)	29 (12.5)	20 (8.7)
	Number of censored subjects, n (%)	203 (87.5)	209 (91.3)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	28.8 (23.5, NE)	NE (NE, NE)
	Median (95% CI)	NE (30.0, NE)	NE (NE, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	0.98 (0.54, 1.75)	
	p-value [3]	0.9332	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.

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Frequent Severe AE by SOC, PT (incidence >= 5% or >=10 patients and incidence >= 1%)
Safety Analysis Set

		EC+FOLFOX (N=232)	Control 1 (N=229)
SOC: Investigations	Number of subjects with events, n (%)	88 (37.9)	65 (28.4)
	Number of censored subjects, n (%)	144 (62.1)	164 (71.6)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	1.1 (0.6, 2.0)	3.7 (2.3, 8.3)
	Median (95% CI)	NE (NE, NE)	NE (NE, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	1.40 (1.02, 1.93)	
	p-value [3]	0.0419	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.

		EC+FOLFOX (N=232)	Control 1 (N=229)
SOC: Investigations, PT: Lipase increased	Number of subjects with events, n (%)	40 (17.2)	14 (6.1)
	Number of censored subjects, n (%)	192 (82.8)	215 (93.9)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Median (95% CI)	NE (NE, NE)	NE (NE, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	2.73 (1.48, 5.01)	
	p-value [3]	0.0008	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.

		EC+FOLFOX (N=232)	Control 1 (N=229)
SOC: Investigations, PT: Neutrophil count decreased	Number of subjects with events, n (%)	44 (19.0)	39 (17.0)
	Number of censored subjects, n (%)	188 (81.0)	190 (83.0)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	NE (NE, NE)	NE (7.4, NE)
	Median (95% CI)	NE (NE, NE)	NE (NE, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	1.11 (0.72, 1.72)	
	p-value [3]	0.6495	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.

		EC+FOLFOX (N=232)	Control 1 (N=229)
SOC: Investigations, PT: White blood cell count decreased	Number of subjects with events, n (%)	13 (5.6)	8 (3.5)
	Number of censored subjects, n (%)	219 (94.4)	221 (96.5)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Median (95% CI)	NE (NE, NE)	NE (NE, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	1.56 (0.65, 3.78)	
	p-value [3]	0.3177	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.

		EC+FOLFOX (N=232)	Control 1 (N=229)
SOC: Metabolism and nutrition disorders	Number of subjects with events, n (%)	23 (9.9)	14 (6.1)
	Number of censored subjects, n (%)	209 (90.1)	215 (93.9)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	NE (30.1, NE)	NE (NE, NE)
	Median (95% CI)	NE (NE, NE)	NE (NE, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	1.26 (0.64, 2.46)	
	p-value [3]	0.5061	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.

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Safety Analysis Set

		EC+FOLFOX (N=232)	Control 1 (N=229)
SOC: Nervous system disorders	Number of subjects with events, n (%)	61 (26.3)	27 (11.8)
	Number of censored subjects, n (%)	171 (73.7)	202 (88.2)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	6.5 (5.7, NE)	NE (8.8, NE)
	Median (95% CI)	NE (NE, NE)	NE (NE, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	1.81 (1.15, 2.85)	
	p-value [3]	0.0092	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.

		EC+FOLFOX (N=232)	Control 1 (N=229)
SOC: Nervous system disorders, PT: Neuropathy peripheral	Number of subjects with events, n (%)	18 (7.8)	8 (3.5)
	Number of censored subjects, n (%)	214 (92.2)	221 (96.5)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Median (95% CI)	NE (NE, NE)	NE (NE, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	1.63 (0.71, 3.76)	
	p-value [3]	0.2441	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.

		EC+FOLFOX (N=232)	Control 1 (N=229)
SOC: Nervous system disorders, PT: Neurotoxicity	Number of subjects with events, n (%)	13 (5.6)	0 (0.0)
	Number of censored subjects, n (%)	219 (94.4)	229 (100.0)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Median (95% CI)	NE (NE, NE)	NE (NE, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	NE	
	p-value [3]		

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.

		EC+FOLFOX (N=232)	Control 1 (N=229)
SOC: Nervous system disorders, PT: Paraesthesia	Number of subjects with events, n (%)	10 (4.3)	4 (1.7)
	Number of censored subjects, n (%)	222 (95.7)	225 (98.3)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Median (95% CI)	NE (NE, NE)	NE (NE, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	1.81 (0.57, 5.79)	
	p-value [3]	0.3099	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.

		EC+FOLFOX (N=232)	Control 1 (N=229)
SOC: Nervous system disorders, PT: Peripheral sensory neuropathy	Number of subjects with events, n (%)	16 (6.9)	8 (3.5)
	Number of censored subjects, n (%)	216 (93.1)	221 (96.5)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Median (95% CI)	NE (NE, NE)	NE (NE, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	1.47 (0.63, 3.45)	
	p-value [3]	0.3711	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.

		EC+FOLFOX (N=232)	Control 1 (N=229)
SOC: Respiratory, thoracic and mediastinal disorders	Number of subjects with events, n (%)	12 (5.2)	13 (5.7)
	Number of censored subjects, n (%)	220 (94.8)	216 (94.3)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Median (95% CI)	NE (NE, NE)	NE (NE, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	0.70 (0.32, 1.54)	
	p-value [3]	0.3714	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.

		EC+FOLFOX (N=232)	Control 1 (N=229)
SOC: Skin and subcutaneous tissue disorders	Number of subjects with events, n (%)	16 (6.9)	2 (0.9)
	Number of censored subjects, n (%)	216 (93.1)	227 (99.1)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Median (95% CI)	NE (NE, NE)	NE (NE, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	4.40 (0.99, 19.60)	
	p-value [3]	0.0349	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.

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Datacut: 06JAN2025
Frequent Severe AE by SOC, PT (incidence >= 5% or >=10 patients and incidence >= 1%)
Safety Analysis Set

		EC+FOLFOX (N=232)	Control 1 (N=229)
SOC: Vascular disorders	Number of subjects with events, n (%)	8 (3.4)	13 (5.7)
	Number of censored subjects, n (%)	224 (96.6)	216 (94.3)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Median (95% CI)	NE (NE, NE)	NE (NE, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	0.45 (0.18, 1.11)	
	p-value [3]	0.0761	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.

		EC+FOLFOX (N=232)	Control 1 (N=229)
SOC: Vascular disorders, PT: Hypertension	Number of subjects with events, n (%)	2 (0.9)	10 (4.4)
	Number of censored subjects, n (%)	230 (99.1)	219 (95.6)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Median (95% CI)	NE (NE, NE)	NE (NE, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	0.14 (0.03, 0.64)	
	p-value [3]	0.0037	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.

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Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Frequent Severe AE by SOC, PT (incidence >= 5% or >=10 patients and incidence >= 1%) - Subgroup analysis
Safety Analysis Set

SOC/PT	Subgroup Level	EC+FOLFOX (N=232) n/ N (%)	EC+FOLFOX (N=232) Median (95% CI)[1]	Control 1 (N=229) n/ N (%)	Control 1 (N=229) Median (95% CI)[1]	Unstratified analysis Hazard Ratio (95% CI)[2]	Unstratified analysis p-Value[3]	Interaction p-Value[4]
SOC: Blood and lymphatic system disorders, PT: Anaemia	Age (Years)							0.0896
	< 65	19/ 148 (12.8)	NE (NE , NE)	1/ 131 (0.8)	NE (NE , NE)	11.30 (1.50, 84.99)	0.0031	
	>= 65	16/ 84 (19.0)	NE (NE , NE)	8/ 98 (8.2)	NE (NE , NE)	1.74 (0.74, 4.11)	0.1998	
	Sex							0.5993
	Male	12/ 121 (9.9)	NE (NE , NE)	2/ 112 (1.8)	NE (NE , NE)	4.27 (0.95, 19.24)	0.0395	
	Female	23/ 111 (20.7)	NE (NE , NE)	7/ 117 (6.0)	NE (NE , NE)	2.36 (1.00, 5.56)	0.0437	
	Region							0.2005
	Europe	12/ 108 (11.1)	NE (NE , NE)	2/ 103 (1.9)	NE (NE , NE)	3.35 (0.73, 15.28)	0.0994	
	USA/Canada	2/ 15 (13.3)	NE (NE , NE)	3/ 17 (17.6)	NE (11.8, NE)	0.70 (0.12, 4.18)	0.6908	
	Rest of World	21/ 109 (19.3)	NE (NE , NE)	4/ 109 (3.7)	NE (NE , NE)	4.02 (1.37, 11.80)	0.0063	
	ECOG-PS at Randomization							0.1757
	0	13/ 130 (10.0)	NE (NE , NE)	1/ 130 (0.8)	NE (NE , NE)	7.66 (0.99, 59.26)	0.0222	
	1	22/ 102 (21.6)	NE (NE , NE)	8/ 99 (8.1)	NE (NE , NE)	2.00 (0.88, 4.54)	0.0899	
	Number of Organs Involved							0.7760
	<= 2	14/ 116 (12.1)	NE (NE , NE)	3/ 119 (2.5)	NE (NE , NE)	3.22 (0.91, 11.35)	0.0553	
	>= 3	21/ 116 (18.1)	NE (NE , NE)	6/ 110 (5.5)	NE (NE , NE)	2.47 (0.99, 6.16)	0.0461	
	Presence of Liver Metastases							0.4882
	Yes	26/ 146 (17.8)	NE (NE , NE)	6/ 149 (4.0)	NE (NE , NE)	3.17 (1.30, 7.75)	0.0077	
	No	9/ 86 (10.5)	NE (NE , NE)	3/ 80 (3.8)	NE (NE , NE)	1.85 (0.48, 7.09)	0.3624	
	Side of Tumor							0.6017
	Left	12/ 88 (13.6)	NE (NE , NE)	4/ 90 (4.4)	NE (NE , NE)	2.33 (0.74, 7.29)	0.1355	
	Right	23/ 144 (16.0)	NE (NE , NE)	5/ 139 (3.6)	NE (NE , NE)	3.01 (1.13, 8.01)	0.0207	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
Subgroup analysis was done for SOCs / PTs with significant overall treatment effect (significant log-rank).
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.
[4] P-Value for interaction from Cox proportional hazards model using ties=exact option with treatment, subgroup and treatment*subgroup interaction as covariates.
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Frequent Severe AE by SOC, PT (incidence >= 5% or >=10 patients and incidence >= 1%) - Subgroup analysis
Safety Analysis Set

SOC/PT	Subgroup Level	EC+FOLFOX (N=232) n/ N (%)	EC+FOLFOX (N=232) Median (95% CI)[1]	Control 1 (N=229) n/ N (%)	Control 1 (N=229) Median (95% CI)[1]	Unstratified analysis Hazard Ratio (95% CI)[2]	Unstratified analysis p-Value[3]	Interaction p-Value[4]
SOC: Gastrointestinal disorders, PT: Diarrhoea	Age (Years)							
	< 65	2/ 148 (1.4)		4/ 131 (3.1)				
	>= 65	1/ 84 (1.2)		7/ 98 (7.1)				
	Sex							
	Male	2/ 121 (1.7)		5/ 112 (4.5)				
	Female	1/ 111 (0.9)		6/ 117 (5.1)				
	Region							
	Europe	0/ 108 (0.0)		6/ 103 (5.8)				
	USA/Canada	1/ 15 (6.7)		1/ 17 (5.9)				
	Rest of World	2/ 109 (1.8)		4/ 109 (3.7)				
	ECOG-PS at Randomization							
	0	1/ 130 (0.8)		4/ 130 (3.1)				
	1	2/ 102 (2.0)		7/ 99 (7.1)				
	Number of Organs Involved							0.8596
	<= 2	2/ 116 (1.7)	NE (NE , NE)	8/ 119 (6.7)	NE (NE , NE)	0.20 (0.04, 0.96)	0.0268	
	>= 3	1/ 116 (0.9)	NE (NE , NE)	3/ 110 (2.7)	NE (NE , NE)	0.26 (0.03, 2.51)	0.2092	
	Presence of Liver Metastases							
	Yes	3/ 146 (2.1)		5/ 149 (3.4)				
	No	0/ 86 (0.0)		6/ 80 (7.5)				
	Side of Tumor							0.9903
	Left	0/ 88 (0.0)	NE (NE , NE)	4/ 90 (4.4)	NE (NE , NE)	NE		
	Right	3/ 144 (2.1)	NE (NE , NE)	7/ 139 (5.0)	NE (NE , NE)	0.33 (0.08, 1.29)	0.0942	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
Subgroup analysis was done for SOCs / PTs with significant overall treatment effect (significant log-rank).
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.
[4] P-Value for interaction from Cox proportional hazards model using ties=exact option with treatment, subgroup and treatment*subgroup interaction as covariates.
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Frequent Severe AE by SOC, PT (incidence >= 5% or >=10 patients and incidence >= 1%) - Subgroup analysis
Safety Analysis Set

SOC/PT	Subgroup Level	EC+FOLFOX (N=232) n/ N (%)	EC+FOLFOX (N=232) Median (95% CI)[1]	Control 1 (N=229) n/ N (%)	Control 1 (N=229) Median (95% CI)[1]	Unstratified analysis Hazard Ratio (95% CI)[2]	Unstratified analysis p-Value[3]	Interaction p-Value[4]
SOC: Investigations	Age (Years)							0.5618
	< 65	56/ 148 (37.8)	NE (NE , NE)	34/ 131 (26.0)	NE (NE , NE)	1.54 (1.01, 2.36)	0.0462	
	>= 65	32/ 84 (38.1)	NE (NE , NE)	31/ 98 (31.6)	NE (10.1, NE)	1.24 (0.76, 2.04)	0.4056	
	Sex							0.7070
	Male	42/ 121 (34.7)	NE (NE , NE)	27/ 112 (24.1)	NE (NE , NE)	1.52 (0.94, 2.47)	0.0887	
	Female	46/ 111 (41.4)	NE (6.6, NE)	38/ 117 (32.5)	NE (10.1, NE)	1.35 (0.88, 2.08)	0.1852	
	Region							0.4287
	Europe	30/ 108 (27.8)	NE (NE , NE)	16/ 103 (15.5)	NE (NE , NE)	1.82 (0.99, 3.34)	0.0528	
	USA/Canada	9/ 15 (60.0)	0.9 (0.5, NE)	6/ 17 (35.3)	NE (1.0, NE)	1.98 (0.70, 5.59)	0.1940	
	Rest of World	49/ 109 (45.0)	NE (2.8, NE)	43/ 109 (39.4)	NE (7.4, NE)	1.21 (0.80, 1.83)	0.3618	
	ECOG-PS at Randomization							0.0219
	0	46/ 130 (35.4)	NE (NE , NE)	44/ 130 (33.8)	NE (8.3, NE)	1.00 (0.66, 1.52)	0.9989	
	1	42/ 102 (41.2)	NE (3.4, NE)	21/ 99 (21.2)	NE (NE , NE)	2.24 (1.33, 3.78)	0.0022	
	Number of Organs Involved							0.6633
	<= 2	45/ 116 (38.8)	NE (NE , NE)	37/ 119 (31.1)	NE (NE , NE)	1.28 (0.83, 1.99)	0.2672	
	>= 3	43/ 116 (37.1)	NE (NE , NE)	28/ 110 (25.5)	NE (NE , NE)	1.56 (0.97, 2.51)	0.0694	
	Presence of Liver Metastases							0.4803
	Yes	60/ 146 (41.1)	NE (9.4, NE)	43/ 149 (28.9)	NE (10.1, NE)	1.51 (1.02, 2.24)	0.0405	
	No	28/ 86 (32.6)	NE (NE , NE)	22/ 80 (27.5)	NE (NE , NE)	1.23 (0.70, 2.15)	0.4859	
	Side of Tumor							0.7713
	Left	34/ 88 (38.6)	NE (9.4, NE)	24/ 90 (26.7)	NE (NE , NE)	1.45 (0.86, 2.45)	0.1668	
	Right	54/ 144 (37.5)	NE (NE , NE)	41/ 139 (29.5)	NE (NE , NE)	1.37 (0.91, 2.05)	0.1375	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
Subgroup analysis was done for SOCs / PTs with significant overall treatment effect (significant log-rank).
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.
[4] P-Value for interaction from Cox proportional hazards model using ties=exact option with treatment, subgroup and treatment*subgroup interaction as covariates.
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Frequent Severe AE by SOC, PT (incidence >= 5% or >=10 patients and incidence >= 1%) - Subgroup analysis
Safety Analysis Set

SOC/PT	Subgroup Level	EC+FOLFOX (N=232) n/ N (%)	EC+FOLFOX (N=232) Median (95% CI)[1]	Control 1 (N=229) n/ N (%)	Control 1 (N=229) Median (95% CI)[1]	Unstratified analysis Hazard Ratio (95% CI)[2]	Unstratified analysis p-Value[3]	Interaction p-Value[4]
SOC: Investigations, PT: Lipase increased	Age (Years)							0.8914
	< 65	26/ 148 (17.6)	NE (NE , NE)	8/ 131 (6.1)	NE (NE , NE)	2.85 (1.29, 6.29)	0.0068	
	>= 65	14/ 84 (16.7)	NE (NE , NE)	6/ 98 (6.1)	NE (NE , NE)	2.53 (0.97, 6.60)	0.0485	
	Sex							0.2090
	Male	23/ 121 (19.0)	NE (NE , NE)	5/ 112 (4.5)	NE (NE , NE)	4.18 (1.59, 11.00)	0.0016	
	Female	17/ 111 (15.3)	NE (NE , NE)	9/ 117 (7.7)	NE (NE , NE)	1.91 (0.85, 4.29)	0.1097	
	Region							0.6734
	Europe	16/ 108 (14.8)	NE (NE , NE)	7/ 103 (6.8)	NE (NE , NE)	1.96 (0.80, 4.77)	0.1324	
	USA/Canada	3/ 15 (20.0)	NE (NE , NE)	1/ 17 (5.9)	NE (NE , NE)	2.99 (0.31, 28.80)	0.3185	
	Rest of World	21/ 109 (19.3)	NE (NE , NE)	6/ 109 (5.5)	NE (NE , NE)	3.62 (1.46, 8.96)	0.0029	
	ECOG-PS at Randomization							0.1202
	0	22/ 130 (16.9)	NE (NE , NE)	11/ 130 (8.5)	NE (NE , NE)	1.88 (0.91, 3.89)	0.0811	
	1	18/ 102 (17.6)	NE (NE , NE)	3/ 99 (3.0)	NE (NE , NE)	5.76 (1.70, 19.57)	0.0015	
	Number of Organs Involved							0.3740
	<= 2	22/ 116 (19.0)	NE (NE , NE)	10/ 119 (8.4)	NE (NE , NE)	2.21 (1.05, 4.68)	0.0326	
	>= 3	18/ 116 (15.5)	NE (NE , NE)	4/ 110 (3.6)	NE (NE , NE)	4.02 (1.36, 11.90)	0.0064	
	Presence of Liver Metastases							0.1688
	Yes	23/ 146 (15.8)	NE (NE , NE)	11/ 149 (7.4)	NE (NE , NE)	2.00 (0.97, 4.10)	0.0547	
	No	17/ 86 (19.8)	NE (NE , NE)	3/ 80 (3.8)	NE (NE , NE)	5.42 (1.59, 18.50)	0.0025	
	Side of Tumor							0.6447
	Left	14/ 88 (15.9)	NE (NE , NE)	6/ 90 (6.7)	NE (NE , NE)	2.30 (0.88, 5.99)	0.0787	
	Right	26/ 144 (18.1)	NE (NE , NE)	8/ 139 (5.8)	NE (NE , NE)	3.04 (1.38, 6.72)	0.0039	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
Subgroup analysis was done for SOCs / PTs with significant overall treatment effect (significant log-rank).
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.
[4] P-Value for interaction from Cox proportional hazards model using ties=exact option with treatment, subgroup and treatment*subgroup interaction as covariates.
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Frequent Severe AE by SOC, PT (incidence >= 5% or >=10 patients and incidence >= 1%) - Subgroup analysis
Safety Analysis Set

SOC/PT	Subgroup Level	EC+FOLFOX (N=232) n/ N (%)	EC+FOLFOX (N=232) Median (95% CI)[1]	Control 1 (N=229) n/ N (%)	Control 1 (N=229) Median (95% CI)[1]	Unstratified analysis Hazard Ratio (95% CI)[2]	Unstratified analysis p-Value[3]	Interaction p-Value[4]
SOC: Nervous system disorders	Age (Years)							0.3237
	< 65	40/ 148 (27.0)	NE (NE , NE)	13/ 131 (9.9)	NE (NE , NE)	2.26 (1.21, 4.23)	0.0089	
	>= 65	21/ 84 (25.0)	NE (NE , NE)	14/ 98 (14.3)	NE (NE , NE)	1.39 (0.71, 2.74)	0.3378	
	Sex							0.5060
	Male	27/ 121 (22.3)	NE (NE , NE)	13/ 112 (11.6)	NE (NE , NE)	1.55 (0.80, 3.01)	0.1899	
	Female	34/ 111 (30.6)	NE (NE , NE)	14/ 117 (12.0)	NE (NE , NE)	2.11 (1.13, 3.94)	0.0160	
	Region							0.3861
	Europe	39/ 108 (36.1)	NE (8.5, NE)	12/ 103 (11.7)	NE (NE , NE)	2.44 (1.28, 4.67)	0.0053	
	USA/Canada	5/ 15 (33.3)	NE (4.6, NE)	5/ 17 (29.4)	NE (6.6, NE)	1.19 (0.34, 4.23)	0.7869	
	Rest of World	17/ 109 (15.6)	NE (NE , NE)	10/ 109 (9.2)	NE (NE , NE)	1.35 (0.62, 2.96)	0.4490	
	ECOG-PS at Randomization							0.1795
	0	35/ 130 (26.9)	NE (NE , NE)	12/ 130 (9.2)	NE (NE , NE)	2.47 (1.28, 4.76)	0.0053	
	1	26/ 102 (25.5)	NE (NE , NE)	15/ 99 (15.2)	NE (NE , NE)	1.28 (0.67, 2.42)	0.4516	
	Number of Organs Involved							0.8683
	<= 2	29/ 116 (25.0)	NE (NE , NE)	13/ 119 (10.9)	NE (NE , NE)	1.94 (1.01, 3.74)	0.0432	
	>= 3	32/ 116 (27.6)	NE (NE , NE)	14/ 110 (12.7)	NE (NE , NE)	1.70 (0.90, 3.18)	0.0965	
	Presence of Liver Metastases							0.3764
	Yes	32/ 146 (21.9)	NE (NE , NE)	16/ 149 (10.7)	NE (NE , NE)	1.54 (0.84, 2.81)	0.1569	
	No	29/ 86 (33.7)	NE (9.1, NE)	11/ 80 (13.8)	NE (NE , NE)	2.28 (1.14, 4.58)	0.0170	
	Side of Tumor							0.2651
	Left	20/ 88 (22.7)	NE (NE , NE)	12/ 90 (13.3)	NE (NE , NE)	1.31 (0.64, 2.68)	0.4626	
	Right	41/ 144 (28.5)	NE (NE , NE)	15/ 139 (10.8)	NE (NE , NE)	2.23 (1.23, 4.02)	0.0066	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
Subgroup analysis was done for SOCs / PTs with significant overall treatment effect (significant log-rank).
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.
[4] P-Value for interaction from Cox proportional hazards model using ties=exact option with treatment, subgroup and treatment*subgroup interaction as covariates.
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Frequent Severe AE by SOC, PT (incidence >= 5% or >=10 patients and incidence >= 1%) - Subgroup analysis
Safety Analysis Set

SOC/PT	Subgroup Level	EC+FOLFOX (N=232) n/ N (%)	EC+FOLFOX (N=232) Median (95% CI)[1]	Control 1 (N=229) n/ N (%)	Control 1 (N=229) Median (95% CI)[1]	Unstratified analysis Hazard Ratio (95% CI)[2]	Unstratified analysis p-Value[3]	Interaction p-Value[4]
SOC: Skin and subcutaneous tissue disorders	Age (Years)							0.9888
	< 65	11/ 148 (7.4)	NE (NE , NE)	0/ 131 (0.0)	NE (NE , NE)	NE		
	>= 65	5/ 84 (6.0)	NE (NE , NE)	2/ 98 (2.0)	NE (NE , NE)	1.68 (0.31, 8.99)	0.5412	
	Sex							0.5810
	Male	5/ 121 (4.1)	NE (NE , NE)	1/ 112 (0.9)	NE (NE , NE)	2.05 (0.23, 18.32)	0.5128	
	Female	11/ 111 (9.9)	NE (NE , NE)	1/ 117 (0.9)	NE (NE , NE)	7.21 (0.91, 57.05)	0.0304	
	Region							
	Europe	8/ 108 (7.4)		1/ 103 (1.0)				
	USA/Canada	1/ 15 (6.7)		0/ 17 (0.0)				
	Rest of World	7/ 109 (6.4)		1/ 109 (0.9)				
	ECOG-PS at Randomization							0.9891
	0	8/ 130 (6.2)	NE (NE , NE)	0/ 130 (0.0)	NE (NE , NE)	NE		
	1	8/ 102 (7.8)	NE (NE , NE)	2/ 99 (2.0)	NE (NE , NE)	2.29 (0.47, 11.14)	0.2941	
	Number of Organs Involved							0.6111
	<= 2	11/ 116 (9.5)	NE (NE , NE)	1/ 119 (0.8)	NE (NE , NE)	5.94 (0.74, 47.40)	0.0590	
	>= 3	5/ 116 (4.3)	NE (NE , NE)	1/ 110 (0.9)	NE (NE , NE)	2.90 (0.33, 25.71)	0.3181	
	Presence of Liver Metastases							0.9959
	Yes	7/ 146 (4.8)	NE (NE , NE)	1/ 149 (0.7)	NE (NE , NE)	3.92 (0.47, 32.92)	0.1769	
	No	9/ 86 (10.5)	NE (NE , NE)	1/ 80 (1.3)	NE (NE , NE)	4.80 (0.59, 39.30)	0.1096	
	Side of Tumor							0.5717
	Left	5/ 88 (5.7)	NE (NE , NE)	1/ 90 (1.1)	NE (NE , NE)	1.99 (0.21, 18.45)	0.5402	
	Right	11/ 144 (7.6)	NE (NE , NE)	1/ 139 (0.7)	NE (NE , NE)	6.79 (0.86, 53.58)	0.0366	

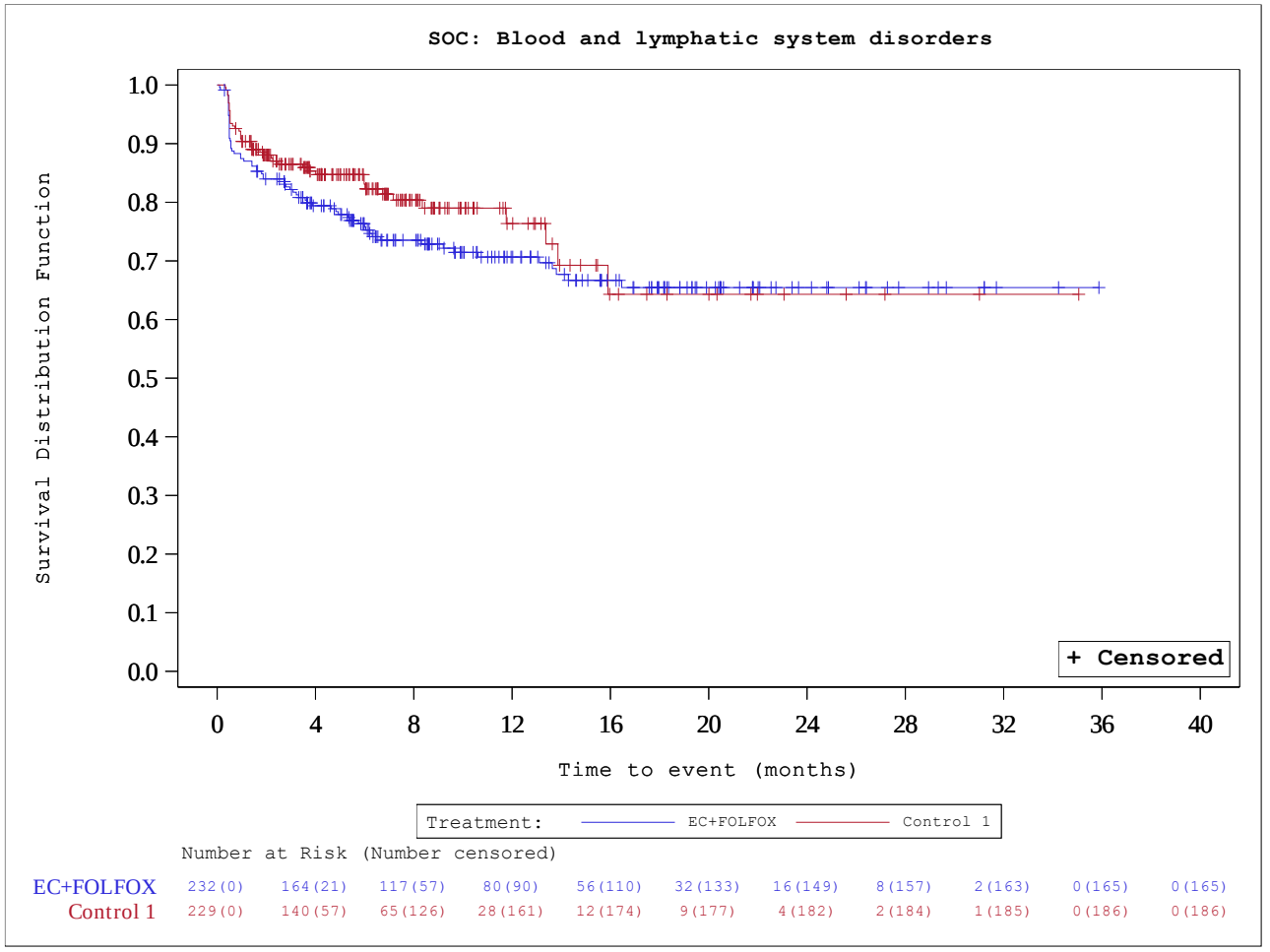
Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
Subgroup analysis was done for SOCs / PTs with significant overall treatment effect (significant log-rank).
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.
[4] P-Value for interaction from Cox proportional hazards model using ties=exact option with treatment, subgroup and treatment*subgroup interaction as covariates.
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Frequent Severe AE by SOC, PT (incidence >= 5% or >=10 patients and incidence >= 1%) - Subgroup analysis
Safety Analysis Set

SOC/PT	Subgroup Level	EC+FOLFOX (N=232) n/ N (%)	EC+FOLFOX (N=232) Median (95% CI)[1]	Control 1 (N=229) n/ N (%)	Control 1 (N=229) Median (95% CI)[1]	Unstratified analysis Hazard Ratio (95% CI)[2]	Unstratified analysis p-Value[3]	Interaction p-Value[4]
SOC: Vascular disorders, PT: Hypertension	Age (Years)							
	< 65	1/ 148 (0.7)		6/ 131 (4.6)				
	>= 65	1/ 84 (1.2)		4/ 98 (4.1)				
	Sex							
	Male	1/ 121 (0.8)		8/ 112 (7.1)				
	Female	1/ 111 (0.9)		2/ 117 (1.7)				
	Region							
	Europe	1/ 108 (0.9)		5/ 103 (4.9)				
	USA/Canada	0/ 15 (0.0)		4/ 17 (23.5)				
	Rest of World	1/ 109 (0.9)		1/ 109 (0.9)				
	ECOG-PS at Randomization							
	0	1/ 130 (0.8)		5/ 130 (3.8)				
	1	1/ 102 (1.0)		5/ 99 (5.1)				
	Number of Organs Involved							
	<= 2	1/ 116 (0.9)		4/ 119 (3.4)				
	>= 3	1/ 116 (0.9)		6/ 110 (5.5)				
	Presence of Liver Metastases							
	Yes	1/ 146 (0.7)		7/ 149 (4.7)				
	No	1/ 86 (1.2)		3/ 80 (3.8)				
	Side of Tumor							
	Left	0/ 88 (0.0)		3/ 90 (3.3)				
	Right	2/ 144 (1.4)		7/ 139 (5.0)				

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
Subgroup analysis was done for SOCs / PTs with significant overall treatment effect (significant log-rank).
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 1.
[3] P-value from 2-sided log-rank test.
[4] P-Value for interaction from Cox proportional hazards model using ties=exact option with treatment, subgroup and treatment*subgroup interaction as covariates.
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Kaplan Meier Plot of frequent Frequent Severe AE by SOC, PT (incidence >= 5% or >=10 patients and incidence >= 1%)
Safety Analysis Set



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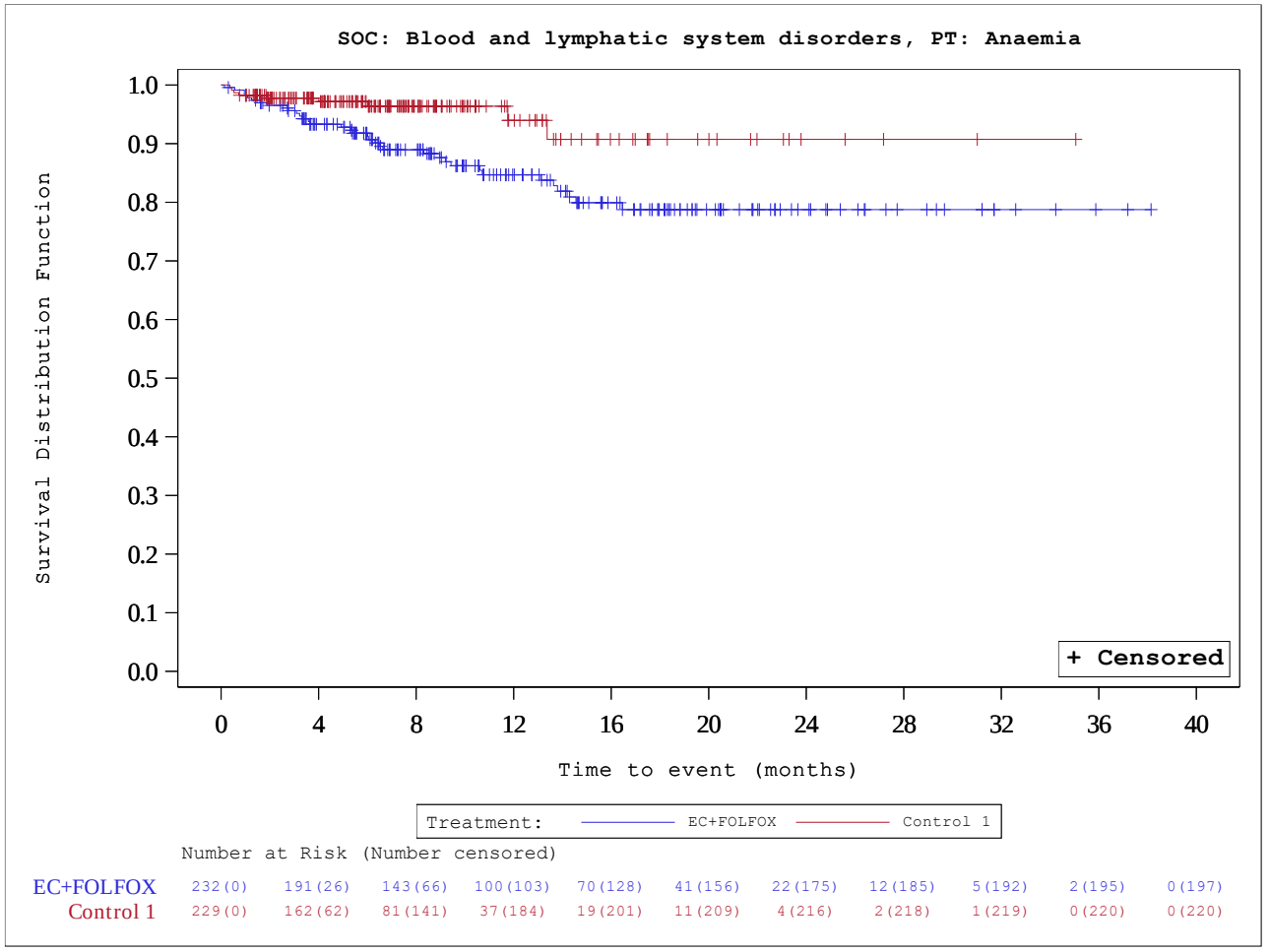

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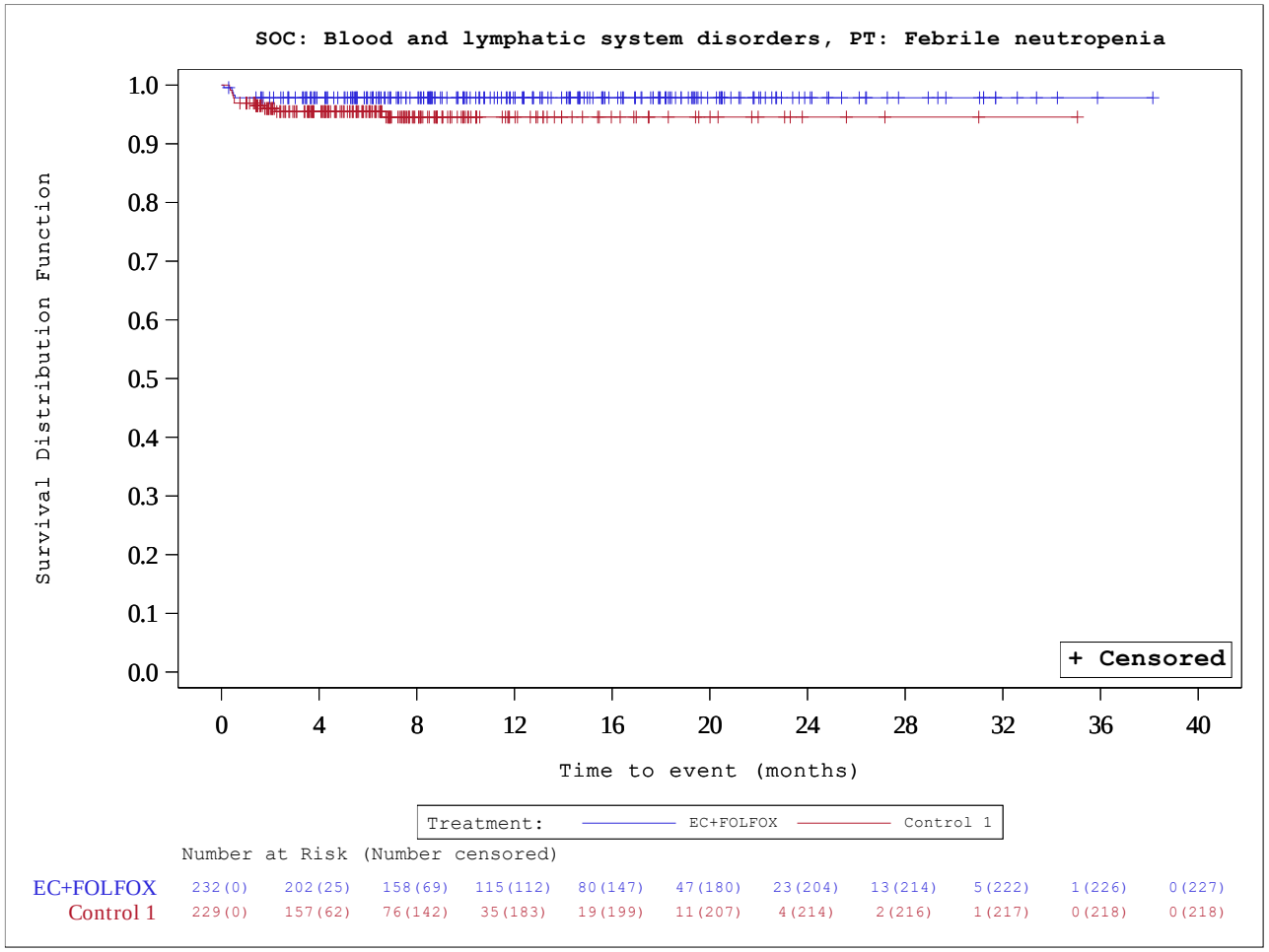

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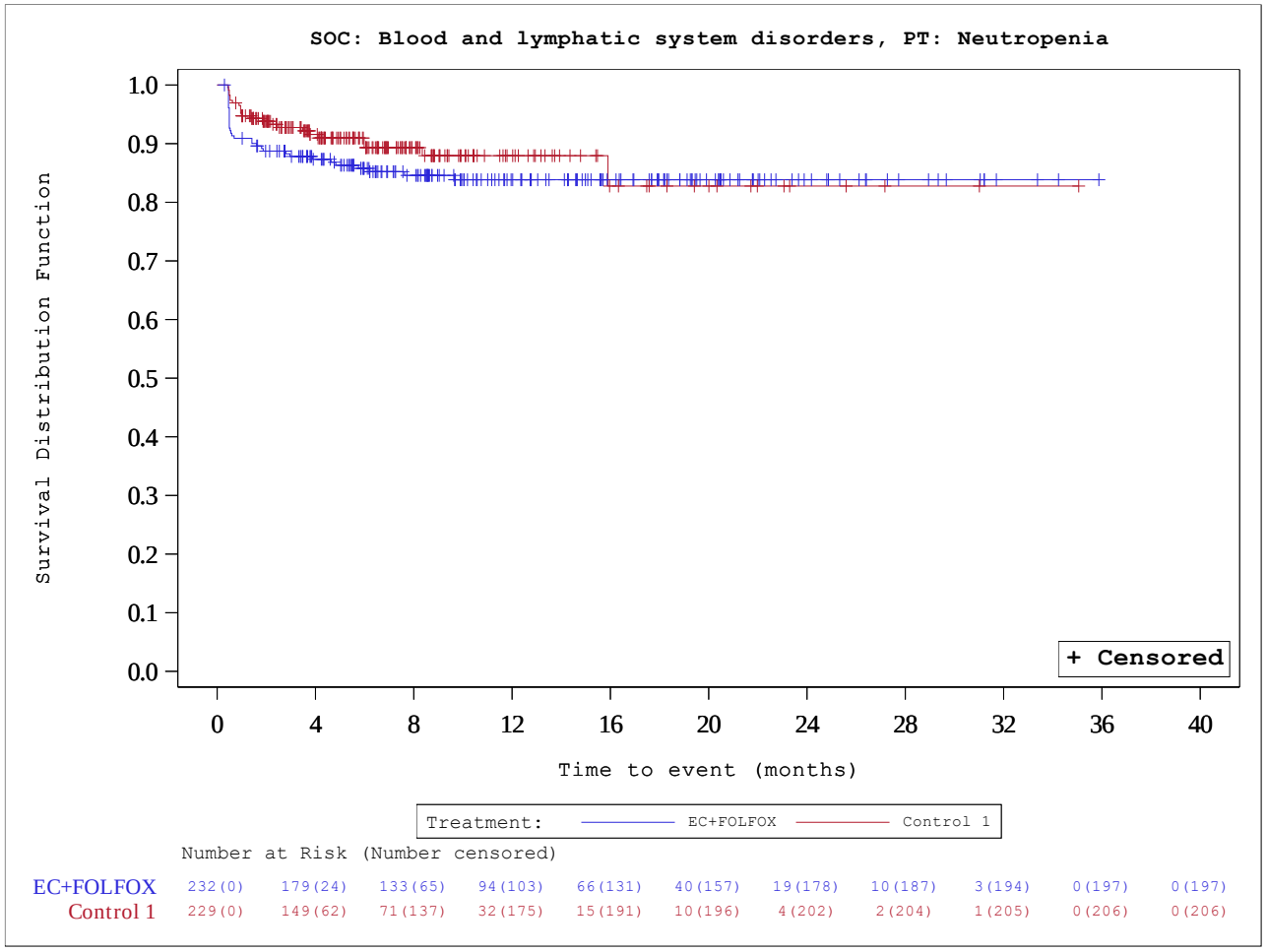

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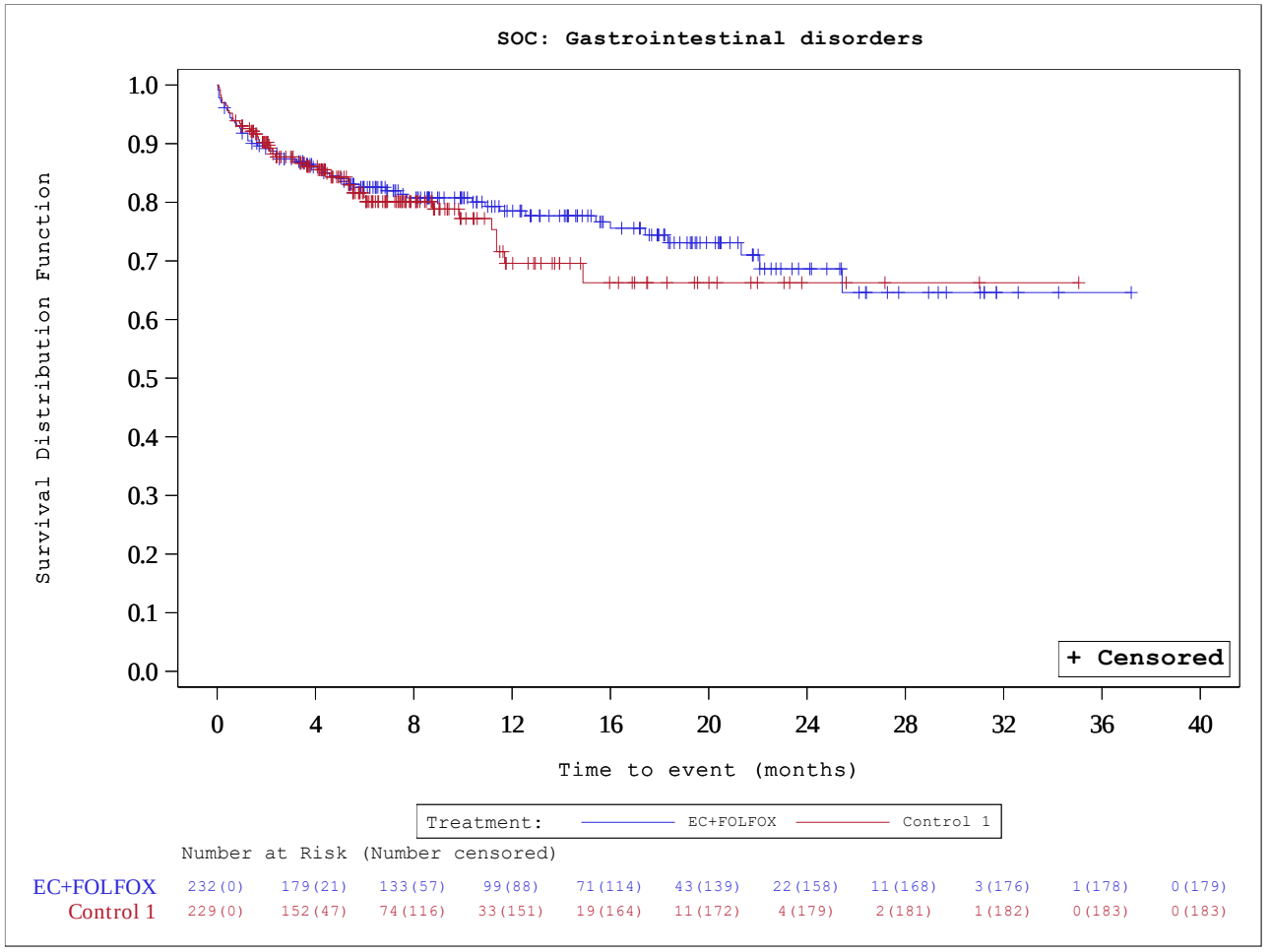

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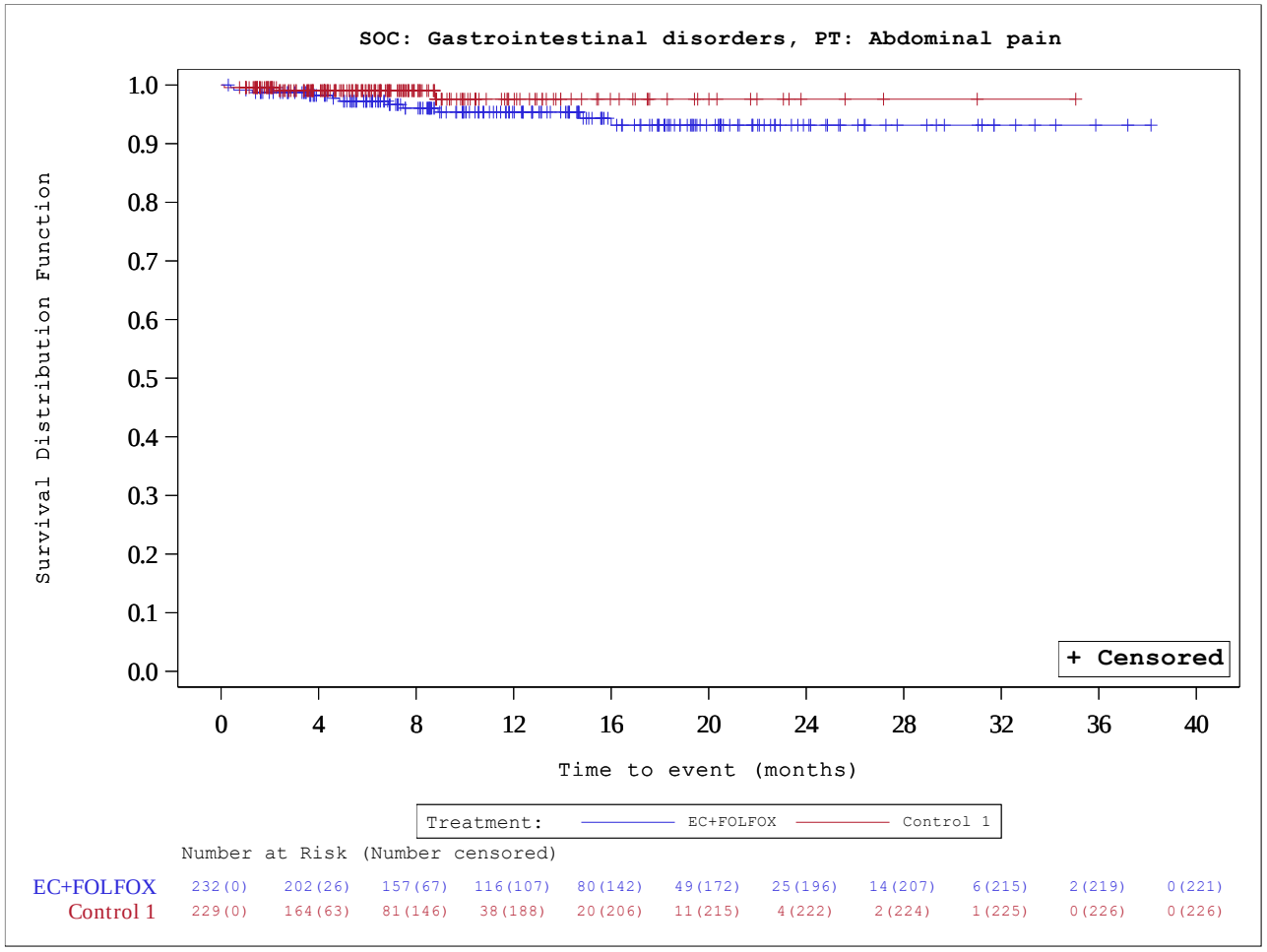

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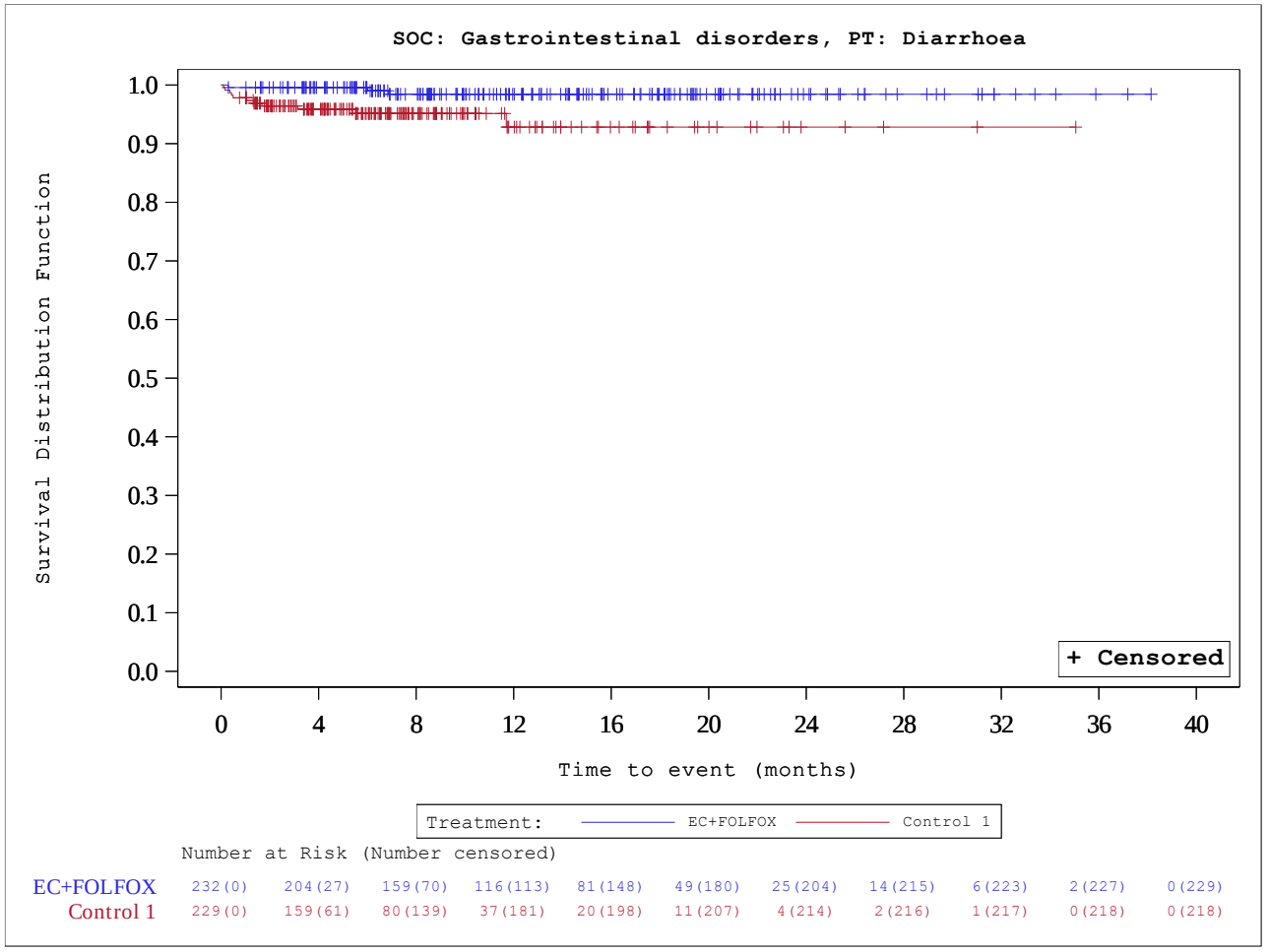

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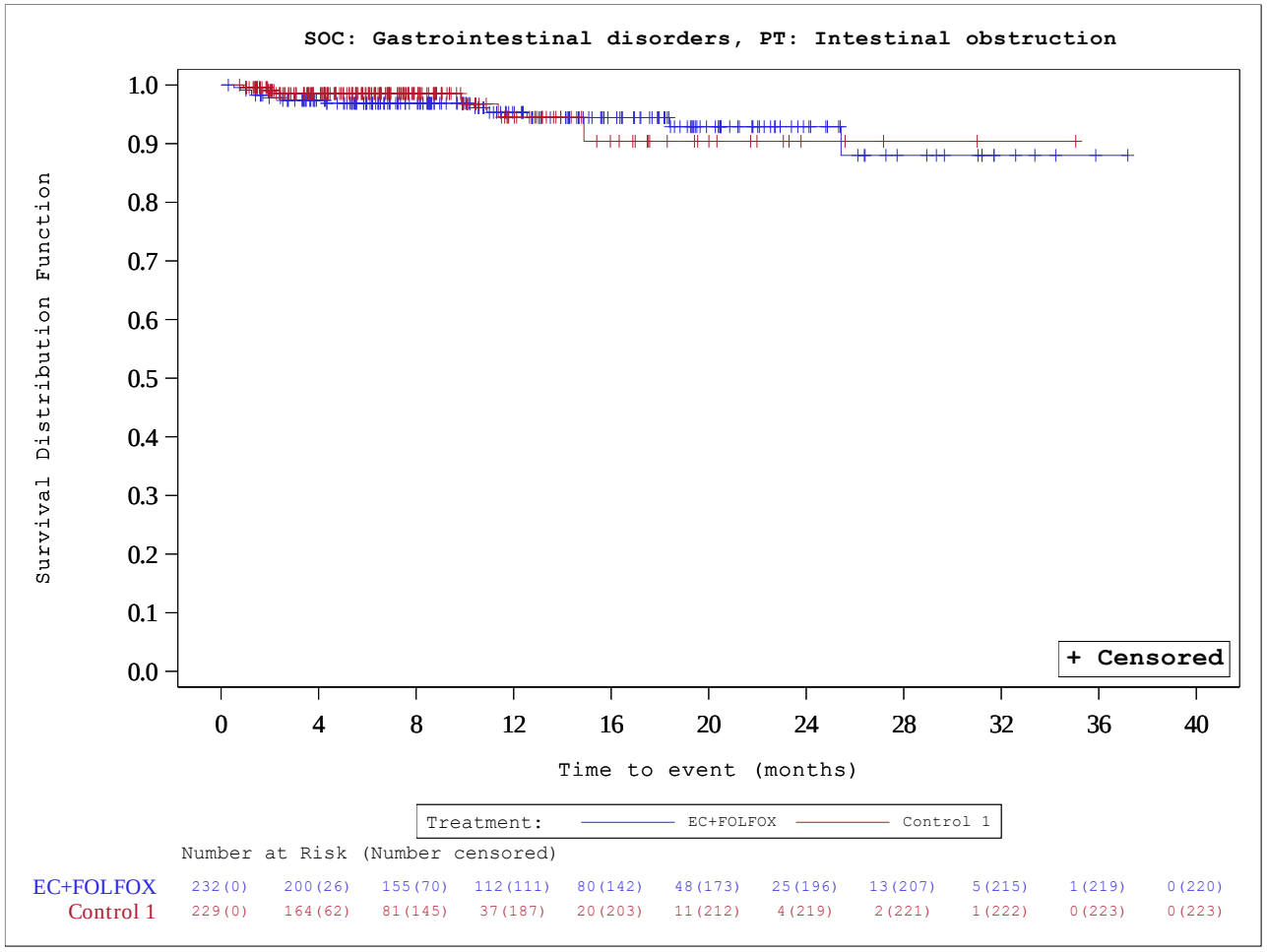

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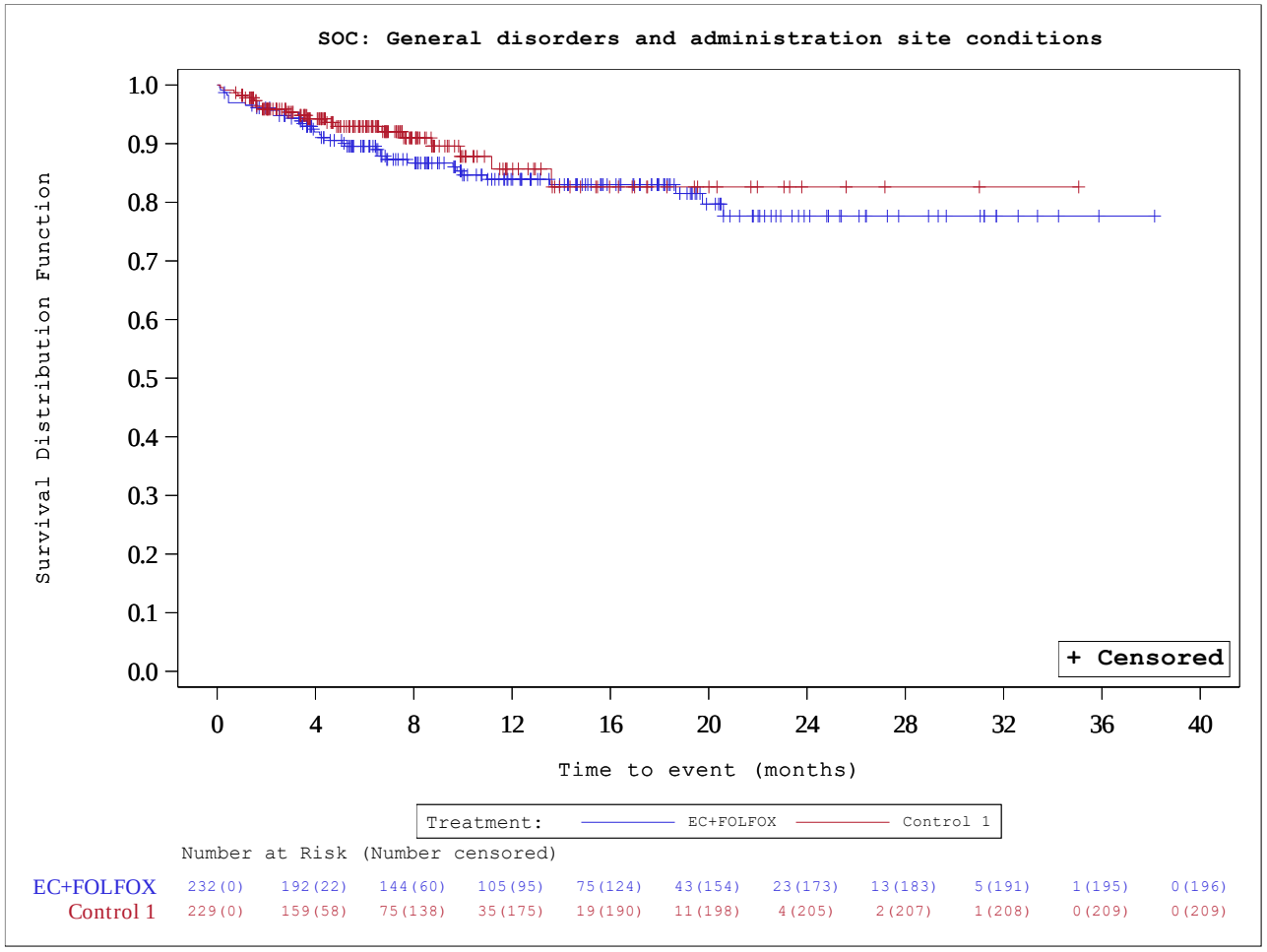

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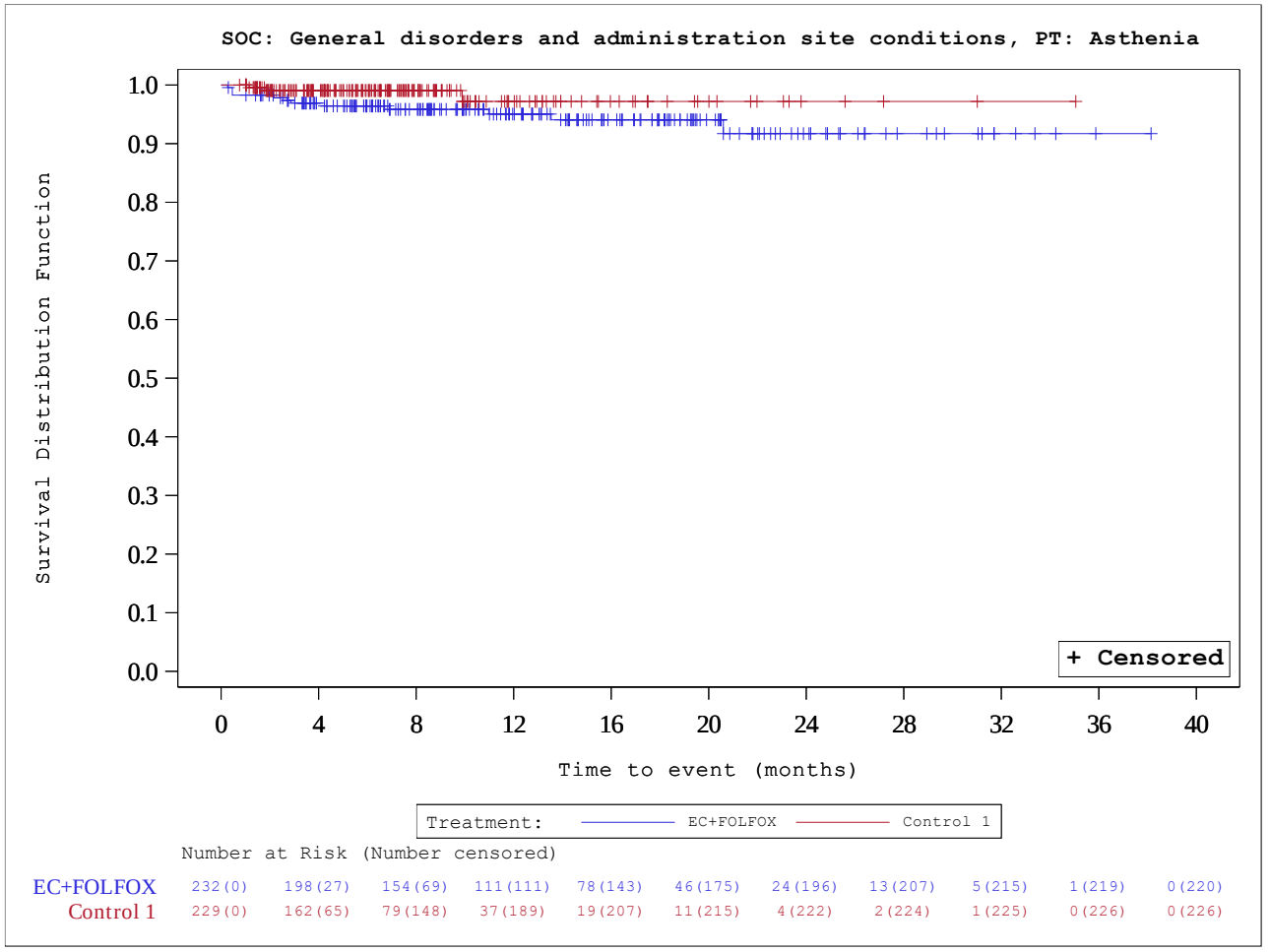

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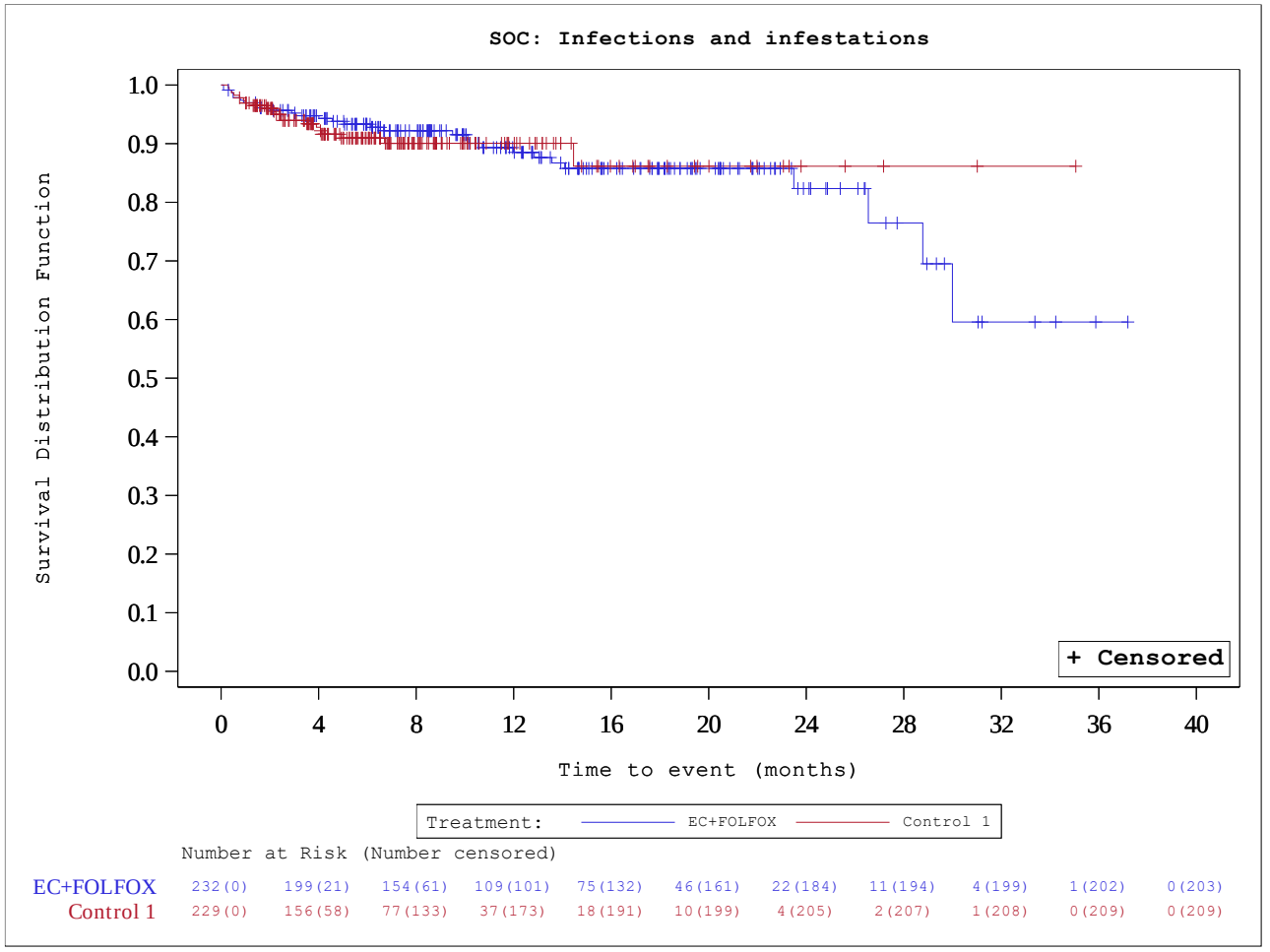

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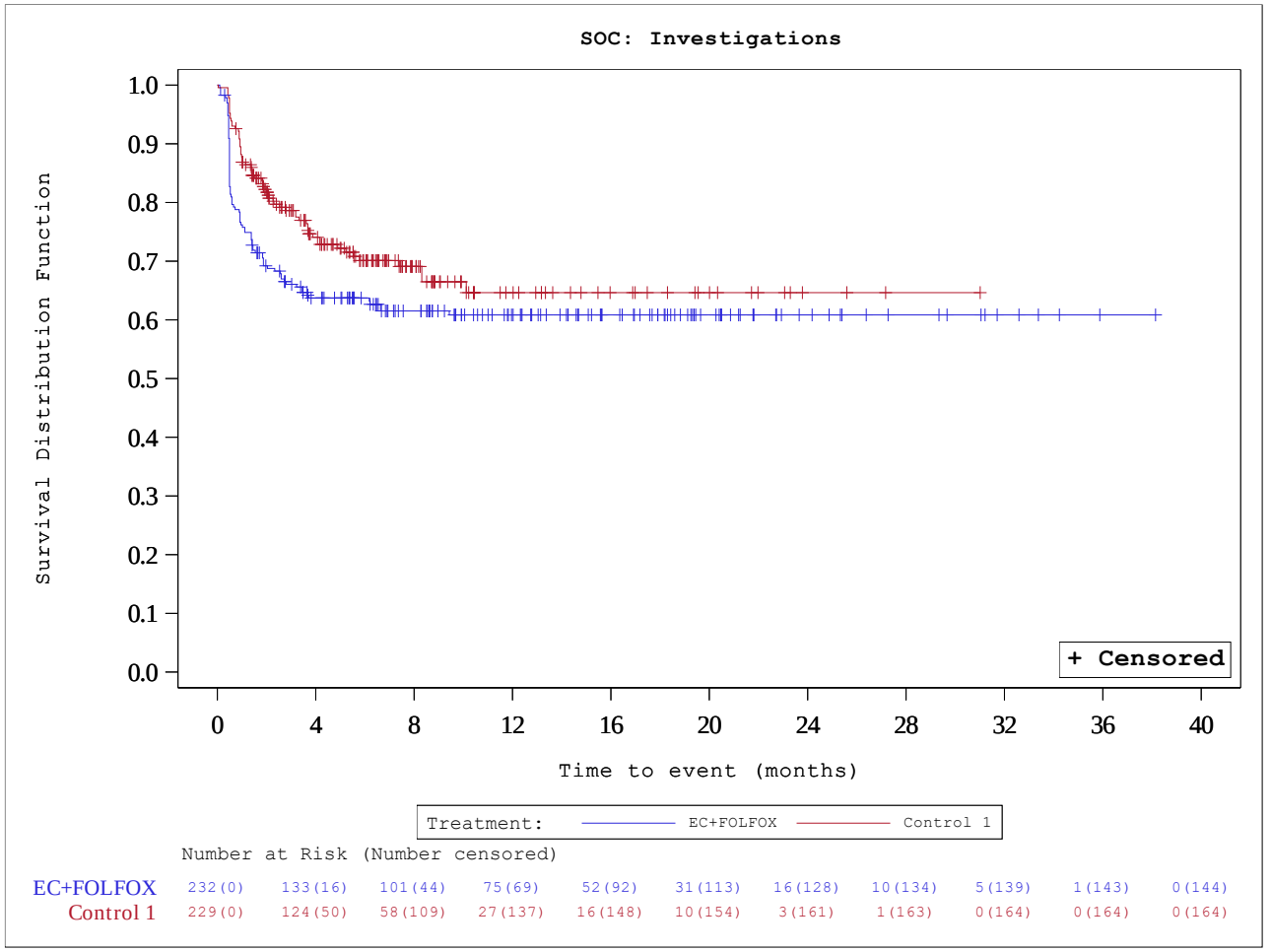

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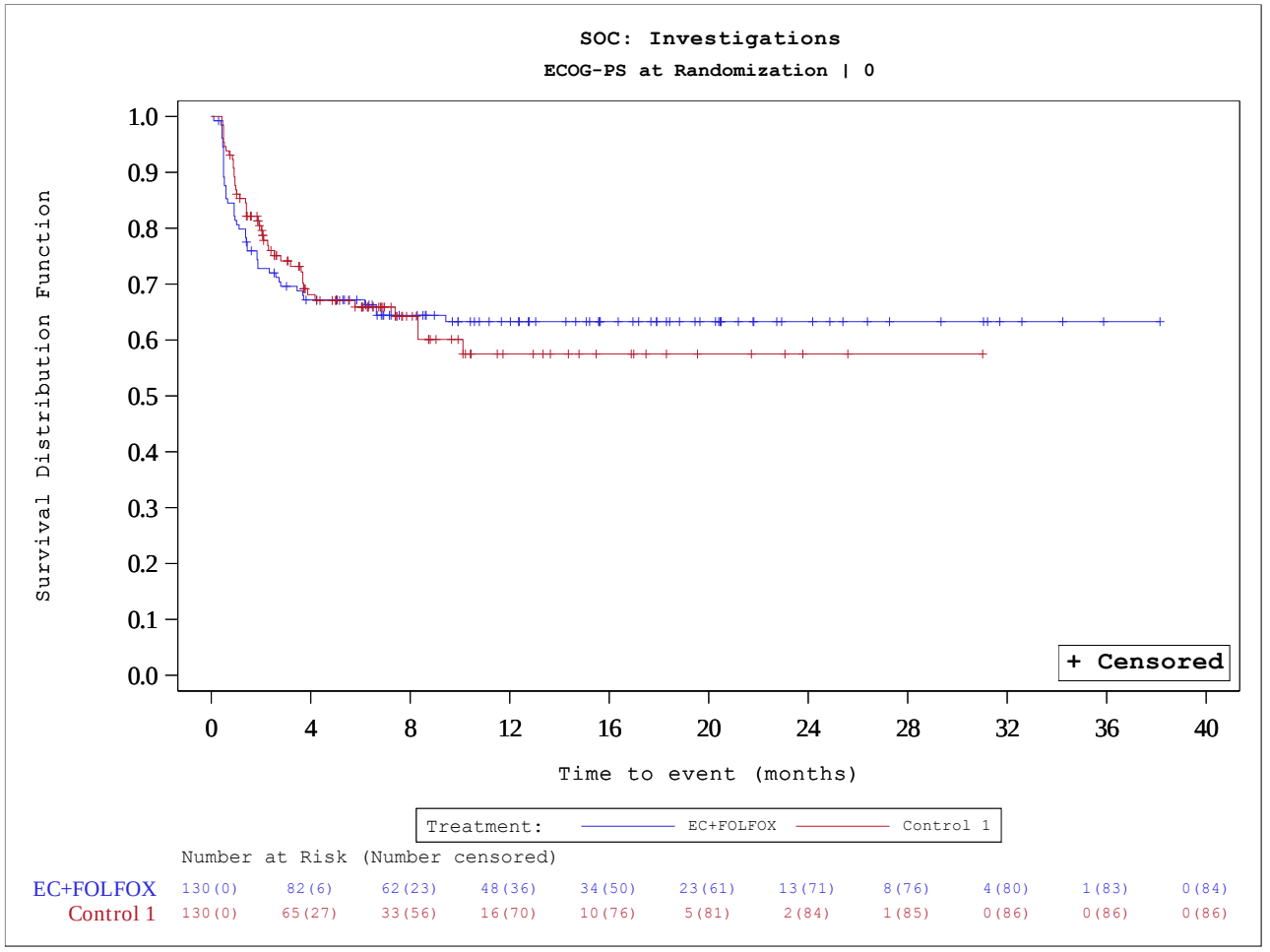

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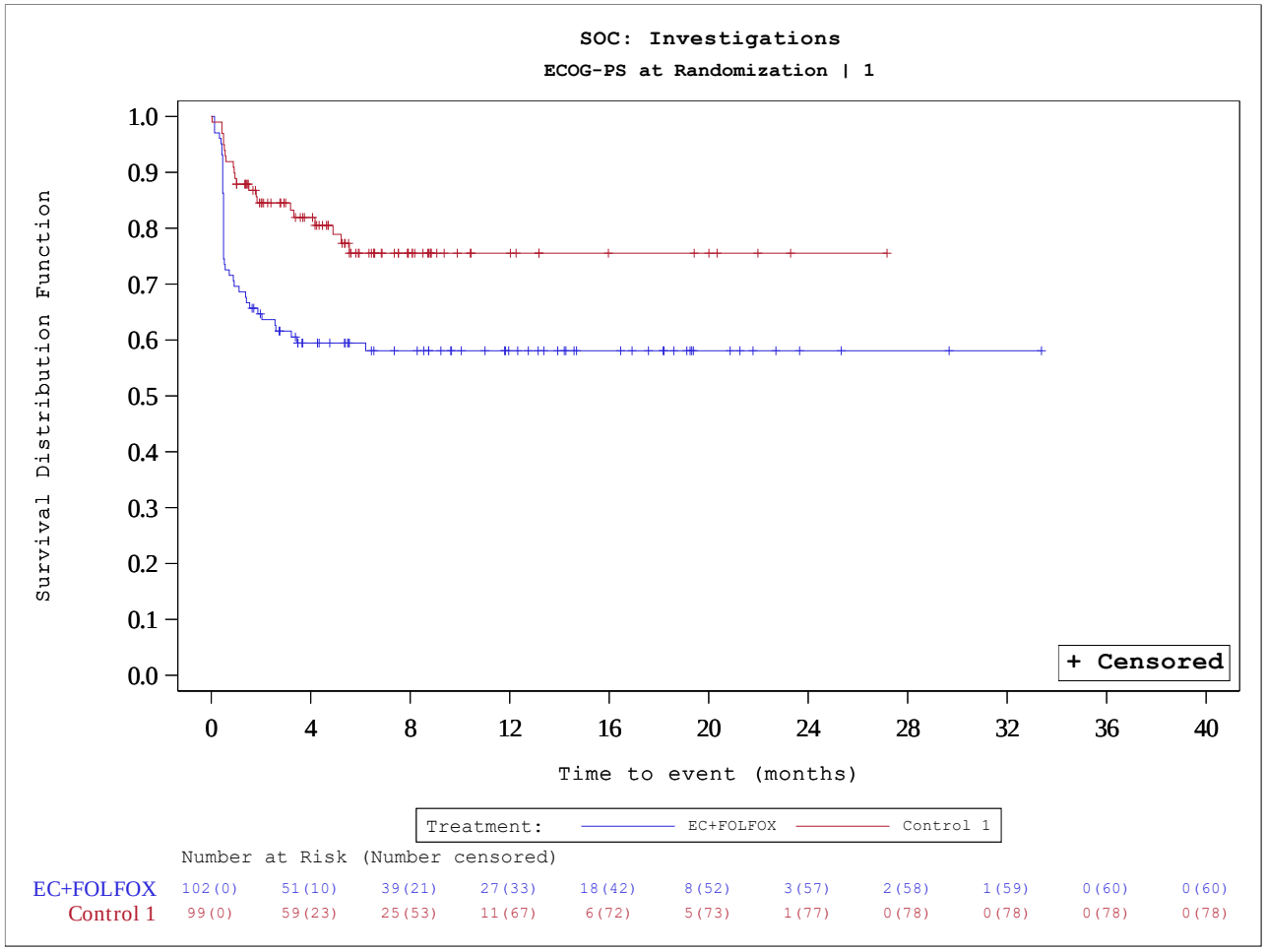

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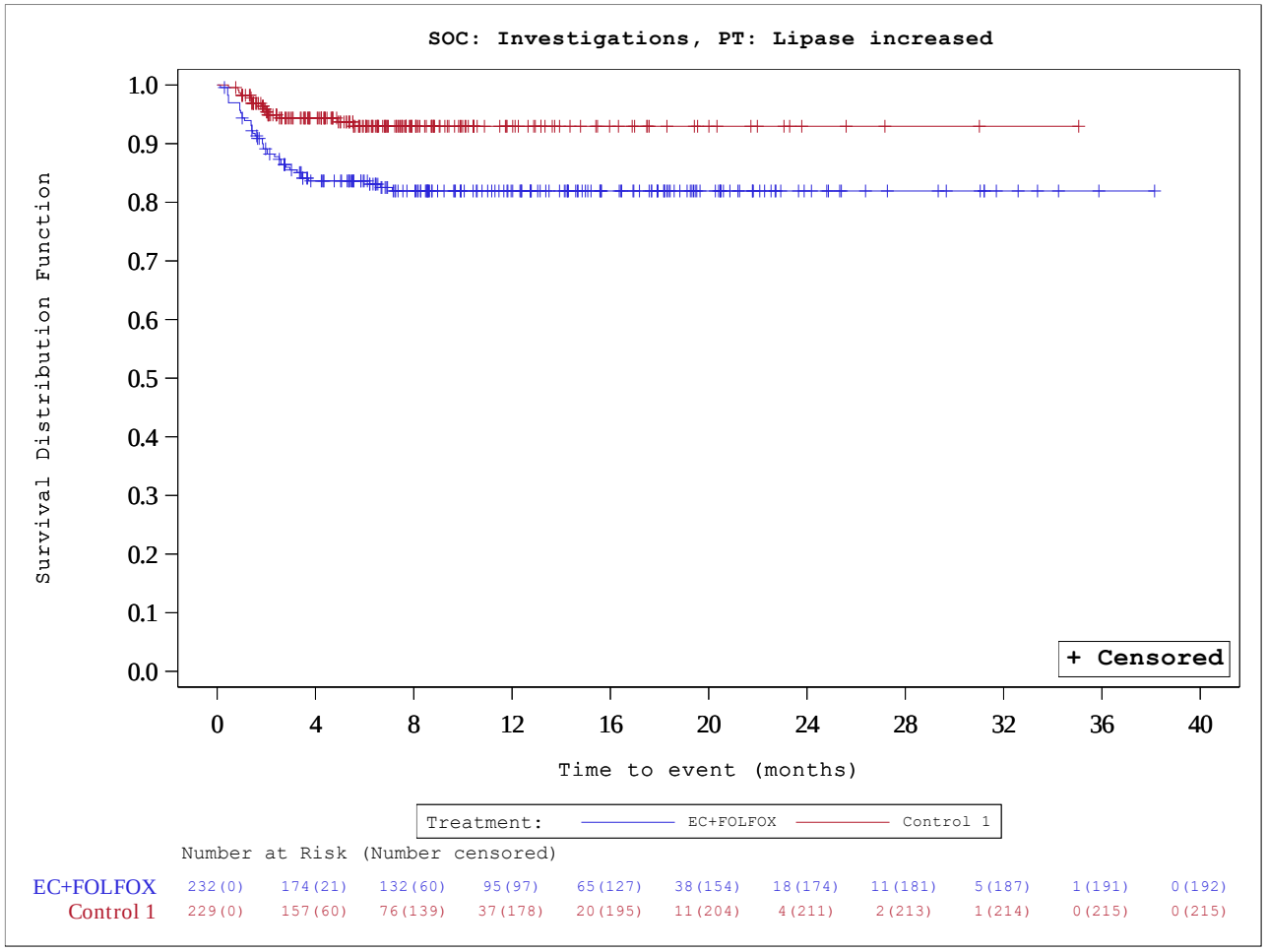

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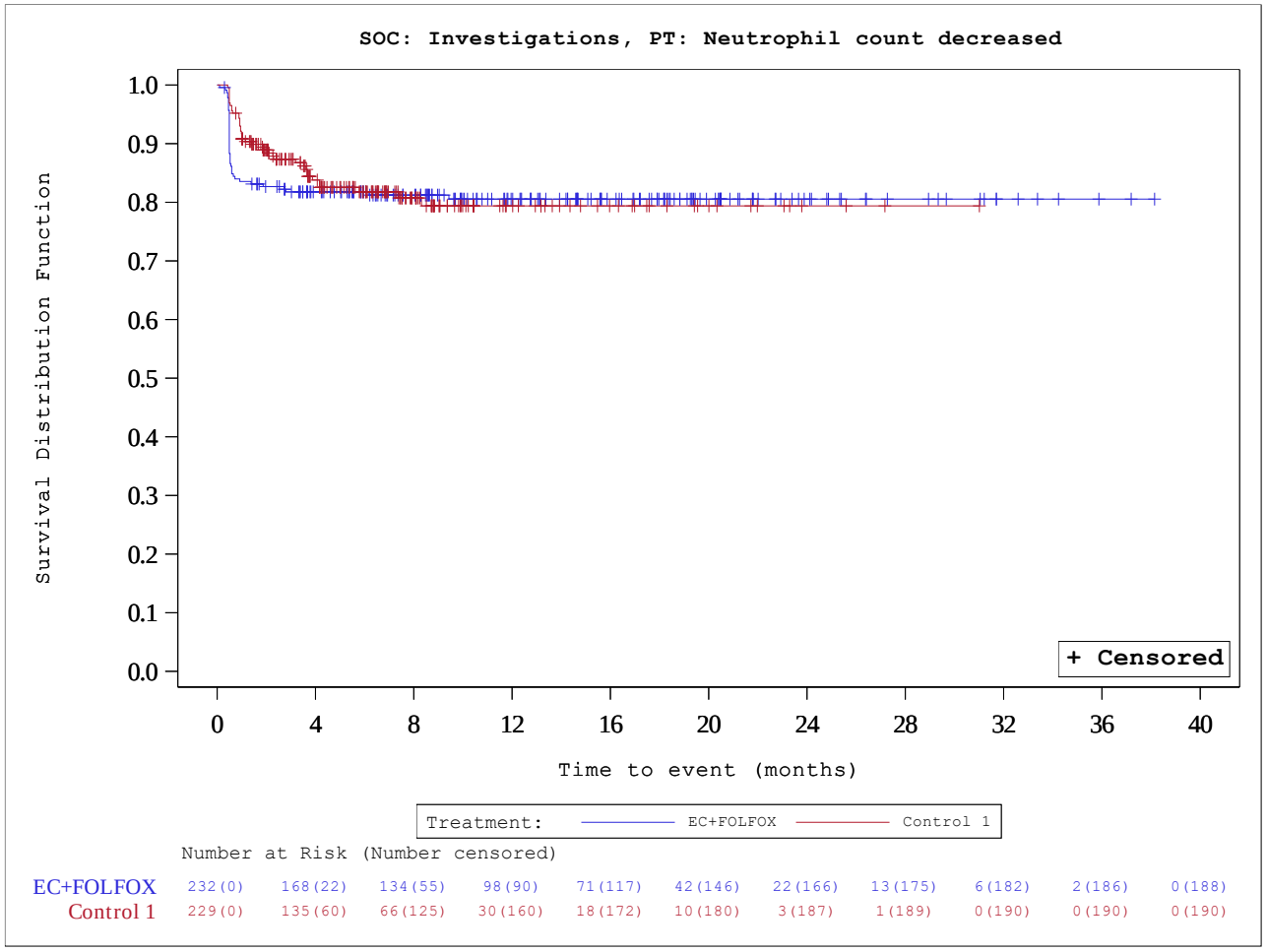

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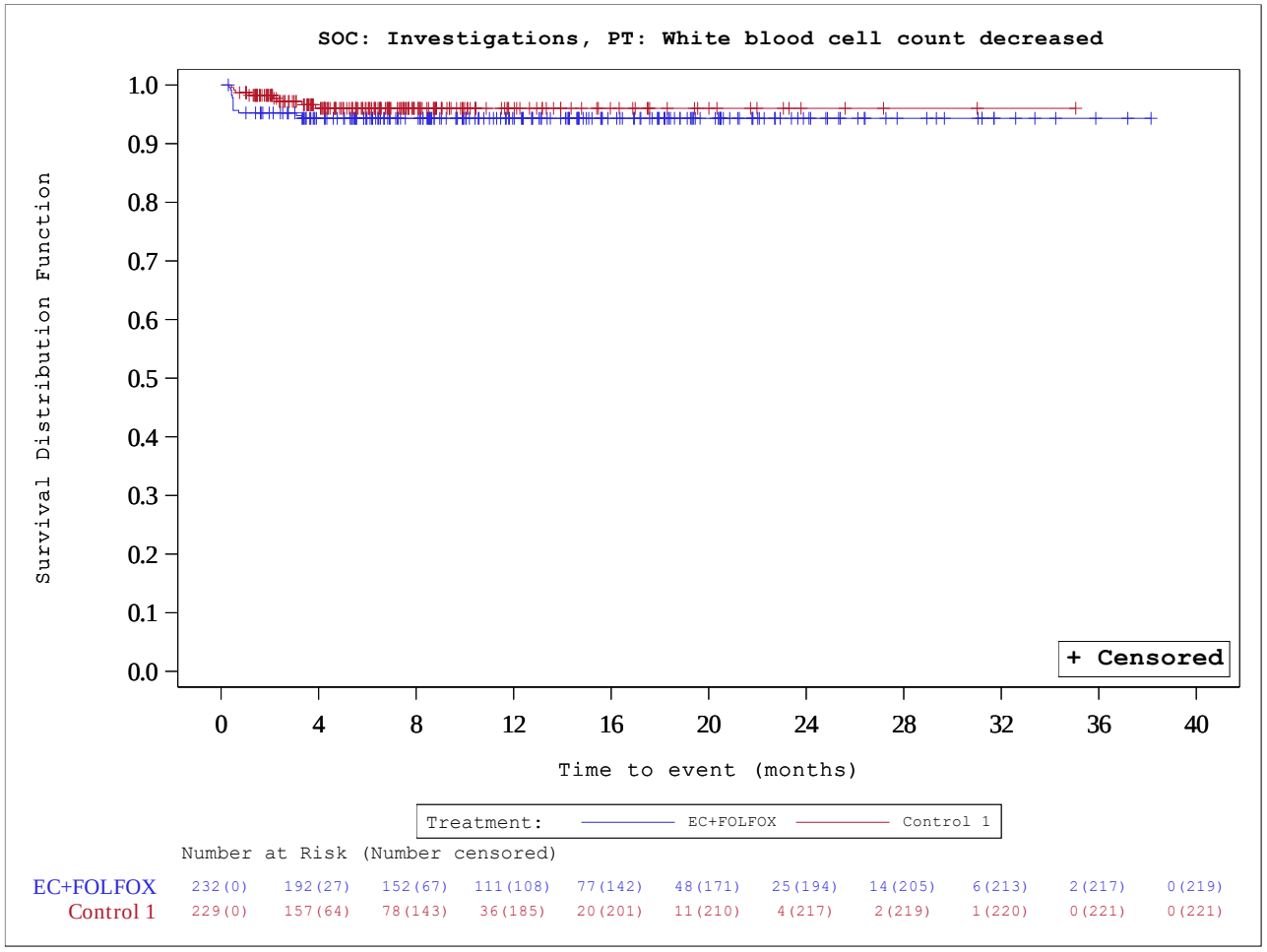

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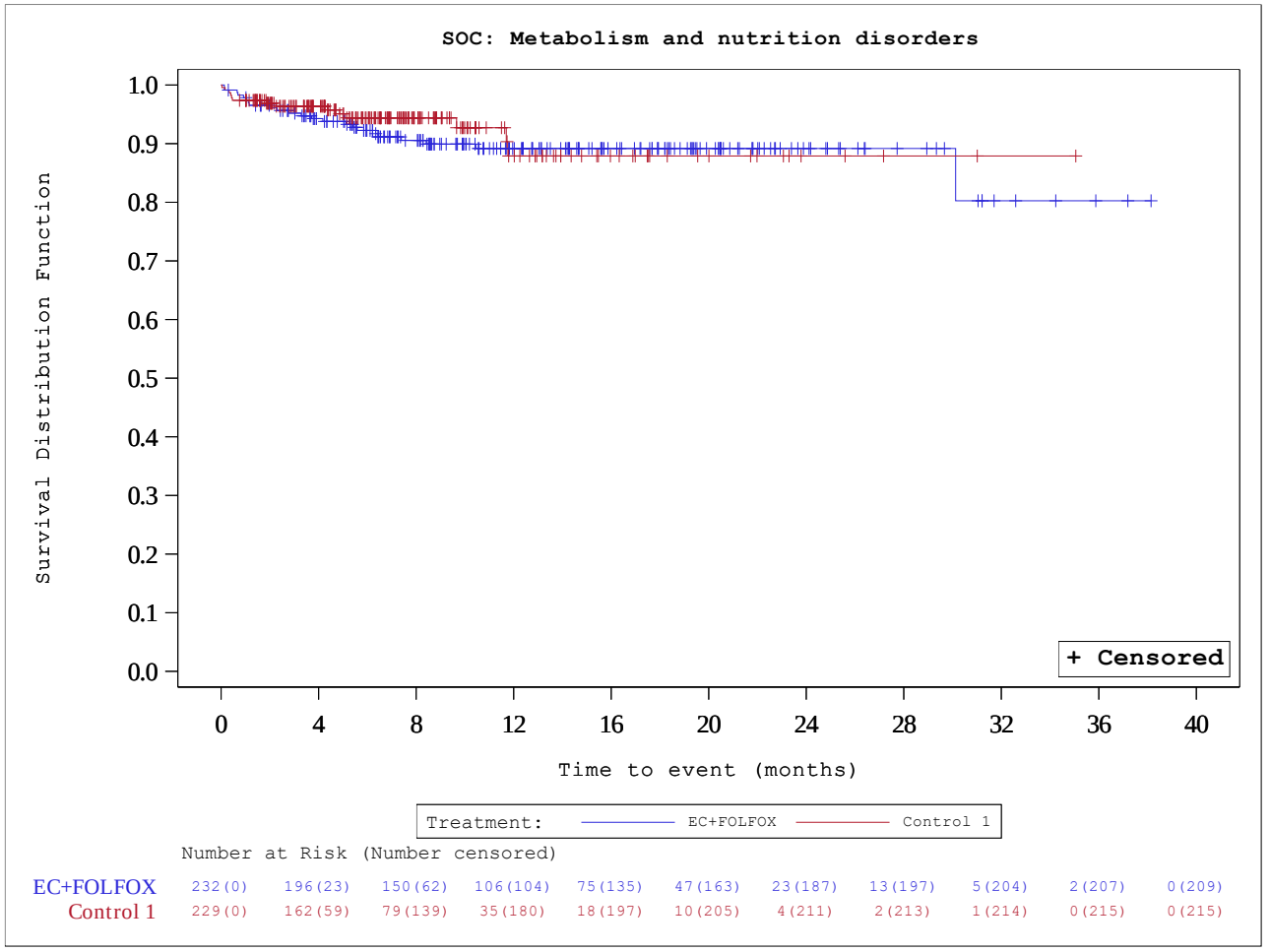

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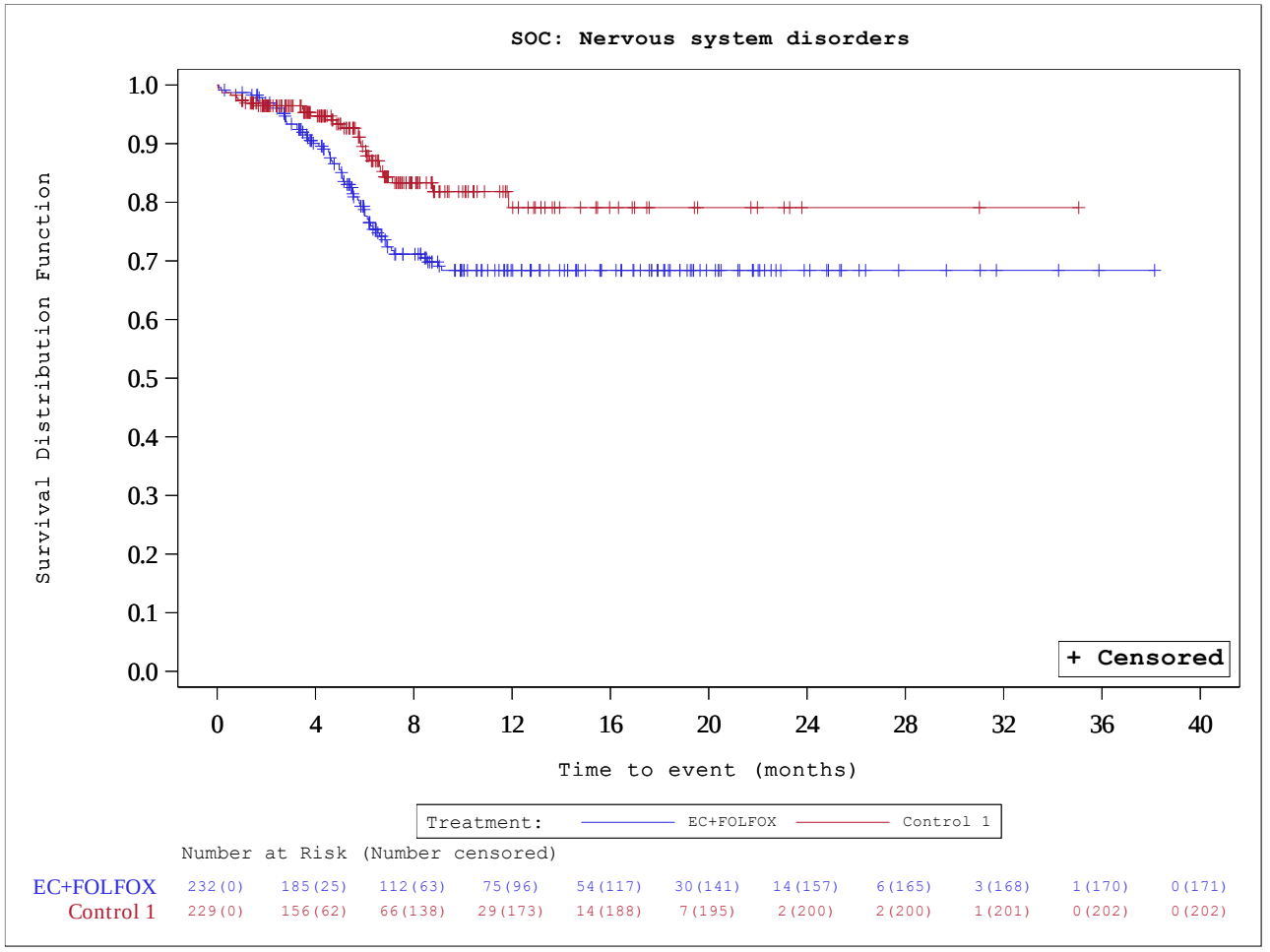

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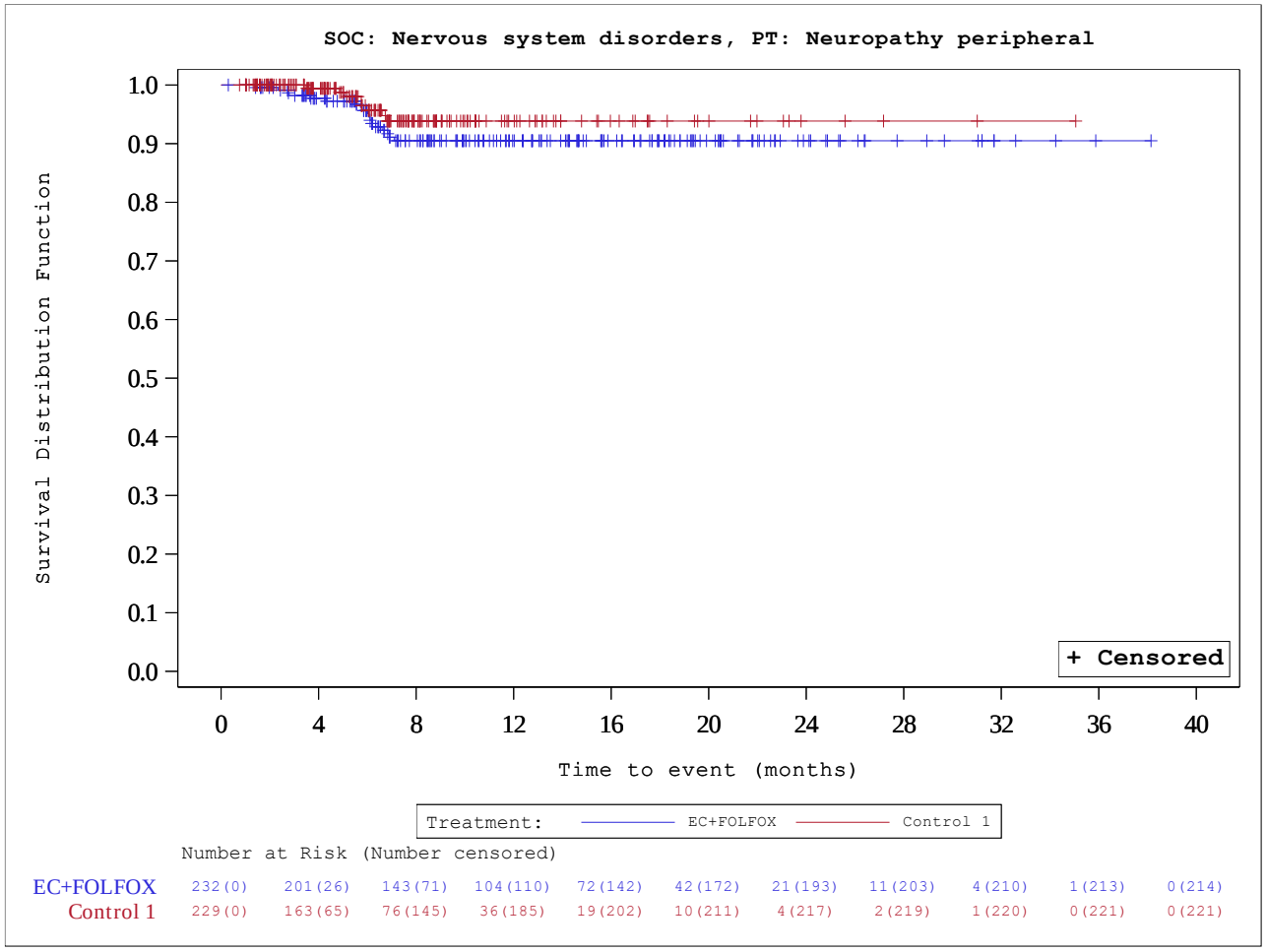

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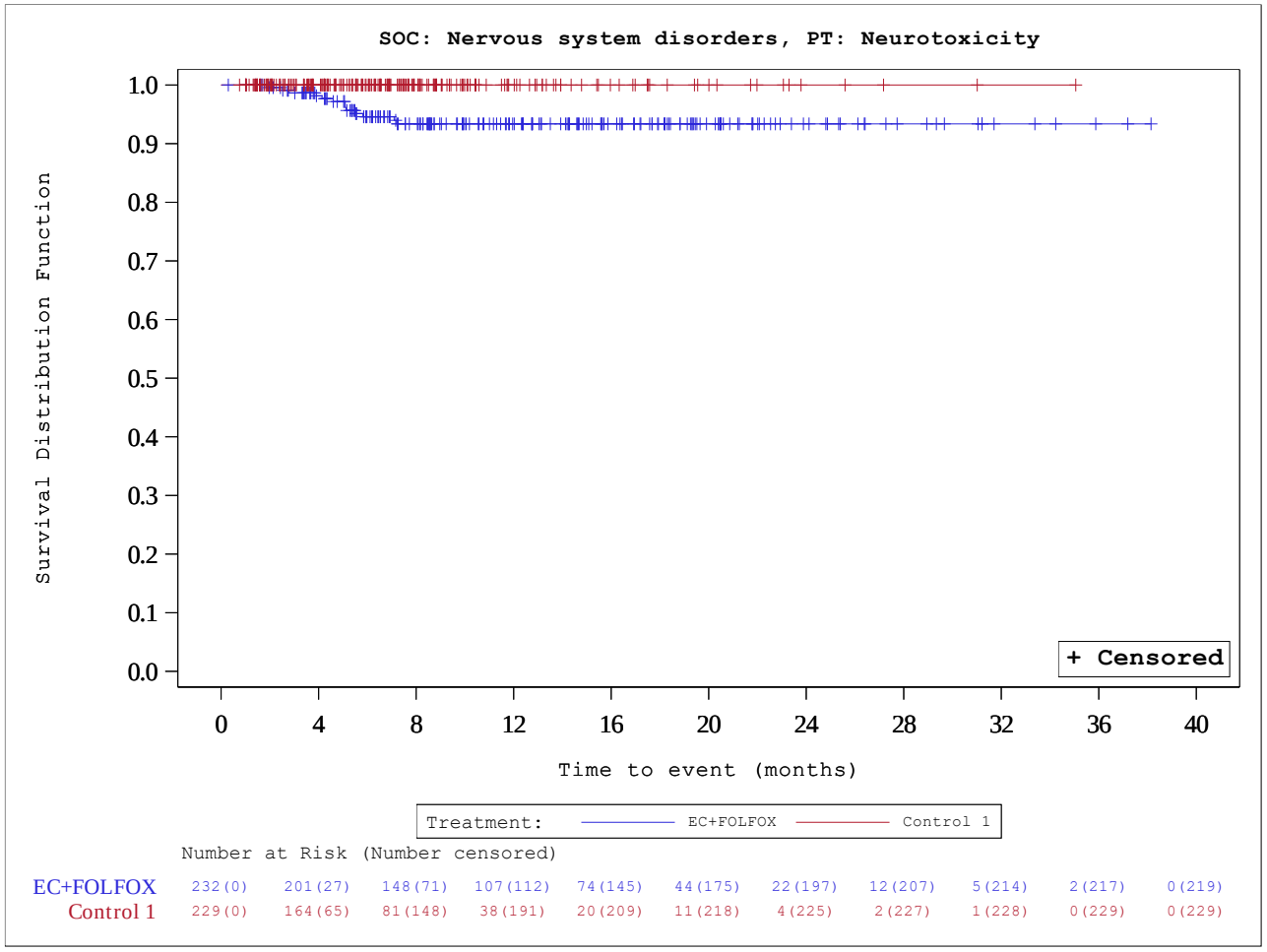

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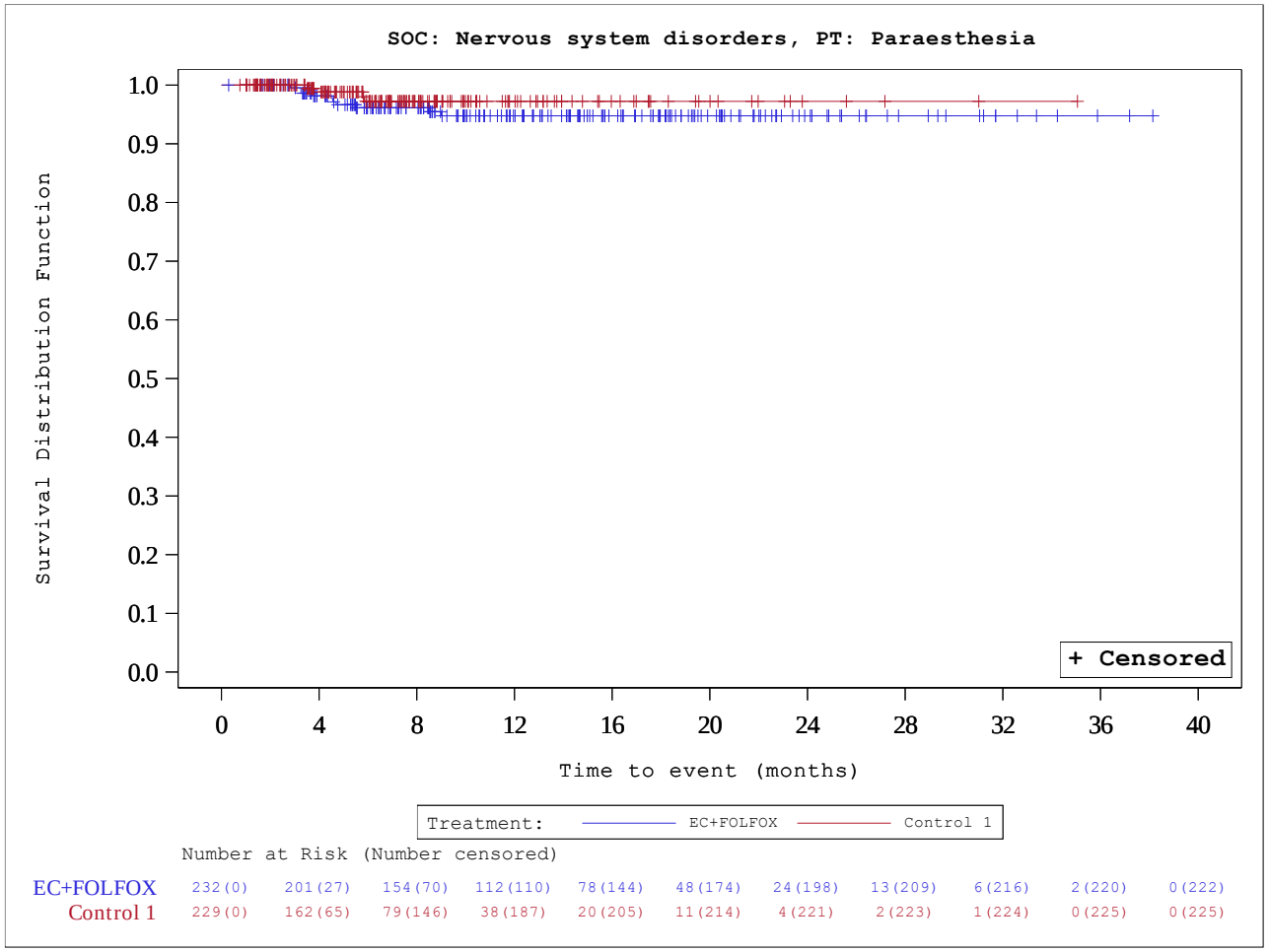

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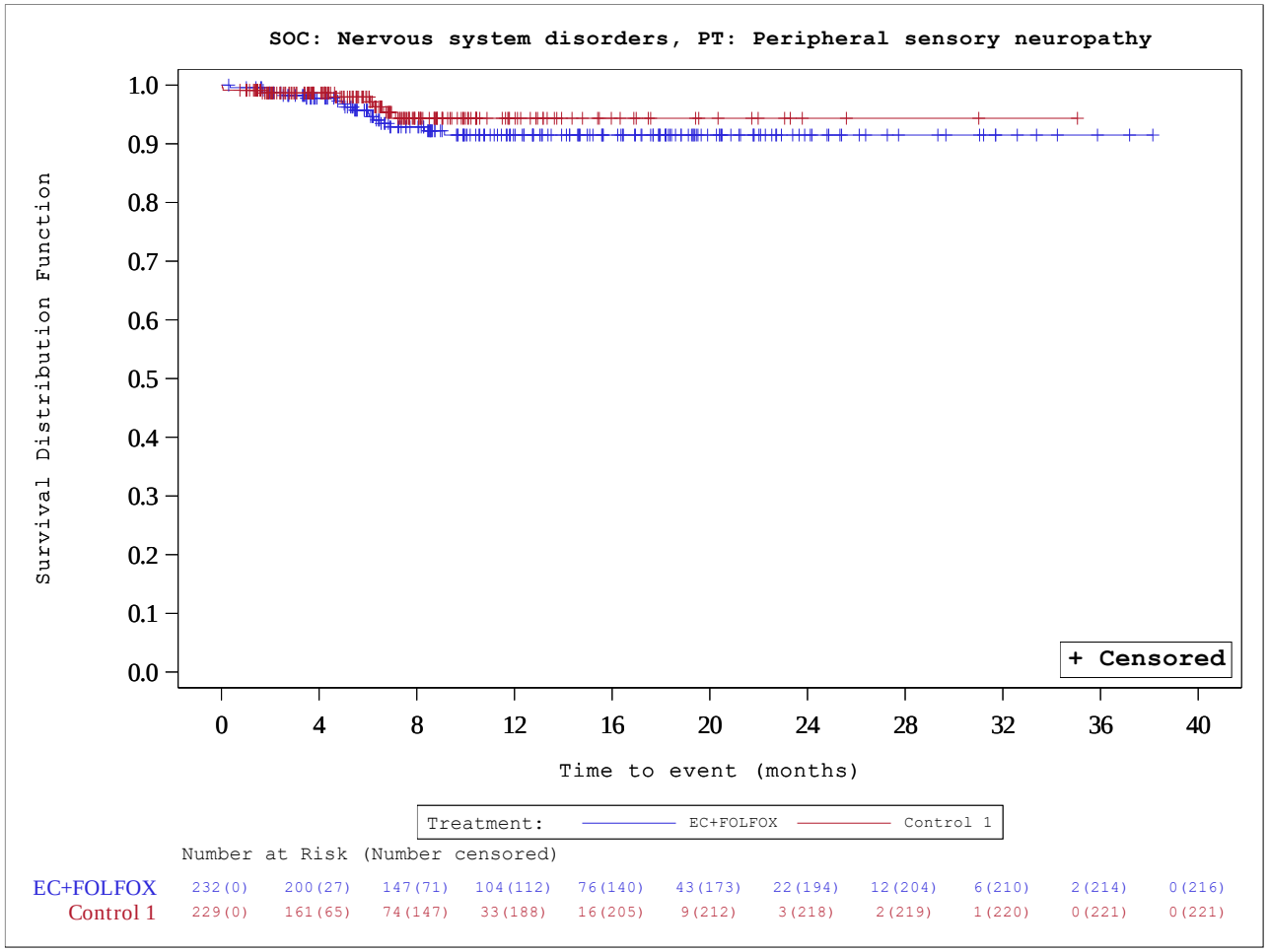

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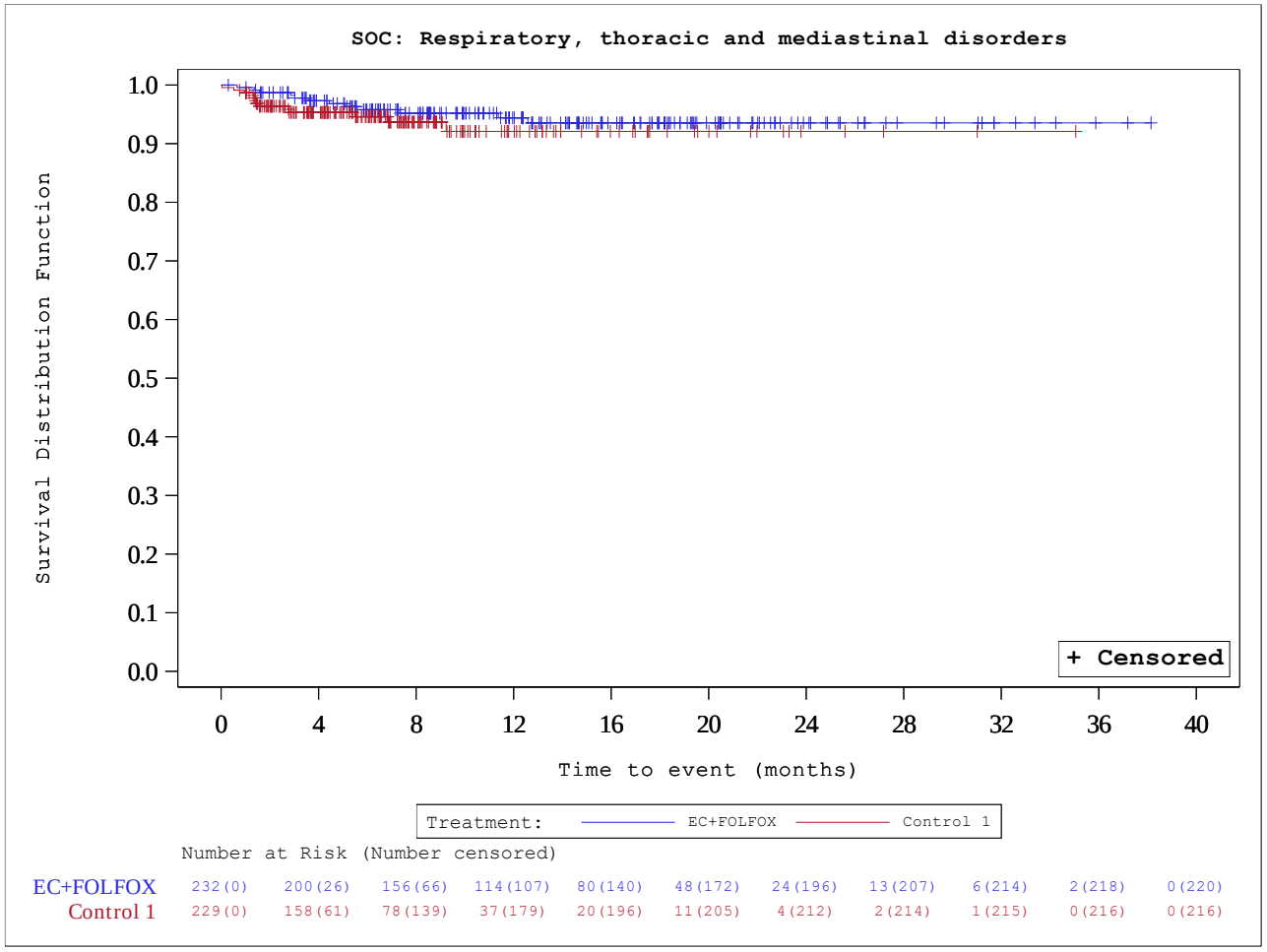

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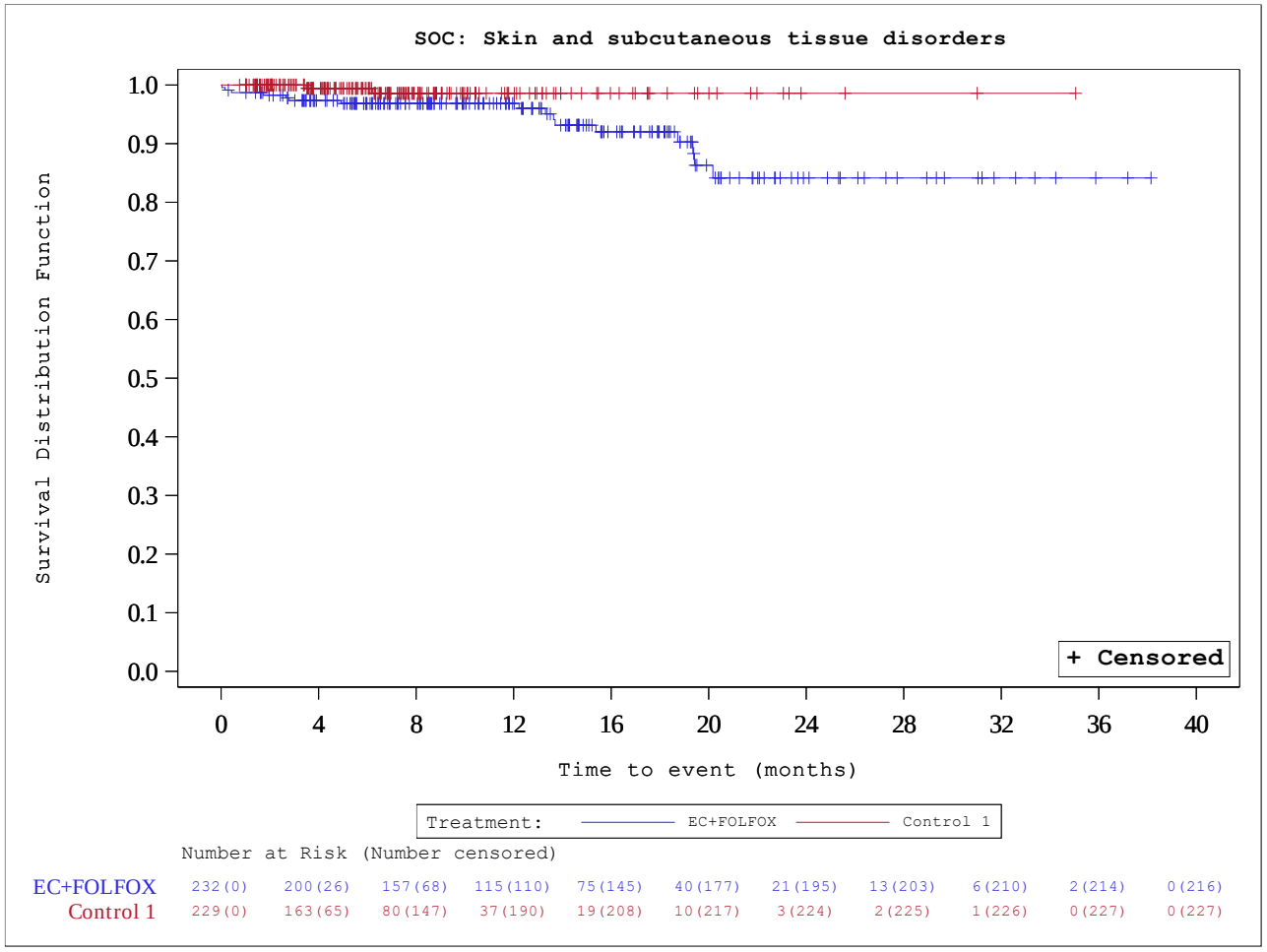
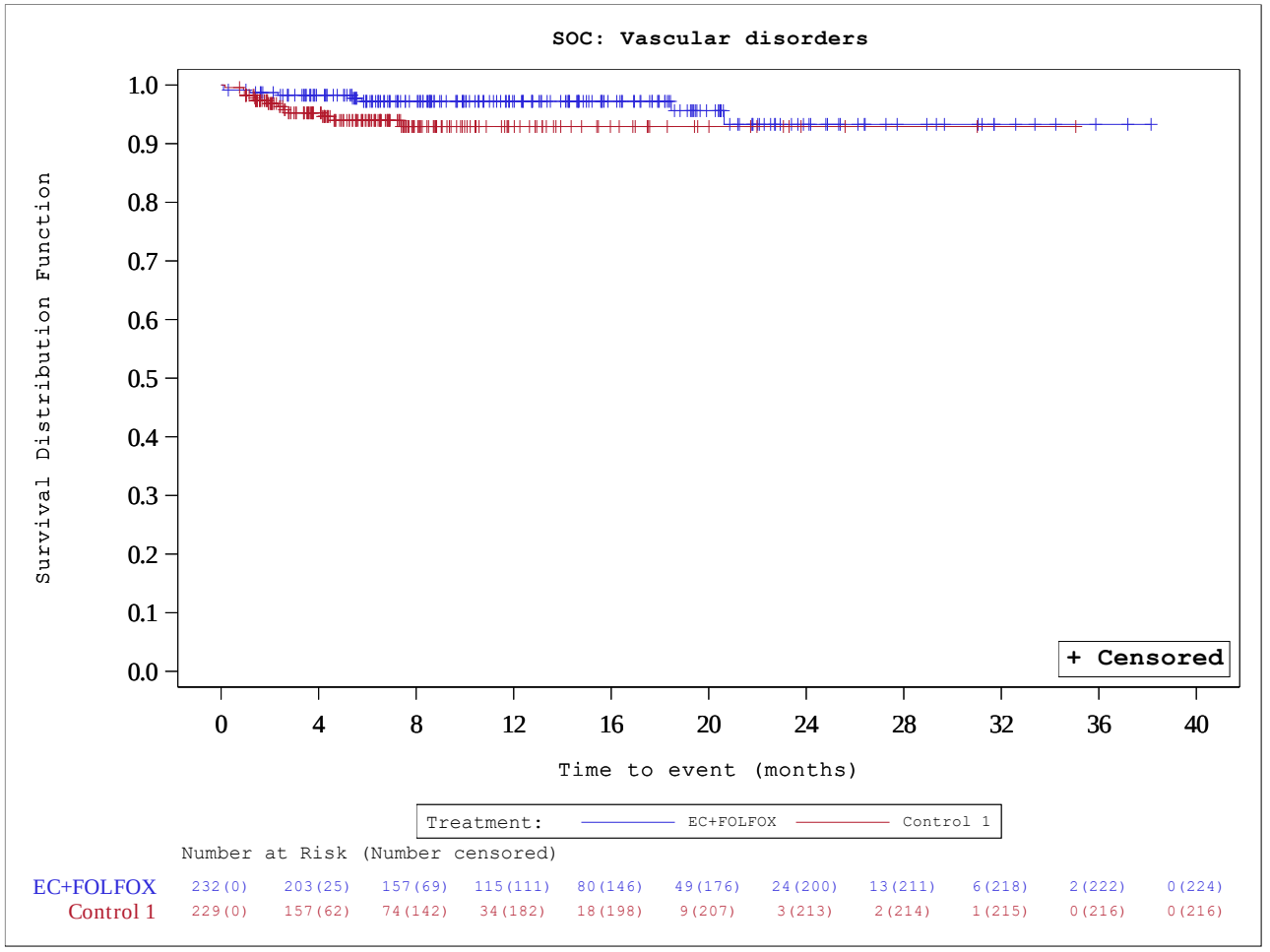
Kaplan Meier Plot of frequent Frequent Severe AE by SOC, PT (incidence >= 5% or >=10 patients and incidence >= 1%)
Safety Analysis Set



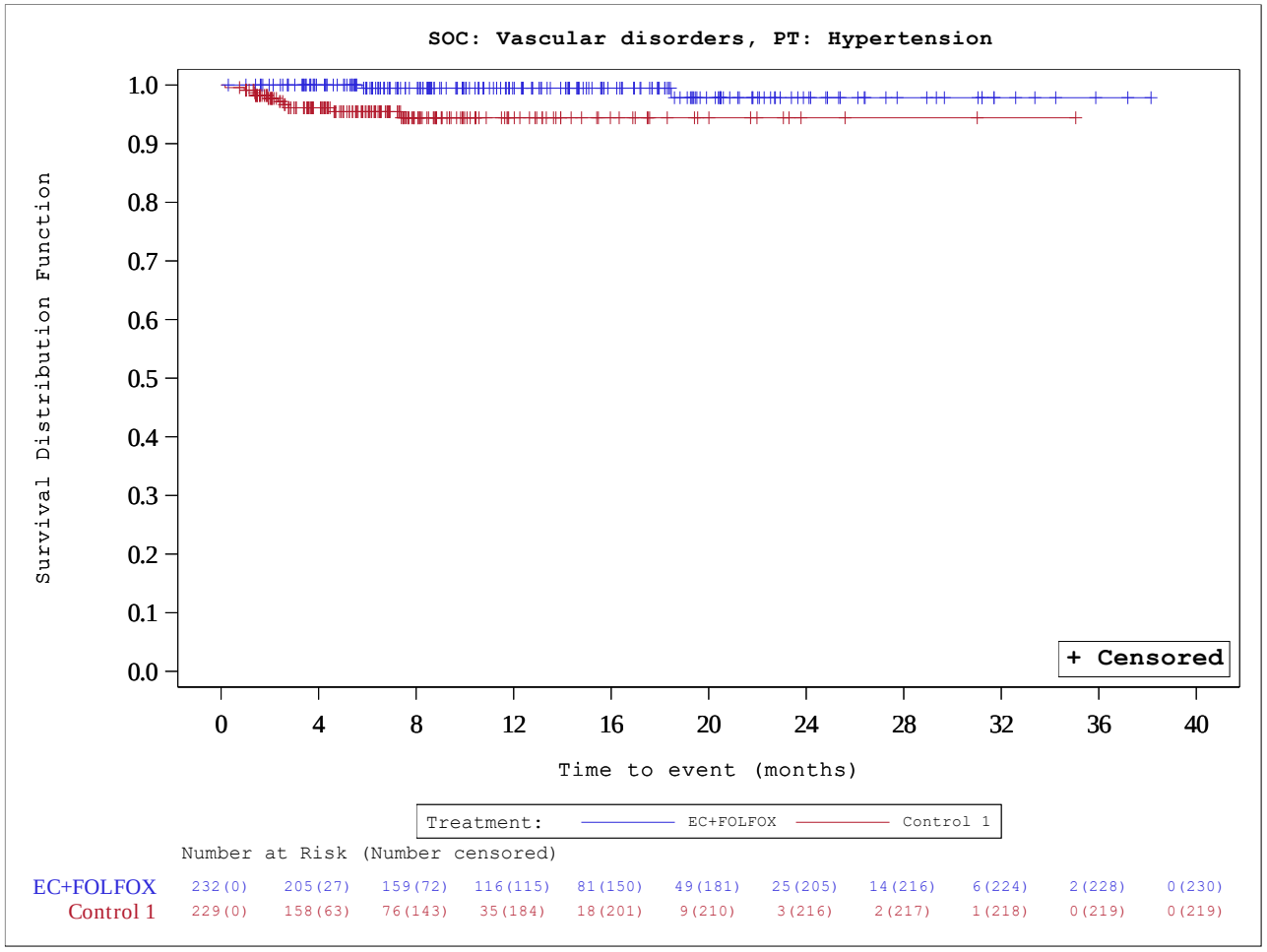
Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
Subgroup analysis was done for SOCs / PTs with significant overall treatment effect (significant log-rank).
Kaplan-Meier Plots for subgroups only created if p-value for interaction < 0.05.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Kaplan Meier Plot of frequent Frequent Severe AE by SOC, PT (incidence >= 5% or >=10 patients and incidence >= 1%)
Safety Analysis Set



Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
Subgroup analysis was done for SOCs / PTs with significant overall treatment effect (significant log-rank).
Kaplan-Meier Plots for subgroups only created if p-value for interaction < 0.05.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Kaplan Meier Plot of frequent Frequent Severe AE by SOC, PT (incidence >= 5% or >=10 patients and incidence >= 1%)
Safety Analysis Set



Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
Subgroup analysis was done for SOCs / PTs with significant overall treatment effect (significant log-rank).
Kaplan-Meier Plots for subgroups only created if p-value for interaction < 0.05.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Duration of frequent significant AE (months)
Safety Analysis Set

SOC - PT		EC+FOLFOX (N=232)	Control 1 (N=229)
Blood and lymphatic system disorders - Anaemia	n (missing)	107 (0)	58 (0)
	Mean (SD)	3.04 (4.710)	2.02 (3.027)
	Median	1.15	0.72
	Q1, Q3	0.46, 3.48	0.49, 2.07
	Min, Max	0.0, 25.8	0.0, 13.8
Ear and labyrinth disorders	n (missing)	5 (0)	10 (0)
	Mean (SD)	6.05 (5.141)	2.73 (3.337)
	Median	8.08	1.17
	Q1, Q3	0.59, 10.32	0.49, 5.29
	Min, Max	0.5, 10.8	0.0, 10.3
Eye disorders	n (missing)	34 (0)	13 (0)
	Mean (SD)	4.54 (5.322)	4.87 (5.540)
	Median	1.13	2.56
	Q1, Q3	0.53, 7.20	0.95, 5.88
	Min, Max	0.1, 17.4	0.0, 14.8
Gastrointestinal disorders - Abdominal pain	n (missing)	47 (0)	53 (0)
	Mean (SD)	1.58 (3.026)	1.58 (3.102)
	Median	0.30	0.30
	Q1, Q3	0.07, 2.14	0.13, 1.41
	Min, Max	0.0, 14.7	0.0, 18.1
Gastrointestinal disorders - Diarrhoea	n (missing)	97 (0)	115 (0)
	Mean (SD)	1.66 (4.254)	2.34 (4.612)
	Median	0.13	0.26
	Q1, Q3	0.07, 0.56	0.10, 1.84
	Min, Max	0.0, 23.0	0.0, 22.7
Gastrointestinal disorders - Gastrooesophageal reflux disease	n (missing)	6 (0)	11 (0)
	Mean (SD)	9.00 (8.979)	4.50 (3.936)
	Median	6.80	3.88
	Q1, Q3	3.75, 10.18	1.02, 7.26
	Min, Max	0.5, 26.0	0.1, 11.2
Gastrointestinal disorders - Haemorrhoids	n (missing)	24 (0)	8 (0)
	Mean (SD)	6.79 (8.920)	5.37 (7.038)
	Median	2.55	1.26
	Q1, Q3	0.56, 12.30	0.59, 11.10
	Min, Max	0.1, 27.3	0.1, 17.0
Gastrointestinal disorders - Vomiting	n (missing)	84 (0)	51 (0)
	Mean (SD)	0.76 (2.400)	0.86 (2.328)
	Median	0.10	0.10
	Q1, Q3	0.03, 0.26	0.03, 0.49
	Min, Max	0.0, 18.0	0.0, 12.4
General disorders and administration site conditions	n (missing)	187 (0)	148 (0)
	Mean (SD)	3.13 (5.502)	2.94 (4.831)
	Median	0.49	0.46
	Q1, Q3	0.16, 3.38	0.13, 3.10
	Min, Max	0.0, 30.3	0.0, 21.3

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
Duration is defined as the time from AE onset to AE end date + 1.
Division by 30.4375 for day-to-month calculation.
Significant denotes to SOCs / PTs with p-value from 2-sided log-rank test < 0.05.
Frequent indicates SOCs / PTs with criteria: incidence >= 10% or >=10 patients and incidence >= 1%.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Duration of frequent significant AE (months)
Safety Analysis Set

SOC - PT		EC+FOLFOX (N=232)	Control 1 (N=229)
General disorders and administration site conditions - Asthenia	n (missing)	68 (0)	34 (0)
	Mean (SD)	2.13 (3.887)	2.59 (3.925)
	Median	0.57	0.80
	Q1, Q3	0.25, 1.87	0.23, 2.99
	Min, Max	0.0, 18.1	0.1, 14.3
General disorders and administration site conditions - Pain	n (missing)	19 (0)	5 (0)
	Mean (SD)	3.34 (5.331)	0.43 (0.703)
	Median	0.30	0.10
	Q1, Q3	0.07, 4.17	0.07, 0.26
	Min, Max	0.0, 17.4	0.0, 1.7
General disorders and administration site conditions - Pyrexia	n (missing)	67 (0)	36 (0)
	Mean (SD)	0.26 (0.601)	0.16 (0.276)
	Median	0.07	0.10
	Q1, Q3	0.03, 0.23	0.03, 0.15
	Min, Max	0.0, 4.1	0.0, 1.6
Investigations	n (missing)	164 (0)	138 (0)
	Mean (SD)	1.30 (2.236)	1.74 (3.573)
	Median	0.49	0.49
	Q1, Q3	0.26, 1.17	0.30, 1.41
	Min, Max	0.0, 14.5	0.0, 27.3
Investigations - Electrocardiogram QT prolonged	n (missing)	11 (0)	1 (0)
	Mean (SD)	1.04 (1.822)	0.03 (-)
	Median	0.46	0.03
	Q1, Q3	0.26, 0.92	0.03, 0.03
	Min, Max	0.0, 6.4	0.0, 0.0
Investigations - Lipase increased	n (missing)	52 (0)	27 (0)
	Mean (SD)	1.62 (2.402)	1.65 (2.108)
	Median	0.92	0.95
	Q1, Q3	0.46, 1.56	0.46, 1.84
	Min, Max	0.0, 14.6	0.0, 10.0
Investigations - Weight decreased	n (missing)	44 (0)	22 (0)
	Mean (SD)	3.40 (5.599)	3.09 (5.627)
	Median	1.41	1.58
	Q1, Q3	0.79, 3.38	0.69, 2.92
	Min, Max	0.3, 32.4	0.3, 27.3
Metabolism and nutrition disorders	n (missing)	144 (0)	99 (0)
	Mean (SD)	3.10 (5.470)	2.54 (4.013)
	Median	0.69	0.53
	Q1, Q3	0.36, 2.86	0.23, 2.79
	Min, Max	0.0, 28.3	0.0, 18.4
Metabolism and nutrition disorders - Hyperglycaemia	n (missing)	20 (0)	4 (0)
	Mean (SD)	2.68 (4.219)	2.58 (2.601)
	Median	1.26	1.63
	Q1, Q3	0.51, 3.14	0.90, 4.25
	Min, Max	0.2, 18.6	0.7, 6.4

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
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Division by 30.4375 for day-to-month calculation.
Significant denotes to SOCs / PTs with p-value from 2-sided log-rank test < 0.05.
Frequent indicates SOCs / PTs with criteria: incidence >= 10% or >=10 patients and incidence >= 1%.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Duration of frequent significant AE (months)
Safety Analysis Set

SOC - PT		EC+FOLFOX (N=232)	Control 1 (N=229)
Metabolism and nutrition disorders - Hypoalbuminaemia	n (missing)	30 (0)	14 (0)
	Mean (SD)	1.47 (2.622)	0.56 (0.326)
	Median	0.49	0.49
	Q1, Q3	0.36, 1.28	0.36, 0.66
	Min, Max	0.1, 12.2	0.2, 1.3
Metabolism and nutrition disorders - Hypomagnesaemia	n (missing)	38 (0)	11 (0)
	Mean (SD)	1.66 (2.976)	1.93 (4.765)
	Median	0.64	0.39
	Q1, Q3	0.43, 1.41	0.16, 0.95
	Min, Max	0.0, 14.8	0.1, 16.2
Metabolism and nutrition disorders - Hypophosphataemia	n (missing)	14 (0)	3 (0)
	Mean (SD)	1.02 (1.126)	0.82 (0.913)
	Median	0.49	0.36
	Q1, Q3	0.33, 1.25	0.23, 1.87
	Min, Max	0.1, 3.4	0.2, 1.9
Musculoskeletal and connective tissue disorders	n (missing)	133 (0)	50 (0)
	Mean (SD)	4.74 (6.059)	2.70 (3.743)
	Median	2.10	1.38
	Q1, Q3	0.46, 6.83	0.26, 4.04
	Min, Max	0.0, 28.8	0.0, 19.8
Musculoskeletal and connective tissue disorders - Arthralgia	n (missing)	73 (0)	12 (0)
	Mean (SD)	4.95 (6.654)	3.37 (4.497)
	Median	2.10	1.36
	Q1, Q3	0.46, 6.41	0.59, 3.70
	Min, Max	0.1, 28.8	0.2, 13.5
Musculoskeletal and connective tissue disorders - Myalgia	n (missing)	38 (0)	9 (0)
	Mean (SD)	4.89 (4.321)	2.47 (3.879)
	Median	3.71	0.72
	Q1, Q3	1.05, 7.26	0.26, 3.32
	Min, Max	0.0, 14.3	0.1, 12.2
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	n (missing)	43 (0)	9 (0)
	Mean (SD)	6.96 (6.978)	4.65 (4.922)
	Median	3.75	3.25
	Q1, Q3	0.85, 13.40	0.69, 7.82
	Min, Max	0.0, 19.8	0.3, 14.7
Renal and urinary disorders - Proteinuria	n (missing)	6 (0)	18 (0)
	Mean (SD)	3.00 (3.735)	2.39 (3.124)
	Median	1.05	0.97
	Q1, Q3	0.92, 4.53	0.46, 3.52
	Min, Max	0.4, 10.0	0.1, 11.0
Skin and subcutaneous tissue disorders	n (missing)	188 (0)	79 (0)
	Mean (SD)	8.33 (8.043)	6.75 (7.065)
	Median	6.23	3.88
	Q1, Q3	1.18, 13.39	1.08, 11.30
	Min, Max	0.0, 34.0	0.0, 29.2

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
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Significant denotes to SOCs / PTs with p-value from 2-sided log-rank test < 0.05.
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Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Duration of frequent significant AE (months)
Safety Analysis Set

SOC - PT		EC+FOLFOX (N=232)	Control 1 (N=229)
Skin and subcutaneous tissue disorders - Alopecia	n (missing)	53 (0)	26 (0)
	Mean (SD)	10.64 (7.333)	9.11 (5.979)
	Median	8.31	8.66
	Q1, Q3	4.86, 16.62	4.24, 13.27
	Min, Max	0.5, 28.5	1.2, 24.7
Skin and subcutaneous tissue disorders - Dermatitis acneiform	n (missing)	43 (0)	2 (0)
	Mean (SD)	6.72 (6.907)	3.43 (0.906)
	Median	4.53	3.43
	Q1, Q3	0.76, 11.89	2.79, 4.07
	Min, Max	0.1, 24.6	2.8, 4.1
Skin and subcutaneous tissue disorders - Dry skin	n (missing)	38 (0)	11 (0)
	Mean (SD)	7.87 (7.115)	7.72 (6.936)
	Median	6.46	4.76
	Q1, Q3	1.64, 12.58	1.58, 13.08
	Min, Max	0.4, 25.4	0.5, 21.0
Skin and subcutaneous tissue disorders - Pigmentation disorder	n (missing)	17 (0)	2 (0)
	Mean (SD)	14.20 (9.679)	17.63 (16.425)
	Median	13.01	17.63
	Q1, Q3	5.88, 21.45	6.01, 29.24
	Min, Max	0.7, 28.1	6.0, 29.2
Skin and subcutaneous tissue disorders - Pruritus	n (missing)	32 (0)	7 (0)
	Mean (SD)	4.29 (5.983)	2.41 (4.029)
	Median	1.82	0.92
	Q1, Q3	0.46, 5.83	0.23, 2.79
	Min, Max	0.0, 25.1	0.0, 11.3
Skin and subcutaneous tissue disorders - Rash	n (missing)	70 (0)	9 (0)
	Mean (SD)	5.61 (7.090)	4.58 (4.489)
	Median	2.22	3.52
	Q1, Q3	0.49, 9.07	0.36, 8.34
	Min, Max	0.0, 26.7	0.0, 11.1
Skin and subcutaneous tissue disorders - Skin hyperpigmentation	n (missing)	43 (0)	7 (0)
	Mean (SD)	13.28 (7.659)	12.21 (5.389)
	Median	12.42	13.54
	Q1, Q3	6.24, 18.66	6.05, 15.44
	Min, Max	1.3, 34.0	4.9, 20.1
Skin and subcutaneous tissue disorders - Skin lesion	n (missing)	13 (0)	2 (0)
	Mean (SD)	5.00 (6.191)	1.05 (0.465)
	Median	4.17	1.05
	Q1, Q3	0.92, 6.01	0.72, 1.38
	Min, Max	0.3, 23.7	0.7, 1.4
Vascular disorders	n (missing)	36 (0)	51 (0)
	Mean (SD)	3.38 (6.152)	4.62 (5.381)
	Median	0.49	2.07
	Q1, Q3	0.21, 2.18	0.26, 8.44
	Min, Max	0.0, 21.7	0.0, 21.3

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
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Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Duration of frequent significant AE (months)
Safety Analysis Set

SOC - PT		EC+FOLFOX (N=232)	Control 1 (N=229)
Vascular disorders - Hypertension	n (missing)	9 (0)	35 (0)
	Mean (SD)	0.57 (0.541)	5.31 (4.997)
	Median	0.46	3.84
	Q1, Q3	0.30, 0.53	1.38, 9.76
	Min, Max	0.0, 1.9	0.0, 19.9

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
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Significant denotes to SOCs / PTs with p-value from 2-sided log-rank test < 0.05.
Frequent indicates SOCs / PTs with criteria: incidence >= 10% or >=10 patients and incidence >= 1%.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Duration of frequent significant severe AE (months)
Safety Analysis Set

SOC - PT		EC+FOLFOX (N=232)	Control 1 (N=229)
Blood and lymphatic system disorders - Anaemia	n (missing)	35 (0)	9 (0)
	Mean (SD)	0.41 (0.395)	0.37 (0.276)
	Median	0.30	0.26
	Q1, Q3	0.16, 0.49	0.20, 0.56
	Min, Max	0.0, 2.0	0.1, 0.9
Gastrointestinal disorders - Diarrhoea	n (missing)	3 (0)	11 (0)
	Mean (SD)	0.10 (0.000)	1.08 (2.056)
	Median	0.10	0.30
	Q1, Q3	0.10, 0.10	0.10, 0.53
	Min, Max	0.1, 0.1	0.0, 6.9
Investigations	n (missing)	88 (0)	65 (0)
	Mean (SD)	0.70 (0.963)	0.64 (0.690)
	Median	0.44	0.43
	Q1, Q3	0.23, 0.76	0.23, 0.69
	Min, Max	0.0, 5.5	0.0, 2.8
Investigations - Lipase increased	n (missing)	40 (0)	14 (0)
	Mean (SD)	1.48 (1.472)	1.48 (0.897)
	Median	0.95	1.26
	Q1, Q3	0.49, 1.74	0.66, 2.30
	Min, Max	0.1, 6.4	0.5, 2.8
Nervous system disorders	n (missing)	61 (0)	27 (0)
	Mean (SD)	5.25 (6.049)	4.42 (5.242)
	Median	2.07	1.81
	Q1, Q3	0.46, 8.31	0.30, 7.95
	Min, Max	0.0, 23.4	0.0, 20.1
Skin and subcutaneous tissue disorders	n (missing)	16 (0)	2 (0)
	Mean (SD)	1.30 (1.878)	11.83 (11.662)
	Median	0.76	11.83
	Q1, Q3	0.39, 0.99	3.58, 20.07
	Min, Max	0.1, 6.1	3.6, 20.1
Vascular disorders - Hypertension	n (missing)	2 (0)	10 (0)
	Mean (SD)	0.38 (0.209)	3.13 (4.219)
	Median	0.38	1.07
	Q1, Q3	0.23, 0.53	0.03, 5.55
	Min, Max	0.2, 0.5	0.0, 12.2

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Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Resolved and unresolved events of frequent significant Any AE
Safety Analysis Set

SOC PT or SOC - PT	EC+FOLFOX (N=232)				Control 1 (N=229)			
	Patients with event	Any event	Resolved event	Unresolved event	Patients with event	Any event	Resolved event	Unresolved event
Blood and lymphatic system disorders - Anaemia	107 (46.1)	370	321 (86.8)	49 (13.2)	58 (25.3)	134	110 (82.1)	24 (17.9)
Ear and labyrinth disorders	5 (2.2)	7	2 (28.6)	5 (71.4)	10 (4.4)	13	11 (84.6)	2 (15.4)
Eye disorders	34 (14.7)	60	34 (56.7)	26 (43.3)	13 (5.7)	22	14 (63.6)	8 (36.4)
Gastrointestinal disorders - Abdominal pain	47 (20.3)	87	71 (81.6)	16 (18.4)	53 (23.1)	96	73 (76.0)	23 (24.0)
Diarrhoea	97 (41.8)	204	186 (91.2)	18 (8.8)	115 (50.2)	251	223 (88.8)	28 (11.2)
Gastrooesophageal reflux disease	6 (2.6)	7	2 (28.6)	5 (71.4)	11 (4.8)	11	4 (36.4)	7 (63.6)
Haemorrhoids	24 (10.3)	30	16 (53.3)	14 (46.7)	8 (3.5)	8	4 (50.0)	4 (50.0)
Vomiting	84 (36.2)	195	186 (95.4)	9 (4.6)	51 (22.3)	113	106 (93.8)	7 (6.2)
General disorders and administration site conditions	187 (80.6)	733	606 (82.7)	127 (17.3)	148 (64.6)	434	336 (77.4)	98 (22.6)
Asthenia	68 (29.3)	214	182 (85.0)	32 (15.0)	34 (14.8)	92	74 (80.4)	18 (19.6)
Pain	19 (8.2)	21	13 (61.9)	8 (38.1)	5 (2.2)	6	5 (83.3)	1 (16.7)
Pyrexia	67 (28.9)	123	120 (97.6)	3 (2.4)	36 (15.7)	49	47 (95.9)	2 (4.1)
Investigations	164 (70.7)	1153	1053 (91.3)	100 (8.7)	138 (60.3)	869	771 (88.7)	98 (11.3)
Electrocardiogram QT prolonged	11 (4.7)	30	30 (100.0)	0	1 (0.4)	1	1 (100.0)	0
Lipase increased	52 (22.4)	168	156 (92.9)	12 (7.1)	27 (11.8)	75	64 (85.3)	11 (14.7)
Weight decreased	44 (19.0)	83	61 (73.5)	22 (26.5)	22 (9.6)	29	18 (62.1)	11 (37.9)
Metabolism and nutrition disorders	144 (62.1)	619	521 (84.2)	98 (15.8)	99 (43.2)	348	271 (77.9)	77 (22.1)
Hyperglycaemia	20 (8.6)	44	39 (88.6)	5 (11.4)	4 (1.7)	12	9 (75.0)	3 (25.0)
Hypoalbuminaemia	30 (12.9)	67	59 (88.1)	8 (11.9)	14 (6.1)	46	39 (84.8)	7 (15.2)
Hypomagnesaemia	38 (16.4)	99	86 (86.9)	13 (13.1)	11 (4.8)	25	20 (80.0)	5 (20.0)
Hypophosphataemia	14 (6.0)	25	19 (76.0)	6 (24.0)	3 (1.3)	9	8 (88.9)	1 (11.1)
Musculoskeletal and connective tissue disorders	133 (57.3)	328	213 (64.9)	115 (35.1)	50 (21.8)	100	59 (59.0)	41 (41.0)
Arthralgia	73 (31.5)	138	89 (64.5)	49 (35.5)	12 (5.2)	14	9 (64.3)	5 (35.7)
Myalgia	38 (16.4)	49	28 (57.1)	21 (42.9)	9 (3.9)	10	8 (80.0)	2 (20.0)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	43 (18.5)	62	35 (56.5)	27 (43.5)	9 (3.9)	9	4 (44.4)	5 (55.6)
Renal and urinary disorders - Proteinuria	6 (2.6)	7	4 (57.1)	3 (42.9)	18 (7.9)	37	30 (81.1)	7 (18.9)
Skin and subcutaneous tissue disorders	188 (81.0)	627	346 (55.2)	281 (44.8)	79 (34.5)	141	68 (48.2)	73 (51.8)
Alopecia	53 (22.8)	58	18 (31.0)	40 (69.0)	26 (11.4)	26	4 (15.4)	22 (84.6)
Dermatitis acneiform	43 (18.5)	76	47 (61.8)	29 (38.2)	2 (0.9)	2	1 (50.0)	1 (50.0)
Dry skin	38 (16.4)	55	28 (50.9)	27 (49.1)	11 (4.8)	12	3 (25.0)	9 (75.0)
Pigmentation disorder	17 (7.3)	18	3 (16.7)	15 (83.3)	2 (0.9)	2	0	2 (100.0)
Pruritus	32 (13.8)	42	31 (73.8)	11 (26.2)	7 (3.1)	9	7 (77.8)	2 (22.2)
Rash	70 (30.2)	101	64 (63.4)	37 (36.6)	9 (3.9)	12	8 (66.7)	4 (33.3)
Skin hyperpigmentation	43 (18.5)	46	6 (13.0)	40 (87.0)	7 (3.1)	7	0	7 (100.0)
Skin lesion	13 (5.6)	13	8 (61.5)	5 (38.5)	2 (0.9)	2	2 (100.0)	0
Vascular disorders	36 (15.5)	62	47 (75.8)	15 (24.2)	51 (22.3)	80	48 (60.0)	32 (40.0)
Hypertension	9 (3.9)	20	18 (90.0)	2 (10.0)	35 (15.3)	51	28 (54.9)	23 (45.1)

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
Significant denotes to SOCs / PTs with p-value from 2-sided log-rank test < 0.05.
Frequent indicates SOCs / PTs with criteria: incidence >= 10% or >=10 patients and incidence >= 1%.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm C
Datacut: 06JAN2025
Resolved and unresolved events of frequent significant severe AE
Safety Analysis Set

SOC PT or SOC - PT	EC+FOLFOX (N=232) Patients with event	Any event	Resolved event	Unresolved event	Control 1 (N=229) Patients with event	Any event	Resolved event	Unresolved event
Blood and lymphatic system disorders - Anaemia	35 (15.1)	66	64 (97.0)	2 (3.0)	9 (3.9)	12	10 (83.3)	2 (16.7)
Gastrointestinal disorders - Diarrhoea	3 (1.3)	4	4 (100.0)	0	11 (4.8)	16	16 (100.0)	0
Investigations	88 (37.9)	173	162 (93.6)	11 (6.4)	65 (28.4)	125	122 (97.6)	3 (2.4)
Lipase increased	40 (17.2)	66	62 (93.9)	4 (6.1)	14 (6.1)	22	20 (90.9)	2 (9.1)
Nervous system disorders	61 (26.3)	73	47 (64.4)	26 (35.6)	27 (11.8)	31	18 (58.1)	13 (41.9)
Skin and subcutaneous tissue disorders	16 (6.9)	17	14 (82.4)	3 (17.6)	2 (0.9)	2	1 (50.0)	1 (50.0)
Vascular disorders - Hypertension	2 (0.9)	2	2 (100.0)	0	10 (4.4)	13	9 (69.2)	4 (30.8)

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
Significant denotes to SOCs / PTs with p-value from 2-sided log-rank test < 0.05.
Frequent indicates SOCs / PTs with the criteria: incidence >= 5% or >=10 patients and incidence >= 1%.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Disposition Events Summary
Full Analysis Set

	EC+FOLFOX (N=236)		Control 2 (N=74)	
	n	(%)	n	(%)
Disposition phase: Treatment				
Entered	236	(100.0)	74	(100.0)
Any reason for discontinuation	169	(71.6)	67	(90.5)
Adverse event	17	(7.2)	5	(6.8)
Death	9	(3.8)	1	(1.4)
Lost to follow-Up	0	(0.0)	1	(1.4)
Progressive disease	101	(42.8)	36	(48.6)
Withdrawal by subject	17	(7.2)	8	(10.8)
Global deterioration of health status	10	(4.2)	6	(8.1)
Other	15	(6.4)	10	(13.5)
Ongoing	67	(28.4)	7	(9.5)
Disposition phase: Long-term follow-up				
Entered	169	(71.6)	67	(90.5)
Any reason for discontinuation	104	(44.1)	42	(56.8)
Death	94	(39.8)	35	(47.3)
Lost to follow-Up	2	(0.8)	0	(0.0)
Withdrawal by subject	8	(3.4)	7	(9.5)
Ongoing	65	(27.5)	25	(33.8)

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Demographic and Disease Characteristics
Full Analysis Set

		EC+FOLFOX (N=236)	Control 2 (N=74)
Age - Group (Years), n (%)	18 - < 65	150 (63.6)	46 (62.2)
	65 - < 75	70 (29.7)	20 (27.0)
	>= 75	16 (6.8)	8 (10.8)
Age (Years)	n (missing)	236 (0)	74 (0)
	Mean (SD)	57.95 (12.707)	59.53 (12.029)
	Median	60.00	61.00
	Q1, Q3	48.50, 68.00	53.00, 69.00
	Min, Max	24.0, 81.0	29.0, 84.0
Sex, n (%)	Male	123 (52.1)	35 (47.3)
	Female	113 (47.9)	39 (52.7)
Race, n (%)	Asian	88 (37.3)	20 (27.0)
	Native Hawaiian or Other Pacific Islander	0	1 (1.4)
	White	141 (59.7)	49 (66.2)
	Not reported	7 (3.0)	3 (4.1)
	Multiracial	0	1 (1.4)
Region, n (%)	Europe	109 (46.2)	43 (58.1)
	USA/Canada	15 (6.4)	8 (10.8)
	Rest of World	112 (47.5)	23 (31.1)
Ethnicity, n (%)	Hispanic or Latino	28 (11.9)	5 (6.8)
	Not Hispanic or Latino	187 (79.2)	64 (86.5)
	Not reported	21 (8.9)	5 (6.8)
Body Site, n (%)	Colon, Ascending	78 (33.1)	26 (35.1)
	Colon, Descending	18 (7.6)	6 (8.1)
	Colon, Rectosigmoid + Colon, Sigmoid	47 (19.9)	15 (20.3)
	Colon, Transverse	39 (16.5)	7 (9.5)
	Colon, Hepatic Flexure	9 (3.8)	2 (2.7)
	Rectum	24 (10.2)	13 (17.6)
	Cecum	20 (8.5)	3 (4.1)
	Colon, Splenic Flexure	1 (0.4)	2 (2.7)
Side of Tumor, n (%)	Left	90 (38.1)	36 (48.6)
	Right	146 (61.9)	38 (51.4)
Stage at Initial Diagnosis, n (%)	Stage I	3 (1.3)	0
	Stage II	13 (5.5)	1 (1.4)
	Stage III	38 (16.1)	26 (35.1)
	Stage IV	182 (77.1)	47 (63.5)
Primary Tumor Resection, n (%)	Completely Resected	116 (49.2)	34 (45.9)
	Partially Resected	14 (5.9)	2 (2.7)
	No Resection	106 (44.9)	38 (51.4)
Number of Organs Involved, n (%)	<= 2	119 (50.4)	34 (45.9)
	>= 3	117 (49.6)	40 (54.1)
Presence of Liver Metastases, n (%)	Yes	147 (62.3)	46 (62.2)
	No	89 (37.7)	28 (37.8)

Age at Screening (years) as reported on CRF.

		EC+FOLFOX (N=236)	Control 2 (N=74)
Time Since Initial Diagnosis (Months)	n (missing)	236 (0)	74 (0)
	Mean (SD)	6.81 (13.183)	7.67 (10.054)
	Median	1.94	2.38
	Q1, Q3	1.33, 3.60	1.31, 15.70
	Min, Max	0.3, 112.5	0.5, 44.6
Time Since Recurrence/Metastatic (Months)	n (missing)	235 (1)	72 (2)
	Mean (SD)	2.26 (3.701)	2.19 (2.122)
	Median	1.54	1.36
	Q1, Q3	1.02, 2.23	1.00, 2.61
	Min, Max	0.0, 40.0	0.3, 11.4
ECOG-PS at Randomization, n (%)	0	131 (55.5)	48 (64.9)
	1	105 (44.5)	26 (35.1)
ECOG-PS at Baseline, n (%)	0	128 (54.2)	41 (55.4)
	1	104 (44.1)	27 (36.5)
	Missing	4 (1.7)	6 (8.1)
BRAF V600E Status, Tumor Tissue (Central), n (%)	Detected	226 (95.8)	62 (83.8)
	Indeterminate	0	1 (1.4)
	Not Detected	4 (1.7)	1 (1.4)
	Not Available	6 (2.5)	10 (13.5)
BRAF V600E Status (Local), n (%)	Detected	222 (94.1)	67 (90.5)
	Not Available	14 (5.9)	7 (9.5)
BRAF V600E Status Central vs. Local, n (%)	Detected vs. Detected	216 (91.5)	61 (82.4)
	Detected vs. Not Available	10 (4.2)	1 (1.4)
	Indeterminate vs. Detected	0	1 (1.4)
	Not Detected vs. Detected	4 (1.7)	1 (1.4)
	Not Available vs. Detected	2 (0.8)	4 (5.4)
	Not Available vs. Not Available	4 (1.7)	6 (8.1)
KRAS Mutation Status (Local), n (%)	Not Detected	231 (97.9)	68 (91.9)
	Not Available	5 (2.1)	6 (8.1)
NRAS Mutation Status (Local), n (%)	Not Detected	230 (97.5)	68 (91.9)
	Not Available	6 (2.5)	6 (8.1)
MSI/MMR Status (Local), n (%)	MSI-H/dMMR	1 (0.4)	0
	MSS/pMMR	229 (97.0)	68 (91.9)
	Not Available	6 (2.5)	6 (8.1)
CEA at Baseline - Group (ug/L), n (%)	<= 5	64 (27.1)	19 (25.7)
	> 5	167 (70.8)	49 (66.2)
	Missing	5 (2.1)	6 (8.1)
CEA at Baseline (ug/L)	n (missing)	230 (6)	68 (6)
	Mean (SD)	149.91 (547.713)	127.11 (413.309)
	Median	13.60	14.80
	Q1, Q3	4.60, 67.16	3.75, 47.30
	Min, Max	0.5, 6236.0	0.8, 2954.0
CRP at Baseline - Group (mg/L), n (%)	<= 10	125 (53.0)	40 (54.1)
	> 10	105 (44.5)	28 (37.8)
	Missing	6 (2.5)	6 (8.1)

Age at Screening (years) as reported on CRF.

		EC+FOLFOX (N=236)	Control 2 (N=74)
CRP at Baseline (mg/L)	n (missing)	229 (7)	68 (6)
	Mean (SD)	23.72 (36.094)	24.73 (40.245)
	Median	8.20	6.05
	Q1, Q3	2.50, 29.90	2.70, 29.75
	Min, Max	0.2, 208.8	0.4, 208.8

Age at Screening (years) as reported on CRF.

		EC+FOLFOX (N=232)
Treatment duration of regime EC+FOLFOX (Weeks)	n (missing)	232 (0)
	Mean (SD)	55.45 (35.413)
	Median	49.79
	Q1, Q3	26.07, 79.50
	Min, Max	1.3, 161.9
Cetuximab	n (missing)	232 (0)
	Mean (SD)	53.81 (36.180)
	Median	49.07
	Q1, Q3	23.93, 77.50
	Min, Max	1.3, 160.7
Encorafenib	n (missing)	232 (0)
	Mean (SD)	54.31 (36.208)
	Median	49.43
	Q1, Q3	23.86, 78.07
	Min, Max	0.4, 161.9
Fluorouracil	n (missing)	232 (0)
	Mean (SD)	46.73 (34.142)
	Median	37.50
	Q1, Q3	20.07, 68.14
	Min, Max	1.3, 160.7
Leucovorin	n (missing)	232 (0)
	Mean (SD)	46.53 (34.378)
	Median	36.71
	Q1, Q3	19.86, 68.14
	Min, Max	1.3, 160.7
Oxaliplatin	n (missing)	232 (0)
	Mean (SD)	23.25 (15.964)
	Median	21.29
	Q1, Q3	15.29, 27.07
	Min, Max	1.3, 141.1

Cetuximab: Defined as time from the date of first cetuximab dose to the date of last cetuximab dose + 14.
Encorafenib: Defined as time from the date of first encorafenib dose to the date of last encorafenib dose + 1.
Fluorouracil: Defined as time from the date of first fluorouracil dose to the date of last fluorouracil dose + 14 for bolus. Defined as time from the date of first fluorouracil dose to the date of last fluorouracil dose + 12 for infusion. Use maximum time of bolus and infusion.
Leucovorin: Defined as time from the date of first leucovorin dose to the date of last leucovorin dose + 14.
Oxaliplatin: Defined as time from the date of first oxaliplatin dose to the date of last oxaliplatin dose + 14.
Division by 7 for day-to-week calculation.

		Control 2 (N=68)
Treatment duration of regime FOLFIRI (Weeks)	n	9
	Mean (SD)	24.14 (17.333)
	Median	23.43
	Q1, Q3	7.00, 36.00
	Min, Max	2.0, 52.4
Fluorouracil	n	9
	Mean (SD)	24.14 (17.333)
	Median	23.43
	Q1, Q3	7.00, 36.00
	Min, Max	2.0, 52.4
Irinotecan	n	9
	Mean (SD)	24.14 (17.333)
	Median	23.43
	Q1, Q3	7.00, 36.00
	Min, Max	2.0, 52.4
Leucovorin	n	9
	Mean (SD)	24.14 (17.333)
	Median	23.43
	Q1, Q3	7.00, 36.00
	Min, Max	2.0, 52.4

Fluorouracil: Defined as time from the date of first fluorouracil dose to the date of last fluorouracil dose + 14 for bolus. Defined as time from the date of first fluorouracil dose to the date of last fluorouracil dose + 12 for infusion. Use maximum time of bolus and infusion.
Irinotecan: Defined as time from the date of first irinotecan dose to the date of last irinotecan dose + 14.
Leucovorin: Defined as time from the date of first leucovorin dose to the date of last leucovorin dose + 14.
Division by 7 for day-to-week calculation.

		Control 2 (N=68)
Treatment duration of regime FOLFIRI+Bevacizumab (Weeks)	n	59
	Mean (SD)	39.93 (28.767)
	Median	32.86
	Q1, Q3	14.57, 60.00
	Min, Max	2.0, 100.1
Bevacizumab	n	59
	Mean (SD)	35.45 (28.452)
	Median	30.00
	Q1, Q3	13.71, 53.00
	Min, Max	2.0, 100.1
Fluorouracil	n	59
	Mean (SD)	39.93 (28.767)
	Median	32.86
	Q1, Q3	14.57, 60.00
	Min, Max	2.0, 100.1
Irinotecan	n	59
	Mean (SD)	38.56 (27.684)
	Median	32.57
	Q1, Q3	14.14, 59.00
	Min, Max	2.0, 100.1
Leucovorin	n	59
	Mean (SD)	37.29 (29.221)
	Median	31.00
	Q1, Q3	13.71, 59.00
	Min, Max	2.0, 100.1

Bevacizumab: Defined as time from the date of first bevacizumab dose to the date of last bevacizumab dose + 14.
Fluorouracil: Defined as time from the date of first fluorouracil dose to the date of last fluorouracil dose + 14 for bolus. Defined as time from the date of first fluorouracil dose to the date of last fluorouracil dose + 12 for infusion. Use maximum time of bolus and infusion.
Irinotecan: Defined as time from the date of first irinotecan dose to the date of last irinotecan dose + 14.
Leucovorin: Defined as time from the date of first leucovorin dose to the date of last leucovorin dose + 14.
Division by 7 for day-to-week calculation.

		Control 2 (N=68)
Treatment duration of regime FOLFIRI and FOLFIRI+Bevacizumab (Weeks)	n	68
	Mean (SD)	37.84 (27.952)
	Median	32.07
	Q1, Q3	14.36, 54.71
	Min, Max	2.0, 100.1
Bevacizumab	n	59
	Mean (SD)	35.45 (28.452)
	Median	30.00
	Q1, Q3	13.71, 53.00
	Min, Max	2.0, 100.1
Fluorouracil	n	68
	Mean (SD)	37.84 (27.952)
	Median	32.07
	Q1, Q3	14.36, 54.71
	Min, Max	2.0, 100.1
Irinotecan	n	68
	Mean (SD)	36.65 (26.899)
	Median	32.07
	Q1, Q3	14.07, 52.07
	Min, Max	2.0, 100.1
Leucovorin	n	68
	Mean (SD)	35.55 (28.199)
	Median	30.07
	Q1, Q3	13.00, 51.21
	Min, Max	2.0, 100.1

Bevacizumab: Defined as time from the date of first bevacizumab dose to the date of last bevacizumab dose + 14.
Fluorouracil: Defined as time from the date of first fluorouracil dose to the date of last fluorouracil dose + 14 for bolus. Defined as time from the date of first fluorouracil dose to the date of last fluorouracil dose + 12 for infusion. Use maximum time of bolus and infusion.
Irinotecan: Defined as time from the date of first irinotecan dose to the date of last irinotecan dose + 14.
Leucovorin: Defined as time from the date of first leucovorin dose to the date of last leucovorin dose + 14.
Division by 7 for day-to-week calculation.

		EC+FOLFOX (N=232)	Control 2 (N=68)
Treatment duration of all regimens (Weeks)	n (missing)	232 (0)	68 (0)
	Mean (SD)	55.45 (35.413)	37.84 (27.952)
	Median	49.79	32.07
	Q1, Q3	26.07, 79.50	14.36, 54.71
	Min, Max	1.3, 161.9	2.0, 100.1

Defined as time from the date of first drug dose to the date of last drug dose + 1/+ 7/+ 14/+ 21.
Division by 7 for day-to-week calculation.

		EC+FOLFOX (N=236)	Control 2 (N=74)
Overall Survival Follow-up duration (Months)	n (missing)	236 (0)	74 (0)
	Mean (SD)	17.73 (7.810)	14.01 (7.459)
	Median	18.14	17.72
	Q1, Q3	12.67, 22.85	7.59, 20.40
	Min, Max	0.2, 37.3	0.0, 23.6

Defined as the time from randomization to the date of death due to any cause. Patients last known to be alive will be censored at the date of last contact.
Division by 30.4375 for day-to-month calculation.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Follow-up Duration of Progression Free Survival
Full Analysis Set

		EC+FOLFOX (N=236)	Control 2 (N=74)
PFS based on BICR Assessment Follow-up duration (Months)	n (missing)	236 (0)	74 (0)
	Mean (SD)	10.76 (7.660)	7.15 (6.378)
	Median	9.76	6.23
	Q1, Q3	5.27, 15.41	1.51, 9.82
	Min, Max	0.0, 36.8	0.0, 21.8

Please refer to table 4 and table 5 in the statistical analysis plan for details regarding censoring.
Division by 30.4375 for day-to-month calculation.

		EC+FOLFOX (N=236)	Control 2 (N=74)
Duration of Objective Response based on BICR Assessment Follow-up duration (Months)	n (missing)	155 (81)	30 (44)
	Mean (SD)	10.70 (6.818)	8.53 (5.626)
	Median	9.20	7.61
	Q1, Q3	5.42, 15.11	4.24, 12.42
	Min, Max	1.3, 35.2	1.2, 20.3

Please refer to table 4 and table 5 in the statistical analysis plan for details regarding censoring.
Division by 30.4375 for day-to-month calculation.
Including only patients having complete response or partial response.

		EC+FOLFOX (N=236)	Control 2 (N=74)
Time to first deterioration of at least 10 points - EOR01-Global QOL Follow-up duration (Months)	n (missing)	219 (17)	66 (8)
	Mean (SD)	7.06 (6.660)	6.51 (5.908)
	Median	4.37	4.42
	Q1, Q3	1.61, 11.24	1.61, 9.82
	Min, Max	0.0, 35.3	0.1, 23.6
Time to first improvement of at least 10 points - EOR01-Global QOL Follow-up duration (Months)	n (missing)	219 (17)	66 (8)
	Mean (SD)	8.19 (7.571)	7.52 (6.091)
	Median	5.55	5.80
	Q1, Q3	1.74, 13.04	2.00, 11.10
	Min, Max	0.0, 34.3	0.1, 21.8
Time to first deterioration of at least 10 points - EOR01-Physical Functioning Follow-up duration (Months)	n (missing)	219 (17)	66 (8)
	Mean (SD)	7.40 (7.442)	6.56 (5.812)
	Median	4.21	5.06
	Q1, Q3	1.58, 11.27	1.64, 10.35
	Min, Max	0.0, 32.0	0.1, 23.6
Time to first improvement of at least 10 points - EOR01-Physical Functioning Follow-up duration (Months)	n (missing)	219 (17)	66 (8)
	Mean (SD)	9.73 (7.856)	8.22 (6.347)
	Median	8.08	7.18
	Q1, Q3	2.92, 14.03	2.37, 11.14
	Min, Max	0.0, 34.5	0.1, 23.6
Time to first deterioration of at least 10 points - EOR01-Role Functioning Follow-up duration (Months)	n (missing)	219 (17)	66 (8)
	Mean (SD)	5.96 (6.239)	5.58 (5.678)
	Median	3.12	2.81
	Q1, Q3	1.51, 9.23	1.54, 8.57
	Min, Max	0.0, 29.1	0.1, 23.6
Time to first improvement of at least 10 points - EOR01-Role Functioning Follow-up duration (Months)	n (missing)	219 (17)	66 (8)
	Mean (SD)	8.51 (7.869)	7.56 (5.773)
	Median	5.88	6.39
	Q1, Q3	1.87, 13.27	2.73, 11.04
	Min, Max	0.0, 34.5	0.1, 21.8
Time to first deterioration of at least 10 points - EOR01-Emotional Functioning Follow-up duration (Months)	n (missing)	219 (17)	66 (8)
	Mean (SD)	9.45 (7.424)	7.42 (5.806)
	Median	7.66	6.37
	Q1, Q3	3.52, 13.86	2.23, 10.94
	Min, Max	0.0, 35.3	0.1, 23.6
Time to first improvement of at least 10 points - EOR01-Emotional Functioning Follow-up duration (Months)	n (missing)	219 (17)	66 (8)
	Mean (SD)	7.02 (7.153)	6.56 (5.412)
	Median	4.21	5.34
	Q1, Q3	1.61, 11.07	2.00, 9.95
	Min, Max	0.0, 34.3	0.1, 21.7
Time to first deterioration of at least 10 points - EOR01-Cognitive Functioning Follow-up duration (Months)	n (missing)	219 (17)	66 (8)
	Mean (SD)	6.67 (6.553)	6.68 (5.715)
	Median	4.17	5.34
	Q1, Q3	1.61, 9.76	1.68, 9.92
	Min, Max	0.0, 35.3	0.1, 21.7

Defined as the time from the date of randomization to the date of last assessment.
Division by 30.4375 for day-to-month calculation.

		EC+FOLFOX (N=236)	Control 2 (N=74)
Time to first improvement of at least 10 points - EOR01-Cognitive Functioning Follow-up duration (Months)	n (missing)	219 (17)	66 (8)
	Mean (SD)	9.79 (8.260)	7.26 (6.167)
	Median	7.95	5.72
	Q1, Q3	2.76, 14.09	2.00, 11.04
	Min, Max	0.0, 35.3	0.1, 23.6
Time to first deterioration of at least 10 points - EOR01-Social Functioning Follow-up duration (Months)	n (missing)	219 (17)	66 (8)
	Mean (SD)	6.60 (6.727)	5.85 (5.306)
	Median	3.88	4.29
	Q1, Q3	1.58, 9.79	1.54, 8.74
	Min, Max	0.0, 29.1	0.1, 23.6
Time to first improvement of at least 10 points - EOR01-Social Functioning Follow-up duration (Months)	n (missing)	219 (17)	66 (8)
	Mean (SD)	8.50 (7.856)	7.47 (5.818)
	Median	5.59	6.06
	Q1, Q3	2.04, 13.27	2.04, 11.04
	Min, Max	0.0, 34.3	0.1, 21.8
Time to first deterioration of at least 10 points - EOR01-Fatigue Follow-up duration (Months)	n (missing)	219 (17)	66 (8)
	Mean (SD)	5.23 (5.824)	6.04 (5.839)
	Median	2.56	3.24
	Q1, Q3	1.48, 6.97	1.54, 9.03
	Min, Max	0.0, 27.9	0.1, 23.6
Time to first improvement of at least 10 points - EOR01-Fatigue Follow-up duration (Months)	n (missing)	219 (17)	66 (8)
	Mean (SD)	8.02 (7.329)	6.26 (5.093)
	Median	5.72	5.36
	Q1, Q3	2.07, 11.33	1.61, 9.72
	Min, Max	0.0, 34.3	0.1, 21.8
Time to first deterioration of at least 10 points - EOR01-Nausea and Vomiting Follow-up duration (Months)	n (missing)	219 (17)	66 (8)
	Mean (SD)	6.99 (7.126)	5.73 (4.839)
	Median	3.88	4.21
	Q1, Q3	1.58, 10.94	1.68, 8.57
	Min, Max	0.0, 34.3	0.1, 20.6
Time to first improvement of at least 10 points - EOR01-Nausea and Vomiting Follow-up duration (Months)	n (missing)	219 (17)	66 (8)
	Mean (SD)	10.84 (8.062)	8.16 (6.207)
	Median	9.72	7.24
	Q1, Q3	4.14, 17.05	2.37, 11.14
	Min, Max	0.0, 35.3	0.1, 23.6
Time to first deterioration of at least 10 points - EOR01-Pain Follow-up duration (Months)	n (missing)	219 (17)	66 (8)
	Mean (SD)	7.38 (6.481)	6.83 (5.456)
	Median	5.49	5.78
	Q1, Q3	2.10, 11.01	2.04, 9.82
	Min, Max	0.0, 29.1	0.1, 23.6
Time to first improvement of at least 10 points - EOR01-Pain Follow-up duration (Months)	n (missing)	219 (17)	66 (8)
	Mean (SD)	7.16 (7.788)	6.99 (6.213)
	Median	3.22	5.72
	Q1, Q3	1.51, 11.30	1.54, 10.94
	Min, Max	0.0, 34.5	0.1, 23.6

Defined as the time from the date of randomization to the date of last assessment.
Division by 30.4375 for day-to-month calculation.

		EC+FOLFOX (N=236)	Control 2 (N=74)
Time to first deterioration of at least 10 points - EOR01-Dyspnoea Follow-up duration (Months)	n (missing)	219 (17)	66 (8)
	Mean (SD)	8.00 (7.260)	7.17 (6.106)
	Median	5.52	5.72
	Q1, Q3	1.68, 12.48	2.04, 10.35
	Min, Max	0.0, 29.8	0.1, 23.6
Time to first improvement of at least 10 points - EOR01-Dyspnoea Follow-up duration (Months)	n (missing)	219 (17)	66 (8)
	Mean (SD)	10.37 (8.101)	7.57 (5.798)
	Median	8.67	6.77
	Q1, Q3	3.48, 16.69	2.46, 11.10
	Min, Max	0.0, 35.3	0.1, 21.8
Time to first deterioration of at least 10 points - EOR01-Insomnia Follow-up duration (Months)	n (missing)	219 (17)	66 (8)
	Mean (SD)	8.59 (7.382)	6.07 (5.290)
	Median	6.51	4.24
	Q1, Q3	2.17, 13.83	1.61, 9.82
	Min, Max	0.0, 32.0	0.1, 20.6
Time to first improvement of at least 10 points - EOR01-Insomnia Follow-up duration (Months)	n (missing)	219 (17)	66 (8)
	Mean (SD)	8.12 (7.891)	7.66 (6.365)
	Median	5.39	5.95
	Q1, Q3	1.64, 12.71	1.84, 11.10
	Min, Max	0.0, 35.3	0.1, 23.6
Time to first deterioration of at least 10 points - EOR01-Appetite Loss Follow-up duration (Months)	n (missing)	219 (17)	66 (8)
	Mean (SD)	6.21 (6.329)	6.44 (5.166)
	Median	3.25	5.47
	Q1, Q3	1.58, 9.69	2.04, 9.69
	Min, Max	0.0, 32.0	0.1, 21.7
Time to first improvement of at least 10 points - EOR01-Appetite Loss Follow-up duration (Months)	n (missing)	219 (17)	66 (8)
	Mean (SD)	9.55 (8.295)	7.97 (6.196)
	Median	6.93	6.46
	Q1, Q3	2.37, 13.96	2.37, 11.14
	Min, Max	0.0, 35.3	0.1, 23.6
Time to first deterioration of at least 10 points - EOR01-Constipation Follow-up duration (Months)	n (missing)	219 (17)	66 (8)
	Mean (SD)	8.41 (7.145)	6.90 (4.963)
	Median	5.91	5.90
	Q1, Q3	2.10, 13.73	2.23, 10.35
	Min, Max	0.0, 32.0	0.1, 20.6
Time to first improvement of at least 10 points - EOR01-Constipation Follow-up duration (Months)	n (missing)	219 (17)	66 (8)
	Mean (SD)	10.14 (8.357)	7.72 (6.333)
	Median	8.31	5.95
	Q1, Q3	2.37, 16.72	2.23, 11.14
	Min, Max	0.0, 35.3	0.1, 23.6
Time to first deterioration of at least 10 points - EOR01-Diarrhea Follow-up duration (Months)	n (missing)	219 (17)	66 (8)
	Mean (SD)	8.78 (6.940)	6.45 (5.190)
	Median	7.69	5.34
	Q1, Q3	2.73, 13.27	1.84, 9.92
	Min, Max	0.0, 32.0	0.1, 20.6

Defined as the time from the date of randomization to the date of last assessment.
Division by 30.4375 for day-to-month calculation.

		EC+FOLFOX (N=236)	Control 2 (N=74)
Time to first improvement of at least 10 points - EOR01-Diarrhea Follow-up duration (Months)	n (missing)	219 (17)	66 (8)
	Mean (SD)	9.80 (7.967)	7.58 (6.313)
	Median	8.15	5.95
	Q1, Q3	2.56, 15.18	2.00, 11.10
	Min, Max	0.0, 34.5	0.1, 23.6
Time to first deterioration of at least 10 points - EOR01-Financial Difficulties Follow-up duration (Months)	n (missing)	219 (17)	66 (8)
	Mean (SD)	8.60 (7.641)	7.68 (6.130)
	Median	5.88	6.77
	Q1, Q3	2.33, 12.48	2.04, 11.04
	Min, Max	0.0, 32.4	0.1, 23.6
Time to first improvement of at least 10 points - EOR01-Financial Difficulties Follow-up duration (Months)	n (missing)	219 (17)	66 (8)
	Mean (SD)	10.01 (8.108)	7.74 (5.824)
	Median	8.34	6.77
	Q1, Q3	2.76, 15.18	2.73, 11.10
	Min, Max	0.0, 35.3	0.1, 21.8

Defined as the time from the date of randomization to the date of last assessment.
Division by 30.4375 for day-to-month calculation.

		EC+FOLFOX (N=236)	Control 2 (N=74)
Time to first deterioration of at least 15 percent - EQ5D02-EQ-VAS Score Follow-up duration (Months)	n (missing)	215 (21)	65 (9)
	Mean (SD)	8.67 (6.863)	7.26 (6.124)
	Median	6.93	5.59
	Q1, Q3	2.92, 13.73	1.84, 10.61
	Min, Max	0.0, 35.3	0.1, 23.6
Time to first improvement of at least 15 percent - EQ5D02-EQ-VAS Score Follow-up duration (Months)	n (missing)	215 (21)	65 (9)
	Mean (SD)	9.48 (8.110)	7.69 (6.036)
	Median	7.13	6.05
	Q1, Q3	2.76, 14.00	2.73, 11.14
	Min, Max	0.0, 34.5	0.1, 21.8

Defined as the time from the date of randomization to the date of last assessment.
Division by 30.4375 for day-to-month calculation.

		EC+FOLFOX (N=236)	Control 2 (N=74)
Time to first deterioration of at least 15 percent - PGIS01 - Colorectal Cancer Follow-up duration (Months)	n (missing)	219 (17)	66 (8)
	Mean (SD)	8.38 (7.152)	6.39 (5.407)
	Median	5.91	5.47
	Q1, Q3	2.79, 12.45	1.61, 9.72
	Min, Max	0.0, 35.3	0.1, 22.9
Time to first improvement of at least 15 percent - PGIS01 - Colorectal Cancer Follow-up duration (Months)	n (missing)	219 (17)	66 (8)
	Mean (SD)	7.10 (7.716)	7.46 (6.376)
	Median	3.48	5.72
	Q1, Q3	1.51, 11.04	1.84, 11.04
	Min, Max	0.0, 34.5	0.1, 22.9

Defined as the time from the date of randomization to the date of last assessment.
Division by 30.4375 for day-to-month calculation.

		EC+FOLFOX (N=236)	Control 2 (N=74)
Time to first deterioration of at least 15 percent - PGI01-Change Follow-up duration (Months)	n (missing)	212 (24)	62 (12)
	Mean (SD)	7.07 (6.835)	5.07 (5.273)
	Median	4.58	2.66
	Q1, Q3	1.54, 10.15	1.51, 7.72
	Min, Max	0.5, 35.3	1.4, 23.6
Time to first improvement of at least 15 percent - PGI01-Change Follow-up duration (Months)	n (missing)	212 (24)	62 (12)
	Mean (SD)	5.82 (5.460)	5.69 (4.117)
	Median	3.56	4.75
	Q1, Q3	2.02, 8.26	2.04, 8.34
	Min, Max	0.6, 32.4	1.4, 20.1

Defined as the time from the date of randomization to the date of last assessment.
Division by 30.4375 for day-to-month calculation.

		EC+FOLFOX (N=232)	Control 2 (N=68)
Safety Follow-up duration (Months)	n (missing)	232 (0)	68 (0)
	Mean (SD)	13.41 (8.247)	9.10 (6.534)
	Median	12.17	7.39
	Q1, Q3	6.46, 18.97	3.84, 12.86
	Min, Max	0.3, 38.1	0.6, 23.8

Defined as the time from the date of first dose to the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
Division by 30.4375 for day-to-month calculation.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
All Subsequent Systemic Anticancer Treatment
Full Analysis Set

Drug Category Drug	EC+FOLFOX (N=236) n (%)	Control 2 (N=74) n (%)
Any Subsequent Systemic Anticancer Treatment	108 (45.8)	45 (60.8)
FOLFIRI +/- Combination	57 (24.2)	9 (12.2)
FLUOROURACIL	37 (15.7)	6 (8.1)
BEVACIZUMAB	32 (13.6)	6 (8.1)
IRINOTECAN	31 (13.1)	3 (4.1)
CALCIUM FOLINATE;FLUOROURACIL;IRINOTECAN HYDROCHLORIDE	19 (8.1)	3 (4.1)
FOLINIC ACID	17 (7.2)	1 (1.4)
CALCIUM FOLINATE	8 (3.4)	1 (1.4)
AFLIBERCEPT	8 (3.4)	0 (0.0)
IRINOTECAN HYDROCHLORIDE	5 (2.1)	3 (4.1)
CALCIUM LEVOFOLINATE	2 (0.8)	2 (2.7)
LEVOFOLINIC ACID	2 (0.8)	1 (1.4)
AFLIBERCEPT BETA	1 (0.4)	0 (0.0)
CAPECITABINE	1 (0.4)	0 (0.0)
CETUXIMAB	1 (0.4)	0 (0.0)
FLUOROURACIL;FOLINIC ACID;IRINOTECAN	1 (0.4)	0 (0.0)
FOLIC ACID	1 (0.4)	0 (0.0)
IRINOTECAN HYDROCHLORIDE TRIHYDRATE	1 (0.4)	0 (0.0)
RALTITREXED	1 (0.4)	0 (0.0)
RAMUCIRUMAB	0 (0.0)	1 (1.4)
TIPIRACIL HYDROCHLORIDE;TRIFLURIDINE	1 (0.4)	0 (0.0)
BRAF Inhibitor +/- Combination	19 (8.1)	30 (40.5)
CETUXIMAB	16 (6.8)	25 (33.8)
ENCORAFENIB	16 (6.8)	24 (32.4)
BINIMETINIB	5 (2.1)	3 (4.1)
PANITUMUMAB	1 (0.4)	6 (8.1)
DABRAFENIB MESILATE	2 (0.8)	3 (4.1)
TRAMETINIB	1 (0.4)	4 (5.4)
VEMURAFENIB	2 (0.8)	3 (4.1)
FLUOROURACIL	1 (0.4)	2 (2.7)
IRINOTECAN HYDROCHLORIDE	1 (0.4)	2 (2.7)
CALCIUM FOLINATE	1 (0.4)	1 (1.4)
IRINOTECAN	1 (0.4)	1 (1.4)
OXALIPLATIN	0 (0.0)	2 (2.7)
AZENOSERTIB	1 (0.4)	0 (0.0)
BEVACIZUMAB	0 (0.0)	1 (1.4)
BEVACIZUMAB;CALCIUM FOLINATE;FLUOROURACIL;IRINOTECAN HYDROCHLORIDE	1 (0.4)	0 (0.0)
CETUXIMAB;FLUOROURACIL;FOLINIC ACID;IRINOTECAN	1 (0.4)	0 (0.0)
DABRAFENIB	1 (0.4)	0 (0.0)
FLUOROURACIL;FOLINIC ACID;OXALIPLATIN	0 (0.0)	1 (1.4)
FOLINIC ACID	0 (0.0)	1 (1.4)
IMMUNOTHERAPY	0 (0.0)	1 (1.4)
PF-07799933	0 (0.0)	1 (1.4)
RALTITREXED	0 (0.0)	1 (1.4)
SINTILIMAB	0 (0.0)	1 (1.4)
TRAMETINIB DIMETHYL SULFOXIDE	1 (0.4)	0 (0.0)
Single Agent Chemotherapy +/- Combination	17 (7.2)	4 (5.4)
CAPECITABINE	10 (4.2)	3 (4.1)
BEVACIZUMAB	9 (3.8)	3 (4.1)
IRINOTECAN	4 (1.7)	0 (0.0)
GIMERACIL;OTERACIL POTASSIUM;TEGAFUR	1 (0.4)	1 (1.4)
IRINOTECAN HYDROCHLORIDE	2 (0.8)	0 (0.0)
CISPLATIN	1 (0.4)	0 (0.0)
FLUOROURACIL	1 (0.4)	0 (0.0)
FOLINIC ACID	1 (0.4)	0 (0.0)
GEMCITABINE HYDROCHLORIDE	1 (0.4)	0 (0.0)

WHODD GLOBALB3 MAR2024 coding dictionary applied.
Drug category is determined by medical review of all subsequent anticancer systemic treatment before database lock.

Drug Category Drug	EC+FOLFOX (N=236) n (%)	Control 2 (N=74) n (%)
MITOMYCIN	1 (0.4)	0 (0.0)
OXALIPLATIN	0 (0.0)	1 (1.4)
TEGAFUR;URACIL	0 (0.0)	1 (1.4)
CAPIRI +/- Combination	11 (4.7)	0 (0.0)
CAPECITABINE	11 (4.7)	0 (0.0)
BEVACIZUMAB	10 (4.2)	0 (0.0)
IRINOTECAN	9 (3.8)	0 (0.0)
IRINOTECAN HYDROCHLORIDE	2 (0.8)	0 (0.0)
FOLFOX +/- Combination	10 (4.2)	14 (18.9)
FLUOROURACIL	7 (3.0)	9 (12.2)
OXALIPLATIN	7 (3.0)	9 (12.2)
BEVACIZUMAB	7 (3.0)	8 (10.8)
FLUOROURACIL;FOLINIC ACID;OXALIPLATIN	3 (1.3)	5 (6.8)
FOLINIC ACID	2 (0.8)	4 (5.4)
CALCIUM FOLINATE	1 (0.4)	3 (4.1)
CALCIUM LEVOFOLINATE	2 (0.8)	0 (0.0)
CETUXIMAB	1 (0.4)	0 (0.0)
LEVOMEFOLIC ACID	0 (0.0)	1 (1.4)
Trifluridine/Tipiracil +/- VEGF Inhibitor	10 (4.2)	3 (4.1)
BEVACIZUMAB	9 (3.8)	1 (1.4)
TIPIRACIL HYDROCHLORIDE;TRIFLURIDINE	5 (2.1)	2 (2.7)
TIPIRACIL;TRIFLURIDINE	4 (1.7)	1 (1.4)
TIPIRACIL	1 (0.4)	0 (0.0)
TRIFLURIDINE	1 (0.4)	0 (0.0)
Other	8 (3.4)	0 (0.0)
BEVACIZUMAB	4 (1.7)	0 (0.0)
RALTITREXED	2 (0.8)	0 (0.0)
CETUXIMAB	1 (0.4)	0 (0.0)
INVESTIGATIONAL DRUG	1 (0.4)	0 (0.0)
IRINOTECAN	1 (0.4)	0 (0.0)
FOLFOXIRI +/- Combination	3 (1.3)	0 (0.0)
FLUOROURACIL	2 (0.8)	0 (0.0)
IRINOTECAN	2 (0.8)	0 (0.0)
OXALIPLATIN	2 (0.8)	0 (0.0)
BEVACIZUMAB	1 (0.4)	0 (0.0)
CALCIUM FOLINATE	1 (0.4)	0 (0.0)
CALCIUM FOLINATE;FLUOROURACIL;IRINOTECAN HYDROCHLORIDE	1 (0.4)	0 (0.0)
FLUOROURACIL;FOLINIC ACID;OXALIPLATIN	1 (0.4)	0 (0.0)
LEVOFOLINIC ACID	1 (0.4)	0 (0.0)
Regorafenib	3 (1.3)	3 (4.1)
REGORAFENIB	3 (1.3)	3 (4.1)
ENVAFOLIMAB	1 (0.4)	0 (0.0)
KN046	1 (0.4)	0 (0.0)
CAPOX +/- Combination	2 (0.8)	4 (5.4)
CAPECITABINE	2 (0.8)	4 (5.4)
OXALIPLATIN	2 (0.8)	4 (5.4)
BEVACIZUMAB	2 (0.8)	2 (2.7)
Fruquintinib	1 (0.4)	1 (1.4)
FRUQUINTINIB	1 (0.4)	1 (1.4)
Immunotherapy	1 (0.4)	0 (0.0)
BEVACIZUMAB	1 (0.4)	0 (0.0)

WHODD GLOBALB3 MAR2024 coding dictionary applied.
Drug category is determined by medical review of all subsequent anticancer systemic treatment before database lock.

Drug Category Drug	EC+FOLFOX (N=236) n (%)	Control 2 (N=74) n (%)
CHIDAMIDE	1 (0.4)	0 (0.0)
SINTILIMAB	1 (0.4)	0 (0.0)

WHODD GLOBALB3 MAR2024 coding dictionary applied.
Drug category is determined by medical review of all subsequent anticancer systemic treatment before database lock.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
First Subsequent Systemic Anticancer Treatment
Full Analysis Set

Drug Category Drug	EC+FOLFOX (N=236) n (%)	Control 2 (N=74) n (%)
Any Subsequent Systemic Anticancer Treatment	108 (45.8)	45 (60.8)
FOLFIRI +/- Combination	54 (22.9)	7 (9.5)
FLUOROURACIL	21 (8.9)	3 (4.1)
BEVACIZUMAB	15 (6.4)	3 (4.1)
CALCIUM FOLINATE;FLUOROURACIL;IRINOTECAN HYDROCHLORIDE	8 (3.4)	1 (1.4)
AFLIBERCEPT	5 (2.1)	0 (0.0)
CALCIUM FOLINATE	2 (0.8)	0 (0.0)
CALCIUM LEVOFOLINATE	1 (0.4)	0 (0.0)
FLUOROURACIL;FOLINIC ACID;IRINOTECAN	1 (0.4)	0 (0.0)
FOLIC ACID	1 (0.4)	0 (0.0)
BRAF Inhibitor +/- Combination	10 (4.2)	25 (33.8)
CETUXIMAB	3 (1.3)	14 (18.9)
ENCORAFENIB	3 (1.3)	4 (5.4)
BINIMETINIB	1 (0.4)	2 (2.7)
DABRAFENIB MESILATE	0 (0.0)	2 (2.7)
BEVACIZUMAB	0 (0.0)	1 (1.4)
BEVACIZUMAB;CALCIUM FOLINATE;FLUOROURACIL;IRINOTECAN HYDROCHLORIDE	1 (0.4)	0 (0.0)
CALCIUM FOLINATE	0 (0.0)	1 (1.4)
CETUXIMAB;FLUOROURACIL;FOLINIC ACID;IRINOTECAN	1 (0.4)	0 (0.0)
FLUOROURACIL	1 (0.4)	0 (0.0)
FLUOROURACIL;FOLINIC ACID;OXALIPLATIN	0 (0.0)	1 (1.4)
Single Agent Chemotherapy +/- Combination	15 (6.4)	2 (2.7)
BEVACIZUMAB	6 (2.5)	2 (2.7)
CAPECITABINE	5 (2.1)	0 (0.0)
IRINOTECAN	2 (0.8)	0 (0.0)
CISPLATIN	1 (0.4)	0 (0.0)
GEMCITABINE HYDROCHLORIDE	1 (0.4)	0 (0.0)
CAPIRI +/- Combination	11 (4.7)	0 (0.0)
BEVACIZUMAB	9 (3.8)	0 (0.0)
CAPECITABINE	1 (0.4)	0 (0.0)
IRINOTECAN HYDROCHLORIDE	1 (0.4)	0 (0.0)
FOLFOX +/- Combination	7 (3.0)	7 (9.5)
BEVACIZUMAB	5 (2.1)	3 (4.1)
FLUOROURACIL;FOLINIC ACID;OXALIPLATIN	2 (0.8)	2 (2.7)
CALCIUM FOLINATE	0 (0.0)	1 (1.4)
FLUOROURACIL	0 (0.0)	1 (1.4)
Trifluridine/Tipiracil +/- VEGF Inhibitor	2 (0.8)	1 (1.4)
BEVACIZUMAB	1 (0.4)	1 (1.4)
TIPIRACIL;TRIFLURIDINE	1 (0.4)	0 (0.0)
Other	5 (2.1)	0 (0.0)
BEVACIZUMAB	3 (1.3)	0 (0.0)
INVESTIGATIONAL DRUG	1 (0.4)	0 (0.0)
RALTITREXED	1 (0.4)	0 (0.0)
FOLFOXIRI +/- Combination	2 (0.8)	0 (0.0)
CALCIUM FOLINATE	1 (0.4)	0 (0.0)
FLUOROURACIL;FOLINIC ACID;OXALIPLATIN	1 (0.4)	0 (0.0)
Regorafenib	0 (0.0)	1 (1.4)
REGORAFENIB	0 (0.0)	1 (1.4)
CAPOX +/- Combination	2 (0.8)	2 (2.7)

WHODD GLOBALB3 MAR2024 coding dictionary applied.
Drug category is determined by medical review of all subsequent anticancer systemic treatment before database lock.

Drug Category Drug	EC+FOLFOX (N=236) n (%)	Control 2 (N=74) n (%)
BEVACIZUMAB	2 (0.8)	1 (1.4)
CAPECITABINE	0 (0.0)	1 (1.4)

WHODD GLOBALB3 MAR2024 coding dictionary applied.
Drug category is determined by medical review of all subsequent anticancer systemic treatment before database lock.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Concomitant Medication
Safety Analysis Set

ATC 2	EC+FOLFOX (N=232) n (%)	Control 2 (N=68) n (%)
ANY CONCOMITANT MEDICATION	232 (100.0)	68 (100.0)
STOMATOLOGICAL PREPARATIONS	222 (95.7)	66 (97.1)
ANTIEMETICS AND ANTINAUSEANTS	220 (94.8)	63 (92.6)
OPHTHALMOLOGICALS	220 (94.8)	66 (97.1)
CORTICOSTEROIDS, DERMATOLOGICAL PREPARATIONS	218 (94.0)	61 (89.7)
CORTICOSTEROIDS FOR SYSTEMIC USE	216 (93.1)	61 (89.7)
OTOLOGICALS	214 (92.2)	65 (95.6)
VASOPROTECTIVES	214 (92.2)	65 (95.6)
NASAL PREPARATIONS	212 (91.4)	62 (91.2)
OPHTHALMOLOGICAL AND OTOLOGICAL PREPARATIONS	208 (89.7)	60 (88.2)
DRUGS FOR OBSTRUCTIVE AIRWAY DISEASES	204 (87.9)	57 (83.8)
ANTIPRURITICS, INCL. ANTIHISTAMINES, ANESTHETICS, ETC.	191 (82.3)	25 (36.8)
ANTIHISTAMINES FOR SYSTEMIC USE	188 (81.0)	23 (33.8)
ANALGESICS	170 (73.3)	53 (77.9)
DRUGS FOR ACID RELATED DISORDERS	169 (72.8)	46 (67.6)
ANTIBACTERIALS FOR SYSTEMIC USE	165 (71.1)	35 (51.5)
PSYCHOLEPTICS	150 (64.7)	41 (60.3)
ANTIDIARRHEALS, INTESTINAL ANTIINFLAMMATORY/ANTIINFECTIVE AGENTS	143 (61.6)	42 (61.8)
ANTIBIOTICS AND CHEMOTHERAPEUTICS FOR DERMATOLOGICAL USE	140 (60.3)	20 (29.4)
DRUGS FOR FUNCTIONAL GASTROINTESTINAL DISORDERS	138 (59.5)	56 (82.4)
DRUGS FOR CONSTIPATION	130 (56.0)	42 (61.8)
OTHER DERMATOLOGICAL PREPARATIONS	127 (54.7)	28 (41.2)
BLOOD SUBSTITUTES AND PERFUSION SOLUTIONS	124 (53.4)	36 (52.9)
ANTIINFLAMMATORY AND ANTIRHEUMATIC PRODUCTS	117 (50.4)	27 (39.7)
TOPICAL PRODUCTS FOR JOINT AND MUSCULAR PAIN	117 (50.4)	26 (38.2)
MINERAL SUPPLEMENTS	116 (50.0)	29 (42.6)
ANTI-ACNE PREPARATIONS	112 (48.3)	18 (26.5)
HOMEOPATHIC PREPARATION	110 (47.4)	24 (35.3)
ANTITHROMBOTIC AGENTS	109 (47.0)	35 (51.5)
ANTIANEMIC PREPARATIONS	100 (43.1)	18 (26.5)
CARDIAC THERAPY	97 (41.8)	49 (72.1)
THROAT PREPARATIONS	93 (40.1)	23 (33.8)
GYNECOLOGICAL ANTIINFECTIVES AND ANTISEPTICS	91 (39.2)	20 (29.4)
ALL OTHER THERAPEUTIC PRODUCTS	86 (37.1)	45 (66.2)
OTHER GYNECOLOGICALS	82 (35.3)	20 (29.4)
UROLOGICALS	82 (35.3)	10 (14.7)
ANTIEPILEPTICS	81 (34.9)	16 (23.5)
COUGH AND COLD PREPARATIONS	79 (34.1)	21 (30.9)
IMMUNOSTIMULANTS	75 (32.3)	26 (38.2)
EMOLLIENTS AND PROTECTIVES	70 (30.2)	17 (25.0)
LIPID MODIFYING AGENTS	68 (29.3)	17 (25.0)
VITAMINS	68 (29.3)	18 (26.5)
BILE AND LIVER THERAPY	66 (28.4)	18 (26.5)
AGENTS ACTING ON THE RENIN-ANGIOTENSIN SYSTEM	59 (25.4)	19 (27.9)
MEDICATED DRESSINGS	57 (24.6)	13 (19.1)
OTHER ALIMENTARY TRACT AND METABOLISM PRODUCTS	57 (24.6)	12 (17.6)
ANESTHETICS	54 (23.3)	17 (25.0)
DIURETICS	53 (22.8)	11 (16.2)
UNSPECIFIED HERBAL AND TRADITIONAL MEDICINE	53 (22.8)	14 (20.6)
ALL OTHER NON-THERAPEUTIC PRODUCTS	52 (22.4)	12 (17.6)
GENERAL NUTRIENTS	51 (22.0)	12 (17.6)
OTHER NERVOUS SYSTEM DRUGS	49 (21.1)	15 (22.1)
PREPARATIONS FOR TREATMENT OF WOUNDS AND ULCERS	49 (21.1)	13 (19.1)
ANTIHEMORRHAGICS	44 (19.0)	10 (14.7)
PSYCHOANALEPTICS	44 (19.0)	13 (19.1)
ANTI-PARKINSON DRUGS	41 (17.7)	10 (14.7)
ANTIFUNGALS FOR DERMATOLOGICAL USE	40 (17.2)	7 (10.3)
DRUGS USED IN DIABETES	39 (16.8)	10 (14.7)
BETA BLOCKING AGENTS	36 (15.5)	10 (14.7)
DIAGNOSTIC AGENTS	36 (15.5)	10 (14.7)

WHODD GLOBALB3 MAR2024 coding dictionary applied.
Only medications are listed with a prevalence of >= 5% in one of the two treatment arms.

ATC 2	EC+FOLFOX (N=232) n (%)	Control 2 (N=68) n (%)
CALCIUM CHANNEL BLOCKERS	35 (15.1)	14 (20.6)
ANTIPROTOZOALS	34 (14.7)	8 (11.8)
MUSCLE RELAXANTS	31 (13.4)	4 (5.9)
ANTINEOPLASTIC AGENTS	27 (11.6)	9 (13.2)
SEX HORMONES AND MODULATORS OF THE GENITAL SYSTEM	27 (11.6)	4 (5.9)
ANTIVIRALS FOR SYSTEMIC USE	25 (10.8)	5 (7.4)
ENDOCRINE THERAPY	25 (10.8)	4 (5.9)
ANTIHYPERTENSIVES	24 (10.3)	5 (7.4)
APPETITE STIMULANTS	23 (9.9)	5 (7.4)
VACCINES	22 (9.5)	3 (4.4)
ANTIMYCOTICS FOR SYSTEMIC USE	21 (9.1)	3 (4.4)
THYROID THERAPY	20 (8.6)	4 (5.9)
ANTISEPTICS AND DISINFECTANTS	17 (7.3)	4 (5.9)
OTHER RESPIRATORY SYSTEM PRODUCTS	17 (7.3)	4 (5.9)
DIGESTIVES, INCL. ENZYMES	11 (4.7)	4 (5.9)
ANTIGOUT PREPARATIONS	9 (3.9)	4 (5.9)
PITUITARY AND HYPOTHALAMIC HORMONES AND ANALOGUES	9 (3.9)	4 (5.9)
**Uncoded ATC Level 2 Text	6 (2.6)	4 (5.9)

WHODD GLOBALB3 MAR2024 coding dictionary applied.
Only medications are listed with a prevalence of >= 5% in one of the two treatment arms.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Overall Survival (Months)
Full Analysis Set

	EC+FOLFOX (N=236)	Control 2 (N=74)
Number of subjects with events, n (%)	94 (39.8)	35 (47.3)
Number of censored subjects, n (%)	142 (60.2)	39 (52.7)
Kaplan-Meier estimates of Time to Event (Months) [1]		
25%-ile (95% CI)	14.7 (11.9, 17.9)	8.9 (7.2, 12.6)
Median (95% CI)	30.3 (21.7, NE)	20.3 (13.2, NE)
75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
Stratified analysis [2]		
Hazard Ratio (95% CI) [3]	0.59 (0.39, 0.87)	
p-value [4]	0.0072	

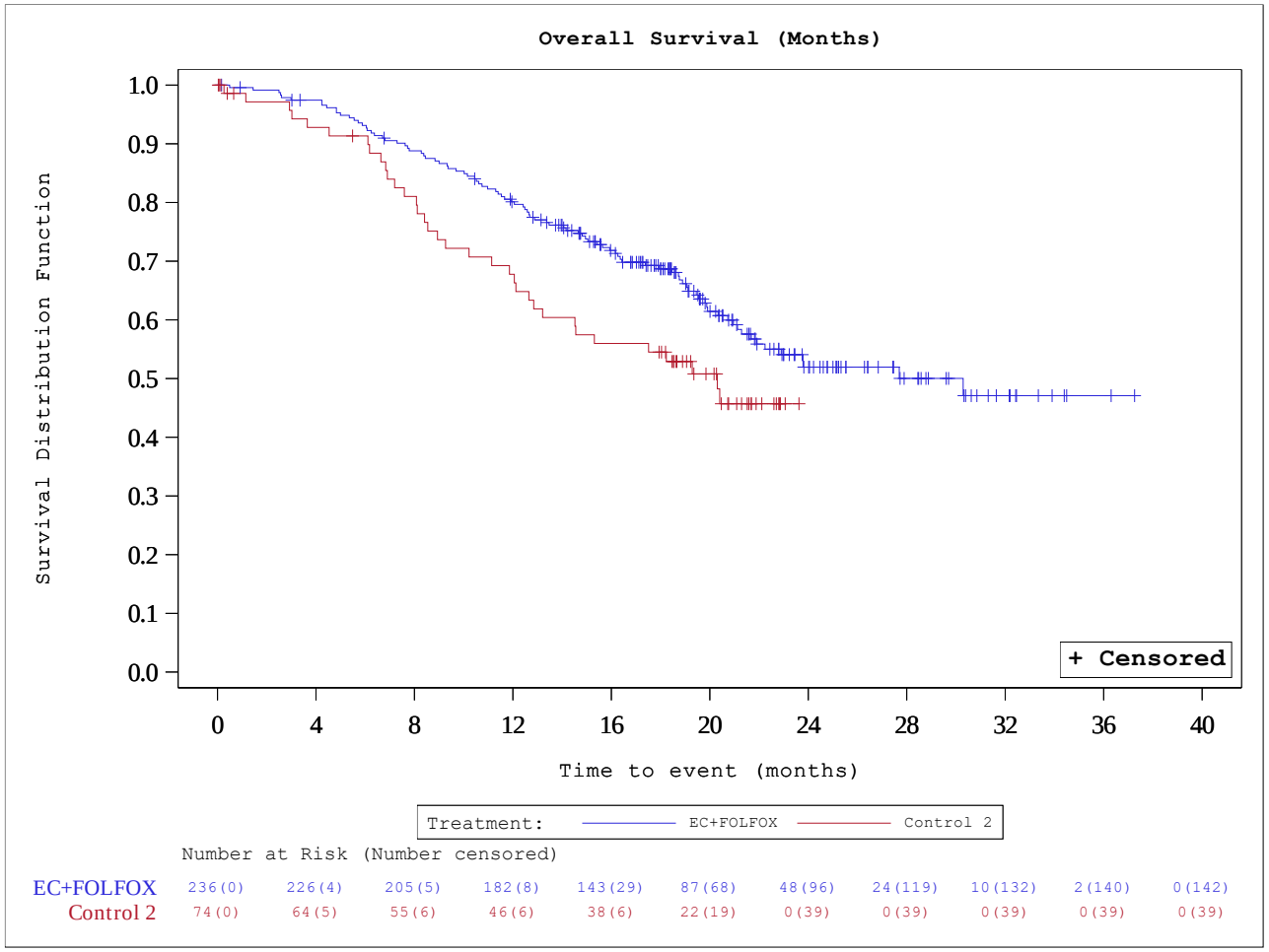
[1] Based on the Brookmeyer and Crowley method.
[2] Stratified by ECOG PS by Randomization.
[3] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[4] P-value from 2-sided log-rank test.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Overall Survival (Months) - Subgroup analysis
Full Analysis Set

Subgroup Level	EC+FOLFOX (N=236) n/ N (%)	EC+FOLFOX (N=236) Median (95% CI)[1]	Control 2 (N=74) n/ N (%)	Control 2 (N=74) Median (95% CI)[1]	Unstratified analysis Hazard Ratio (95% CI)[2]	Unstratified analysis p-Value[3]	Interaction p-Value[4]
Age (Years)							0.7104
< 65	56/ 150 (37.3)	NE (21.3, NE)	21/ 46 (45.7)	20.4 (13.2, NE)	0.70 (0.42, 1.15)	0.1577	
>= 65	38/ 86 (44.2)	27.7 (19.8, NE)	14/ 28 (50.0)	20.3 (8.5, NE)	0.59 (0.32, 1.10)	0.0942	
Sex							0.8284
Male	54/ 123 (43.9)	22.2 (19.5, NE)	18/ 35 (51.4)	14.9 (8.9, NE)	0.62 (0.36, 1.06)	0.0775	
Female	40/ 113 (35.4)	30.3 (23.8, NE)	17/ 39 (43.6)	20.4 (14.5, NE)	0.66 (0.37, 1.17)	0.1518	
Region							0.6999
Europe	46/ 109 (42.2)	30.3 (19.8, NE)	24/ 43 (55.8)	14.5 (8.9, NE)	0.52 (0.32, 0.85)	0.0087	
USA/Canada	7/ 15 (46.7)	20.7 (16.2, NE)	0/ 8 (0.0)	NE (NE , NE)	NE		
Rest of World	41/ 112 (36.6)	27.7 (21.9, NE)	11/ 23 (47.8)	20.4 (13.2, NE)	0.68 (0.35, 1.34)	0.2634	
ECOG-PS at Randomization							0.2770
0	42/ 131 (32.1)	NE (23.8, NE)	17/ 48 (35.4)	NE (18.2, NE)	0.71 (0.40, 1.26)	0.2400	
1	52/ 105 (49.5)	20.3 (17.9, NE)	18/ 26 (69.2)	12.8 (6.8, 20.3)	0.48 (0.28, 0.83)	0.0071	
Number of Organs Involved							0.8373
<= 2	32/ 119 (26.9)	NE (30.3, NE)	11/ 34 (32.4)	NE (20.3, NE)	0.67 (0.33, 1.34)	0.2522	
>= 3	62/ 117 (53.0)	19.1 (16.2, 22.2)	24/ 40 (60.0)	12.1 (8.5, 20.4)	0.62 (0.39, 1.00)	0.0501	
Presence of Liver Metastases							0.7185
Yes	73/ 147 (49.7)	21.0 (18.5, 27.7)	25/ 46 (54.3)	14.6 (9.3, NE)	0.66 (0.42, 1.05)	0.0769	
No	21/ 89 (23.6)	NE (30.3, NE)	10/ 28 (35.7)	NE (19.3, NE)	0.54 (0.25, 1.17)	0.1115	
Side of Tumor							0.5271
Left	38/ 90 (42.2)	30.3 (20.3, NE)	20/ 36 (55.6)	15.3 (12.6, NE)	0.60 (0.35, 1.04)	0.0682	
Right	56/ 146 (38.4)	27.7 (21.3, NE)	15/ 38 (39.5)	NE (11.9, NE)	0.76 (0.43, 1.35)	0.3536	

[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.
[4] P-Value for interaction from Cox proportional hazards model using ties=exact option with treatment, subgroup and treatment*subgroup interaction as covariates.
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Kaplan Meier Plot of Overall Survival (Months)
Full Analysis Set



Kaplan-Meier Plots for subgroups only created if p-value for interaction < 0.05.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
PFS based on BICR Assessment (Months)
Full Analysis Set

	EC+FOLFOX (N=236)	Control 2 (N=74)
Number of subjects with events, n (%)	122 (51.7)	42 (56.8)
Number of censored subjects, n (%)	114 (48.3)	32 (43.2)
Kaplan-Meier estimates of Time to Event (Months) [1]		
25%-ile (95% CI)	7.2 (6.2, 8.4)	3.9 (2.9, 6.9)
Median (95% CI)	12.8 (11.2, 15.9)	8.3 (6.9, 9.8)
75%-ile (95% CI)	32.9 (20.0, NE)	18.0 (9.8, NE)
Stratified analysis [2]		
Hazard Ratio (95% CI) [3]	0.52 (0.36, 0.75)	
p-value [4]	0.0003	

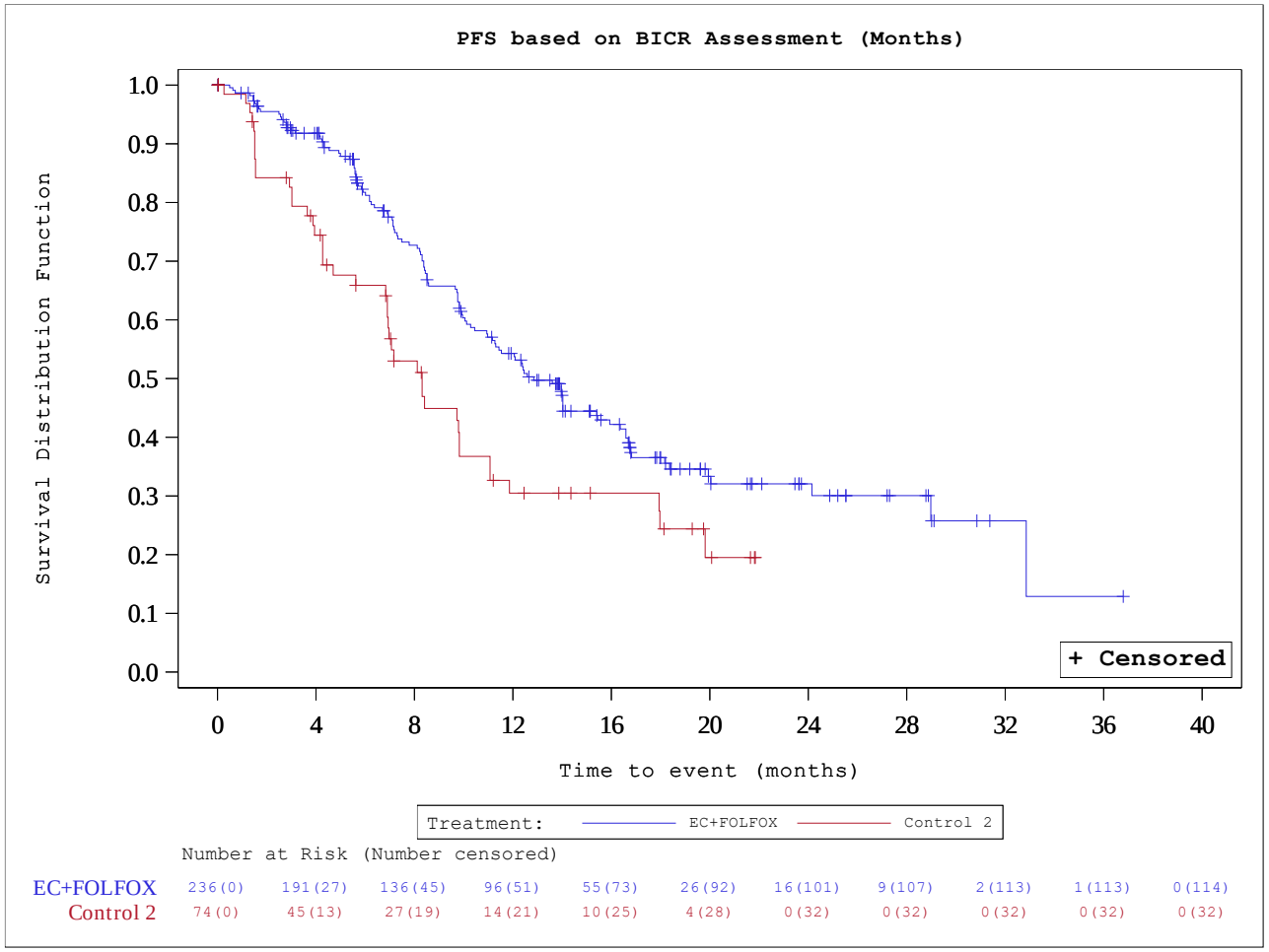
[1] Based on the Brookmeyer and Crowley method.
[2] Stratified by ECOG PS by Randomization.
[3] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[4] P-value from 2-sided log-rank test.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
PFS based on BICR Assessment (Months) - Subgroup analysis
Full Analysis Set

Subgroup Level	EC+FOLFOX (N=236) n/ N (%)	EC+FOLFOX (N=236) Median (95% CI)[1]	Control 2 (N=74) n/ N (%)	Control 2 (N=74) Median (95% CI)[1]	Unstratified analysis Hazard Ratio (95% CI)[2]	Unstratified analysis p-Value[3]	Interaction p-Value[4]
Age (Years)							0.5100
< 65	78/ 150 (52.0)	12.4 (10.1, 15.4)	25/ 46 (54.3)	8.3 (6.9, 11.9)	0.65 (0.41, 1.01)	0.0564	
>= 65	44/ 86 (51.2)	14.0 (11.0, 19.9)	17/ 28 (60.7)	7.2 (3.9, 17.9)	0.49 (0.28, 0.87)	0.0135	
Sex							0.1730
Male	59/ 123 (48.0)	15.4 (10.0, 18.2)	22/ 35 (62.9)	7.1 (4.3, 9.8)	0.46 (0.28, 0.75)	0.0015	
Female	63/ 113 (55.8)	12.4 (10.3, 14.0)	20/ 39 (51.3)	8.4 (6.9, NE)	0.73 (0.44, 1.21)	0.2204	
Region							0.0095
Europe	54/ 109 (49.5)	14.0 (11.3, 18.4)	28/ 43 (65.1)	7.2 (4.7, 9.8)	0.35 (0.22, 0.56)	<.0001	
USA/Canada	11/ 15 (73.3)	11.4 (5.8, 15.4)	1/ 8 (12.5)	NE (NE , NE)	6.71 (0.85, 52.80)	0.0380	
Rest of World	57/ 112 (50.9)	11.5 (9.8, 16.6)	13/ 23 (56.5)	8.1 (5.6, 19.8)	0.63 (0.34, 1.15)	0.1255	
ECOG-PS at Randomization							0.2749
0	60/ 131 (45.8)	15.9 (12.4, 24.1)	24/ 48 (50.0)	9.8 (7.0, 18.0)	0.61 (0.38, 0.98)	0.0416	
1	62/ 105 (59.0)	11.3 (8.5, 14.0)	18/ 26 (69.2)	5.6 (3.6, 8.4)	0.42 (0.25, 0.72)	0.0012	
Number of Organs Involved							0.0792
<= 2	52/ 119 (43.7)	15.9 (12.6, 32.9)	16/ 34 (47.1)	17.9 (8.3, NE)	0.76 (0.43, 1.33)	0.3308	
>= 3	70/ 117 (59.8)	9.8 (8.4, 14.0)	26/ 40 (65.0)	4.3 (3.0, 7.2)	0.42 (0.27, 0.67)	0.0002	
Presence of Liver Metastases							0.6353
Yes	87/ 147 (59.2)	11.0 (8.6, 12.8)	27/ 46 (58.7)	6.9 (4.3, 9.8)	0.61 (0.40, 0.94)	0.0250	
No	35/ 89 (39.3)	18.4 (14.0, 32.9)	15/ 28 (53.6)	9.7 (7.1, 19.8)	0.50 (0.27, 0.93)	0.0252	
Side of Tumor							0.6959
Left	51/ 90 (56.7)	11.2 (8.5, 16.7)	21/ 36 (58.3)	8.3 (5.6, 11.1)	0.57 (0.34, 0.95)	0.0308	
Right	71/ 146 (48.6)	14.0 (11.4, 16.6)	21/ 38 (55.3)	8.1 (4.7, 19.8)	0.62 (0.38, 1.02)	0.0561	

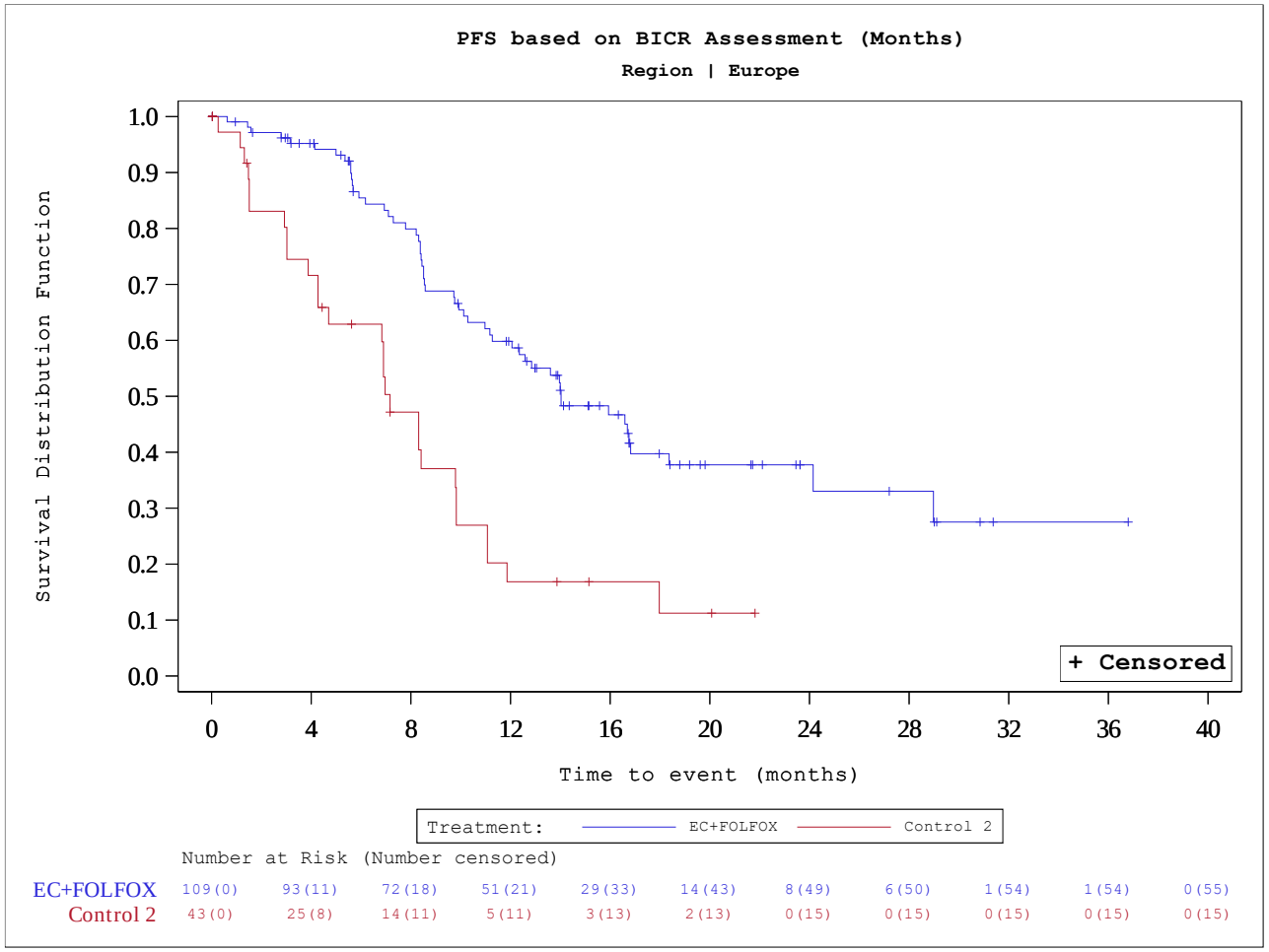
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.
[4] P-Value for interaction from Cox proportional hazards model using ties=exact option with treatment, subgroup and treatment*subgroup interaction as covariates.
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Kaplan Meier Plot of PFS based on BICR Assessment (Months)
Full Analysis Set



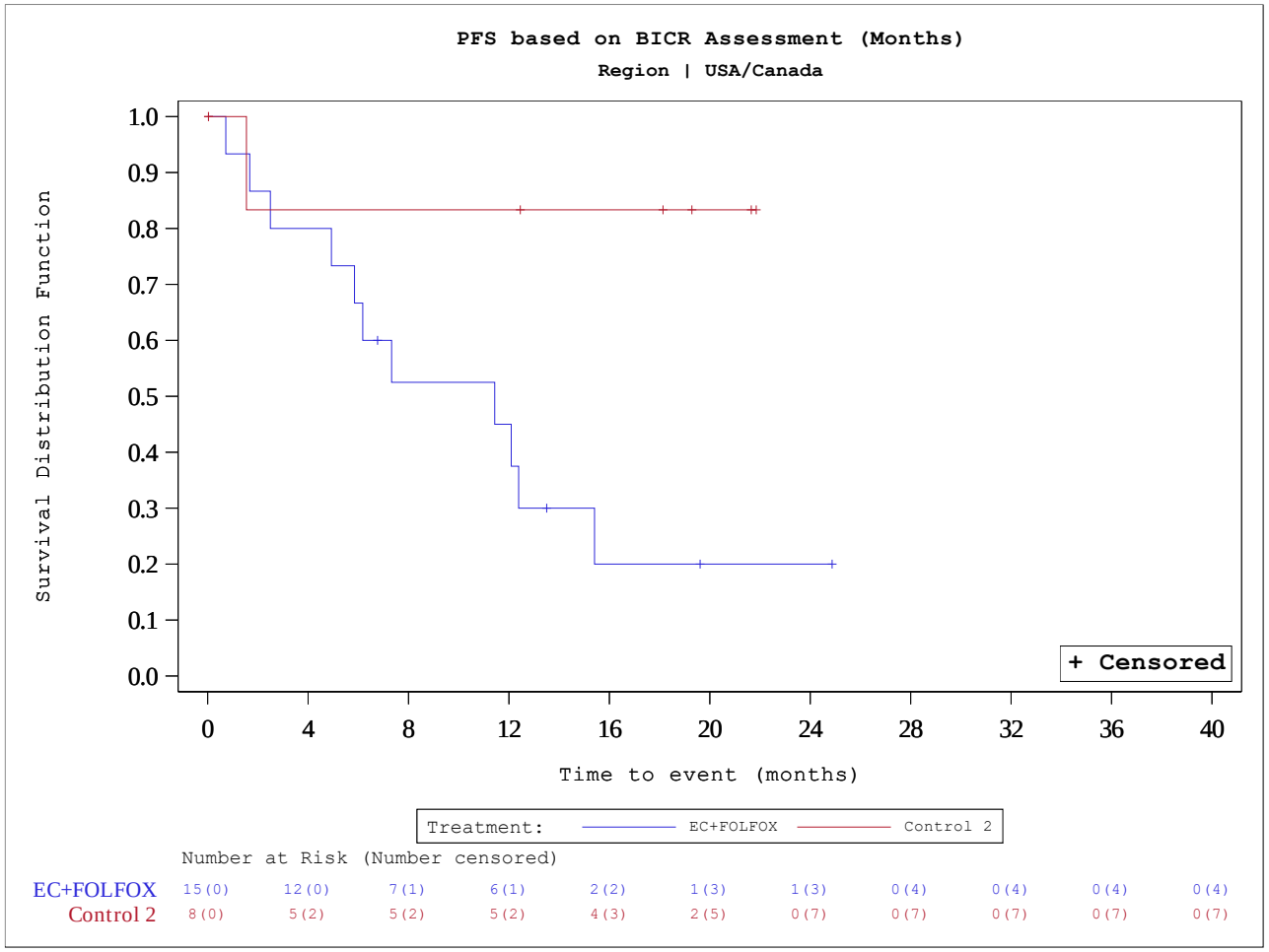
Kaplan-Meier Plots for subgroups only created if p-value for interaction < 0.05.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Kaplan Meier Plot of PFS based on BICR Assessment (Months)
Full Analysis Set



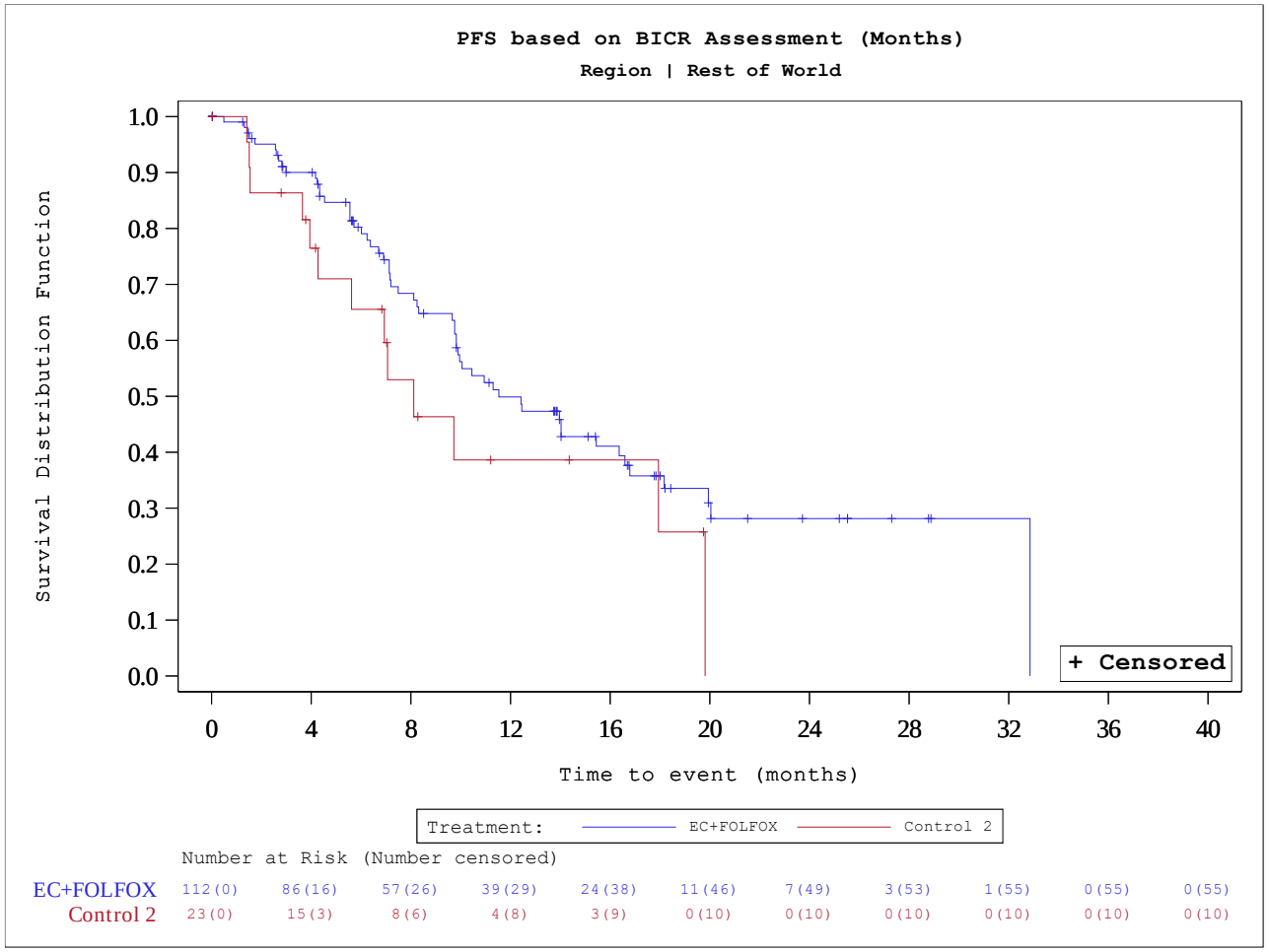
Kaplan-Meier Plots for subgroups only created if p-value for interaction < 0.05.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Kaplan Meier Plot of PFS based on BICR Assessment (Months)
Full Analysis Set



Kaplan-Meier Plots for subgroups only created if p-value for interaction < 0.05.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Kaplan Meier Plot of PFS based on BICR Assessment (Months)
Full Analysis Set



Kaplan-Meier Plots for subgroups only created if p-value for interaction < 0.05.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Duration of Objective Response based on BICR Assessment (Months)
Full Analysis Set

	EC+FOLFOX (N=155)	Control 2 (N=30)
Number of subjects with events, n (%)	74 (47.7)	14 (46.7)
Number of censored subjects, n (%)	81 (52.3)	16 (53.3)
Kaplan-Meier estimates of Time to Event (Months) [1]		
25%-ile (95% CI)	7.1 (6.6, 8.4)	7.0 (4.2, 8.4)
Median (95% CI)	13.9 (10.9, 18.5)	12.4 (8.2, NE)
75%-ile (95% CI)	27.6 (22.6, NE)	NE (12.4, NE)
Stratified analysis [2]		
Hazard Ratio (95% CI) [3]	0.70 (0.39, 1.27)	
p-value [4]	0.2440	

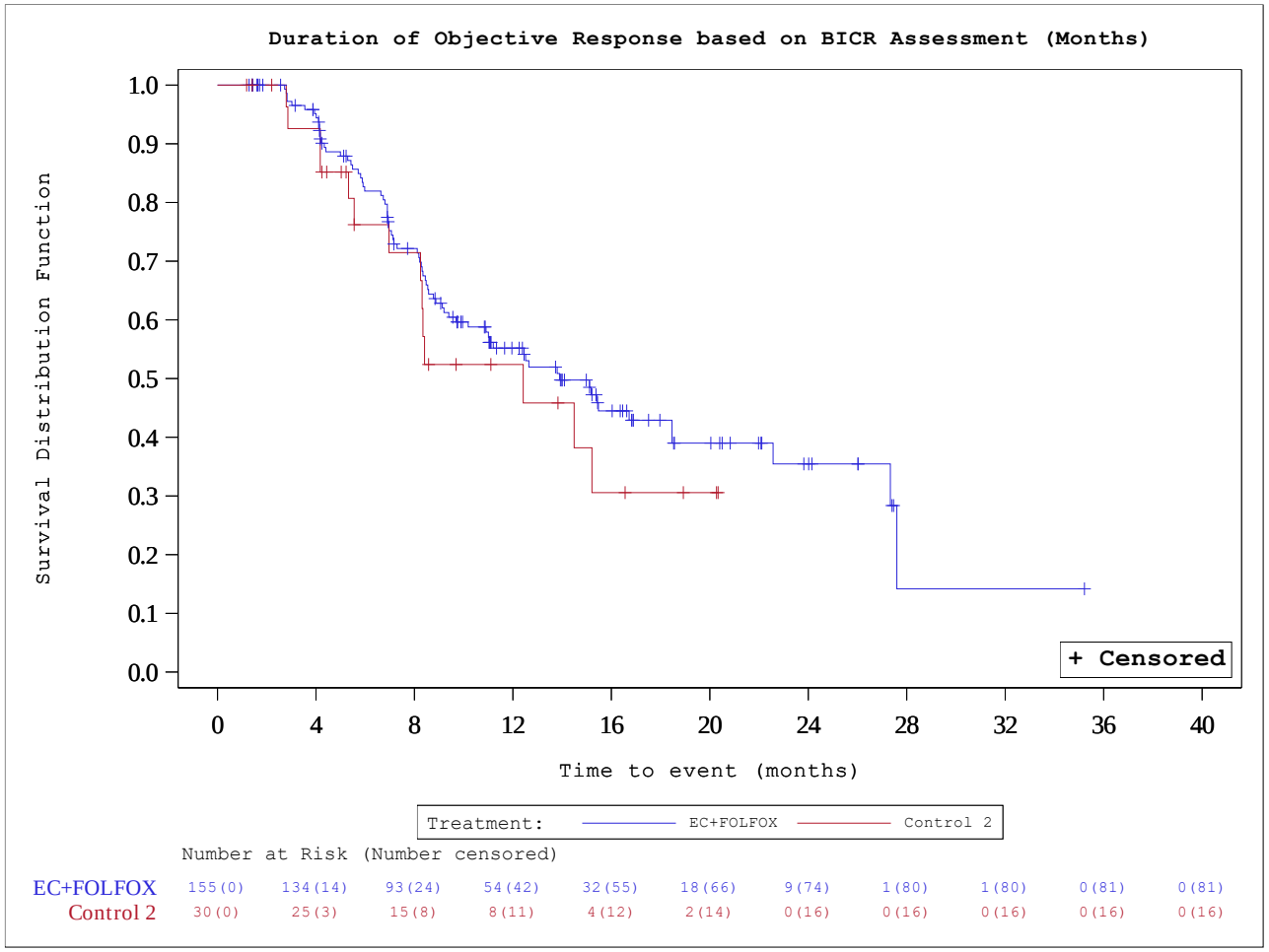
[1] Based on the Brookmeyer and Crowley method.
[2] Stratified by ECOG PS by Randomization.
[3] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[4] P-value from 2-sided log-rank test.
Including only patients having complete response or partial response.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Duration of Objective Response based on BICR Assessment (Months) - Subgroup analysis
Full Analysis Set

Subgroup Level	EC+FOLFOX (N=155) n/ N (%)	EC+FOLFOX (N=155) Median (95% CI)[1]	Control 2 (N=30) n/ N (%)	Control 2 (N=30) Median (95% CI)[1]	Unstratified analysis Hazard Ratio (95% CI)[2]	Unstratified analysis p-Value[3]	Interaction p-Value[4]
Age (Years)							0.7690
< 65	50/ 100 (50.0)	12.5 (8.8, 18.5)	9/ 18 (50.0)	8.3 (7.0, NE)	0.75 (0.37, 1.52)	0.4236	
>= 65	24/ 55 (43.6)	15.2 (10.9, 27.3)	5/ 12 (41.7)	15.2 (8.3, NE)	0.79 (0.30, 2.09)	0.6310	
Sex							0.8008
Male	38/ 82 (46.3)	15.5 (8.6, 27.6)	7/ 12 (58.3)	12.4 (8.3, NE)	0.73 (0.32, 1.64)	0.4465	
Female	36/ 73 (49.3)	13.8 (10.2, 18.5)	7/ 18 (38.9)	8.3 (7.0, NE)	0.84 (0.37, 1.89)	0.6644	
Region							0.7901
Europe	36/ 76 (47.4)	15.1 (9.7, 27.6)	10/ 15 (66.7)	8.3 (5.6, 12.4)	0.47 (0.23, 0.96)	0.0360	
USA/Canada	6/ 8 (75.0)	9.3 (4.2, NE)	0/ 4 (0.0)	NE (NE , NE)	NE		
Rest of World	32/ 71 (45.1)	15.4 (8.9, 27.3)	4/ 11 (36.4)	14.5 (5.3, 15.2)	0.65 (0.23, 1.86)	0.4195	
ECOG-PS at Randomization							0.5378
0	40/ 89 (44.9)	18.5 (9.7, 27.6)	11/ 24 (45.8)	14.5 (8.3, NE)	0.76 (0.39, 1.50)	0.4377	
1	34/ 66 (51.5)	12.6 (8.9, 16.7)	3/ 6 (50.0)	7.0 (5.6, NE)	0.51 (0.15, 1.69)	0.2700	
Number of Organs Involved							0.4327
<= 2	28/ 77 (36.4)	27.3 (12.5, NE)	8/ 18 (44.4)	14.5 (7.0, NE)	0.60 (0.27, 1.32)	0.2006	
>= 3	46/ 78 (59.0)	9.2 (7.3, 15.4)	6/ 12 (50.0)	8.3 (8.2, NE)	0.97 (0.41, 2.27)	0.9361	
Presence of Liver Metastases							0.0833
Yes	56/ 100 (56.0)	10.2 (8.4, 13.9)	8/ 18 (44.4)	8.4 (8.2, NE)	1.12 (0.53, 2.34)	0.7746	
No	18/ 55 (32.7)	27.3 (27.3, 27.6)	6/ 12 (50.0)	14.5 (7.0, 15.2)	0.39 (0.15, 1.01)	0.0440	
Side of Tumor							0.0993
Left	31/ 60 (51.7)	15.1 (8.3, 27.3)	8/ 14 (57.1)	8.3 (5.3, 12.4)	0.47 (0.21, 1.06)	0.0610	
Right	43/ 95 (45.3)	13.8 (10.2, 27.6)	6/ 16 (37.5)	15.2 (8.3, NE)	1.18 (0.50, 2.78)	0.7058	

[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.
[4] P-Value for interaction from Cox proportional hazards model using ties=exact option with treatment, subgroup and treatment*subgroup interaction as covariates.
Including only patients having complete response or partial response.
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Kaplan Meier Plot of Duration of Objective Response based on BICR Assessment (Months)
Full Analysis Set



Kaplan-Meier Plots for subgroups only created if p-value for interaction < 0.05.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Time to first deterioration of at least 10 points - EOR01-Global QOL (Months)
Full Analysis Set

	EC+FOLFOX (N=219)	Control 2 (N=66)
Number of subjects with events, n (%)	121 (55.3)	27 (40.9)
Number of censored subjects, n (%)	98 (44.7)	39 (59.1)
Kaplan-Meier estimates of Time to Event (Months) [1]		
25%-ile (95% CI)	2.0 (1.6, 2.9)	2.9 (1.6, 7.7)
Median (95% CI)	5.8 (4.4, 9.8)	12.3 (6.7, NE)
75%-ile (95% CI)	NE (23.0, NE)	NE (15.5, NE)
Stratified analysis [2]		
Hazard Ratio (95% CI) [3]	1.30 (0.86, 1.98)	
p-value [4]	0.2136	

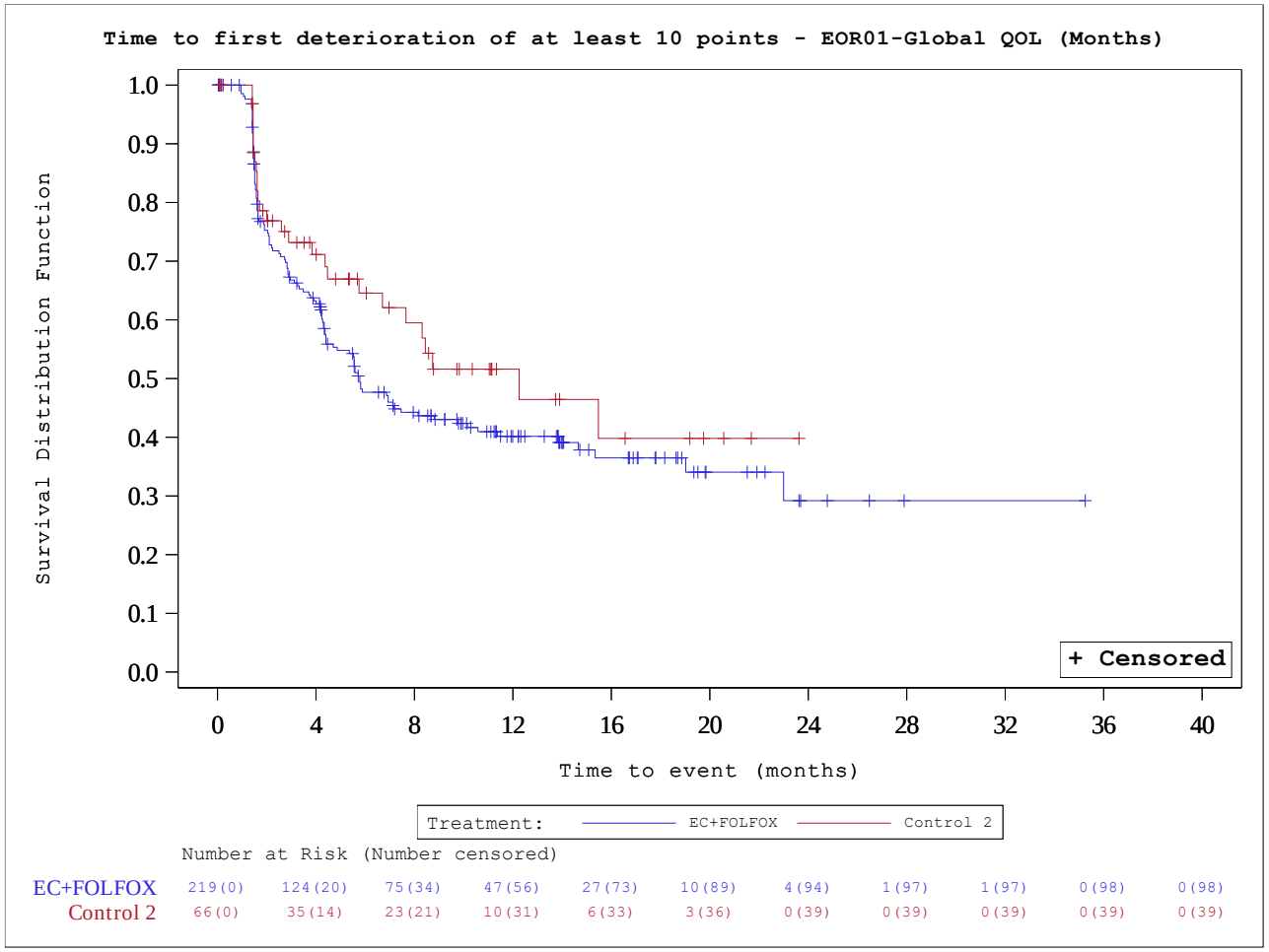
[1] Based on the Brookmeyer and Crowley method.
[2] Stratified by ECOG PS by Randomization.
[3] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[4] P-value from 2-sided log-rank test.
Including only patients from the full analysis set who completed a baseline (last PRO assessment prior to or on the first dose of study treatment) and at least 1 post-baseline PRO assessment.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Time to first deterioration of at least 10 points - EOR01-Global QOL (Months) - Subgroup analysis
Full Analysis Set

Subgroup Level	EC+FOLFOX (N=219) n/ N (%)	EC+FOLFOX (N=219) Median (95% CI)[1]	Control 2 (N=66) n/ N (%)	Control 2 (N=66) Median (95% CI)[1]	Unstratified analysis Hazard Ratio (95% CI)[2]	Unstratified analysis p-Value[3]	Interaction p-Value[4]
Age (Years)							0.6239
< 65	72/ 139 (51.8)	6.9 (4.4, 15.3)	16/ 41 (39.0)	15.5 (6.7, NE)	1.23 (0.71, 2.11)	0.4467	
>= 65	49/ 80 (61.3)	5.6 (3.8, 8.1)	11/ 25 (44.0)	8.7 (4.5, NE)	1.50 (0.78, 2.89)	0.2263	
Sex							0.1830
Male	62/ 114 (54.4)	5.9 (4.7, 10.6)	15/ 31 (48.4)	8.3 (3.8, 15.5)	1.00 (0.57, 1.76)	0.9981	
Female	59/ 105 (56.2)	5.5 (4.0, 19.0)	12/ 35 (34.3)	NE (6.7, NE)	1.74 (0.94, 3.24)	0.0752	
Region							0.2840
Europe	54/ 104 (51.9)	8.8 (4.4, NE)	17/ 38 (44.7)	8.7 (5.7, 15.5)	0.97 (0.56, 1.69)	0.9244	
USA/Canada	5/ 8 (62.5)	3.8 (1.6, NE)	1/ 6 (16.7)	NE (NE , NE)	4.24 (0.49, 36.42)	0.1453	
Rest of World	62/ 107 (57.9)	5.6 (4.2, 6.9)	9/ 22 (40.9)	NE (1.7, NE)	1.50 (0.75, 3.03)	0.2453	
ECOG-PS at Randomization							0.6708
0	65/ 123 (52.8)	5.8 (4.3, 19.0)	19/ 43 (44.2)	12.3 (4.5, NE)	1.23 (0.73, 2.04)	0.4331	
1	56/ 96 (58.3)	5.6 (4.3, 10.2)	8/ 23 (34.8)	8.4 (4.4, NE)	1.47 (0.70, 3.09)	0.3040	
Number of Organs Involved							0.0002
<= 2	71/ 110 (64.5)	4.3 (2.9, 5.7)	9/ 33 (27.3)	NE (12.3, NE)	3.02 (1.51, 6.06)	0.0010	
>= 3	50/ 109 (45.9)	10.2 (5.8, NE)	18/ 33 (54.5)	4.4 (2.6, 8.7)	0.55 (0.32, 0.95)	0.0293	
Presence of Liver Metastases							0.1371
Yes	69/ 135 (51.1)	7.1 (5.5, 19.0)	18/ 40 (45.0)	7.7 (4.4, NE)	1.03 (0.61, 1.73)	0.9151	
No	52/ 84 (61.9)	4.7 (3.9, 7.2)	9/ 26 (34.6)	NE (8.3, NE)	2.02 (0.99, 4.11)	0.0476	
Side of Tumor							0.8747
Left	40/ 83 (48.2)	8.8 (5.6, NE)	12/ 33 (36.4)	15.5 (8.4, NE)	1.24 (0.65, 2.36)	0.5173	
Right	81/ 136 (59.6)	4.4 (3.8, 7.1)	15/ 33 (45.5)	8.3 (3.8, NE)	1.31 (0.76, 2.28)	0.3300	

[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.
[4] P-Value for interaction from Cox proportional hazards model using ties=exact option with treatment, subgroup and treatment*subgroup interaction as covariates.
Including only patients from the full analysis set who completed a baseline (last PRO assessment prior to or on the first dose of study treatment) and at least 1 post-baseline PRO assessment.
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Kaplan Meier Plot of Time to first deterioration of at least 10 points - EOR01-Global QOL (Months)
Full Analysis Set



Kaplan-Meier Plots for subgroups only created if p-value for interaction < 0.05.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
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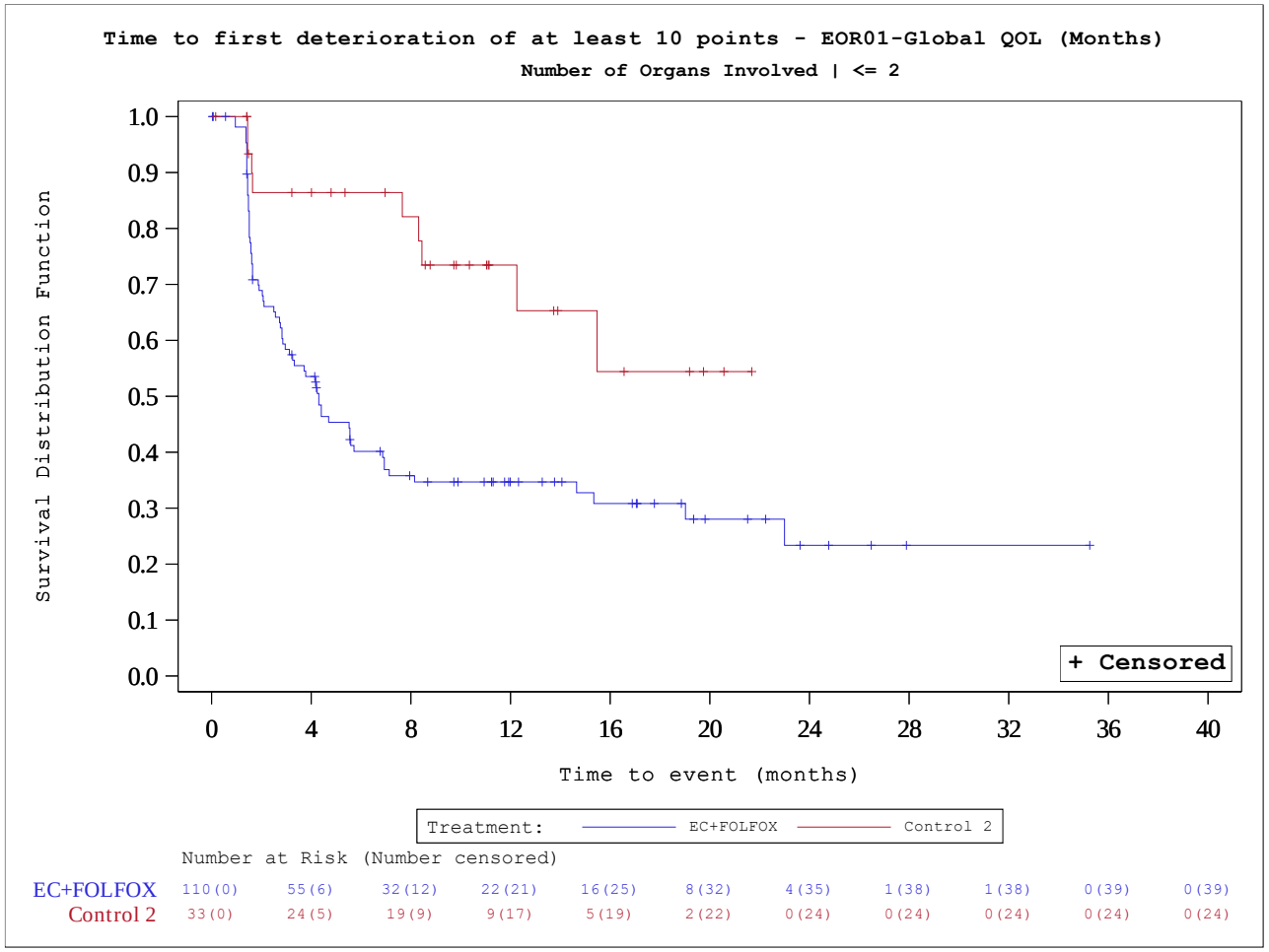
Kaplan Meier Plot of Time to first deterioration of at least 10 points - EOR01-Global QOL (Months)
Full Analysis Set



Kaplan-Meier Plots for subgroups only created if p-value for interaction < 0.05.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
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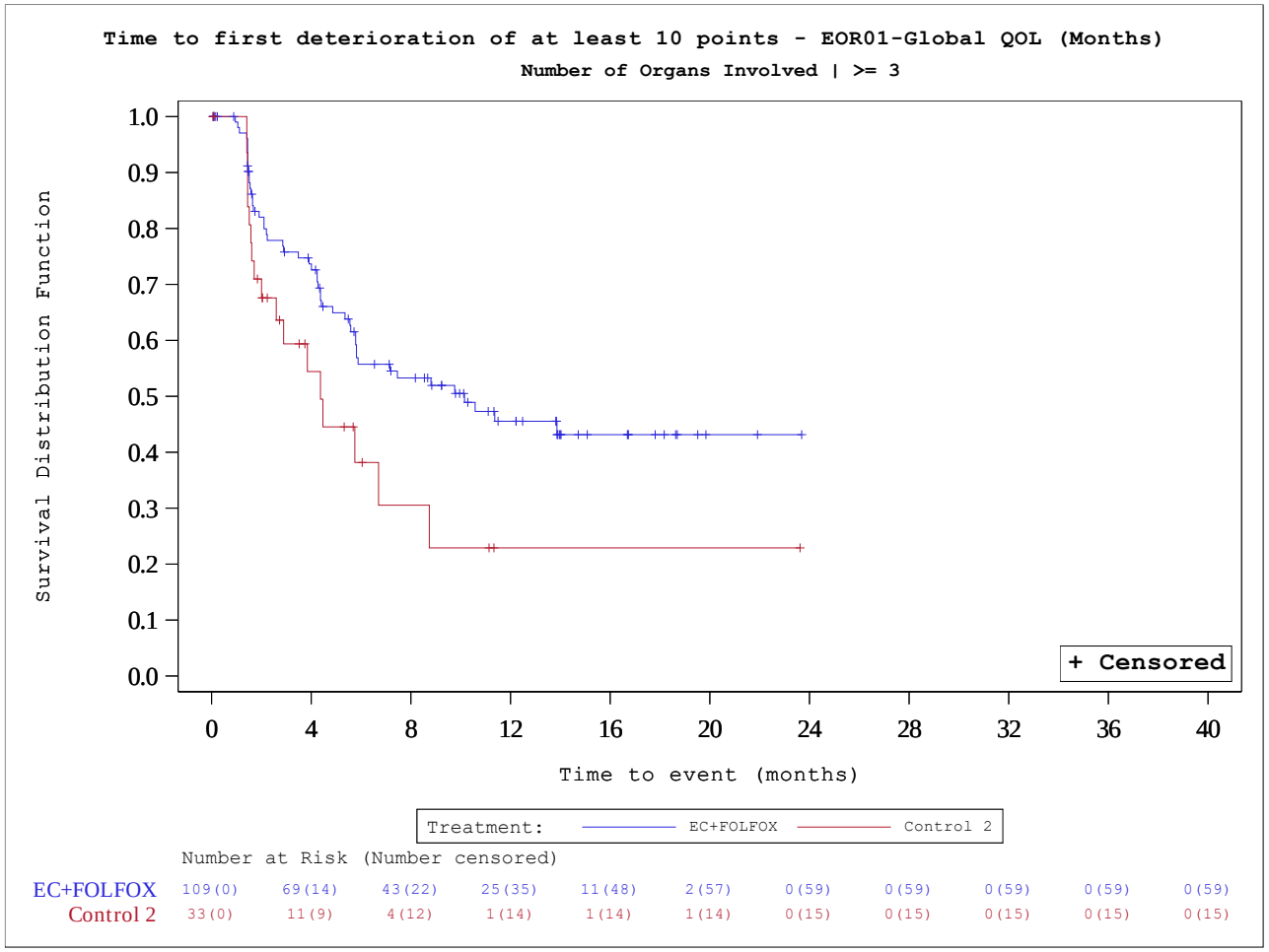
Full Analysis Set



Kaplan-Meier Plots for subgroups only created if p-value for interaction < 0.05.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Time to first improvement of at least 10 points - EOR01-Global QOL (Months)
Full Analysis Set

	EC+FOLFOX (N=219)	Control 2 (N=66)
Number of subjects with events, n (%)	96 (43.8)	16 (24.2)
Number of censored subjects, n (%)	123 (56.2)	50 (75.8)
Kaplan-Meier estimates of Time to Event (Months) [1]		
25%-ile (95% CI)	2.9 (1.9, 4.1)	5.6 (2.8, NE)
Median (95% CI)	15.0 (8.3, NE)	NE (NE, NE)
75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
Stratified analysis [2]		
Hazard Ratio (95% CI) [3]	1.74 (1.02, 2.96)	
p-value [4]	0.0389	

[1] Based on the Brookmeyer and Crowley method.
[2] Stratified by ECOG PS by Randomization.
[3] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio > 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[4] P-value from 2-sided log-rank test.
Including only patients from the full analysis set who completed a baseline (last PRO assessment prior to or on the first dose of study treatment) and at least 1 post-baseline PRO assessment.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Time to first improvement of at least 10 points - EOR01-Global QOL (Months) - Subgroup analysis
Full Analysis Set

Subgroup Level	EC+FOLFOX (N=219) n/ N (%)	EC+FOLFOX (N=219) Median (95% CI)[1]	Control 2 (N=66) n/ N (%)	Control 2 (N=66) Median (95% CI)[1]	Unstratified analysis Hazard Ratio (95% CI)[2]	Unstratified analysis p-Value[3]	Interaction p-Value[4]
Age (Years)							0.5417
< 65	64/ 139 (46.0)	12.7 (7.0, NE)	12/ 41 (29.3)	NE (11.1, NE)	1.62 (0.87, 3.00)	0.1237	
>= 65	32/ 80 (40.0)	15.3 (8.1, NE)	4/ 25 (16.0)	NE (NE , NE)	2.36 (0.83, 6.70)	0.0931	
Sex							0.9424
Male	45/ 114 (39.5)	23.7 (7.6, NE)	6/ 31 (19.4)	NE (NE , NE)	1.90 (0.81, 4.46)	0.1349	
Female	51/ 105 (48.6)	8.8 (6.8, 18.3)	10/ 35 (28.6)	NE (11.1, NE)	1.85 (0.94, 3.64)	0.0719	
Region							0.5418
Europe	46/ 104 (44.2)	15.3 (6.8, NE)	7/ 38 (18.4)	NE (NE , NE)	2.27 (1.03, 5.04)	0.0373	
USA/Canada	2/ 8 (25.0)	NE (2.8, NE)	2/ 6 (33.3)	NE (2.9, NE)	0.73 (0.10, 5.17)	0.7490	
Rest of World	48/ 107 (44.9)	14.3 (5.7, NE)	7/ 22 (31.8)	NE (5.6, NE)	1.52 (0.69, 3.36)	0.3020	
ECOG-PS at Randomization							0.8135
0	47/ 123 (38.2)	23.7 (8.5, NE)	10/ 43 (23.3)	NE (NE , NE)	1.65 (0.83, 3.28)	0.1469	
1	49/ 96 (51.0)	7.6 (3.9, 18.3)	6/ 23 (26.1)	NE (11.1, NE)	1.88 (0.80, 4.39)	0.1391	
Number of Organs Involved							0.8108
<= 2	42/ 110 (38.2)	23.7 (14.3, NE)	7/ 33 (21.2)	NE (NE , NE)	1.67 (0.75, 3.73)	0.2026	
>= 3	54/ 109 (49.5)	7.6 (4.1, 15.3)	9/ 33 (27.3)	NE (7.0, NE)	1.96 (0.97, 3.98)	0.0577	
Presence of Liver Metastases							0.4278
Yes	64/ 135 (47.4)	8.5 (4.6, NE)	9/ 40 (22.5)	NE (NE , NE)	2.15 (1.07, 4.33)	0.0269	
No	32/ 84 (38.1)	23.7 (12.7, NE)	7/ 26 (26.9)	NE (11.1, NE)	1.35 (0.60, 3.08)	0.4702	
Side of Tumor							0.4888
Left	43/ 83 (51.8)	7.5 (3.7, NE)	8/ 33 (24.2)	NE (11.1, NE)	2.31 (1.09, 4.92)	0.0254	
Right	53/ 136 (39.0)	18.3 (8.8, NE)	8/ 33 (24.2)	NE (NE , NE)	1.54 (0.73, 3.24)	0.2506	

[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio > 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.
[4] P-Value for interaction from Cox proportional hazards model using ties=exact option with treatment, subgroup and treatment*subgroup interaction as covariates.
Including only patients from the full analysis set who completed a baseline (last PRO assessment prior to or on the first dose of study treatment) and at least 1 post-baseline PRO assessment.
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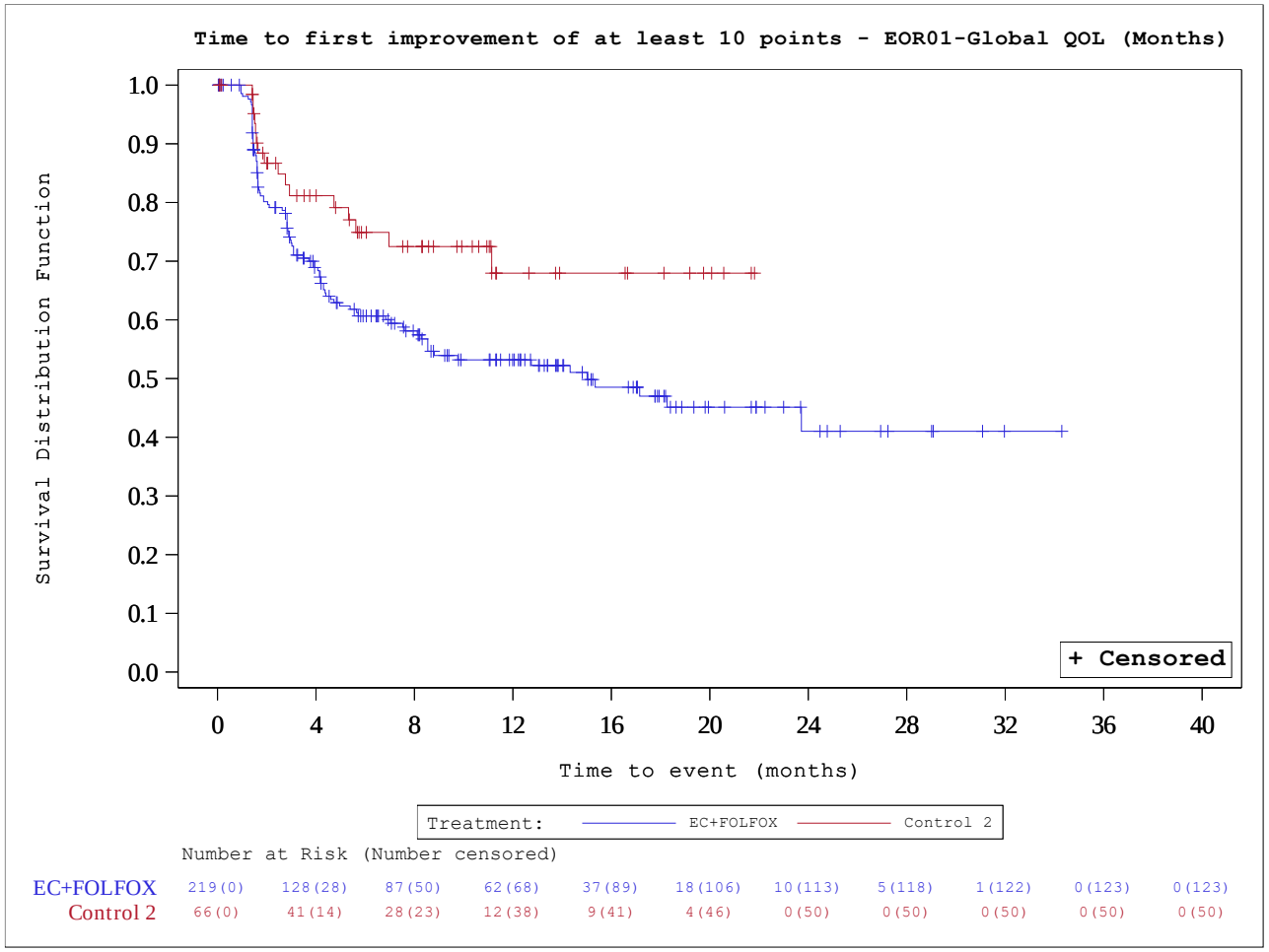
Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Kaplan Meier Plot of Time to first improvement of at least 10 points - EOR01-Global QOL (Months)
Full Analysis Set



Kaplan-Meier Plots for subgroups only created if p-value for interaction < 0.05.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Time to first deterioration of at least 10 points - EOR01-Physical Functioning (Months)
Full Analysis Set

	EC+FOLFOX (N=219)	Control 2 (N=66)
Number of subjects with events, n (%)	128 (58.4)	28 (42.4)
Number of censored subjects, n (%)	91 (41.6)	38 (57.6)
Kaplan-Meier estimates of Time to Event (Months) [1]		
25%-ile (95% CI)	1.7 (1.6, 2.3)	2.8 (1.6, 7.2)
Median (95% CI)	5.8 (4.2, 8.0)	11.2 (6.7, NE)
75%-ile (95% CI)	29.8 (20.5, NE)	NE (16.4, NE)
Stratified analysis [2]		
Hazard Ratio (95% CI) [3]	1.35 (0.89, 2.04)	
p-value [4]	0.1550	

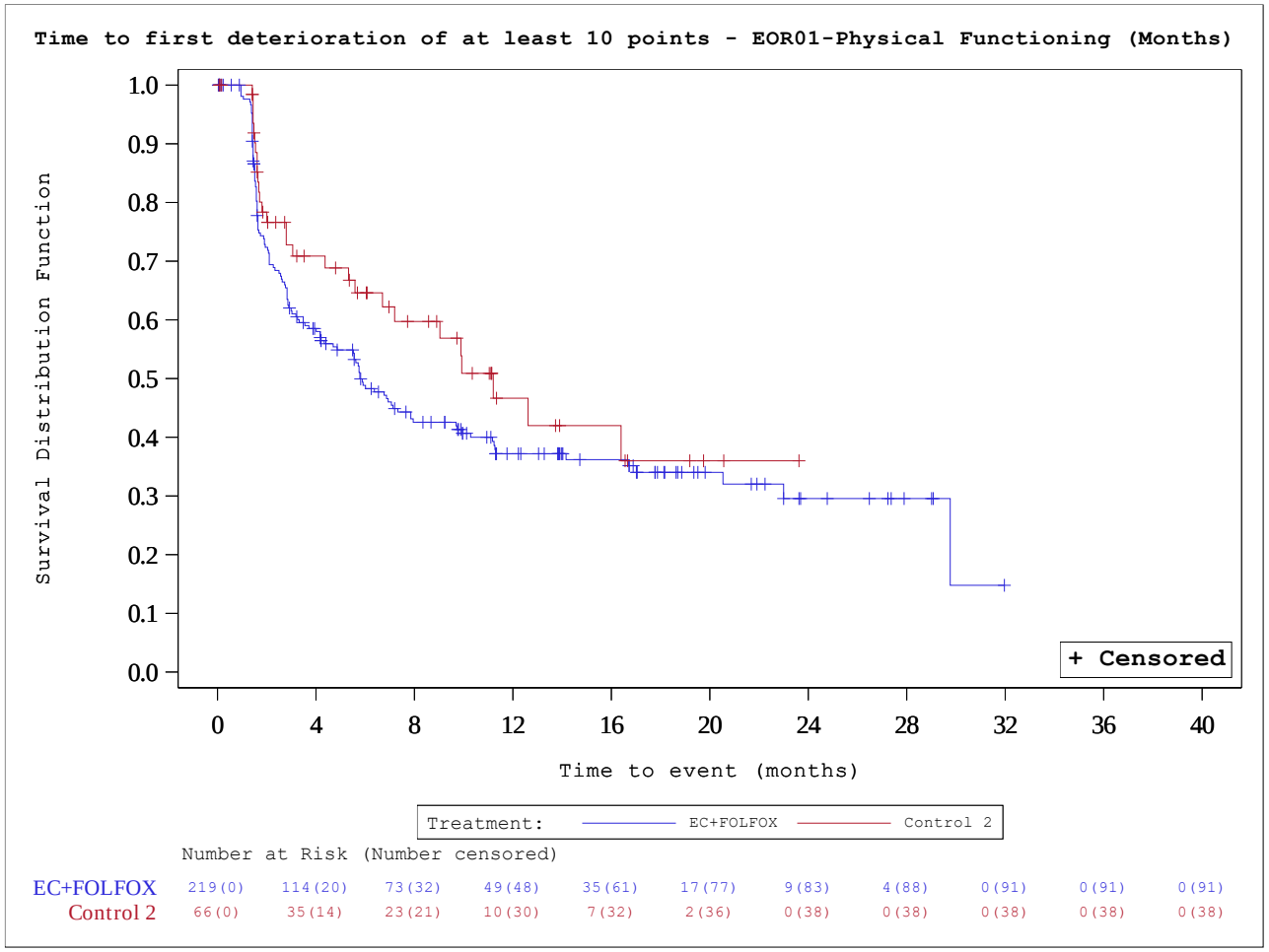
[1] Based on the Brookmeyer and Crowley method.
[2] Stratified by ECOG PS by Randomization.
[3] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[4] P-value from 2-sided log-rank test.
Including only patients from the full analysis set who completed a baseline (last PRO assessment prior to or on the first dose of study treatment) and at least 1 post-baseline PRO assessment.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Time to first deterioration of at least 10 points - EOR01-Physical Functioning (Months) - Subgroup analysis
Full Analysis Set

Subgroup Level	EC+FOLFOX (N=219) n/ N (%)	EC+FOLFOX (N=219) Median (95% CI)[1]	Control 2 (N=66) n/ N (%)	Control 2 (N=66) Median (95% CI)[1]	Unstratified analysis Hazard Ratio (95% CI)[2]	Unstratified analysis p-Value[3]	Interaction p-Value[4]
Age (Years)							0.9227
< 65	79/ 139 (56.8)	6.4 (5.5, 11.2)	17/ 41 (41.5)	11.2 (5.6, NE)	1.34 (0.79, 2.26)	0.2777	
>= 65	49/ 80 (61.3)	3.3 (2.3, 9.7)	11/ 25 (44.0)	9.9 (2.0, NE)	1.39 (0.72, 2.69)	0.3235	
Sex							0.9408
Male	71/ 114 (62.3)	5.7 (3.3, 7.3)	14/ 31 (45.2)	9.9 (5.6, 16.4)	1.32 (0.74, 2.34)	0.3477	
Female	57/ 105 (54.3)	7.1 (4.2, 20.5)	14/ 35 (40.0)	11.2 (5.3, NE)	1.35 (0.75, 2.42)	0.3112	
Region							0.4003
Europe	59/ 104 (56.7)	6.9 (4.3, 23.0)	17/ 38 (44.7)	9.9 (5.3, NE)	1.06 (0.62, 1.82)	0.8336	
USA/Canada	4/ 8 (50.0)	NE (1.6, NE)	1/ 6 (16.7)	NE (NE , NE)	3.03 (0.34, 27.11)	0.2980	
Rest of World	65/ 107 (60.7)	5.6 (2.9, 9.7)	10/ 22 (45.5)	11.2 (3.1, NE)	1.53 (0.79, 2.98)	0.2124	
ECOG-PS at Randomization							0.9900
0	73/ 123 (59.3)	6.9 (3.7, 10.3)	20/ 43 (46.5)	11.2 (6.7, NE)	1.34 (0.81, 2.20)	0.2508	
1	55/ 96 (57.3)	5.7 (3.0, 11.2)	8/ 23 (34.8)	NE (2.8, NE)	1.38 (0.66, 2.90)	0.4011	
Number of Organs Involved							0.0206
<= 2	75/ 110 (68.2)	5.6 (3.2, 7.9)	11/ 33 (33.3)	16.4 (9.0, NE)	2.18 (1.15, 4.11)	0.0138	
>= 3	53/ 109 (48.6)	6.4 (4.2, NE)	17/ 33 (51.5)	6.7 (3.1, 12.6)	0.84 (0.49, 1.46)	0.5259	
Presence of Liver Metastases							0.5567
Yes	82/ 135 (60.7)	5.7 (2.9, 7.3)	19/ 40 (47.5)	7.2 (3.1, NE)	1.22 (0.74, 2.01)	0.4429	
No	46/ 84 (54.8)	7.9 (4.2, 20.5)	9/ 26 (34.6)	16.4 (9.0, NE)	1.58 (0.77, 3.24)	0.2104	
Side of Tumor							0.6665
Left	47/ 83 (56.6)	7.1 (4.0, 11.3)	14/ 33 (42.4)	9.9 (4.4, NE)	1.24 (0.68, 2.26)	0.4825	
Right	81/ 136 (59.6)	5.7 (3.3, 9.7)	14/ 33 (42.4)	12.6 (5.6, NE)	1.45 (0.82, 2.57)	0.1934	

[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.
[4] P-Value for interaction from Cox proportional hazards model using ties=exact option with treatment, subgroup and treatment*subgroup interaction as covariates.
Including only patients from the full analysis set who completed a baseline (last PRO assessment prior to or on the first dose of study treatment) and at least 1 post-baseline PRO assessment.
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Kaplan Meier Plot of Time to first deterioration of at least 10 points - EOR01-Physical Functioning (Months)
Full Analysis Set



Kaplan-Meier Plots for subgroups only created if p-value for interaction < 0.05.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
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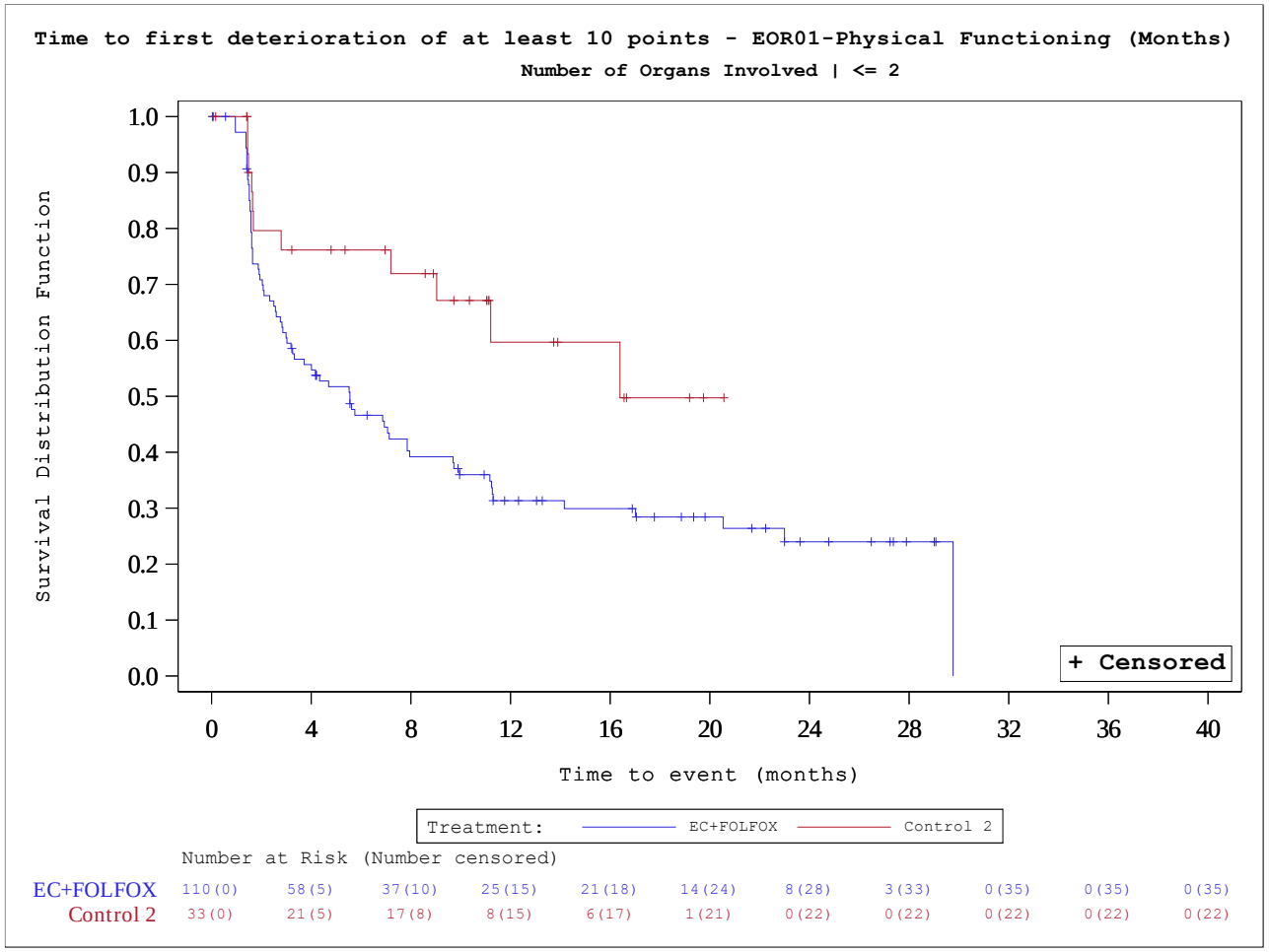
Full Analysis Set



Kaplan-Meier Plots for subgroups only created if p-value for interaction < 0.05.

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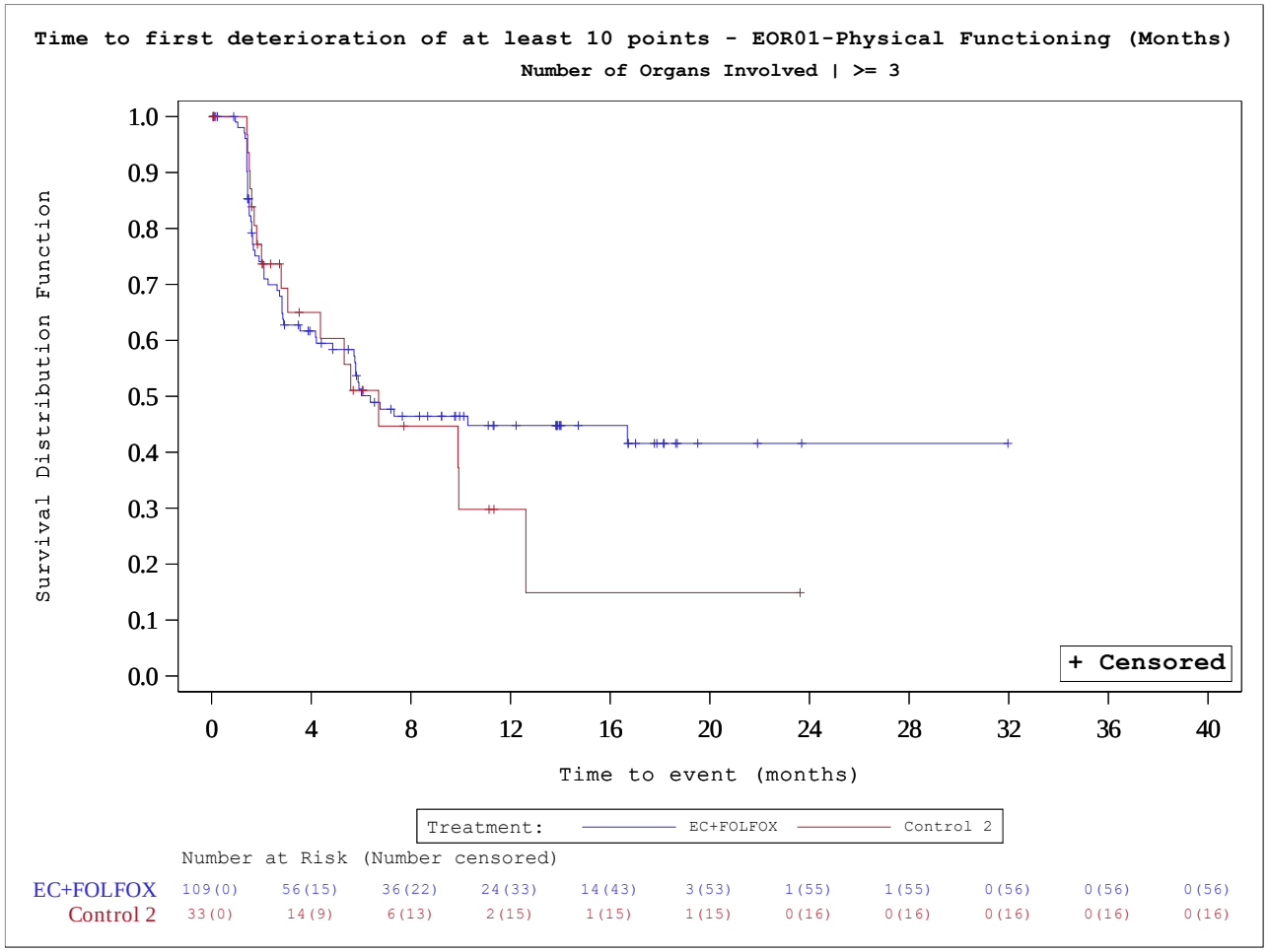
Full Analysis Set



Kaplan-Meier Plots for subgroups only created if p-value for interaction < 0.05.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Time to first improvement of at least 10 points - EOR01-Physical Functioning (Months)
Full Analysis Set

	EC+FOLFOX (N=219)	Control 2 (N=66)
Number of subjects with events, n (%)	61 (27.9)	6 (9.1)
Number of censored subjects, n (%)	158 (72.1)	60 (90.9)
Kaplan-Meier estimates of Time to Event (Months) [1]		
25%-ile (95% CI)	5.7 (4.4, 11.3)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
Stratified analysis [2]		
Hazard Ratio (95% CI) [3]	2.80 (1.21, 6.49)	
p-value [4]	0.0122	

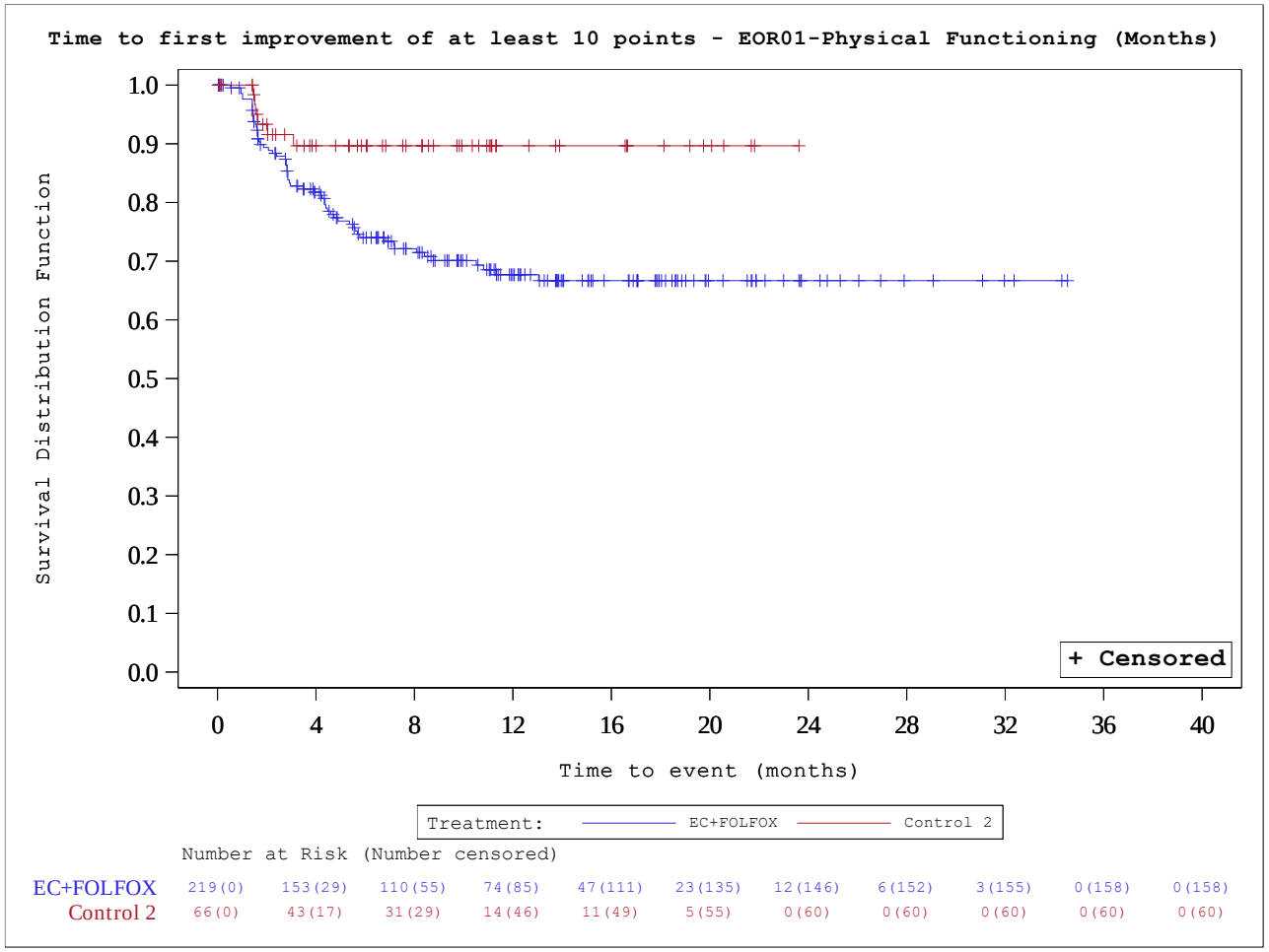
[1] Based on the Brookmeyer and Crowley method.
[2] Stratified by ECOG PS by Randomization.
[3] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio > 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[4] P-value from 2-sided log-rank test.
Including only patients from the full analysis set who completed a baseline (last PRO assessment prior to or on the first dose of study treatment) and at least 1 post-baseline PRO assessment.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Time to first improvement of at least 10 points - EOR01-Physical Functioning (Months) - Subgroup analysis
Full Analysis Set

Subgroup Level	EC+FOLFOX (N=219) n/ N (%)	EC+FOLFOX (N=219) Median (95% CI)[1]	Control 2 (N=66) n/ N (%)	Control 2 (N=66) Median (95% CI)[1]	Unstratified analysis Hazard Ratio (95% CI)[2]	Unstratified analysis p-Value[3]	Interaction p-Value[4]
Age (Years)							0.5193
< 65	45/ 139 (32.4)	NE (NE , NE)	5/ 41 (12.2)	NE (NE , NE)	2.42 (0.96, 6.10)	0.0524	
>= 65	16/ 80 (20.0)	NE (NE , NE)	1/ 25 (4.0)	NE (NE , NE)	5.25 (0.70, 39.58)	0.0720	
Sex							0.3939
Male	25/ 114 (21.9)	NE (NE , NE)	3/ 31 (9.7)	NE (NE , NE)	1.98 (0.60, 6.56)	0.2558	
Female	36/ 105 (34.3)	NE (13.0, NE)	3/ 35 (8.6)	NE (NE , NE)	4.09 (1.26, 13.28)	0.0111	
Region							0.8891
Europe	38/ 104 (36.5)	NE (11.3, NE)	4/ 38 (10.5)	NE (NE , NE)	3.30 (1.18, 9.25)	0.0159	
USA/Canada	1/ 8 (12.5)	NE (10.8, NE)	0/ 6 (0.0)	NE (NE , NE)	NE		
Rest of World	22/ 107 (20.6)	NE (NE , NE)	2/ 22 (9.1)	NE (NE , NE)	2.12 (0.50, 9.02)	0.2977	
ECOG-PS at Randomization							0.1344
0	32/ 123 (26.0)	NE (NE , NE)	2/ 43 (4.7)	NE (NE , NE)	5.58 (1.34, 23.27)	0.0078	
1	29/ 96 (30.2)	NE (NE , NE)	4/ 23 (17.4)	NE (NE , NE)	1.48 (0.52, 4.20)	0.4642	
Number of Organs Involved							0.8119
<= 2	23/ 110 (20.9)	NE (NE , NE)	2/ 33 (6.1)	NE (NE , NE)	3.31 (0.78, 14.03)	0.0851	
>= 3	38/ 109 (34.9)	NE (8.8, NE)	4/ 33 (12.1)	NE (NE , NE)	2.72 (0.97, 7.64)	0.0469	
Presence of Liver Metastases							0.3116
Yes	39/ 135 (28.9)	NE (NE , NE)	5/ 40 (12.5)	NE (NE , NE)	2.16 (0.85, 5.49)	0.0958	
No	22/ 84 (26.2)	NE (NE , NE)	1/ 26 (3.8)	NE (NE , NE)	6.58 (0.89, 48.86)	0.0333	
Side of Tumor							0.7647
Left	27/ 83 (32.5)	NE (NE , NE)	3/ 33 (9.1)	NE (NE , NE)	3.47 (1.05, 11.45)	0.0294	
Right	34/ 136 (25.0)	NE (NE , NE)	3/ 33 (9.1)	NE (NE , NE)	2.61 (0.80, 8.49)	0.0984	

[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio > 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.
[4] P-Value for interaction from Cox proportional hazards model using ties=exact option with treatment, subgroup and treatment*subgroup interaction as covariates.
Including only patients from the full analysis set who completed a baseline (last PRO assessment prior to or on the first dose of study treatment) and at least 1 post-baseline PRO assessment.
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Kaplan Meier Plot of Time to first improvement of at least 10 points - EOR01-Physical Functioning (Months)
Full Analysis Set



Kaplan-Meier Plots for subgroups only created if p-value for interaction < 0.05.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Time to first deterioration of at least 10 points - EOR01-Role Functioning (Months)
Full Analysis Set

	EC+FOLFOX (N=219)	Control 2 (N=66)
Number of subjects with events, n (%)	140 (63.9)	35 (53.0)
Number of censored subjects, n (%)	79 (36.1)	31 (47.0)
Kaplan-Meier estimates of Time to Event (Months) [1]		
25%-ile (95% CI)	1.6 (1.5, 1.7)	1.6 (1.5, 2.8)
Median (95% CI)	4.2 (2.9, 5.9)	5.5 (2.8, 16.4)
75%-ile (95% CI)	17.9 (11.1, NE)	19.7 (9.9, NE)
Stratified analysis [2]		
Hazard Ratio (95% CI) [3]	1.18 (0.81, 1.72)	
p-value [4]	0.3783	

[1] Based on the Brookmeyer and Crowley method.
[2] Stratified by ECOG PS by Randomization.
[3] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[4] P-value from 2-sided log-rank test.
Including only patients from the full analysis set who completed a baseline (last PRO assessment prior to or on the first dose of study treatment) and at least 1 post-baseline PRO assessment.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Time to first deterioration of at least 10 points - EOR01-Role Functioning (Months) - Subgroup analysis
Full Analysis Set

Subgroup Level	EC+FOLFOX (N=219) n/ N (%)	EC+FOLFOX (N=219) Median (95% CI)[1]	Control 2 (N=66) n/ N (%)	Control 2 (N=66) Median (95% CI)[1]	Unstratified analysis Hazard Ratio (95% CI)[2]	Unstratified analysis p-Value[3]	Interaction p-Value[4]
Age (Years)							0.7524
< 65	87/ 139 (62.6)	4.9 (2.8, 7.1)	21/ 41 (51.2)	5.5 (3.0, 19.7)	1.24 (0.77, 2.00)	0.3715	
>= 65	53/ 80 (66.3)	3.1 (2.1, 5.7)	14/ 25 (56.0)	2.6 (1.6, NE)	1.08 (0.60, 1.96)	0.7850	
Sex							0.9129
Male	71/ 114 (62.3)	5.6 (3.3, 7.1)	15/ 31 (48.4)	7.4 (2.4, 16.4)	1.23 (0.70, 2.15)	0.4633	
Female	69/ 105 (65.7)	2.9 (2.3, 5.7)	20/ 35 (57.1)	4.4 (1.7, 19.7)	1.17 (0.71, 1.93)	0.5211	
Region							0.2762
Europe	67/ 104 (64.4)	4.2 (2.5, 8.3)	20/ 38 (52.6)	7.2 (2.0, 9.9)	1.01 (0.61, 1.67)	0.9491	
USA/Canada	6/ 8 (75.0)	1.9 (1.4, NE)	2/ 6 (33.3)	NE (1.6, NE)	2.64 (0.53, 13.19)	0.2119	
Rest of World	67/ 107 (62.6)	4.8 (2.8, 7.1)	13/ 22 (59.1)	4.7 (2.8, 19.7)	1.14 (0.63, 2.06)	0.6773	
ECOG-PS at Randomization							0.1056
0	80/ 123 (65.0)	3.3 (2.1, 6.9)	22/ 43 (51.2)	7.4 (3.0, NE)	1.46 (0.91, 2.33)	0.1171	
1	60/ 96 (62.5)	4.8 (3.0, 9.2)	13/ 23 (56.5)	2.8 (1.4, 19.7)	0.78 (0.43, 1.43)	0.4335	
Number of Organs Involved							0.1642
<= 2	76/ 110 (69.1)	3.3 (2.0, 5.7)	16/ 33 (48.5)	9.0 (1.7, 19.7)	1.51 (0.88, 2.59)	0.1305	
>= 3	64/ 109 (58.7)	4.9 (3.0, 9.7)	19/ 33 (57.6)	3.0 (2.4, 7.4)	0.85 (0.51, 1.43)	0.5456	
Presence of Liver Metastases							0.6828
Yes	84/ 135 (62.2)	4.2 (2.8, 6.9)	22/ 40 (55.0)	4.4 (2.4, 9.9)	1.10 (0.69, 1.76)	0.6800	
No	56/ 84 (66.7)	4.8 (2.7, 7.1)	13/ 26 (50.0)	9.0 (2.6, 19.7)	1.30 (0.71, 2.38)	0.3937	
Side of Tumor							0.7535
Left	51/ 83 (61.4)	4.9 (2.8, 7.1)	18/ 33 (54.5)	5.5 (2.8, 19.7)	1.12 (0.66, 1.92)	0.6750	
Right	89/ 136 (65.4)	3.8 (2.7, 6.1)	17/ 33 (51.5)	4.7 (2.0, NE)	1.25 (0.74, 2.10)	0.3900	

[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.
[4] P-Value for interaction from Cox proportional hazards model using ties=exact option with treatment, subgroup and treatment*subgroup interaction as covariates.
Including only patients from the full analysis set who completed a baseline (last PRO assessment prior to or on the first dose of study treatment) and at least 1 post-baseline PRO assessment.
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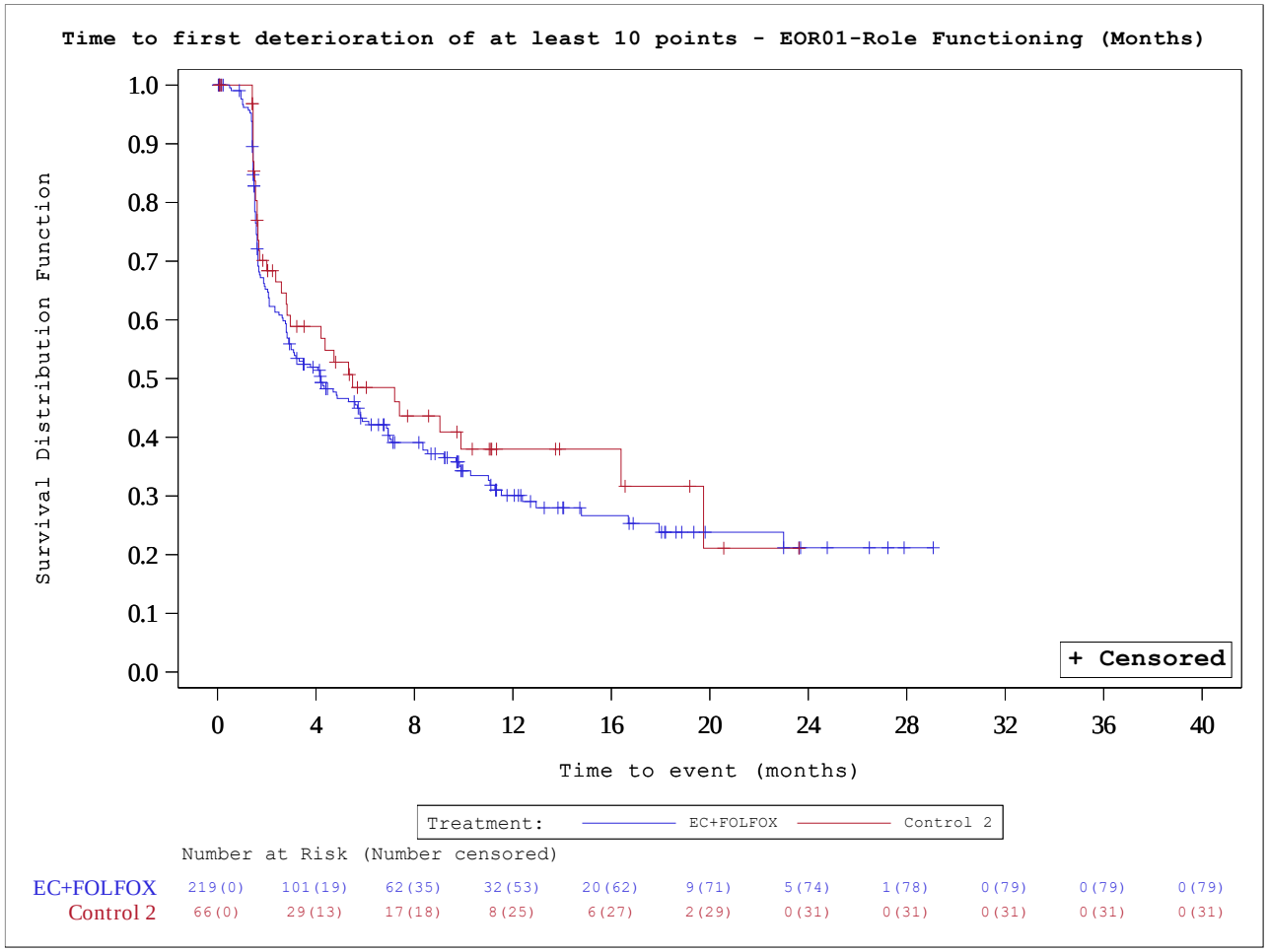
Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Kaplan Meier Plot of Time to first deterioration of at least 10 points - EOR01-Role Functioning (Months)
Full Analysis Set



Kaplan-Meier Plots for subgroups only created if p-value for interaction < 0.05.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
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Time to first improvement of at least 10 points - EOR01-Role Functioning (Months)
Full Analysis Set

	EC+FOLFOX (N=219)	Control 2 (N=66)
Number of subjects with events, n (%)	85 (38.8)	10 (15.2)
Number of censored subjects, n (%)	134 (61.2)	56 (84.8)
Kaplan-Meier estimates of Time to Event (Months) [1]		
25%-ile (95% CI)	2.8 (1.9, 4.2)	NE (4.3, NE)
Median (95% CI)	24.6 (13.4, NE)	NE (NE, NE)
75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
Stratified analysis [2]		
Hazard Ratio (95% CI) [3]	2.55 (1.32, 4.91)	
p-value [4]	0.0039	

[1] Based on the Brookmeyer and Crowley method.
[2] Stratified by ECOG PS by Randomization.
[3] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio > 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[4] P-value from 2-sided log-rank test.
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Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Time to first improvement of at least 10 points - EOR01-Role Functioning (Months) - Subgroup analysis
Full Analysis Set

Subgroup Level	EC+FOLFOX (N=219) n/ N (%)	EC+FOLFOX (N=219) Median (95% CI)[1]	Control 2 (N=66) n/ N (%)	Control 2 (N=66) Median (95% CI)[1]	Unstratified analysis Hazard Ratio (95% CI)[2]	Unstratified analysis p-Value[3]	Interaction p-Value[4]
Age (Years)							0.1334
< 65	58/ 139 (41.7)	14.0 (9.7, NE)	9/ 41 (22.0)	NE (NE , NE)	1.87 (0.93, 3.78)	0.0761	
>= 65	27/ 80 (33.8)	NE (24.6, NE)	1/ 25 (4.0)	NE (NE , NE)	9.49 (1.29, 69.91)	0.0068	
Sex							0.0805
Male	41/ 114 (36.0)	NE (NE , NE)	7/ 31 (22.6)	NE (NE , NE)	1.57 (0.70, 3.50)	0.2664	
Female	44/ 105 (41.9)	24.6 (9.7, NE)	3/ 35 (8.6)	NE (NE , NE)	5.21 (1.61, 16.81)	0.0020	
Region							0.5321
Europe	48/ 104 (46.2)	13.4 (4.7, NE)	5/ 38 (13.2)	NE (NE , NE)	3.71 (1.47, 9.34)	0.0028	
USA/Canada	4/ 8 (50.0)	9.7 (2.8, NE)	1/ 6 (16.7)	NE (2.9, NE)	3.42 (0.38, 30.74)	0.2467	
Rest of World	33/ 107 (30.8)	NE (14.0, NE)	4/ 22 (18.2)	NE (NE , NE)	1.72 (0.61, 4.85)	0.3012	
ECOG-PS at Randomization							0.4105
0	41/ 123 (33.3)	NE (24.6, NE)	7/ 43 (16.3)	NE (NE , NE)	2.04 (0.91, 4.56)	0.0758	
1	44/ 96 (45.8)	13.4 (4.5, NE)	3/ 23 (13.0)	NE (NE , NE)	3.69 (1.14, 11.89)	0.0192	
Number of Organs Involved							0.2661
<= 2	41/ 110 (37.3)	NE (14.0, NE)	3/ 33 (9.1)	NE (NE , NE)	4.29 (1.33, 13.89)	0.0079	
>= 3	44/ 109 (40.4)	13.7 (5.6, NE)	7/ 33 (21.2)	NE (7.0, NE)	1.92 (0.86, 4.26)	0.1050	
Presence of Liver Metastases							0.1856
Yes	50/ 135 (37.0)	NE (13.4, NE)	8/ 40 (20.0)	NE (NE , NE)	1.90 (0.90, 4.01)	0.0876	
No	35/ 84 (41.7)	24.6 (6.4, NE)	2/ 26 (7.7)	NE (NE , NE)	5.59 (1.34, 23.30)	0.0076	
Side of Tumor							0.9891
Left	34/ 83 (41.0)	24.6 (7.2, NE)	5/ 33 (15.2)	NE (NE , NE)	2.66 (1.04, 6.83)	0.0338	
Right	51/ 136 (37.5)	NE (12.7, NE)	5/ 33 (15.2)	NE (NE , NE)	2.66 (1.06, 6.66)	0.0298	

[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio > 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.
[4] P-Value for interaction from Cox proportional hazards model using ties=exact option with treatment, subgroup and treatment*subgroup interaction as covariates.
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Pierre Fabre Pharma GmbH: Final
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Population: arm B vs. arm E
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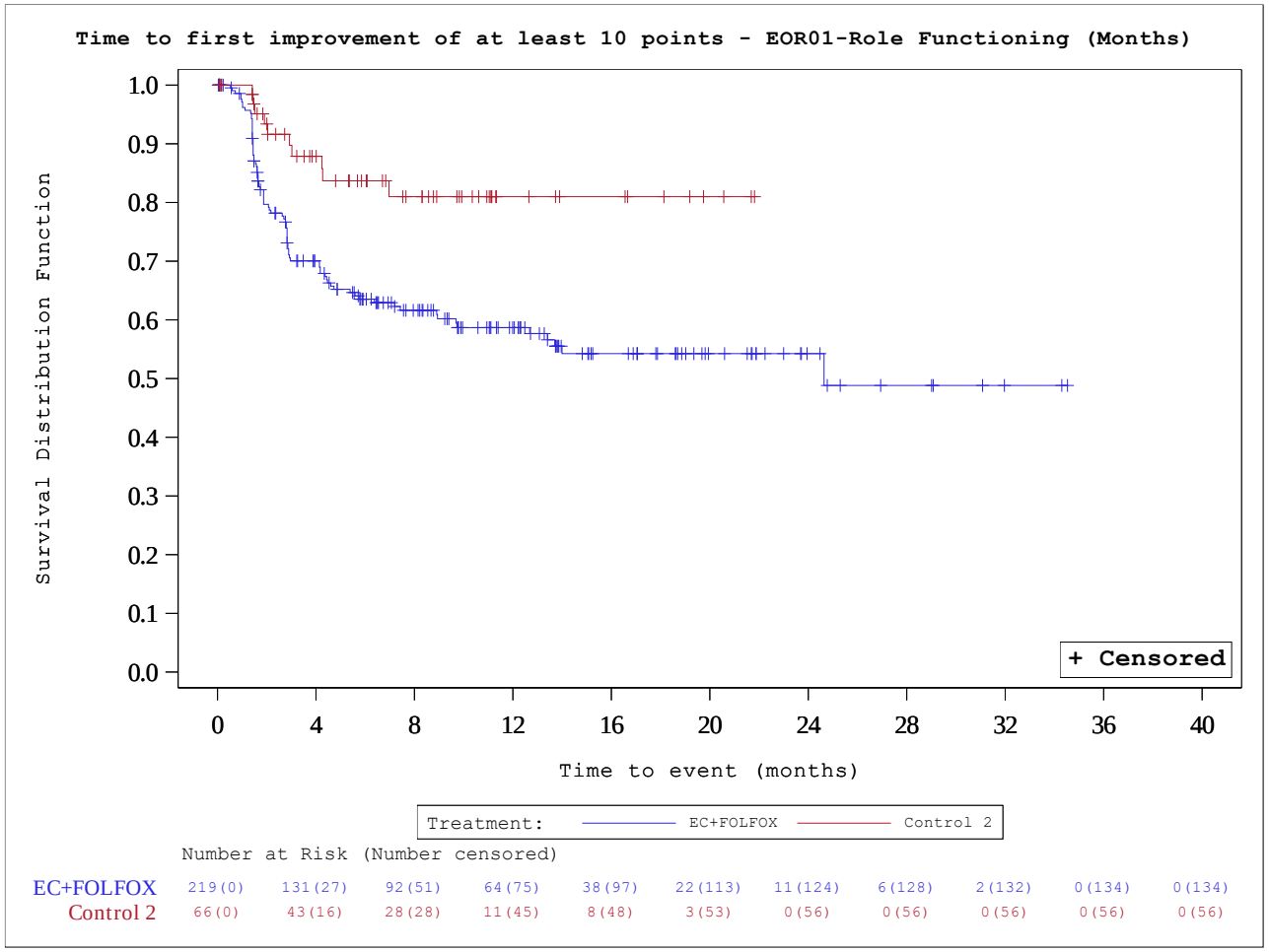
Kaplan Meier Plot of Time to first improvement of at least 10 points - EOR01-Role Functioning (Months)
Full Analysis Set



Kaplan-Meier Plots for subgroups only created if p-value for interaction < 0.05.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Time to first deterioration of at least 10 points - EOR01-Emotional Functioning (Months)
Full Analysis Set

	EC+FOLFOX (N=219)	Control 2 (N=66)
Number of subjects with events, n (%)	85 (38.8)	18 (27.3)
Number of censored subjects, n (%)	134 (61.2)	48 (72.7)
Kaplan-Meier estimates of Time to Event (Months) [1]		
25%-ile (95% CI)	5.4 (4.2, 7.1)	7.2 (4.2, NE)
Median (95% CI)	19.0 (13.9, NE)	NE (15.5, NE)
75%-ile (95% CI)	NE (25.7, NE)	NE (NE, NE)
Stratified analysis [2]		
Hazard Ratio (95% CI) [3]	1.14 (0.68, 1.91)	
p-value [4]	0.6150	

[1] Based on the Brookmeyer and Crowley method.
[2] Stratified by ECOG PS by Randomization.
[3] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[4] P-value from 2-sided log-rank test.
Including only patients from the full analysis set who completed a baseline (last PRO assessment prior to or on the first dose of study treatment) and at least 1 post-baseline PRO assessment.

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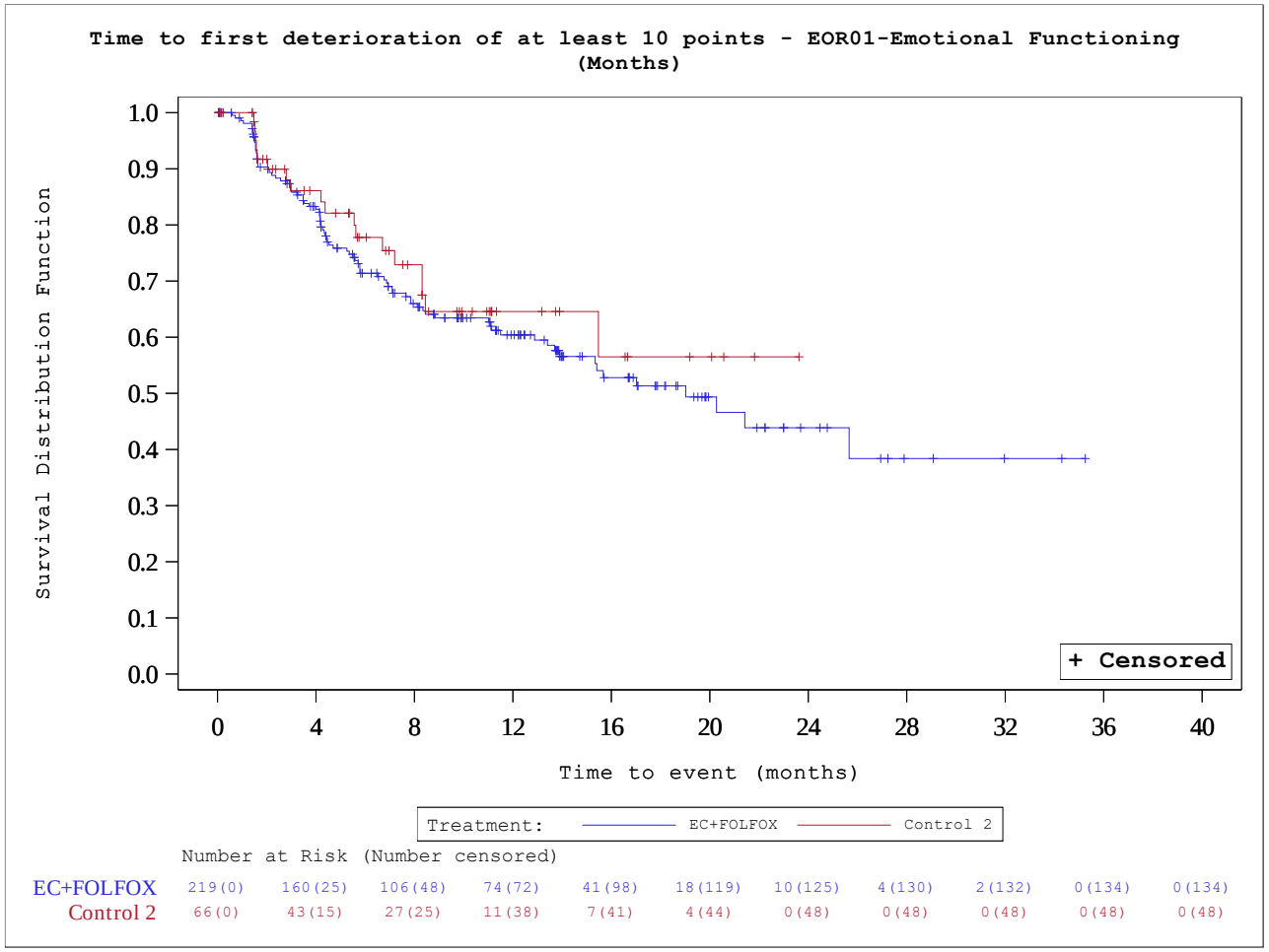
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Time to first deterioration of at least 10 points - EOR01-Emotional Functioning (Months) - Subgroup analysis
Full Analysis Set

Subgroup Level	EC+FOLFOX (N=219) n/ N (%)	EC+FOLFOX (N=219) Median (95% CI)[1]	Control 2 (N=66) n/ N (%)	Control 2 (N=66) Median (95% CI)[1]	Unstratified analysis Hazard Ratio (95% CI)[2]	Unstratified analysis p-Value[3]	Interaction p-Value[4]
Age (Years)							0.9115
< 65	61/ 139 (43.9)	15.4 (8.8, NE)	13/ 41 (31.7)	15.5 (8.3, NE)	1.25 (0.68, 2.27)	0.4718	
>= 65	24/ 80 (30.0)	25.7 (15.7, NE)	5/ 25 (20.0)	NE (NE , NE)	1.12 (0.42, 2.98)	0.8176	
Sex							0.5345
Male	41/ 114 (36.0)	NE (12.9, NE)	9/ 31 (29.0)	15.5 (8.3, NE)	1.03 (0.50, 2.13)	0.9252	
Female	44/ 105 (41.9)	19.0 (11.1, 25.7)	9/ 35 (25.7)	NE (8.4, NE)	1.38 (0.67, 2.84)	0.3759	
Region							0.9227
Europe	42/ 104 (40.4)	21.4 (12.9, NE)	10/ 38 (26.3)	15.5 (8.4, NE)	1.19 (0.59, 2.38)	0.6224	
USA/Canada	2/ 8 (25.0)	NE (4.2, NE)	1/ 6 (16.7)	NE (3.0, NE)	1.35 (0.12, 14.95)	0.8055	
Rest of World	41/ 107 (38.3)	15.4 (11.1, NE)	7/ 22 (31.8)	NE (5.6, NE)	1.01 (0.45, 2.27)	0.9724	
ECOG-PS at Randomization							0.1880
0	47/ 123 (38.2)	21.4 (13.9, NE)	10/ 43 (23.3)	NE (15.5, NE)	1.51 (0.76, 3.00)	0.2333	
1	38/ 96 (39.6)	17.0 (11.0, NE)	8/ 23 (34.8)	8.4 (5.6, NE)	0.72 (0.33, 1.58)	0.4147	
Number of Organs Involved							0.6222
<= 2	49/ 110 (44.5)	15.7 (12.9, NE)	10/ 33 (30.3)	NE (8.4, NE)	1.38 (0.70, 2.73)	0.3532	
>= 3	36/ 109 (33.0)	21.4 (11.5, NE)	8/ 33 (24.2)	NE (8.3, NE)	1.04 (0.48, 2.25)	0.9157	
Presence of Liver Metastases							0.5894
Yes	55/ 135 (40.7)	19.0 (11.1, 25.7)	10/ 40 (25.0)	NE (8.3, NE)	1.33 (0.68, 2.62)	0.4043	
No	30/ 84 (35.7)	21.4 (15.4, NE)	8/ 26 (30.8)	NE (8.4, NE)	1.05 (0.48, 2.31)	0.8963	
Side of Tumor							0.1354
Left	31/ 83 (37.3)	20.3 (11.1, NE)	11/ 33 (33.3)	15.5 (8.3, NE)	0.81 (0.40, 1.63)	0.5578	
Right	54/ 136 (39.7)	19.0 (13.4, NE)	7/ 33 (21.2)	NE (NE , NE)	1.76 (0.80, 3.87)	0.1557	

[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.
[4] P-Value for interaction from Cox proportional hazards model using ties=exact option with treatment, subgroup and treatment*subgroup interaction as covariates.
Including only patients from the full analysis set who completed a baseline (last PRO assessment prior to or on the first dose of study treatment) and at least 1 post-baseline PRO assessment.
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Kaplan Meier Plot of Time to first deterioration of at least 10 points - EOR01-Emotional Functioning (Months)
Full Analysis Set



Kaplan-Meier Plots for subgroups only created if p-value for interaction < 0.05.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
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Time to first improvement of at least 10 points - EOR01-Emotional Functioning (Months)
Full Analysis Set

	EC+FOLFOX (N=219)	Control 2 (N=66)
Number of subjects with events, n (%)	110 (50.2)	18 (27.3)
Number of censored subjects, n (%)	109 (49.8)	48 (72.7)
Kaplan-Meier estimates of Time to Event (Months) [1]		
25%-ile (95% CI)	1.7 (1.6, 2.3)	4.5 (2.8, NE)
Median (95% CI)	6.4 (4.2, 16.8)	NE (10.0, NE)
75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
Stratified analysis [2]		
Hazard Ratio (95% CI) [3]	2.00 (1.22, 3.30)	
p-value [4]	0.0055	

[1] Based on the Brookmeyer and Crowley method.
[2] Stratified by ECOG PS by Randomization.
[3] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio > 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[4] P-value from 2-sided log-rank test.
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Time to first improvement of at least 10 points - EOR01-Emotional Functioning (Months) - Subgroup analysis
Full Analysis Set

Subgroup Level	EC+FOLFOX (N=219) n/ N (%)	EC+FOLFOX (N=219) Median (95% CI)[1]	Control 2 (N=66) n/ N (%)	Control 2 (N=66) Median (95% CI)[1]	Unstratified analysis Hazard Ratio (95% CI)[2]	Unstratified analysis p-Value[3]	Interaction p-Value[4]
Age (Years)							0.5835
< 65	69/ 139 (49.6)	8.1 (4.1, NE)	12/ 41 (29.3)	NE (7.1, NE)	1.81 (0.98, 3.34)	0.0547	
>= 65	41/ 80 (51.3)	5.9 (4.2, NE)	6/ 25 (24.0)	NE (8.3, NE)	2.43 (1.03, 5.72)	0.0371	
Sex							0.6147
Male	55/ 114 (48.2)	7.0 (4.2, NE)	8/ 31 (25.8)	NE (10.0, NE)	1.74 (0.83, 3.66)	0.1372	
Female	55/ 105 (52.4)	5.6 (2.5, NE)	10/ 35 (28.6)	NE (8.3, NE)	2.26 (1.15, 4.44)	0.0149	
Region							0.2283
Europe	63/ 104 (60.6)	4.2 (2.3, 6.0)	9/ 38 (23.7)	NE (8.3, NE)	2.84 (1.41, 5.72)	0.0022	
USA/Canada	3/ 8 (37.5)	NE (2.8, NE)	1/ 6 (16.7)	NE (7.1, NE)	2.80 (0.29, 27.30)	0.3552	
Rest of World	44/ 107 (41.1)	NE (7.0, NE)	8/ 22 (36.4)	NE (4.2, NE)	1.19 (0.56, 2.52)	0.6582	
ECOG-PS at Randomization							0.2723
0	60/ 123 (48.8)	6.4 (4.2, NE)	14/ 43 (32.6)	NE (10.0, NE)	1.66 (0.93, 2.97)	0.0851	
1	50/ 96 (52.1)	5.9 (3.1, 14.1)	4/ 23 (17.4)	NE (8.3, NE)	3.14 (1.13, 8.70)	0.0203	
Number of Organs Involved							0.6137
<= 2	50/ 110 (45.5)	14.1 (5.6, NE)	9/ 33 (27.3)	NE (10.0, NE)	1.77 (0.87, 3.60)	0.1114	
>= 3	60/ 109 (55.0)	4.2 (2.8, 8.3)	9/ 33 (27.3)	NE (7.1, NE)	2.31 (1.14, 4.65)	0.0162	
Presence of Liver Metastases							0.3465
Yes	71/ 135 (52.6)	4.9 (3.4, 16.8)	10/ 40 (25.0)	NE (8.3, NE)	2.45 (1.26, 4.76)	0.0061	
No	39/ 84 (46.4)	11.1 (4.2, NE)	8/ 26 (30.8)	NE (2.8, NE)	1.48 (0.69, 3.17)	0.3121	
Side of Tumor							0.8456
Left	39/ 83 (47.0)	11.1 (3.9, NE)	8/ 33 (24.2)	NE (10.0, NE)	2.10 (0.98, 4.50)	0.0513	
Right	71/ 136 (52.2)	5.4 (4.2, 11.3)	10/ 33 (30.3)	NE (7.1, NE)	1.88 (0.97, 3.65)	0.0562	

[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio > 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.
[4] P-Value for interaction from Cox proportional hazards model using ties=exact option with treatment, subgroup and treatment*subgroup interaction as covariates.
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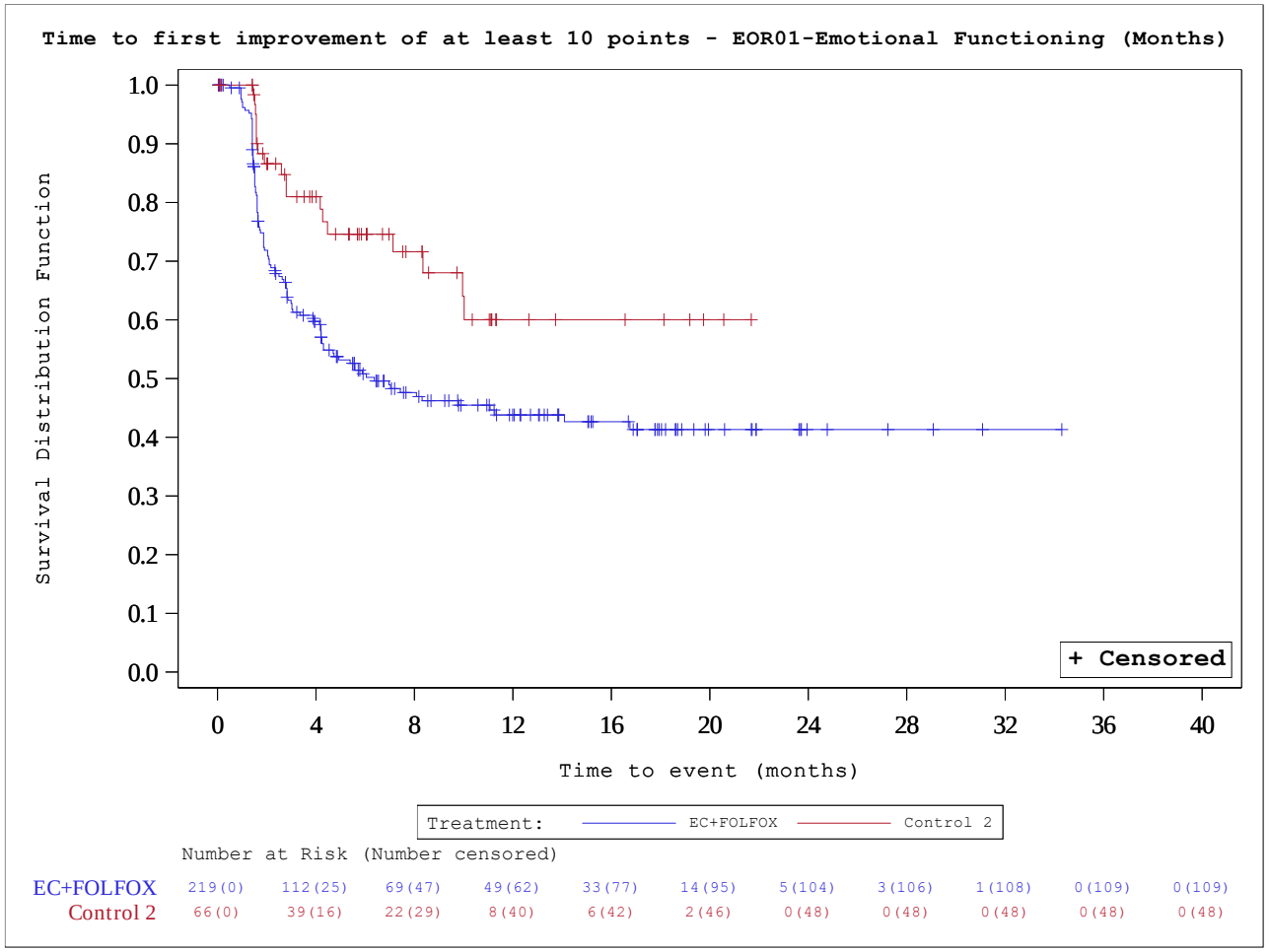

Kaplan-Meier Plots for subgroups only created if p-value for interaction < 0.05.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
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Time to first deterioration of at least 10 points - EOR01-Cognitive Functioning (Months)
Full Analysis Set

	EC+FOLFOX (N=219)	Control 2 (N=66)
Number of subjects with events, n (%)	132 (60.3)	25 (37.9)
Number of censored subjects, n (%)	87 (39.7)	41 (62.1)
Kaplan-Meier estimates of Time to Event (Months) [1]		
25%-ile (95% CI)	2.1 (1.6, 2.9)	4.4 (1.7, 7.1)
Median (95% CI)	5.7 (4.2, 7.0)	15.5 (7.1, NE)
75%-ile (95% CI)	24.2 (13.1, NE)	NE (NE, NE)
Stratified analysis [2]		
Hazard Ratio (95% CI) [3]	1.62 (1.05, 2.48)	
p-value [4]	0.0271	

[1] Based on the Brookmeyer and Crowley method.
[2] Stratified by ECOG PS by Randomization.
[3] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[4] P-value from 2-sided log-rank test.
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Time to first deterioration of at least 10 points - EOR01-Cognitive Functioning (Months) - Subgroup analysis
Full Analysis Set

Subgroup Level	EC+FOLFOX (N=219) n/ N (%)	EC+FOLFOX (N=219) Median (95% CI)[1]	Control 2 (N=66) n/ N (%)	Control 2 (N=66) Median (95% CI)[1]	Unstratified analysis Hazard Ratio (95% CI)[2]	Unstratified analysis p-Value[3]	Interaction p-Value[4]
Age (Years)							0.4498
< 65	86/ 139 (61.9)	5.8 (4.2, 7.5)	17/ 41 (41.5)	15.5 (4.7, NE)	1.48 (0.88, 2.49)	0.1364	
>= 65	46/ 80 (57.5)	5.3 (3.8, 8.0)	8/ 25 (32.0)	NE (5.8, NE)	2.14 (1.01, 4.54)	0.0418	
Sex							0.3269
Male	66/ 114 (57.9)	5.8 (4.3, 8.8)	13/ 31 (41.9)	8.3 (5.6, NE)	1.35 (0.74, 2.45)	0.3257	
Female	66/ 105 (62.9)	5.6 (3.5, 7.5)	12/ 35 (34.3)	NE (5.7, NE)	2.09 (1.13, 3.86)	0.0160	
Region							0.8433
Europe	59/ 104 (56.7)	7.0 (4.2, 11.0)	12/ 38 (31.6)	15.5 (7.2, NE)	1.76 (0.94, 3.27)	0.0719	
USA/Canada	5/ 8 (62.5)	7.1 (1.6, NE)	2/ 6 (33.3)	NE (2.9, NE)	2.01 (0.39, 10.41)	0.3968	
Rest of World	68/ 107 (63.6)	5.3 (3.0, 6.2)	11/ 22 (50.0)	5.7 (2.8, NE)	1.39 (0.74, 2.63)	0.3067	
ECOG-PS at Randomization							0.6884
0	68/ 123 (55.3)	6.8 (4.3, 10.6)	17/ 43 (39.5)	15.5 (5.8, NE)	1.51 (0.89, 2.57)	0.1255	
1	64/ 96 (66.7)	4.8 (3.5, 6.2)	8/ 23 (34.8)	8.3 (5.6, NE)	1.82 (0.87, 3.80)	0.1045	
Number of Organs Involved							0.0251
<= 2	70/ 110 (63.6)	4.7 (3.1, 7.0)	10/ 33 (30.3)	NE (8.3, NE)	2.69 (1.38, 5.22)	0.0023	
>= 3	62/ 109 (56.9)	5.8 (4.3, 8.3)	15/ 33 (45.5)	5.7 (4.4, NE)	0.98 (0.56, 1.73)	0.9485	
Presence of Liver Metastases							0.0281
Yes	78/ 135 (57.8)	5.8 (4.0, 8.3)	19/ 40 (47.5)	7.1 (4.4, NE)	1.14 (0.69, 1.89)	0.6023	
No	54/ 84 (64.3)	5.7 (4.2, 7.1)	6/ 26 (23.1)	NE (15.5, NE)	3.41 (1.46, 7.94)	0.0025	
Side of Tumor							0.5705
Left	48/ 83 (57.8)	7.5 (5.3, 10.6)	13/ 33 (39.4)	15.5 (5.7, NE)	1.43 (0.77, 2.64)	0.2514	
Right	84/ 136 (61.8)	4.4 (3.5, 6.1)	12/ 33 (36.4)	8.3 (5.6, NE)	1.86 (1.02, 3.41)	0.0401	

[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.
[4] P-Value for interaction from Cox proportional hazards model using ties=exact option with treatment, subgroup and treatment*subgroup interaction as covariates.
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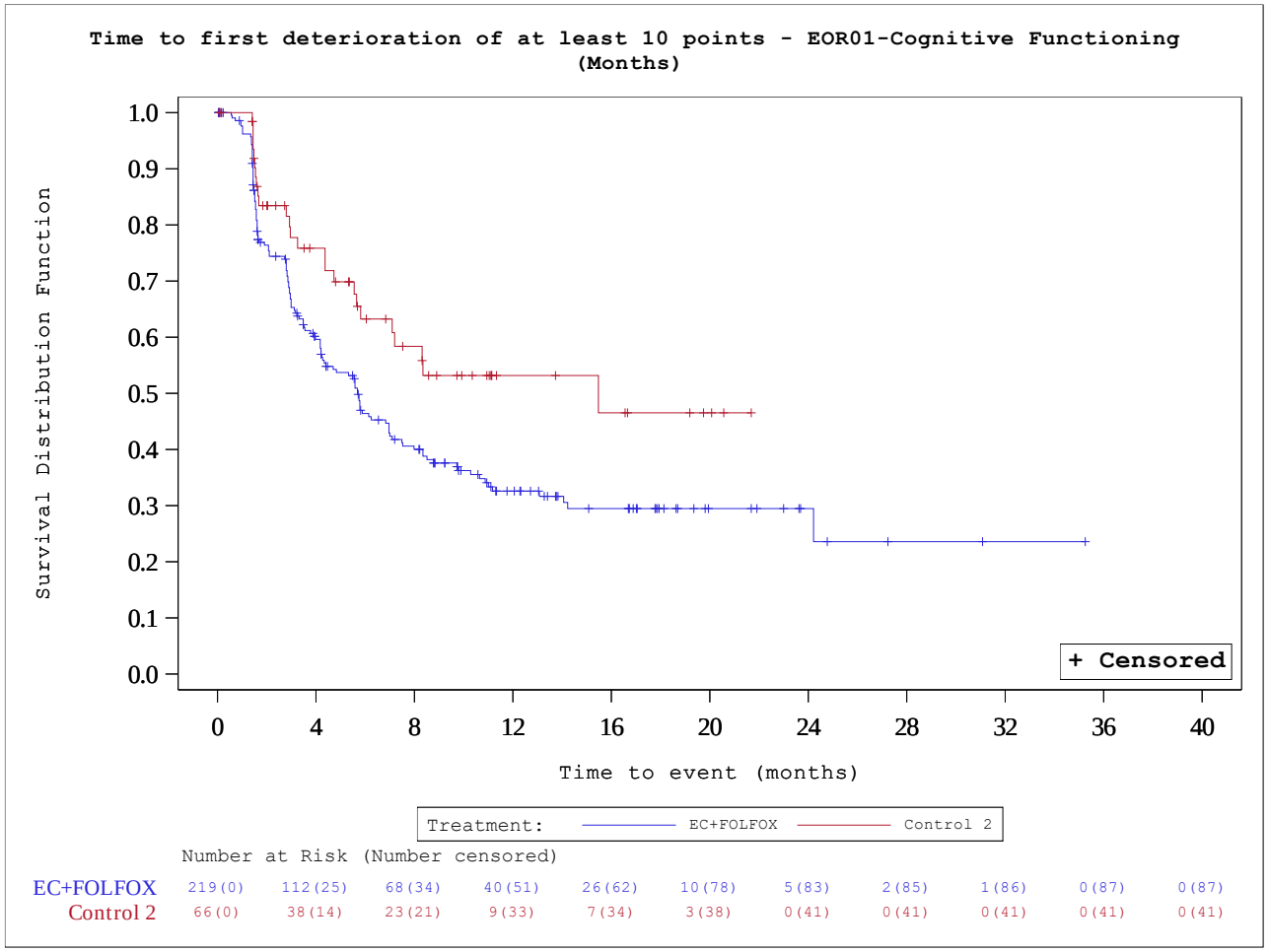

Kaplan-Meier Plots for subgroups only created if p-value for interaction < 0.05.

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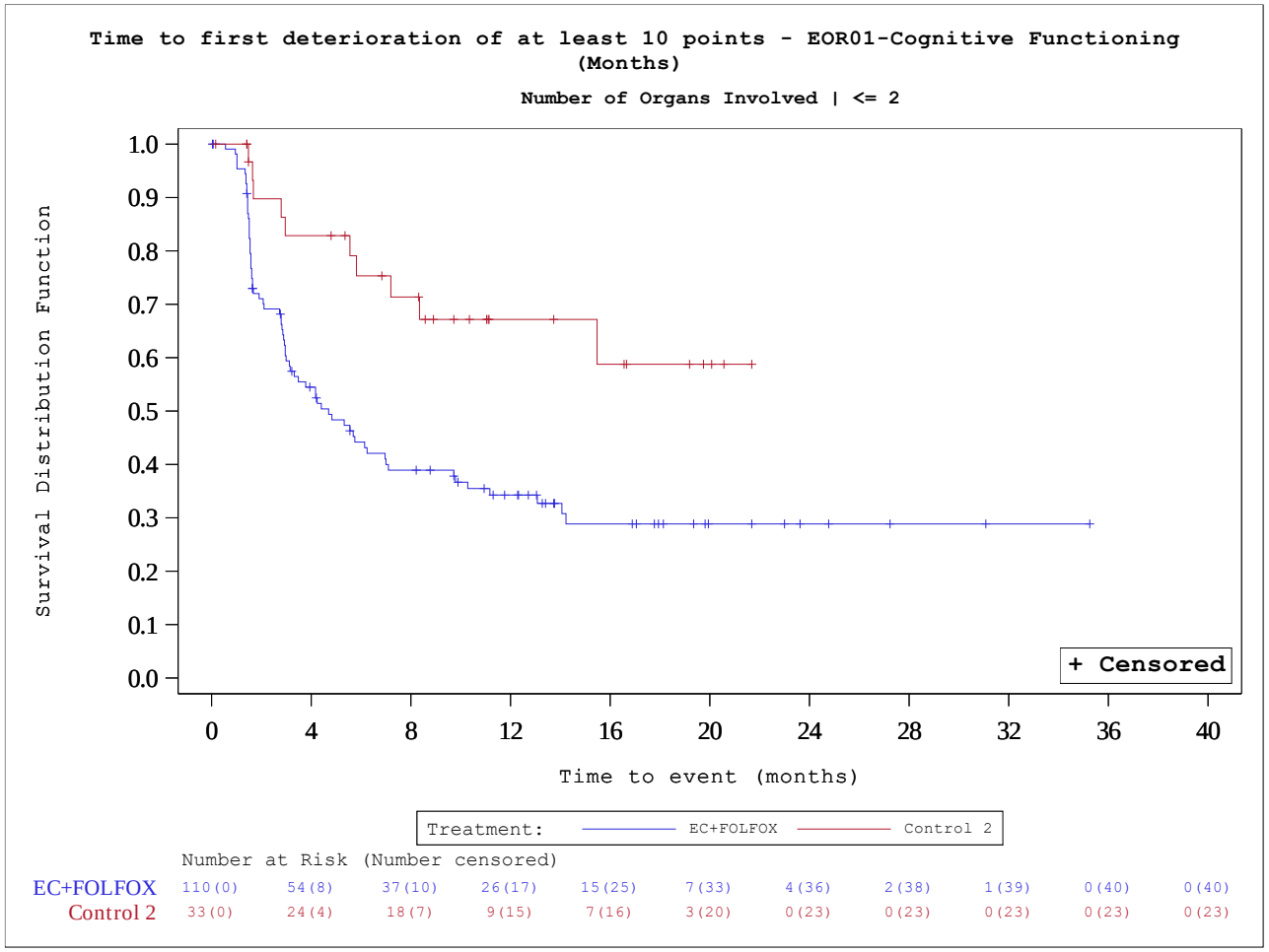

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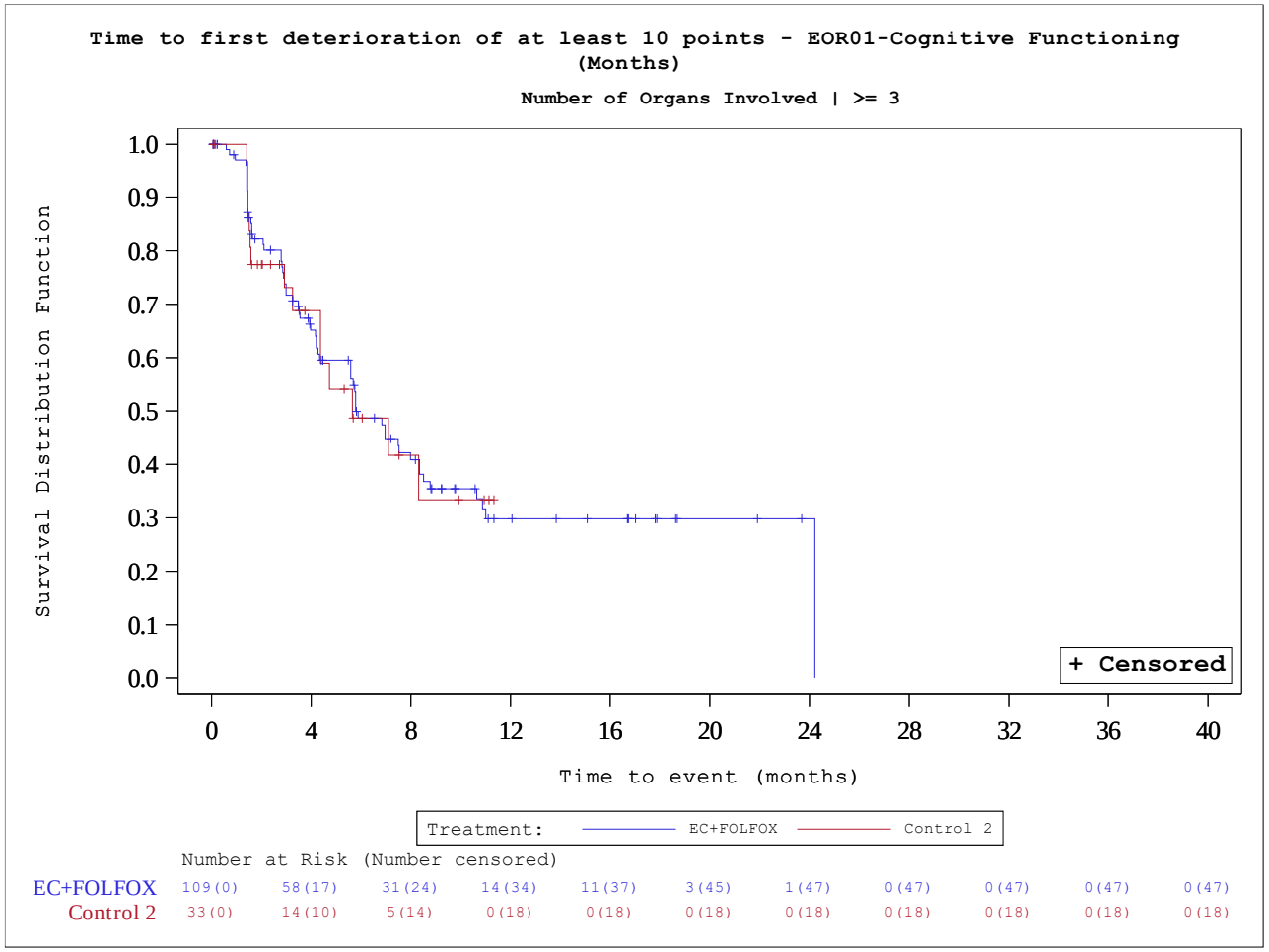

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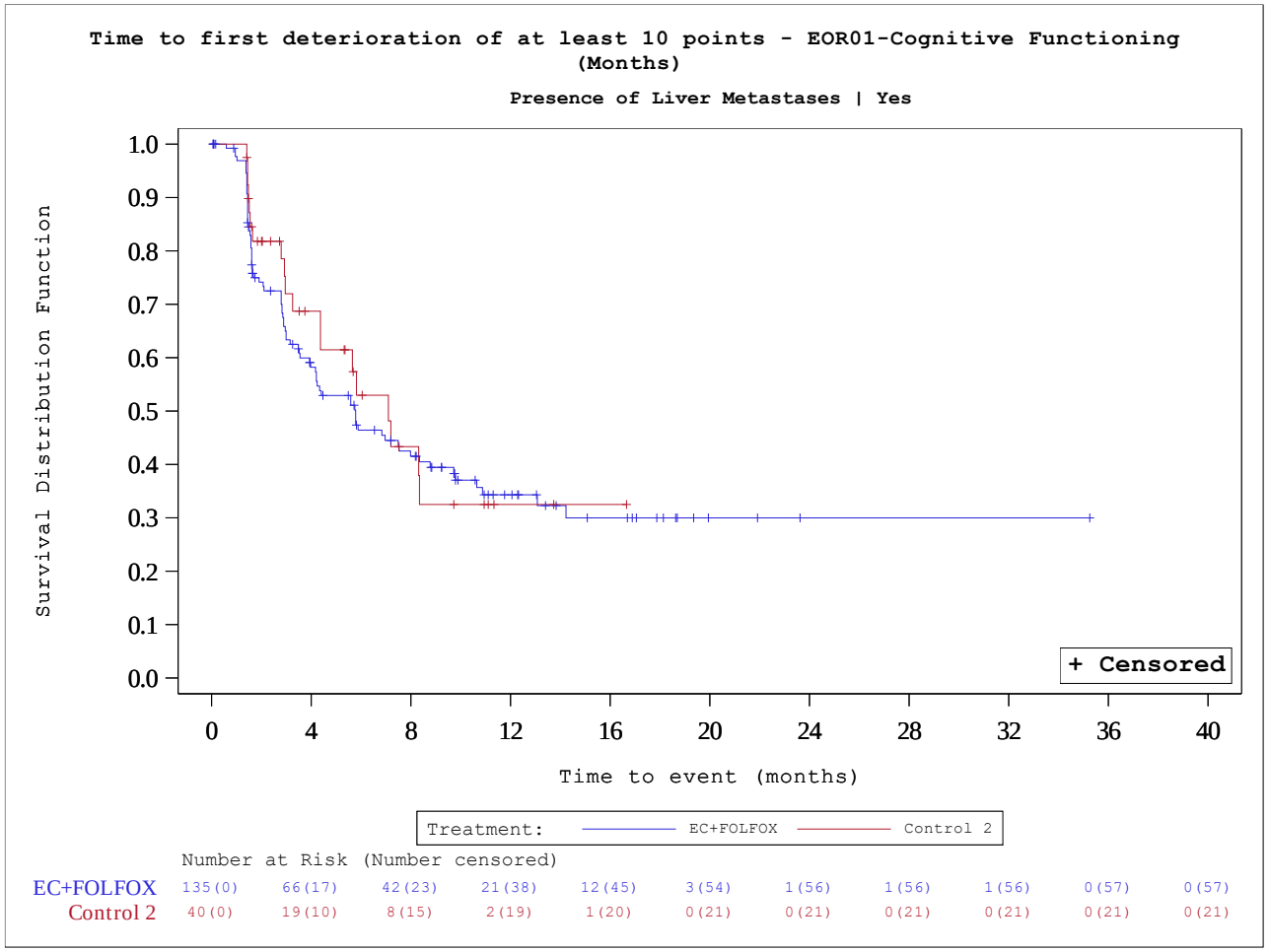

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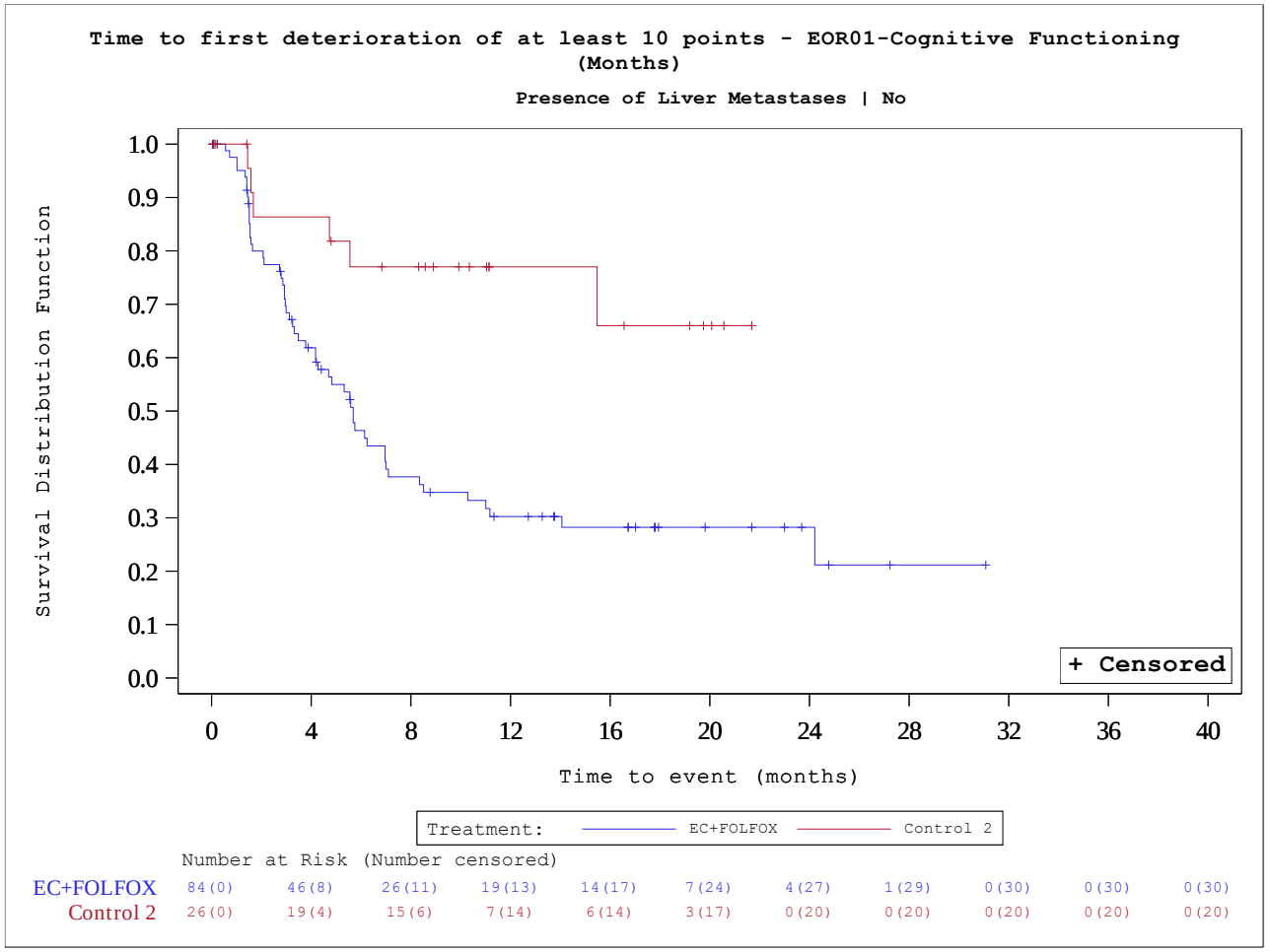

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Time to first improvement of at least 10 points - EOR01-Cognitive Functioning (Months)
Full Analysis Set

	EC+FOLFOX (N=219)	Control 2 (N=66)
Number of subjects with events, n (%)	66 (30.1)	14 (21.2)
Number of censored subjects, n (%)	153 (69.9)	52 (78.8)
Kaplan-Meier estimates of Time to Event (Months) [1]		
25%-ile (95% CI)	4.3 (3.0, 11.3)	7.5 (2.8, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
Stratified analysis [2]		
Hazard Ratio (95% CI) [3]	1.25 (0.70, 2.23)	
p-value [4]	0.4473	

[1] Based on the Brookmeyer and Crowley method.
[2] Stratified by ECOG PS by Randomization.
[3] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio > 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[4] P-value from 2-sided log-rank test.
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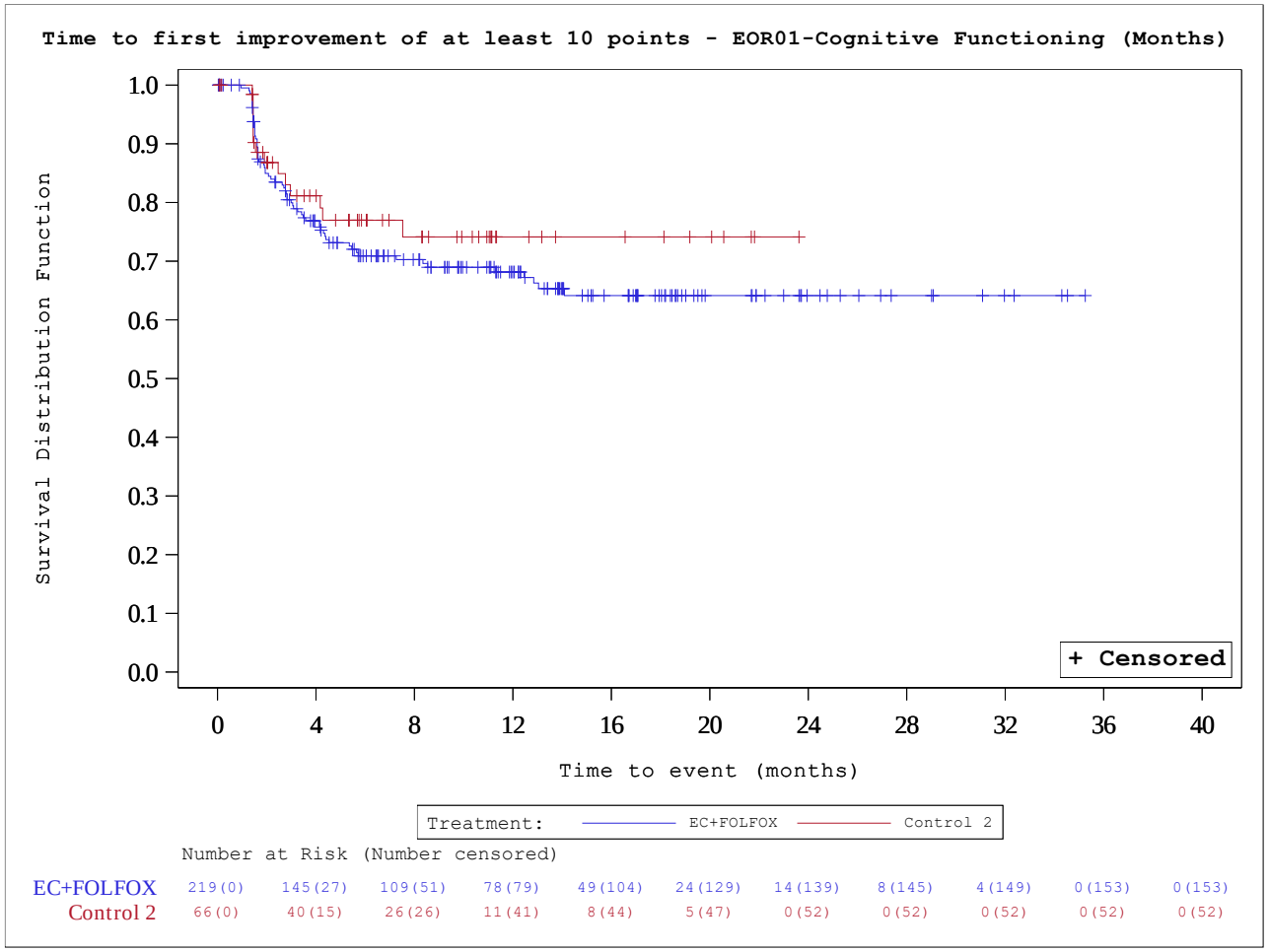
Time to first improvement of at least 10 points - EOR01-Cognitive Functioning (Months) - Subgroup analysis
Full Analysis Set

Subgroup Level	EC+FOLFOX (N=219) n/ N (%)	EC+FOLFOX (N=219) Median (95% CI)[1]	Control 2 (N=66) n/ N (%)	Control 2 (N=66) Median (95% CI)[1]	Unstratified analysis Hazard Ratio (95% CI)[2]	Unstratified analysis p-Value[3]	Interaction p-Value[4]
Age (Years)							0.1915
< 65	40/ 139 (28.8)	NE (NE , NE)	6/ 41 (14.6)	NE (NE , NE)	1.83 (0.78, 4.32)	0.1626	
>= 65	26/ 80 (32.5)	NE (14.1, NE)	8/ 25 (32.0)	NE (7.5, NE)	0.87 (0.39, 1.92)	0.7483	
Sex							0.9201
Male	32/ 114 (28.1)	NE (NE , NE)	6/ 31 (19.4)	NE (NE , NE)	1.25 (0.52, 2.99)	0.6110	
Female	34/ 105 (32.4)	NE (NE , NE)	8/ 35 (22.9)	NE (NE , NE)	1.31 (0.61, 2.84)	0.4863	
Region							0.6438
Europe	34/ 104 (32.7)	NE (NE , NE)	7/ 38 (18.4)	NE (NE , NE)	1.45 (0.64, 3.28)	0.3613	
USA/Canada	3/ 8 (37.5)	NE (2.8, NE)	1/ 6 (16.7)	NE (NE , NE)	2.19 (0.23, 21.06)	0.4877	
Rest of World	29/ 107 (27.1)	NE (NE , NE)	6/ 22 (27.3)	NE (4.3, NE)	0.91 (0.38, 2.20)	0.8336	
ECOG-PS at Randomization							0.4295
0	36/ 123 (29.3)	NE (NE , NE)	8/ 43 (18.6)	NE (NE , NE)	1.52 (0.71, 3.27)	0.2757	
1	30/ 96 (31.3)	NE (14.1, NE)	6/ 23 (26.1)	NE (4.3, NE)	0.92 (0.38, 2.23)	0.8503	
Number of Organs Involved							0.2121
<= 2	33/ 110 (30.0)	NE (NE , NE)	9/ 33 (27.3)	NE (NE , NE)	0.91 (0.43, 1.90)	0.8107	
>= 3	33/ 109 (30.3)	NE (NE , NE)	5/ 33 (15.2)	NE (NE , NE)	1.95 (0.76, 5.00)	0.1577	
Presence of Liver Metastases							0.5172
Yes	38/ 135 (28.1)	NE (NE , NE)	9/ 40 (22.5)	NE (NE , NE)	1.10 (0.53, 2.28)	0.7802	
No	28/ 84 (33.3)	NE (14.1, NE)	5/ 26 (19.2)	NE (NE , NE)	1.65 (0.64, 4.28)	0.2988	
Side of Tumor							0.9213
Left	25/ 83 (30.1)	NE (NE , NE)	7/ 33 (21.2)	NE (NE , NE)	1.35 (0.58, 3.14)	0.4823	
Right	41/ 136 (30.1)	NE (NE , NE)	7/ 33 (21.2)	NE (NE , NE)	1.24 (0.55, 2.75)	0.5952	

[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio > 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.
[4] P-Value for interaction from Cox proportional hazards model using ties=exact option with treatment, subgroup and treatment*subgroup interaction as covariates.
Including only patients from the full analysis set who completed a baseline (last PRO assessment prior to or on the first dose of study treatment) and at least 1 post-baseline PRO assessment.
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Kaplan Meier Plot of Time to first improvement of at least 10 points - EOR01-Cognitive Functioning (Months)
Full Analysis Set



Kaplan-Meier Plots for subgroups only created if p-value for interaction < 0.05.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Time to first deterioration of at least 10 points - EOR01-Social Functioning (Months)
Full Analysis Set

	EC+FOLFOX (N=219)	Control 2 (N=66)
Number of subjects with events, n (%)	123 (56.2)	32 (48.5)
Number of censored subjects, n (%)	96 (43.8)	34 (51.5)
Kaplan-Meier estimates of Time to Event (Months) [1]		
25%-ile (95% CI)	1.7 (1.6, 2.3)	2.8 (1.5, 4.5)
Median (95% CI)	5.5 (4.1, 7.0)	8.7 (4.5, 11.3)
75%-ile (95% CI)	NE (NE, NE)	NE (10.4, NE)
Stratified analysis [2]		
Hazard Ratio (95% CI) [3]	1.12 (0.75, 1.66)	
p-value [4]	0.5728	

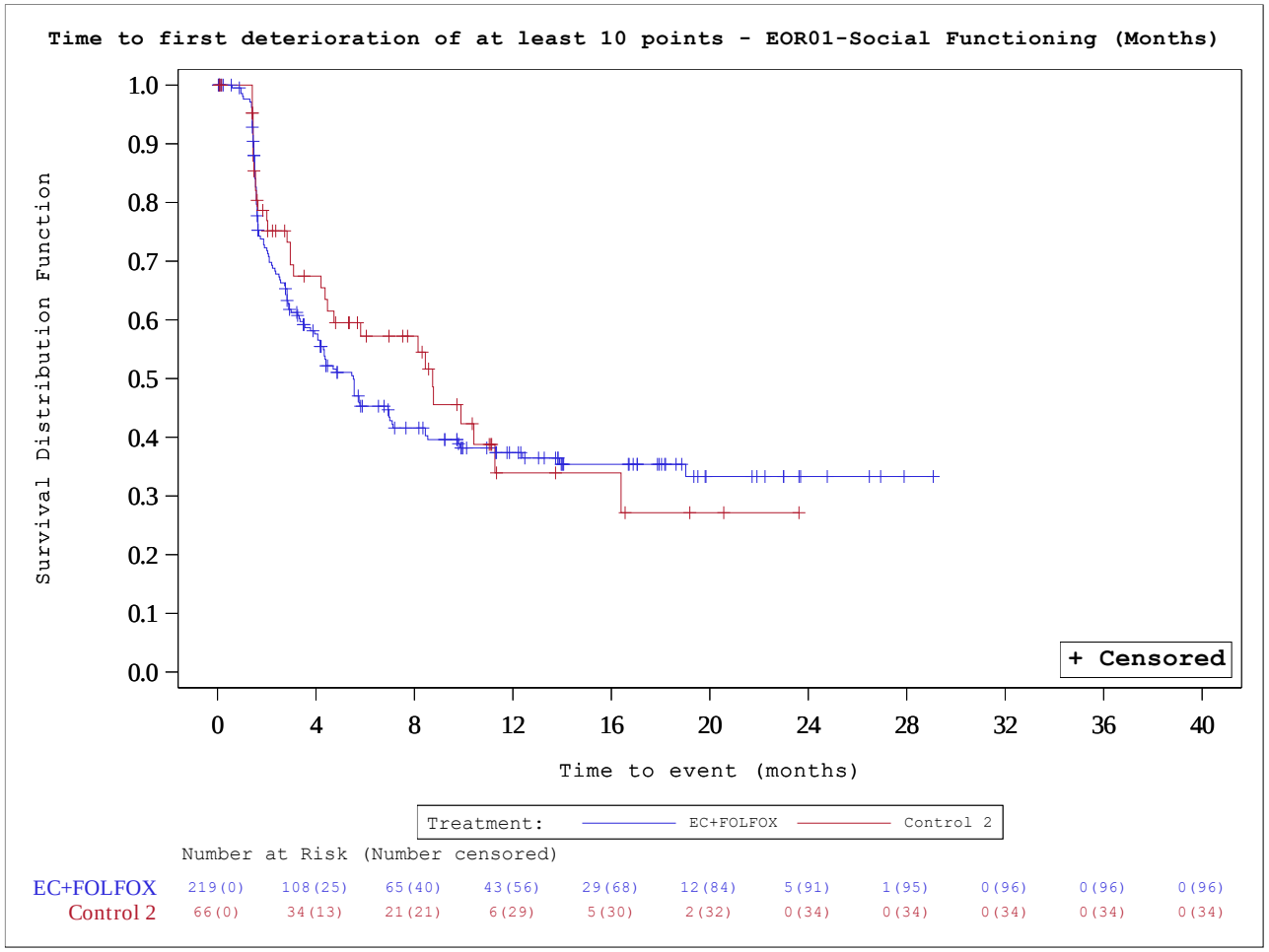
[1] Based on the Brookmeyer and Crowley method.
[2] Stratified by ECOG PS by Randomization.
[3] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[4] P-value from 2-sided log-rank test.
Including only patients from the full analysis set who completed a baseline (last PRO assessment prior to or on the first dose of study treatment) and at least 1 post-baseline PRO assessment.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Time to first deterioration of at least 10 points - EOR01-Social Functioning (Months) - Subgroup analysis
Full Analysis Set

Subgroup Level	EC+FOLFOX (N=219) n/ N (%)	EC+FOLFOX (N=219) Median (95% CI)[1]	Control 2 (N=66) n/ N (%)	Control 2 (N=66) Median (95% CI)[1]	Unstratified analysis Hazard Ratio (95% CI)[2]	Unstratified analysis p-Value[3]	Interaction p-Value[4]
Age (Years)							0.5669
< 65	80/ 139 (57.6)	5.5 (3.0, 7.1)	19/ 41 (46.3)	9.9 (4.4, NE)	1.25 (0.76, 2.06)	0.3859	
>= 65	43/ 80 (53.8)	5.6 (4.1, 13.9)	13/ 25 (52.0)	8.1 (2.8, NE)	0.97 (0.52, 1.81)	0.9163	
Sex							0.5824
Male	63/ 114 (55.3)	5.6 (3.9, 7.1)	13/ 31 (41.9)	8.7 (4.5, 16.4)	1.32 (0.72, 2.39)	0.3663	
Female	60/ 105 (57.1)	5.5 (3.4, 11.3)	19/ 35 (54.3)	8.4 (3.1, NE)	1.02 (0.61, 1.72)	0.9241	
Region							0.5948
Europe	60/ 104 (57.7)	5.6 (3.5, 8.5)	17/ 38 (44.7)	8.7 (3.1, NE)	1.16 (0.68, 1.99)	0.5764	
USA/Canada	3/ 8 (37.5)	NE (1.6, NE)	1/ 6 (16.7)	NE (3.0, NE)	2.32 (0.24, 22.40)	0.4522	
Rest of World	60/ 107 (56.1)	4.4 (3.0, 7.1)	14/ 22 (63.6)	4.7 (2.0, 9.9)	0.90 (0.50, 1.62)	0.7177	
ECOG-PS at Randomization							0.1743
0	70/ 123 (56.9)	5.6 (3.4, 8.5)	20/ 43 (46.5)	10.4 (5.8, NE)	1.35 (0.82, 2.22)	0.2394	
1	53/ 96 (55.2)	4.4 (3.5, 9.9)	12/ 23 (52.2)	4.4 (1.5, 9.9)	0.79 (0.42, 1.48)	0.4656	
Number of Organs Involved							0.6745
<= 2	67/ 110 (60.9)	4.3 (2.8, 7.0)	17/ 33 (51.5)	9.9 (3.0, NE)	1.22 (0.71, 2.07)	0.4722	
>= 3	56/ 109 (51.4)	6.9 (4.3, 11.3)	15/ 33 (45.5)	8.1 (4.4, NE)	1.03 (0.58, 1.82)	0.9288	
Presence of Liver Metastases							0.7486
Yes	76/ 135 (56.3)	5.5 (3.5, 8.4)	18/ 40 (45.0)	8.7 (3.1, NE)	1.21 (0.72, 2.03)	0.4627	
No	47/ 84 (56.0)	5.8 (3.3, 9.8)	14/ 26 (53.8)	8.8 (4.2, NE)	1.08 (0.59, 1.96)	0.8025	
Side of Tumor							0.3041
Left	50/ 83 (60.2)	4.3 (2.8, 7.0)	16/ 33 (48.5)	8.8 (5.8, 11.3)	1.46 (0.83, 2.58)	0.1845	
Right	73/ 136 (53.7)	5.8 (4.1, 11.3)	16/ 33 (48.5)	8.1 (2.8, NE)	0.96 (0.56, 1.64)	0.8824	

[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.
[4] P-Value for interaction from Cox proportional hazards model using ties=exact option with treatment, subgroup and treatment*subgroup interaction as covariates.
Including only patients from the full analysis set who completed a baseline (last PRO assessment prior to or on the first dose of study treatment) and at least 1 post-baseline PRO assessment.
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Kaplan Meier Plot of Time to first deterioration of at least 10 points - EOR01-Social Functioning (Months)
Full Analysis Set



Kaplan-Meier Plots for subgroups only created if p-value for interaction < 0.05.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Time to first improvement of at least 10 points - EOR01-Social Functioning (Months)
Full Analysis Set

	EC+FOLFOX (N=219)	Control 2 (N=66)
Number of subjects with events, n (%)	89 (40.6)	14 (21.2)
Number of censored subjects, n (%)	130 (59.4)	52 (78.8)
Kaplan-Meier estimates of Time to Event (Months) [1]		
25%-ile (95% CI)	2.9 (2.6, 4.1)	10.1 (4.2, NE)
Median (95% CI)	NE (8.4, NE)	NE (NE, NE)
75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
Stratified analysis [2]		
Hazard Ratio (95% CI) [3]	1.93 (1.10, 3.40)	
p-value [4]	0.0204	

[1] Based on the Brookmeyer and Crowley method.
[2] Stratified by ECOG PS by Randomization.
[3] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio > 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[4] P-value from 2-sided log-rank test.
Including only patients from the full analysis set who completed a baseline (last PRO assessment prior to or on the first dose of study treatment) and at least 1 post-baseline PRO assessment.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Time to first improvement of at least 10 points - EOR01-Social Functioning (Months) - Subgroup analysis
Full Analysis Set

Subgroup Level	EC+FOLFOX (N=219) n/ N (%)	EC+FOLFOX (N=219) Median (95% CI)[1]	Control 2 (N=66) n/ N (%)	Control 2 (N=66) Median (95% CI)[1]	Unstratified analysis Hazard Ratio (95% CI)[2]	Unstratified analysis p-Value[3]	Interaction p-Value[4]
Age (Years)							0.1568
< 65	58/ 139 (41.7)	NE (8.4, NE)	11/ 41 (26.8)	NE (10.1, NE)	1.47 (0.77, 2.79)	0.2438	
>= 65	31/ 80 (38.8)	NE (4.2, NE)	3/ 25 (12.0)	NE (NE , NE)	3.93 (1.20, 12.86)	0.0145	
Sex							0.3077
Male	45/ 114 (39.5)	NE (7.5, NE)	8/ 31 (25.8)	NE (10.1, NE)	1.47 (0.69, 3.12)	0.3160	
Female	44/ 105 (41.9)	NE (7.4, NE)	6/ 35 (17.1)	NE (NE , NE)	2.63 (1.12, 6.17)	0.0211	
Region							0.5758
Europe	49/ 104 (47.1)	9.0 (5.0, NE)	8/ 38 (21.1)	NE (10.9, NE)	2.25 (1.07, 4.76)	0.0287	
USA/Canada	4/ 8 (50.0)	NE (2.8, NE)	3/ 6 (50.0)	10.1 (2.9, NE)	1.08 (0.24, 4.89)	0.9400	
Rest of World	36/ 107 (33.6)	NE (11.2, NE)	3/ 22 (13.6)	NE (NE , NE)	2.66 (0.82, 8.65)	0.0900	
ECOG-PS at Randomization							0.5189
0	46/ 123 (37.4)	NE (8.9, NE)	10/ 43 (23.3)	NE (NE , NE)	1.69 (0.85, 3.35)	0.1291	
1	43/ 96 (44.8)	11.0 (4.7, NE)	4/ 23 (17.4)	NE (NE , NE)	2.49 (0.89, 6.95)	0.0701	
Number of Organs Involved							0.7492
<= 2	42/ 110 (38.2)	NE (11.0, NE)	6/ 33 (18.2)	NE (NE , NE)	2.14 (0.91, 5.03)	0.0753	
>= 3	47/ 109 (43.1)	8.4 (5.2, NE)	8/ 33 (24.2)	NE (NE , NE)	1.81 (0.85, 3.82)	0.1169	
Presence of Liver Metastases							0.2609
Yes	57/ 135 (42.2)	11.2 (7.0, NE)	11/ 40 (27.5)	NE (10.1, NE)	1.58 (0.83, 3.01)	0.1632	
No	32/ 84 (38.1)	NE (9.0, NE)	3/ 26 (11.5)	NE (NE , NE)	3.38 (1.04, 11.05)	0.0319	
Side of Tumor							0.3438
Left	32/ 83 (38.6)	NE (8.4, NE)	8/ 33 (24.2)	NE (NE , NE)	1.52 (0.70, 3.29)	0.2921	
Right	57/ 136 (41.9)	13.0 (7.0, NE)	6/ 33 (18.2)	NE (10.9, NE)	2.54 (1.10, 5.90)	0.0241	

[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio > 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.
[4] P-Value for interaction from Cox proportional hazards model using ties=exact option with treatment, subgroup and treatment*subgroup interaction as covariates.
Including only patients from the full analysis set who completed a baseline (last PRO assessment prior to or on the first dose of study treatment) and at least 1 post-baseline PRO assessment.
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Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
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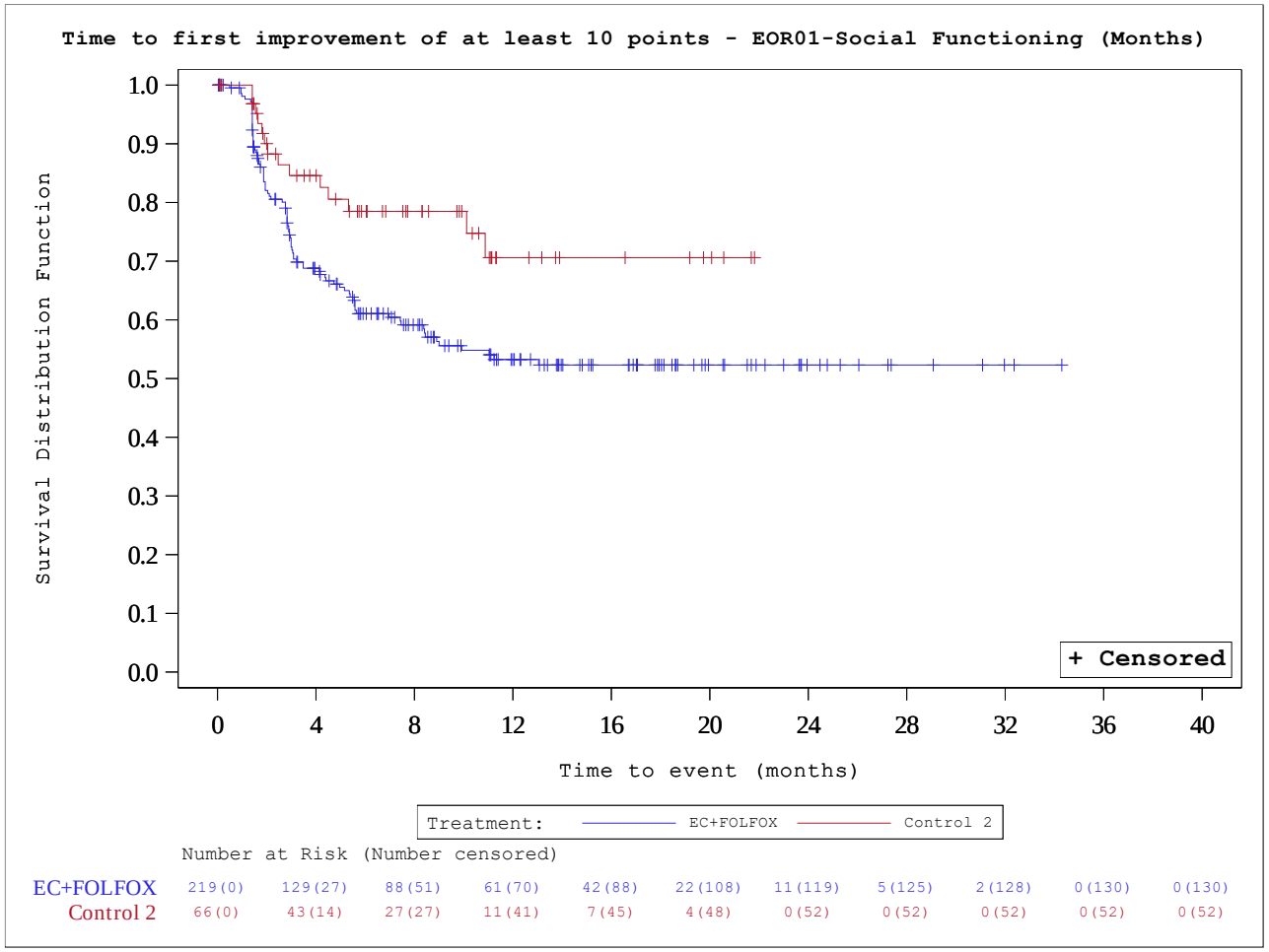
Full Analysis Set



Kaplan-Meier Plots for subgroups only created if p-value for interaction < 0.05.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Time to first deterioration of at least 10 points - EOR01-Fatigue (Months)
Full Analysis Set

	EC+FOLFOX (N=219)	Control 2 (N=66)
Number of subjects with events, n (%)	151 (68.9)	30 (45.5)
Number of censored subjects, n (%)	68 (31.1)	36 (54.5)
Kaplan-Meier estimates of Time to Event (Months) [1]		
25%-ile (95% CI)	1.5 (1.5, 1.6)	1.7 (1.5, 3.0)
Median (95% CI)	2.8 (2.1, 4.0)	7.2 (3.0, NE)
75%-ile (95% CI)	13.9 (7.0, NE)	NE (12.5, NE)
Stratified analysis [2]		
Hazard Ratio (95% CI) [3]	1.74 (1.17, 2.59)	
p-value [4]	0.0052	

[1] Based on the Brookmeyer and Crowley method.
[2] Stratified by ECOG PS by Randomization.
[3] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[4] P-value from 2-sided log-rank test.
Including only patients from the full analysis set who completed a baseline (last PRO assessment prior to or on the first dose of study treatment) and at least 1 post-baseline PRO assessment.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Time to first deterioration of at least 10 points - EOR01-Fatigue (Months) - Subgroup analysis
Full Analysis Set

Subgroup Level	EC+FOLFOX (N=219) n/ N (%)	EC+FOLFOX (N=219) Median (95% CI)[1]	Control 2 (N=66) n/ N (%)	Control 2 (N=66) Median (95% CI)[1]	Unstratified analysis Hazard Ratio (95% CI)[2]	Unstratified analysis p-Value[3]	Interaction p-Value[4]
Age (Years)							0.5427
< 65	97/ 139 (69.8)	2.8 (1.9, 4.4)	17/ 41 (41.5)	9.0 (3.0, NE)	1.94 (1.16, 3.24)	0.0104	
>= 65	54/ 80 (67.5)	2.8 (2.0, 3.8)	13/ 25 (52.0)	7.0 (2.4, NE)	1.51 (0.83, 2.78)	0.1727	
Sex							0.9311
Male	78/ 114 (68.4)	2.9 (1.9, 4.4)	14/ 31 (45.2)	7.2 (2.4, NE)	1.73 (0.98, 3.06)	0.0546	
Female	73/ 105 (69.5)	2.8 (2.0, 3.5)	16/ 35 (45.7)	12.5 (2.6, NE)	1.76 (1.02, 3.02)	0.0370	
Region							0.3626
Europe	71/ 104 (68.3)	4.0 (2.4, 5.7)	17/ 38 (44.7)	9.0 (2.6, NE)	1.49 (0.88, 2.54)	0.1310	
USA/Canada	6/ 8 (75.0)	2.4 (1.6, NE)	1/ 6 (16.7)	NE (NE , NE)	5.66 (0.68, 47.26)	0.0677	
Rest of World	74/ 107 (69.2)	2.6 (1.6, 2.9)	12/ 22 (54.5)	6.7 (2.0, NE)	1.65 (0.90, 3.04)	0.1053	
ECOG-PS at Randomization							0.1698
0	86/ 123 (69.9)	2.8 (2.0, 4.3)	19/ 43 (44.2)	12.5 (5.6, NE)	2.10 (1.27, 3.45)	0.0028	
1	65/ 96 (67.7)	2.8 (1.7, 4.2)	11/ 23 (47.8)	3.0 (1.5, NE)	1.20 (0.63, 2.28)	0.5605	
Number of Organs Involved							0.0692
<= 2	84/ 110 (76.4)	1.9 (1.6, 2.9)	13/ 33 (39.4)	NE (2.9, NE)	2.41 (1.34, 4.33)	0.0022	
>= 3	67/ 109 (61.5)	4.1 (2.8, 5.9)	17/ 33 (51.5)	6.7 (2.4, 12.5)	1.17 (0.69, 2.00)	0.5570	
Presence of Liver Metastases							0.2798
Yes	92/ 135 (68.1)	2.8 (2.1, 4.1)	20/ 40 (50.0)	7.0 (2.4, NE)	1.44 (0.89, 2.34)	0.1305	
No	59/ 84 (70.2)	2.6 (1.7, 4.4)	10/ 26 (38.5)	NE (2.9, NE)	2.35 (1.20, 4.60)	0.0104	
Side of Tumor							0.7791
Left	53/ 83 (63.9)	3.2 (1.6, 6.5)	15/ 33 (45.5)	9.0 (2.9, NE)	1.60 (0.90, 2.84)	0.1026	
Right	98/ 136 (72.1)	2.8 (2.1, 3.5)	15/ 33 (45.5)	6.7 (2.4, NE)	1.80 (1.05, 3.11)	0.0301	

[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.
[4] P-Value for interaction from Cox proportional hazards model using ties=exact option with treatment, subgroup and treatment*subgroup interaction as covariates.
Including only patients from the full analysis set who completed a baseline (last PRO assessment prior to or on the first dose of study treatment) and at least 1 post-baseline PRO assessment.
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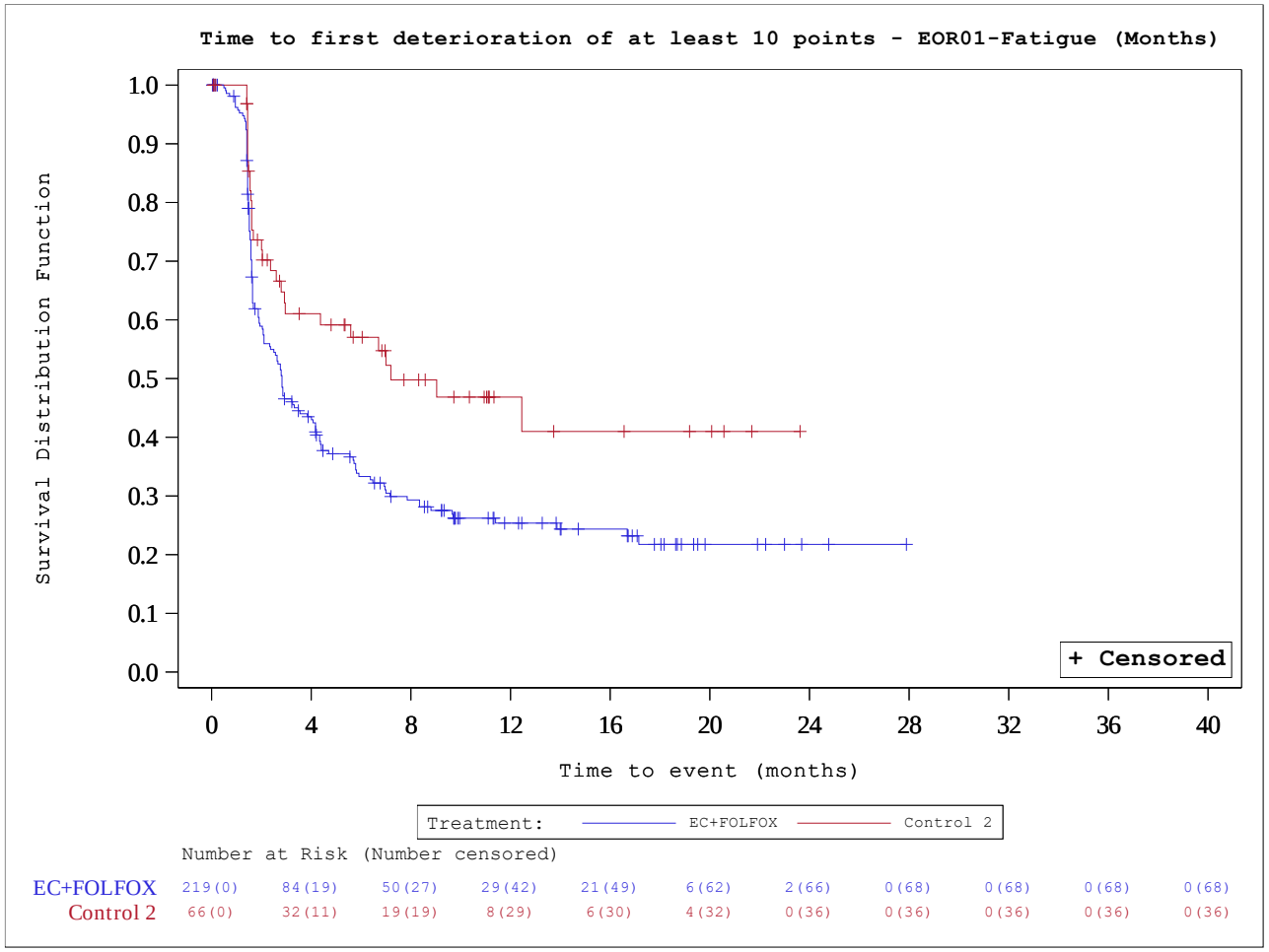
Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Kaplan Meier Plot of Time to first deterioration of at least 10 points - EOR01-Fatigue (Months)
Full Analysis Set



Kaplan-Meier Plots for subgroups only created if p-value for interaction < 0.05.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
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Time to first improvement of at least 10 points - EOR01-Fatigue (Months)
Full Analysis Set

	EC+FOLFOX (N=219)	Control 2 (N=66)
Number of subjects with events, n (%)	97 (44.3)	23 (34.8)
Number of censored subjects, n (%)	122 (55.7)	43 (65.2)
Kaplan-Meier estimates of Time to Event (Months) [1]		
25%-ile (95% CI)	3.0 (2.6, 4.2)	2.9 (1.6, 8.6)
Median (95% CI)	11.1 (8.1, NE)	NE (7.5, NE)
75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
Stratified analysis [2]		
Hazard Ratio (95% CI) [3]	1.16 (0.73, 1.83)	
p-value [4]	0.5250	

[1] Based on the Brookmeyer and Crowley method.
[2] Stratified by ECOG PS by Randomization.
[3] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio > 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[4] P-value from 2-sided log-rank test.
Including only patients from the full analysis set who completed a baseline (last PRO assessment prior to or on the first dose of study treatment) and at least 1 post-baseline PRO assessment.

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Population: arm B vs. arm E
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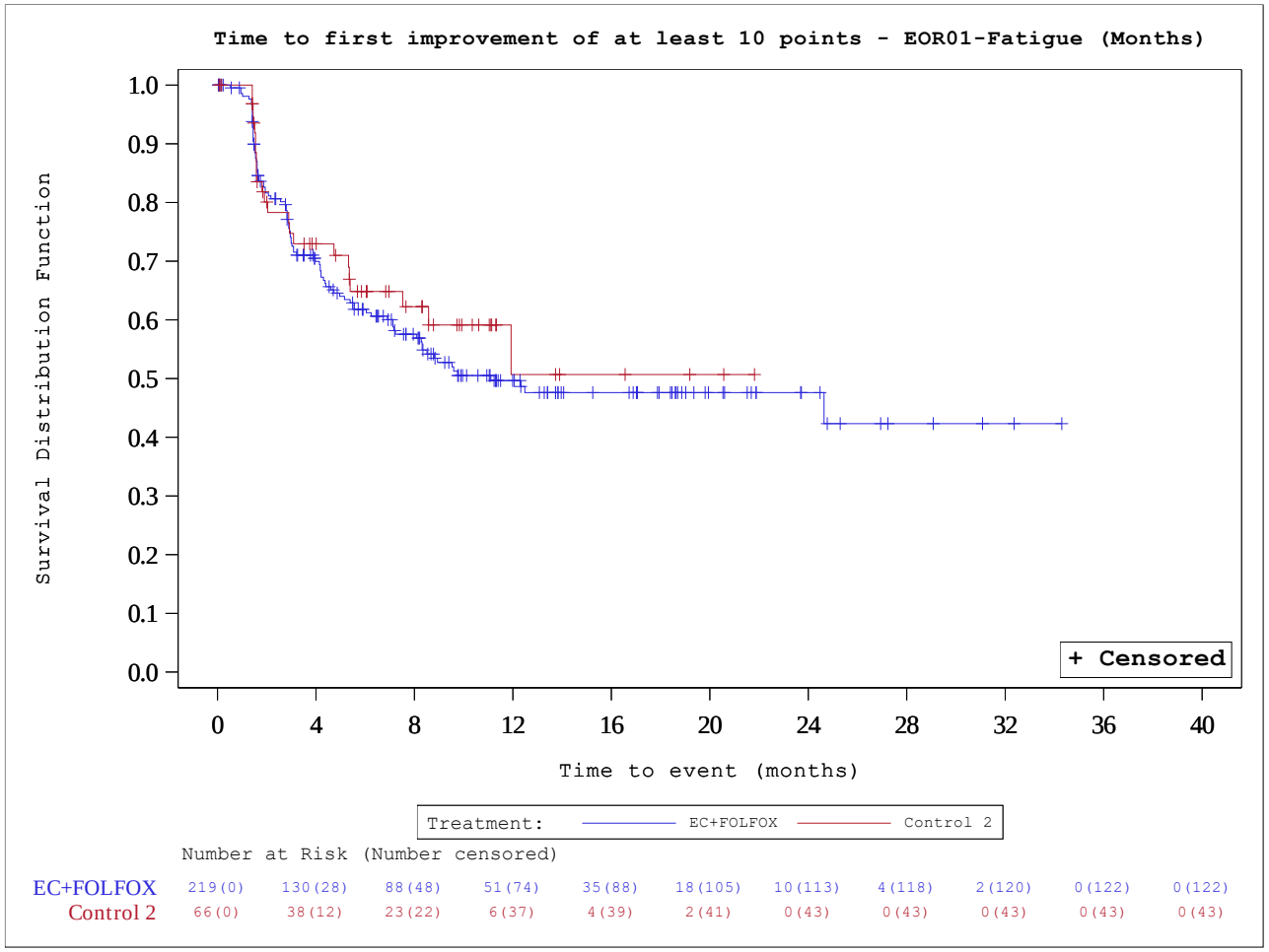
Time to first improvement of at least 10 points - EOR01-Fatigue (Months) - Subgroup analysis
Full Analysis Set

Subgroup Level	EC+FOLFOX (N=219) n/ N (%)	EC+FOLFOX (N=219) Median (95% CI)[1]	Control 2 (N=66) n/ N (%)	Control 2 (N=66) Median (95% CI)[1]	Unstratified analysis Hazard Ratio (95% CI)[2]	Unstratified analysis p-Value[3]	Interaction p-Value[4]
Age (Years)							0.6079
< 65	69/ 139 (49.6)	8.3 (5.6, NE)	15/ 41 (36.6)	11.9 (5.3, NE)	1.27 (0.73, 2.23)	0.3921	
>= 65	28/ 80 (35.0)	24.6 (9.5, NE)	8/ 25 (32.0)	NE (5.4, NE)	0.98 (0.44, 2.16)	0.9627	
Sex							0.8020
Male	50/ 114 (43.9)	8.5 (5.4, NE)	10/ 31 (32.3)	NE (7.5, NE)	1.26 (0.64, 2.49)	0.5037	
Female	47/ 105 (44.8)	12.3 (8.3, NE)	13/ 35 (37.1)	NE (5.3, NE)	1.09 (0.59, 2.02)	0.7929	
Region							0.4264
Europe	46/ 104 (44.2)	24.6 (5.0, NE)	10/ 38 (26.3)	NE (NE , NE)	1.58 (0.80, 3.13)	0.1852	
USA/Canada	3/ 8 (37.5)	NE (5.6, NE)	3/ 6 (50.0)	11.9 (2.9, NE)	0.69 (0.14, 3.46)	0.6506	
Rest of World	48/ 107 (44.9)	9.8 (8.1, NE)	10/ 22 (45.5)	8.6 (4.7, NE)	0.88 (0.45, 1.75)	0.7130	
ECOG-PS at Randomization							0.9412
0	54/ 123 (43.9)	9.8 (7.1, NE)	16/ 43 (37.2)	NE (5.4, NE)	1.16 (0.66, 2.02)	0.6082	
1	43/ 96 (44.8)	11.1 (6.9, NE)	7/ 23 (30.4)	NE (3.1, NE)	1.16 (0.52, 2.60)	0.7069	
Number of Organs Involved							0.3699
<= 2	46/ 110 (41.8)	24.6 (8.3, NE)	9/ 33 (27.3)	NE (11.9, NE)	1.47 (0.72, 3.01)	0.2868	
>= 3	51/ 109 (46.8)	8.5 (5.2, NE)	14/ 33 (42.4)	7.5 (2.9, NE)	0.97 (0.53, 1.75)	0.9174	
Presence of Liver Metastases							0.6736
Yes	60/ 135 (44.4)	9.5 (7.1, NE)	15/ 40 (37.5)	11.9 (5.4, NE)	1.09 (0.62, 1.92)	0.7655	
No	37/ 84 (44.0)	12.5 (6.2, NE)	8/ 26 (30.8)	NE (5.4, NE)	1.33 (0.62, 2.87)	0.4604	
Side of Tumor							0.9639
Left	42/ 83 (50.6)	8.3 (4.6, NE)	12/ 33 (36.4)	NE (5.3, NE)	1.19 (0.62, 2.26)	0.5998	
Right	55/ 136 (40.4)	NE (8.3, NE)	11/ 33 (33.3)	NE (5.4, NE)	1.19 (0.62, 2.28)	0.5916	

[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio > 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.
[4] P-Value for interaction from Cox proportional hazards model using ties=exact option with treatment, subgroup and treatment*subgroup interaction as covariates.
Including only patients from the full analysis set who completed a baseline (last PRO assessment prior to or on the first dose of study treatment) and at least 1 post-baseline PRO assessment.
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Kaplan Meier Plot of Time to first improvement of at least 10 points - EOR01-Fatigue (Months)
Full Analysis Set



Kaplan-Meier Plots for subgroups only created if p-value for interaction < 0.05.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Time to first deterioration of at least 10 points - EOR01-Nausea and Vomiting (Months)
Full Analysis Set

	EC+FOLFOX (N=219)	Control 2 (N=66)
Number of subjects with events, n (%)	115 (52.5)	27 (40.9)
Number of censored subjects, n (%)	104 (47.5)	39 (59.1)
Kaplan-Meier estimates of Time to Event (Months) [1]		
25%-ile (95% CI)	1.6 (1.5, 2.1)	3.0 (1.6, 4.5)
Median (95% CI)	6.9 (3.9, 15.2)	8.6 (4.5, NE)
75%-ile (95% CI)	NE (20.0, NE)	NE (15.5, NE)
Stratified analysis [2]		
Hazard Ratio (95% CI) [3]	1.25 (0.82, 1.90)	
p-value [4]	0.3128	

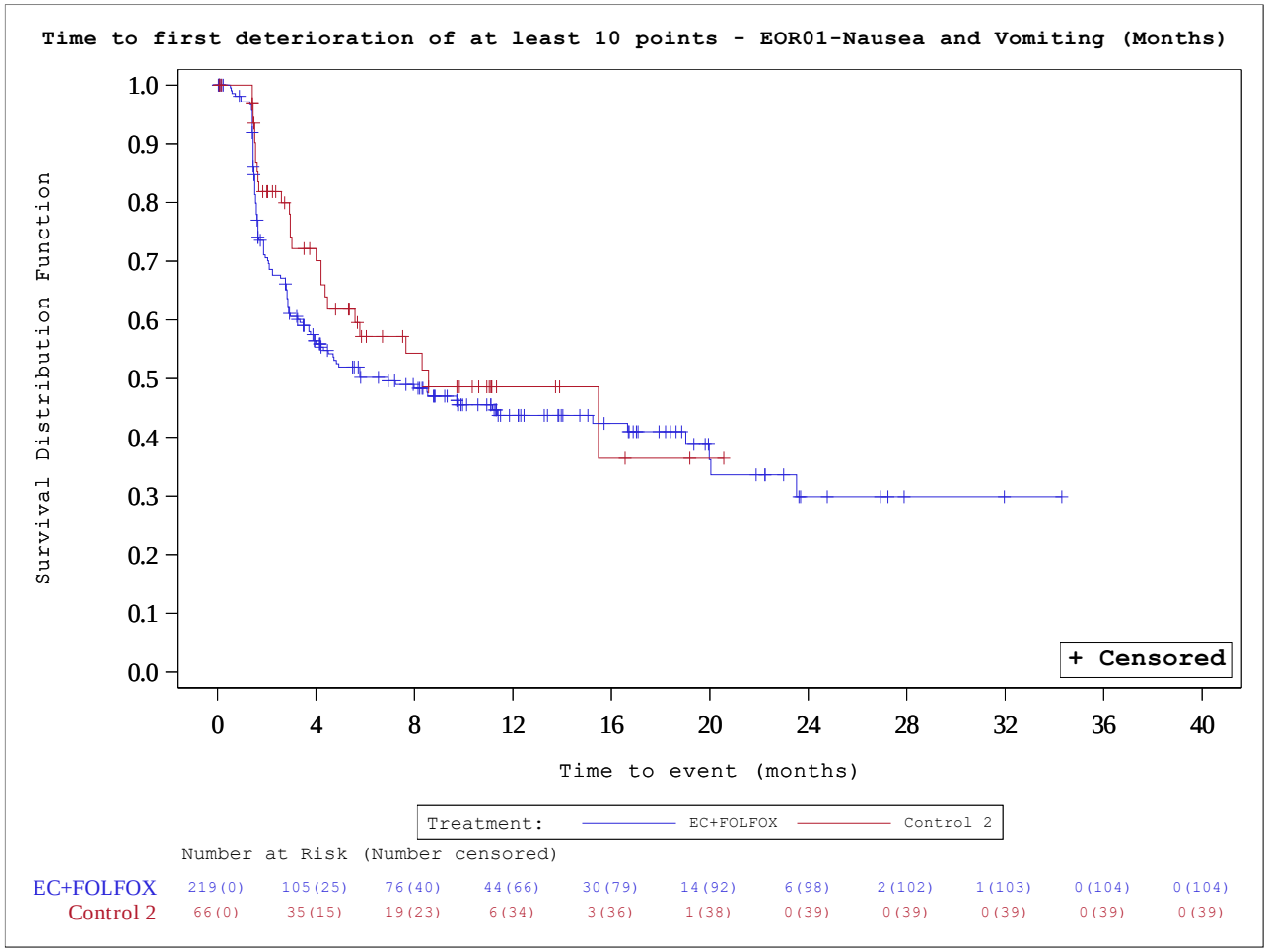
[1] Based on the Brookmeyer and Crowley method.
[2] Stratified by ECOG PS by Randomization.
[3] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[4] P-value from 2-sided log-rank test.
Including only patients from the full analysis set who completed a baseline (last PRO assessment prior to or on the first dose of study treatment) and at least 1 post-baseline PRO assessment.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Time to first deterioration of at least 10 points - EOR01-Nausea and Vomiting (Months) - Subgroup analysis
Full Analysis Set

Subgroup Level	EC+FOLFOX (N=219) n/ N (%)	EC+FOLFOX (N=219) Median (95% CI)[1]	Control 2 (N=66) n/ N (%)	Control 2 (N=66) Median (95% CI)[1]	Unstratified analysis Hazard Ratio (95% CI)[2]	Unstratified analysis p-Value[3]	Interaction p-Value[4]
Age (Years)							0.9346
< 65	80/ 139 (57.6)	4.7 (2.9, 9.8)	19/ 41 (46.3)	8.3 (4.2, NE)	1.25 (0.76, 2.06)	0.3951	
>= 65	35/ 80 (43.8)	15.2 (3.9, NE)	8/ 25 (32.0)	NE (4.5, NE)	1.30 (0.60, 2.82)	0.5038	
Sex							0.6173
Male	50/ 114 (43.9)	16.7 (4.7, NE)	11/ 31 (35.5)	15.5 (4.2, NE)	1.13 (0.59, 2.19)	0.7069	
Female	65/ 105 (61.9)	3.8 (2.8, 8.5)	16/ 35 (45.7)	8.3 (4.2, NE)	1.42 (0.82, 2.46)	0.2064	
Region							0.3277
Europe	53/ 104 (51.0)	4.9 (3.7, NE)	13/ 38 (34.2)	15.5 (5.6, NE)	1.42 (0.77, 2.61)	0.2540	
USA/Canada	6/ 8 (75.0)	2.2 (1.4, NE)	2/ 6 (33.3)	NE (2.9, NE)	3.35 (0.67, 16.73)	0.1189	
Rest of World	56/ 107 (52.3)	8.5 (3.9, 20.0)	12/ 22 (54.5)	5.8 (4.2, NE)	0.90 (0.48, 1.70)	0.7463	
ECOG-PS at Randomization							0.7899
0	65/ 123 (52.8)	7.2 (3.7, 20.0)	18/ 43 (41.9)	15.5 (4.5, NE)	1.28 (0.76, 2.17)	0.3591	
1	50/ 96 (52.1)	5.8 (2.9, NE)	9/ 23 (39.1)	8.6 (4.0, NE)	1.18 (0.58, 2.41)	0.6482	
Number of Organs Involved							0.6544
<= 2	61/ 110 (55.5)	4.8 (3.0, 20.0)	14/ 33 (42.4)	15.5 (4.5, NE)	1.36 (0.76, 2.45)	0.2969	
>= 3	54/ 109 (49.5)	6.9 (4.0, NE)	13/ 33 (39.4)	8.3 (3.0, NE)	1.09 (0.59, 2.01)	0.7913	
Presence of Liver Metastases							0.3971
Yes	64/ 135 (47.4)	11.4 (4.0, 20.0)	17/ 40 (42.5)	7.7 (4.0, NE)	1.08 (0.63, 1.84)	0.7948	
No	51/ 84 (60.7)	4.7 (2.9, 9.8)	10/ 26 (38.5)	15.5 (4.2, NE)	1.61 (0.82, 3.18)	0.1629	
Side of Tumor							0.5727
Left	41/ 83 (49.4)	8.5 (3.7, NE)	14/ 33 (42.4)	15.5 (4.2, NE)	1.12 (0.61, 2.06)	0.7162	
Right	74/ 136 (54.4)	4.9 (3.3, 19.0)	13/ 33 (39.4)	8.3 (4.2, NE)	1.40 (0.77, 2.52)	0.2694	

[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.
[4] P-Value for interaction from Cox proportional hazards model using ties=exact option with treatment, subgroup and treatment*subgroup interaction as covariates.
Including only patients from the full analysis set who completed a baseline (last PRO assessment prior to or on the first dose of study treatment) and at least 1 post-baseline PRO assessment.
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Kaplan Meier Plot of Time to first deterioration of at least 10 points - EOR01-Nausea and Vomiting (Months)
Full Analysis Set



Kaplan-Meier Plots for subgroups only created if p-value for interaction < 0.05.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Time to first improvement of at least 10 points - EOR01-Nausea and Vomiting (Months)
Full Analysis Set

	EC+FOLFOX (N=219)	Control 2 (N=66)
Number of subjects with events, n (%)	31 (14.2)	8 (12.1)
Number of censored subjects, n (%)	188 (85.8)	58 (87.9)
Kaplan-Meier estimates of Time to Event (Months) [1]		
25%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
Stratified analysis [2]		
Hazard Ratio (95% CI) [3]	1.04 (0.48, 2.27)	
p-value [4]	0.9231	

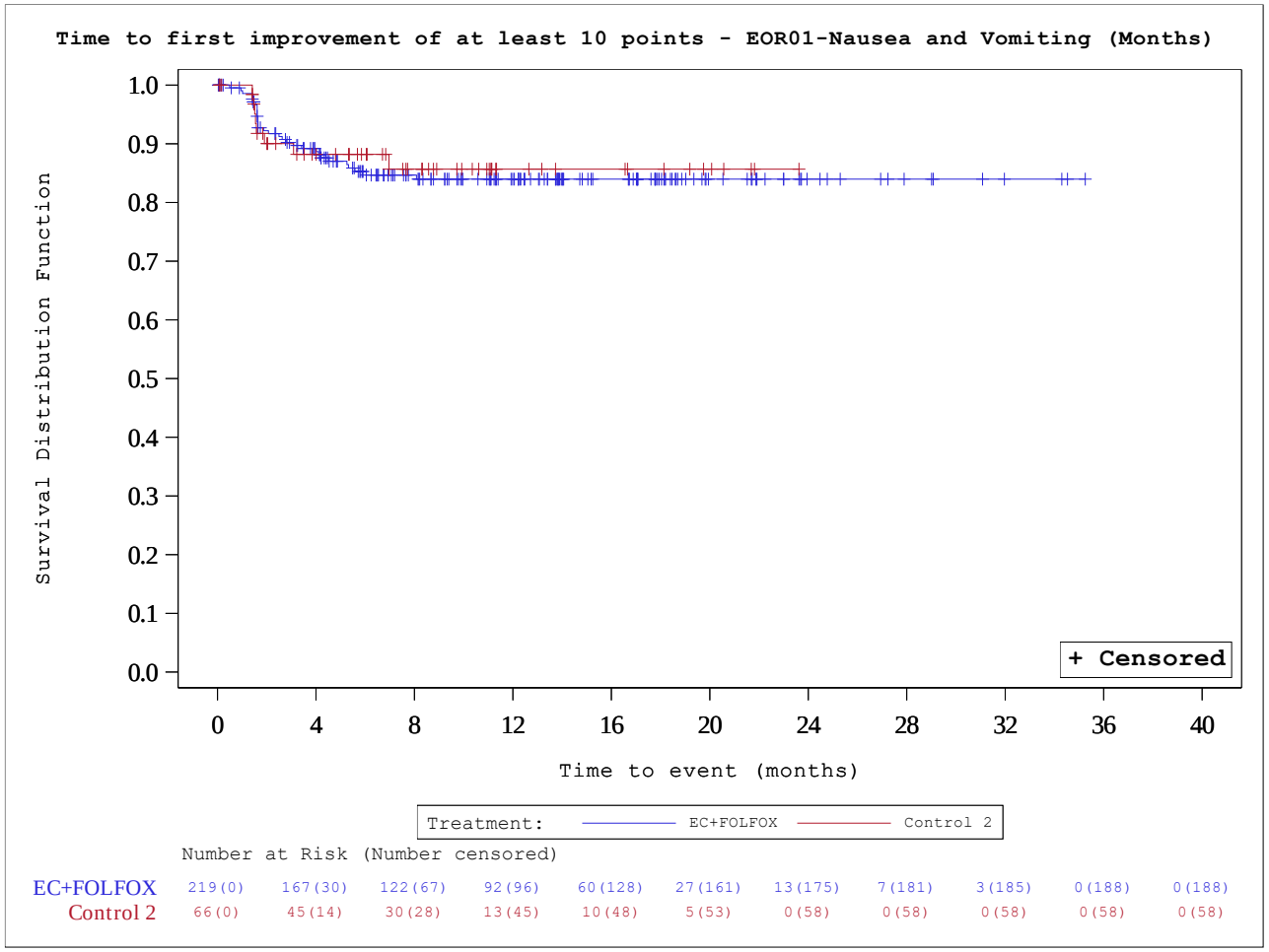
[1] Based on the Brookmeyer and Crowley method.
[2] Stratified by ECOG PS by Randomization.
[3] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio > 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[4] P-value from 2-sided log-rank test.
Including only patients from the full analysis set who completed a baseline (last PRO assessment prior to or on the first dose of study treatment) and at least 1 post-baseline PRO assessment.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Time to first improvement of at least 10 points - EOR01-Nausea and Vomiting (Months) - Subgroup analysis
Full Analysis Set

Subgroup Level	EC+FOLFOX (N=219) n/ N (%)	EC+FOLFOX (N=219) Median (95% CI)[1]	Control 2 (N=66) n/ N (%)	Control 2 (N=66) Median (95% CI)[1]	Unstratified analysis Hazard Ratio (95% CI)[2]	Unstratified analysis p-Value[3]	Interaction p-Value[4]
Age (Years)							0.0960
< 65	25/ 139 (18.0)	NE (NE , NE)	4/ 41 (9.8)	NE (NE , NE)	1.73 (0.60, 4.97)	0.3031	
>= 65	6/ 80 (7.5)	NE (NE , NE)	4/ 25 (16.0)	NE (NE , NE)	0.42 (0.12, 1.51)	0.1737	
Sex							0.8574
Male	13/ 114 (11.4)	NE (NE , NE)	3/ 31 (9.7)	NE (NE , NE)	1.03 (0.29, 3.63)	0.9586	
Female	18/ 105 (17.1)	NE (NE , NE)	5/ 35 (14.3)	NE (NE , NE)	1.20 (0.44, 3.23)	0.7216	
Region							0.6862
Europe	14/ 104 (13.5)	NE (NE , NE)	3/ 38 (7.9)	NE (NE , NE)	1.57 (0.45, 5.45)	0.4766	
USA/Canada	1/ 8 (12.5)	NE (NE , NE)	1/ 6 (16.7)	NE (NE , NE)	0.68 (0.04, 10.98)	0.7878	
Rest of World	16/ 107 (15.0)	NE (NE , NE)	4/ 22 (18.2)	NE (NE , NE)	0.77 (0.26, 2.31)	0.6390	
ECOG-PS at Randomization							0.5711
0	15/ 123 (12.2)	NE (NE , NE)	4/ 43 (9.3)	NE (NE , NE)	1.30 (0.43, 3.91)	0.6433	
1	16/ 96 (16.7)	NE (NE , NE)	4/ 23 (17.4)	NE (NE , NE)	0.81 (0.27, 2.42)	0.7022	
Number of Organs Involved							0.6927
<= 2	14/ 110 (12.7)	NE (NE , NE)	3/ 33 (9.1)	NE (NE , NE)	1.32 (0.38, 4.61)	0.6576	
>= 3	17/ 109 (15.6)	NE (NE , NE)	5/ 33 (15.2)	NE (NE , NE)	0.96 (0.36, 2.61)	0.9408	
Presence of Liver Metastases							0.3317
Yes	18/ 135 (13.3)	NE (NE , NE)	6/ 40 (15.0)	NE (NE , NE)	0.82 (0.32, 2.06)	0.6640	
No	13/ 84 (15.5)	NE (NE , NE)	2/ 26 (7.7)	NE (NE , NE)	1.97 (0.44, 8.71)	0.3649	
Side of Tumor							0.6440
Left	13/ 83 (15.7)	NE (NE , NE)	5/ 33 (15.2)	NE (NE , NE)	0.95 (0.34, 2.66)	0.9177	
Right	18/ 136 (13.2)	NE (NE , NE)	3/ 33 (9.1)	NE (NE , NE)	1.37 (0.40, 4.65)	0.6133	

[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio > 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.
[4] P-Value for interaction from Cox proportional hazards model using ties=exact option with treatment, subgroup and treatment*subgroup interaction as covariates.
Including only patients from the full analysis set who completed a baseline (last PRO assessment prior to or on the first dose of study treatment) and at least 1 post-baseline PRO assessment.
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Kaplan Meier Plot of Time to first improvement of at least 10 points - EOR01-Nausea and Vomiting (Months)
Full Analysis Set



Kaplan-Meier Plots for subgroups only created if p-value for interaction < 0.05.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Time to first deterioration of at least 10 points - EOR01-Pain (Months)
Full Analysis Set

	EC+FOLFOX (N=219)	Control 2 (N=66)
Number of subjects with events, n (%)	125 (57.1)	24 (36.4)
Number of censored subjects, n (%)	94 (42.9)	42 (63.6)
Kaplan-Meier estimates of Time to Event (Months) [1]		
25%-ile (95% CI)	2.9 (2.6, 3.9)	5.7 (2.8, 8.3)
Median (95% CI)	8.1 (6.4, 9.9)	12.6 (8.3, NE)
75%-ile (95% CI)	20.5 (16.7, NE)	NE (15.6, NE)
Stratified analysis [2]		
Hazard Ratio (95% CI) [3]	1.48 (0.95, 2.31)	
p-value [4]	0.0763	

[1] Based on the Brookmeyer and Crowley method.
[2] Stratified by ECOG PS by Randomization.
[3] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[4] P-value from 2-sided log-rank test.
Including only patients from the full analysis set who completed a baseline (last PRO assessment prior to or on the first dose of study treatment) and at least 1 post-baseline PRO assessment.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Time to first deterioration of at least 10 points - EOR01-Pain (Months) - Subgroup analysis
Full Analysis Set

Subgroup Level	EC+FOLFOX (N=219) n/ N (%)	EC+FOLFOX (N=219) Median (95% CI)[1]	Control 2 (N=66) n/ N (%)	Control 2 (N=66) Median (95% CI)[1]	Unstratified analysis Hazard Ratio (95% CI)[2]	Unstratified analysis p-Value[3]	Interaction p-Value[4]
Age (Years)							0.5277
< 65	79/ 139 (56.8)	8.3 (6.4, 11.2)	14/ 41 (34.1)	15.6 (8.3, NE)	1.69 (0.96, 2.98)	0.0682	
>= 65	46/ 80 (57.5)	7.8 (4.2, 11.3)	10/ 25 (40.0)	9.8 (4.4, NE)	1.30 (0.65, 2.59)	0.4587	
Sex							0.7948
Male	64/ 114 (56.1)	7.5 (5.6, 9.7)	11/ 31 (35.5)	NE (5.7, NE)	1.44 (0.76, 2.74)	0.2570	
Female	61/ 105 (58.1)	8.8 (5.8, 13.7)	13/ 35 (37.1)	12.6 (9.7, NE)	1.54 (0.85, 2.81)	0.1529	
Region							0.3269
Europe	61/ 104 (58.7)	8.3 (7.3, 11.1)	12/ 38 (31.6)	NE (7.7, NE)	1.60 (0.86, 2.98)	0.1333	
USA/Canada	5/ 8 (62.5)	3.8 (1.6, NE)	1/ 6 (16.7)	NE (5.7, NE)	4.98 (0.58, 42.92)	0.1055	
Rest of World	59/ 107 (55.1)	8.0 (5.5, 14.8)	11/ 22 (50.0)	9.7 (4.4, NE)	1.08 (0.56, 2.06)	0.8259	
ECOG-PS at Randomization							0.4501
0	72/ 123 (58.5)	7.8 (5.7, 11.1)	15/ 43 (34.9)	NE (7.4, NE)	1.72 (0.98, 3.00)	0.0540	
1	53/ 96 (55.2)	8.8 (5.6, 13.4)	9/ 23 (39.1)	9.7 (8.3, 15.6)	1.13 (0.55, 2.30)	0.7359	
Number of Organs Involved							0.2492
<= 2	75/ 110 (68.2)	5.7 (4.2, 8.3)	13/ 33 (39.4)	12.6 (8.3, NE)	1.94 (1.07, 3.50)	0.0251	
>= 3	50/ 109 (45.9)	11.0 (7.8, 16.7)	11/ 33 (33.3)	NE (4.4, NE)	1.09 (0.56, 2.10)	0.8027	
Presence of Liver Metastases							0.0488
Yes	72/ 135 (53.3)	9.6 (7.3, 11.7)	17/ 40 (42.5)	7.7 (4.4, NE)	1.05 (0.61, 1.78)	0.8673	
No	53/ 84 (63.1)	6.4 (4.2, 9.9)	7/ 26 (26.9)	15.6 (12.6, NE)	2.85 (1.29, 6.28)	0.0067	
Side of Tumor							0.5741
Left	44/ 83 (53.0)	8.3 (6.9, 14.1)	12/ 33 (36.4)	12.6 (7.4, NE)	1.31 (0.69, 2.49)	0.4090	
Right	81/ 136 (59.6)	8.0 (5.6, 9.9)	12/ 33 (36.4)	NE (6.7, NE)	1.68 (0.92, 3.08)	0.0896	

[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.
[4] P-Value for interaction from Cox proportional hazards model using ties=exact option with treatment, subgroup and treatment*subgroup interaction as covariates.
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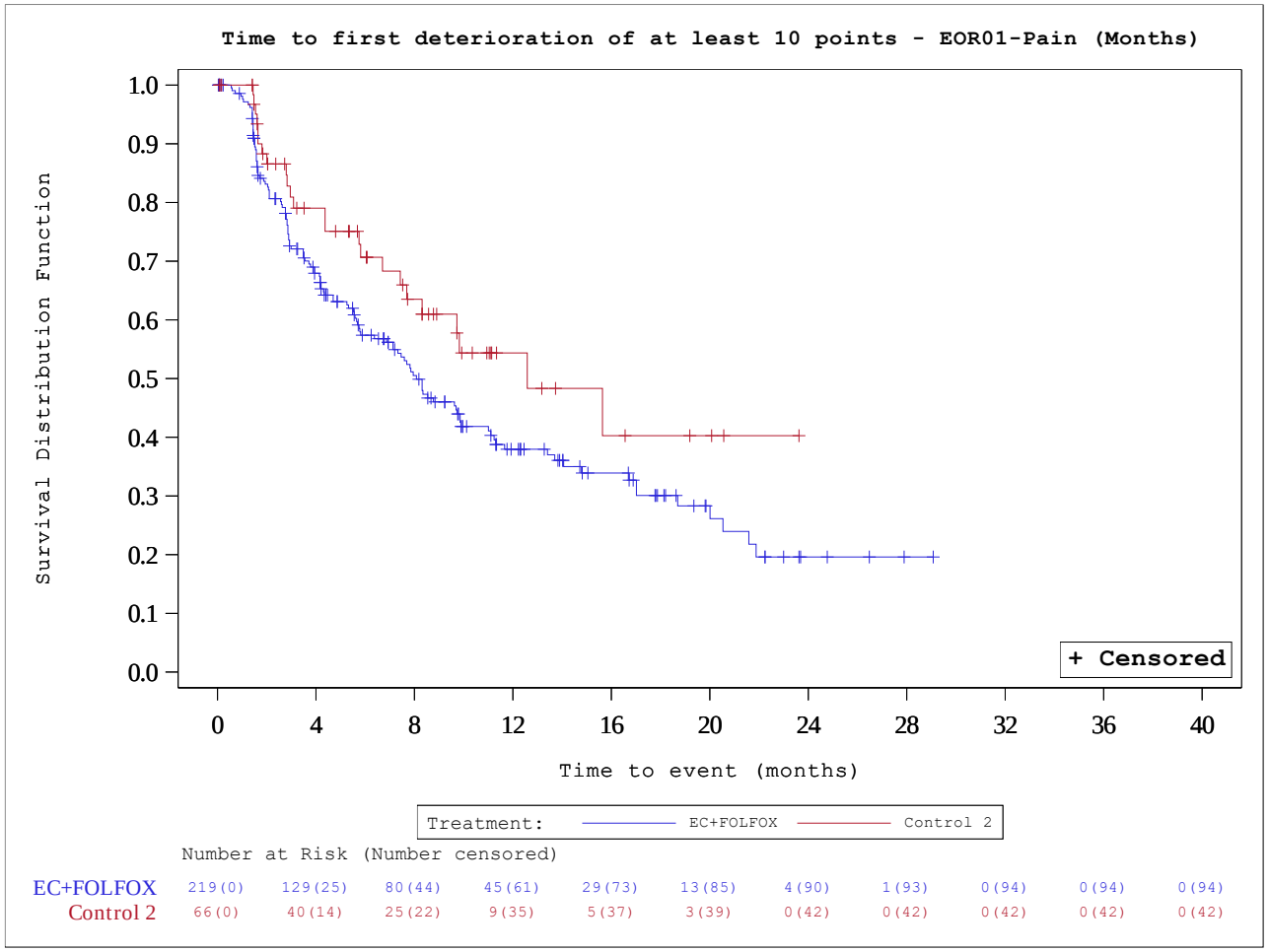
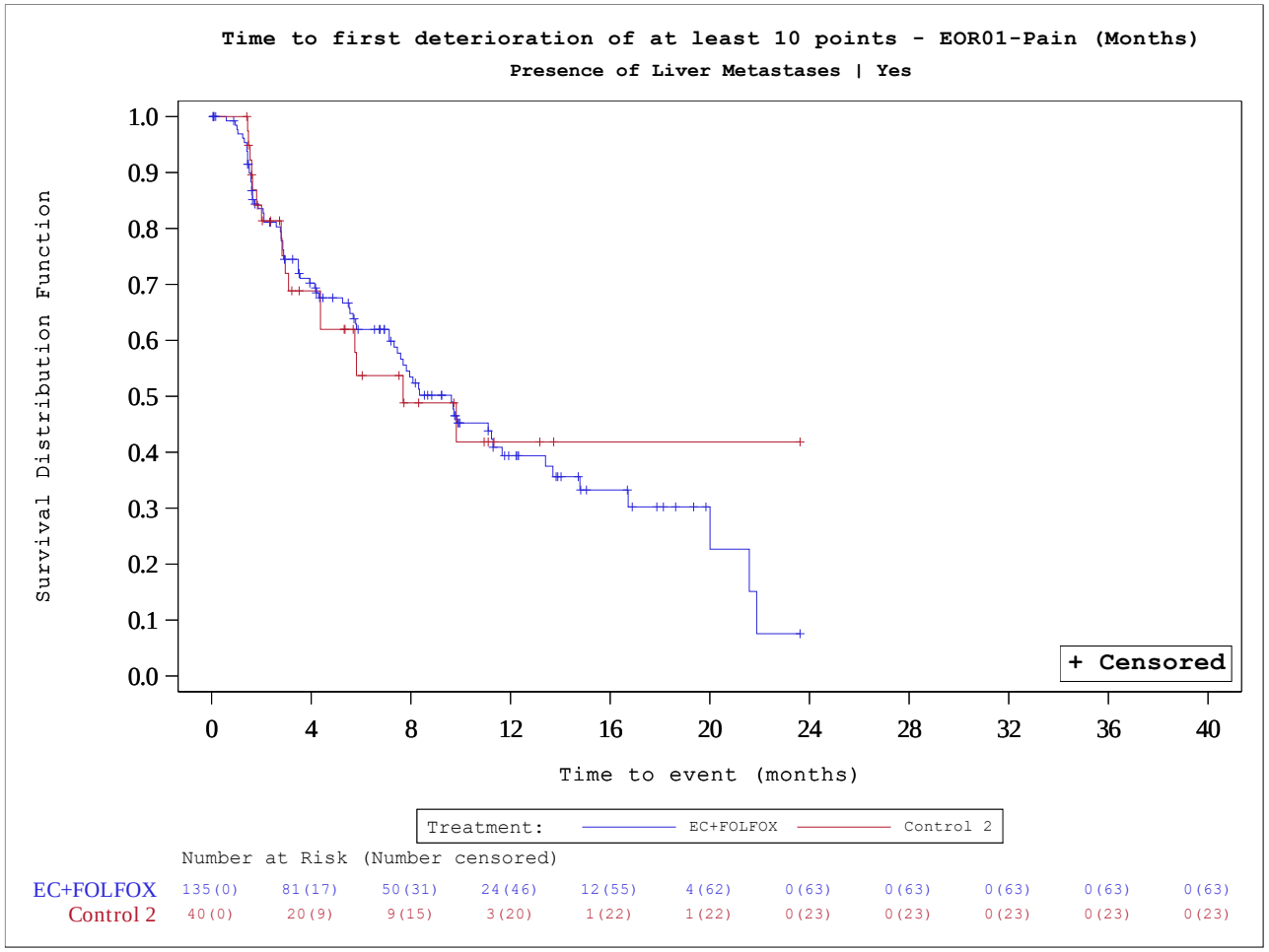
Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Kaplan Meier Plot of Time to first deterioration of at least 10 points - EOR01-Pain (Months)
Full Analysis Set



Kaplan-Meier Plots for subgroups only created if p-value for interaction < 0.05.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Kaplan Meier Plot of Time to first deterioration of at least 10 points - EOR01-Pain (Months)
Full Analysis Set



Kaplan-Meier Plots for subgroups only created if p-value for interaction < 0.05.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
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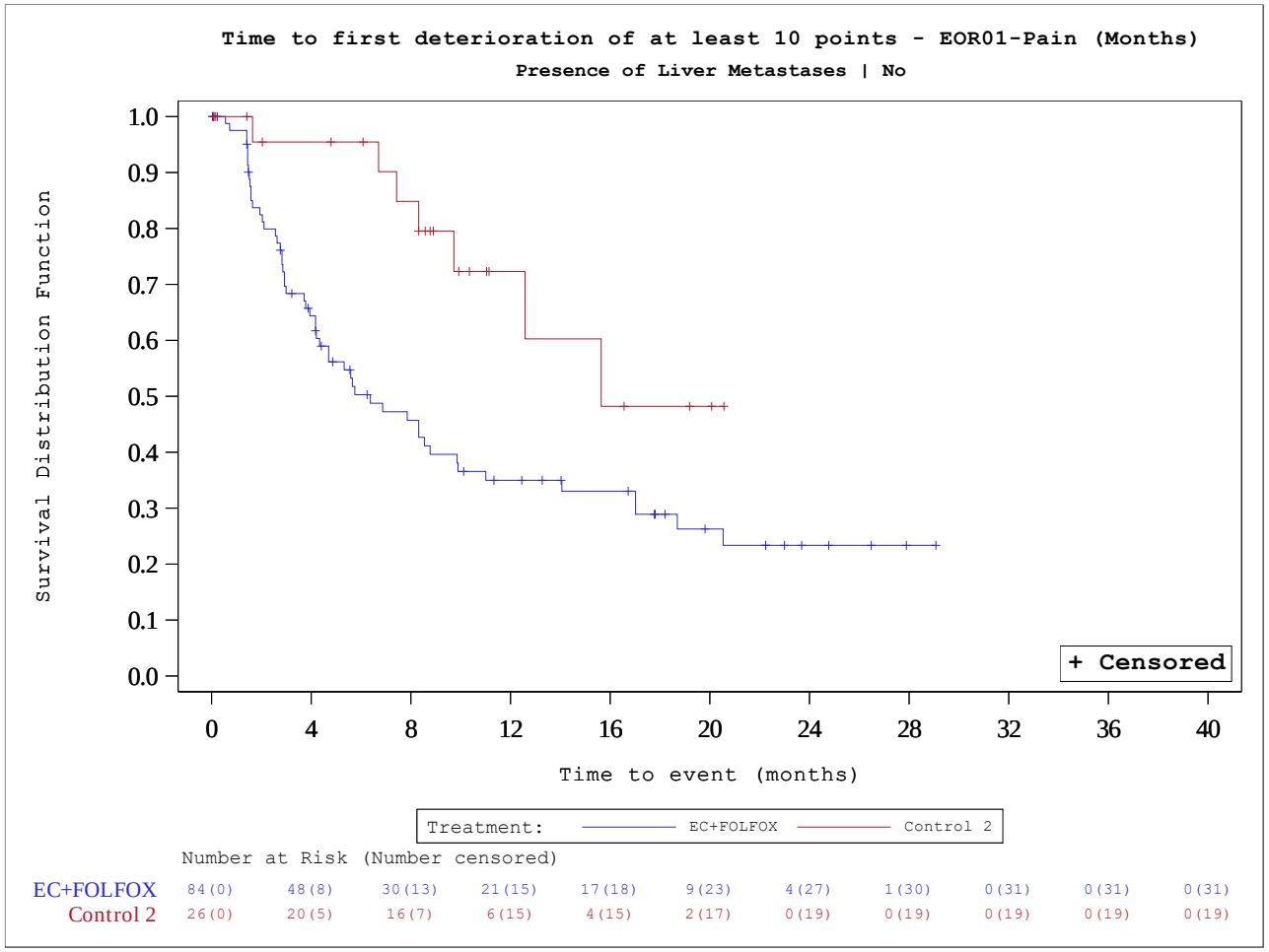


Kaplan-Meier Plots for subgroups only created if p-value for interaction < 0.05.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Time to first improvement of at least 10 points - EOR01-Pain (Months)
Full Analysis Set

	EC+FOLFOX (N=219)	Control 2 (N=66)
Number of subjects with events, n (%)	104 (47.5)	19 (28.8)
Number of censored subjects, n (%)	115 (52.5)	47 (71.2)
Kaplan-Meier estimates of Time to Event (Months) [1]		
25%-ile (95% CI)	1.6 (1.5, 1.6)	2.8 (1.5, NE)
Median (95% CI)	8.3 (3.3, NE)	NE (NE, NE)
75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
Stratified analysis [2]		
Hazard Ratio (95% CI) [3]	1.75 (1.07, 2.86)	
p-value [4]	0.0232	

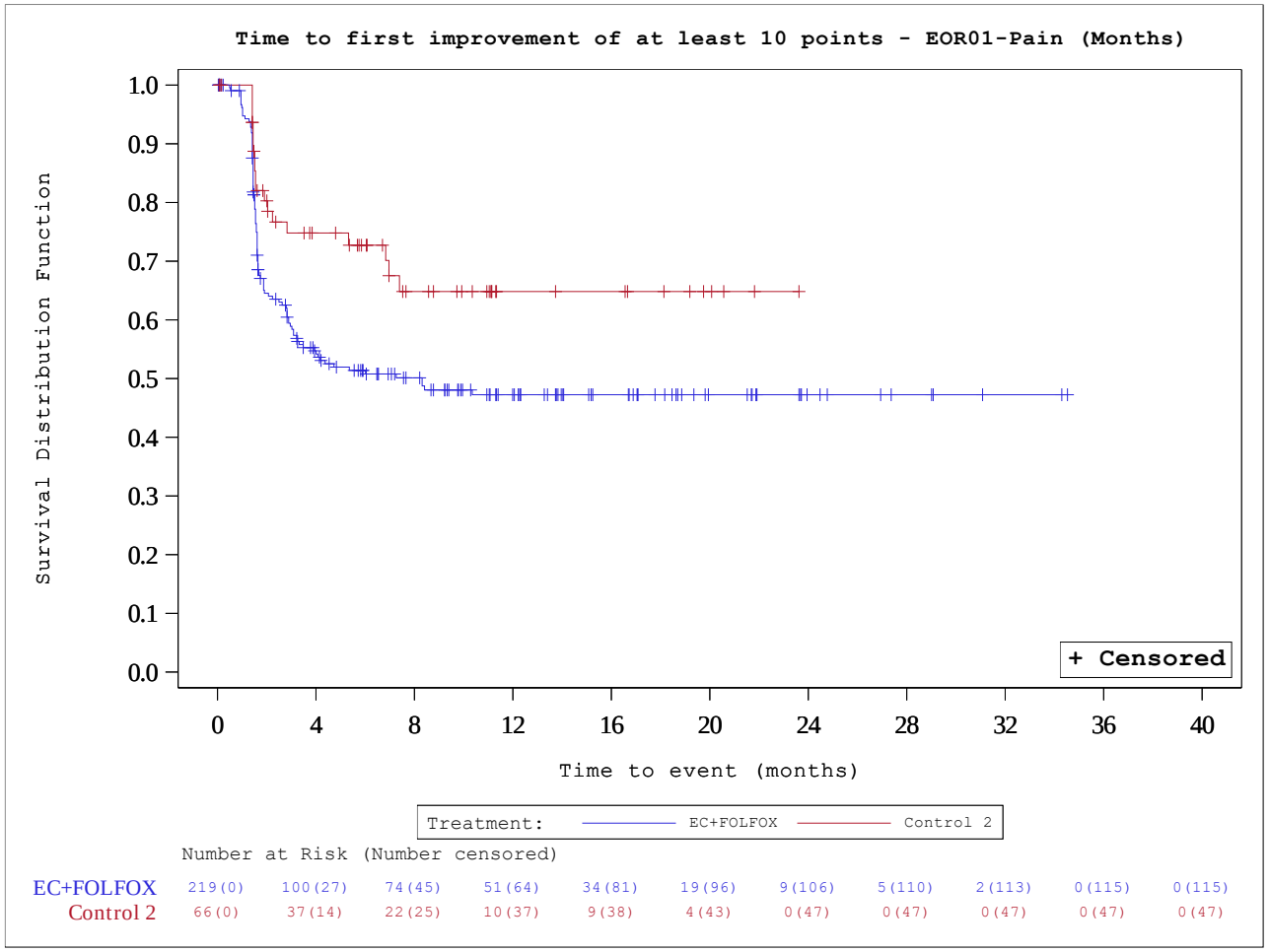
[1] Based on the Brookmeyer and Crowley method.
[2] Stratified by ECOG PS by Randomization.
[3] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio > 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[4] P-value from 2-sided log-rank test.
Including only patients from the full analysis set who completed a baseline (last PRO assessment prior to or on the first dose of study treatment) and at least 1 post-baseline PRO assessment.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Time to first improvement of at least 10 points - EOR01-Pain (Months) - Subgroup analysis
Full Analysis Set

Subgroup Level	EC+FOLFOX (N=219) n/ N (%)	EC+FOLFOX (N=219) Median (95% CI)[1]	Control 2 (N=66) n/ N (%)	Control 2 (N=66) Median (95% CI)[1]	Unstratified analysis Hazard Ratio (95% CI)[2]	Unstratified analysis p-Value[3]	Interaction p-Value[4]
Age (Years)							0.5792
< 65	74/ 139 (53.2)	4.2 (2.6, NE)	12/ 41 (29.3)	NE (7.4, NE)	1.99 (1.08, 3.65)	0.0242	
>= 65	30/ 80 (37.5)	NE (3.9, NE)	7/ 25 (28.0)	NE (7.0, NE)	1.49 (0.65, 3.39)	0.3350	
Sex							0.8628
Male	49/ 114 (43.0)	NE (3.1, NE)	8/ 31 (25.8)	NE (7.4, NE)	1.78 (0.84, 3.76)	0.1243	
Female	55/ 105 (52.4)	4.7 (2.8, NE)	11/ 35 (31.4)	NE (6.8, NE)	1.91 (1.00, 3.66)	0.0444	
Region							0.8638
Europe	54/ 104 (51.9)	4.2 (2.8, NE)	11/ 38 (28.9)	NE (7.0, NE)	1.95 (1.02, 3.73)	0.0398	
USA/Canada	3/ 8 (37.5)	NE (1.6, NE)	1/ 6 (16.7)	NE (NE , NE)	2.50 (0.26, 24.55)	0.4158	
Rest of World	47/ 107 (43.9)	10.3 (2.9, NE)	7/ 22 (31.8)	NE (6.8, NE)	1.50 (0.68, 3.33)	0.3078	
ECOG-PS at Randomization							0.6313
0	54/ 123 (43.9)	NE (3.5, NE)	11/ 43 (25.6)	NE (NE , NE)	1.93 (1.01, 3.68)	0.0431	
1	50/ 96 (52.1)	3.9 (2.2, NE)	8/ 23 (34.8)	NE (2.0, NE)	1.52 (0.72, 3.21)	0.2636	
Number of Organs Involved							0.2718
<= 2	44/ 110 (40.0)	NE (8.3, NE)	10/ 33 (30.3)	NE (7.0, NE)	1.36 (0.68, 2.70)	0.3746	
>= 3	60/ 109 (55.0)	3.2 (1.7, 6.0)	9/ 33 (27.3)	NE (7.4, NE)	2.42 (1.20, 4.88)	0.0104	
Presence of Liver Metastases							0.5669
Yes	64/ 135 (47.4)	6.0 (3.1, NE)	13/ 40 (32.5)	NE (7.0, NE)	1.63 (0.90, 2.95)	0.1057	
No	40/ 84 (47.6)	8.3 (2.8, NE)	6/ 26 (23.1)	NE (NE , NE)	2.19 (0.93, 5.18)	0.0649	
Side of Tumor							0.8788
Left	45/ 83 (54.2)	3.1 (1.9, NE)	11/ 33 (33.3)	NE (5.3, NE)	1.82 (0.94, 3.53)	0.0689	
Right	59/ 136 (43.4)	NE (4.0, NE)	8/ 33 (24.2)	NE (NE , NE)	1.96 (0.94, 4.10)	0.0661	

[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio > 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.
[4] P-Value for interaction from Cox proportional hazards model using ties=exact option with treatment, subgroup and treatment*subgroup interaction as covariates.
Including only patients from the full analysis set who completed a baseline (last PRO assessment prior to or on the first dose of study treatment) and at least 1 post-baseline PRO assessment.
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Kaplan Meier Plot of Time to first improvement of at least 10 points - EOR01-Pain (Months)
Full Analysis Set



Kaplan-Meier Plots for subgroups only created if p-value for interaction < 0.05.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Time to first deterioration of at least 10 points - EOR01-Dyspnoea (Months)
Full Analysis Set

	EC+FOLFOX (N=219)	Control 2 (N=66)
Number of subjects with events, n (%)	103 (47.0)	20 (30.3)
Number of censored subjects, n (%)	116 (53.0)	46 (69.7)
Kaplan-Meier estimates of Time to Event (Months) [1]		
25%-ile (95% CI)	2.7 (1.9, 3.5)	2.8 (2.6, NE)
Median (95% CI)	12.2 (7.0, 19.8)	NE (10.0, NE)
75%-ile (95% CI)	29.8 (NE, NE)	NE (NE, NE)
Stratified analysis [2]		
Hazard Ratio (95% CI) [3]	1.53 (0.94, 2.48)	
p-value [4]	0.0829	

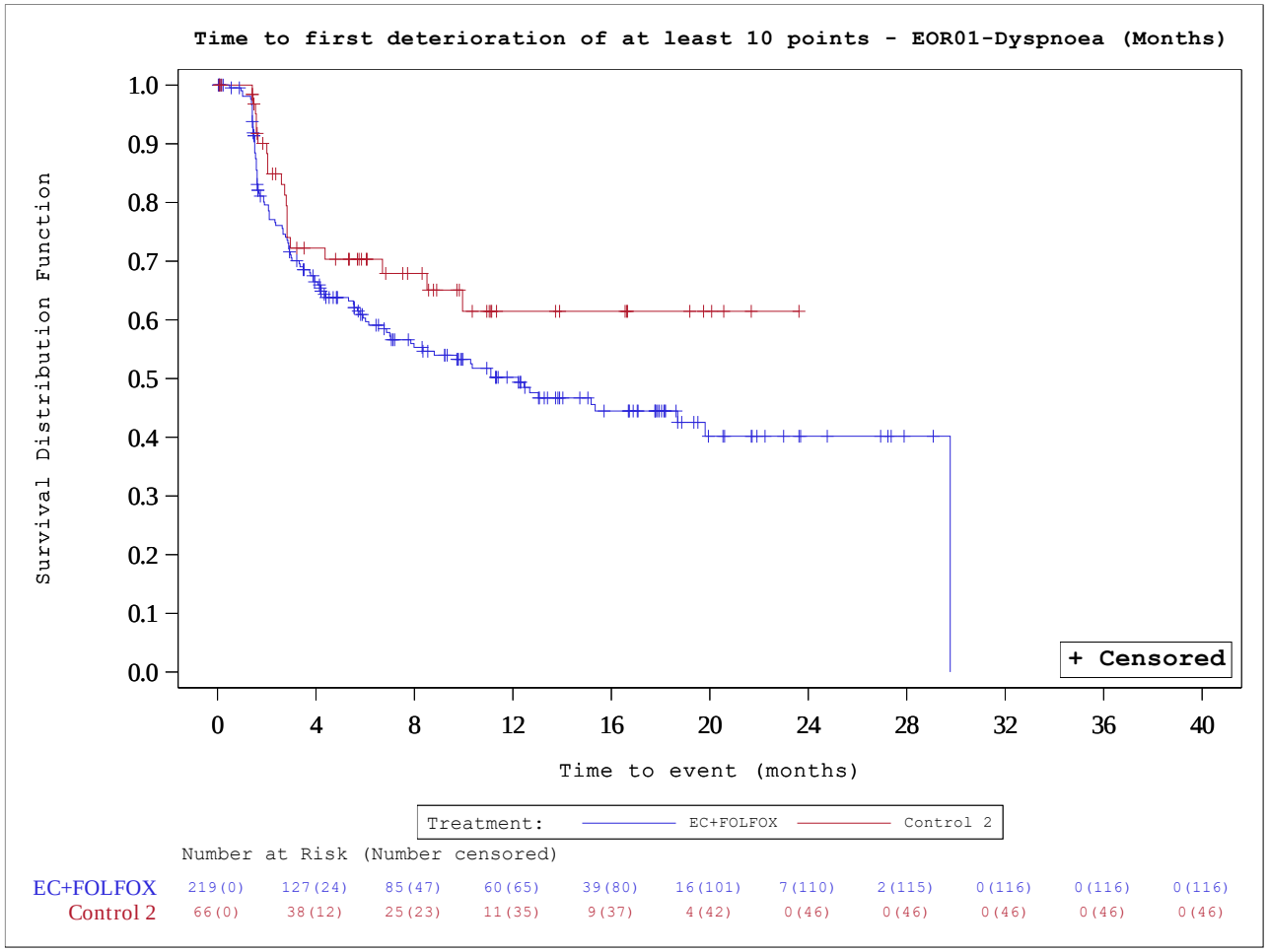
[1] Based on the Brookmeyer and Crowley method.
[2] Stratified by ECOG PS by Randomization.
[3] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[4] P-value from 2-sided log-rank test.
Including only patients from the full analysis set who completed a baseline (last PRO assessment prior to or on the first dose of study treatment) and at least 1 post-baseline PRO assessment.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Time to first deterioration of at least 10 points - EOR01-Dyspnoea (Months) - Subgroup analysis
Full Analysis Set

Subgroup Level	EC+FOLFOX (N=219) n/ N (%)	EC+FOLFOX (N=219) Median (95% CI)[1]	Control 2 (N=66) n/ N (%)	Control 2 (N=66) Median (95% CI)[1]	Unstratified analysis Hazard Ratio (95% CI)[2]	Unstratified analysis p-Value[3]	Interaction p-Value[4]
Age (Years)							0.4040
< 65	67/ 139 (48.2)	12.2 (6.9, 19.8)	14/ 41 (34.1)	NE (6.7, NE)	1.30 (0.73, 2.32)	0.3647	
>= 65	36/ 80 (45.0)	11.1 (3.9, NE)	6/ 25 (24.0)	NE (8.5, NE)	2.05 (0.86, 4.88)	0.0964	
Sex							0.9920
Male	55/ 114 (48.2)	12.2 (5.6, 29.8)	9/ 31 (29.0)	NE (10.0, NE)	1.50 (0.74, 3.05)	0.2556	
Female	48/ 105 (45.7)	11.1 (7.0, NE)	11/ 35 (31.4)	NE (8.5, NE)	1.51 (0.78, 2.91)	0.2139	
Region							0.9764
Europe	52/ 104 (50.0)	12.5 (7.9, 19.8)	11/ 38 (28.9)	NE (8.5, NE)	1.39 (0.72, 2.67)	0.3194	
USA/Canada	4/ 8 (50.0)	12.2 (2.8, NE)	2/ 6 (33.3)	NE (3.0, NE)	1.49 (0.27, 8.16)	0.6428	
Rest of World	47/ 107 (43.9)	11.1 (5.3, NE)	7/ 22 (31.8)	NE (4.4, NE)	1.57 (0.71, 3.48)	0.2639	
ECOG-PS at Randomization							0.0474
0	63/ 123 (51.2)	8.3 (5.6, 19.8)	11/ 43 (25.6)	NE (NE , NE)	2.18 (1.15, 4.14)	0.0148	
1	40/ 96 (41.7)	15.2 (8.8, NE)	9/ 23 (39.1)	NE (2.7, NE)	0.82 (0.39, 1.69)	0.5799	
Number of Organs Involved							0.1895
<= 2	51/ 110 (46.4)	15.3 (6.8, 29.8)	7/ 33 (21.2)	NE (NE , NE)	2.17 (0.99, 4.80)	0.0479	
>= 3	52/ 109 (47.7)	10.3 (5.9, 18.7)	13/ 33 (39.4)	8.5 (4.4, NE)	1.06 (0.57, 1.95)	0.8591	
Presence of Liver Metastases							0.3794
Yes	63/ 135 (46.7)	11.1 (5.9, 29.8)	14/ 40 (35.0)	NE (4.4, NE)	1.28 (0.72, 2.29)	0.4024	
No	40/ 84 (47.6)	12.7 (6.1, NE)	6/ 26 (23.1)	NE (NE , NE)	2.06 (0.87, 4.86)	0.0914	
Side of Tumor							0.2166
Left	44/ 83 (53.0)	9.7 (5.8, 18.7)	8/ 33 (24.2)	NE (NE , NE)	2.10 (0.99, 4.47)	0.0489	
Right	59/ 136 (43.4)	15.2 (6.1, NE)	12/ 33 (36.4)	NE (3.0, NE)	1.17 (0.63, 2.17)	0.6245	

[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.
[4] P-Value for interaction from Cox proportional hazards model using ties=exact option with treatment, subgroup and treatment*subgroup interaction as covariates.
Including only patients from the full analysis set who completed a baseline (last PRO assessment prior to or on the first dose of study treatment) and at least 1 post-baseline PRO assessment.
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Kaplan Meier Plot of Time to first deterioration of at least 10 points - EOR01-Dyspnoea (Months)
Full Analysis Set



Kaplan-Meier Plots for subgroups only created if p-value for interaction < 0.05.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
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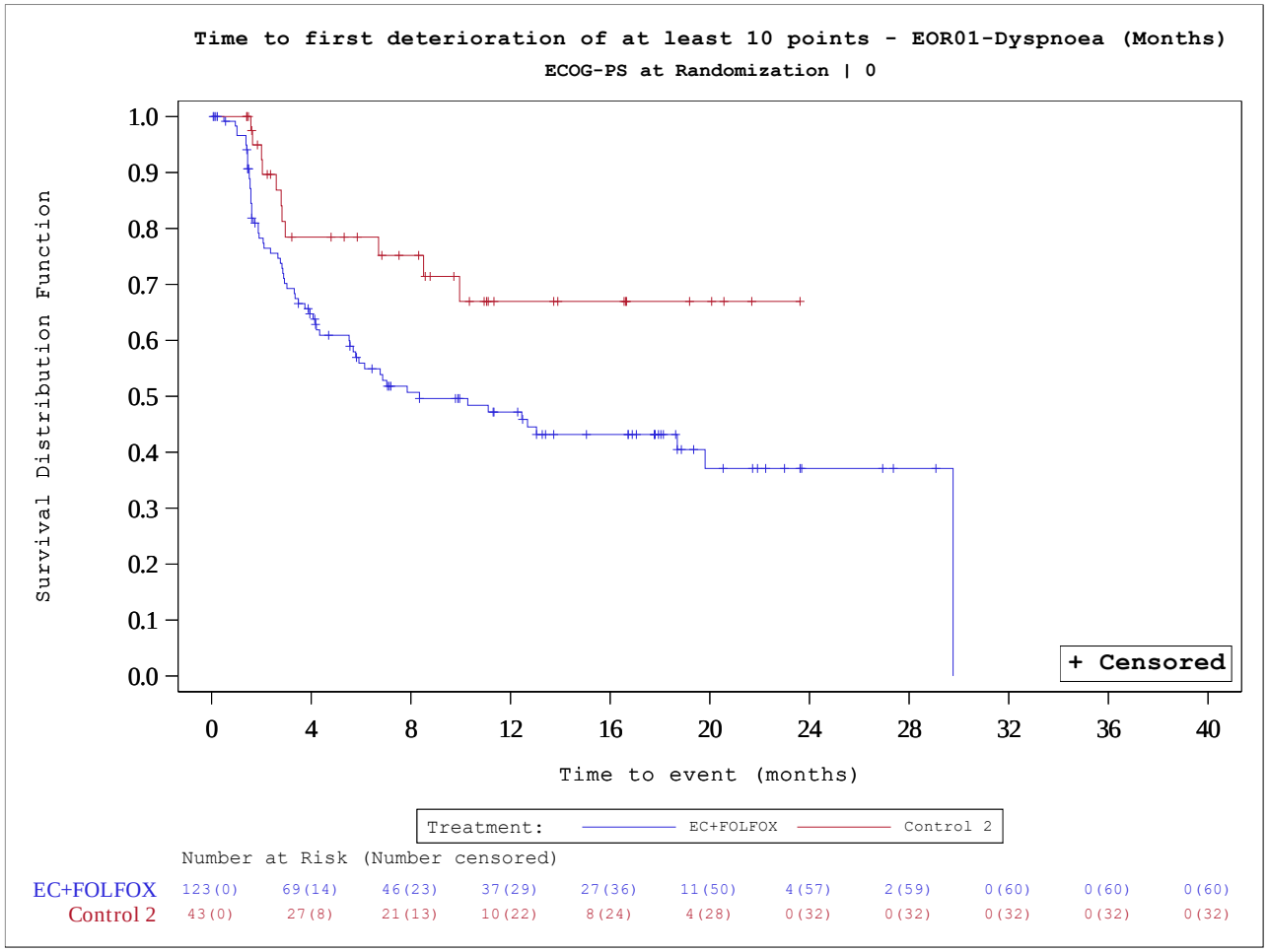
Full Analysis Set



Kaplan-Meier Plots for subgroups only created if p-value for interaction < 0.05.

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Encorafenib (PF-07263896) Protocol C4221015
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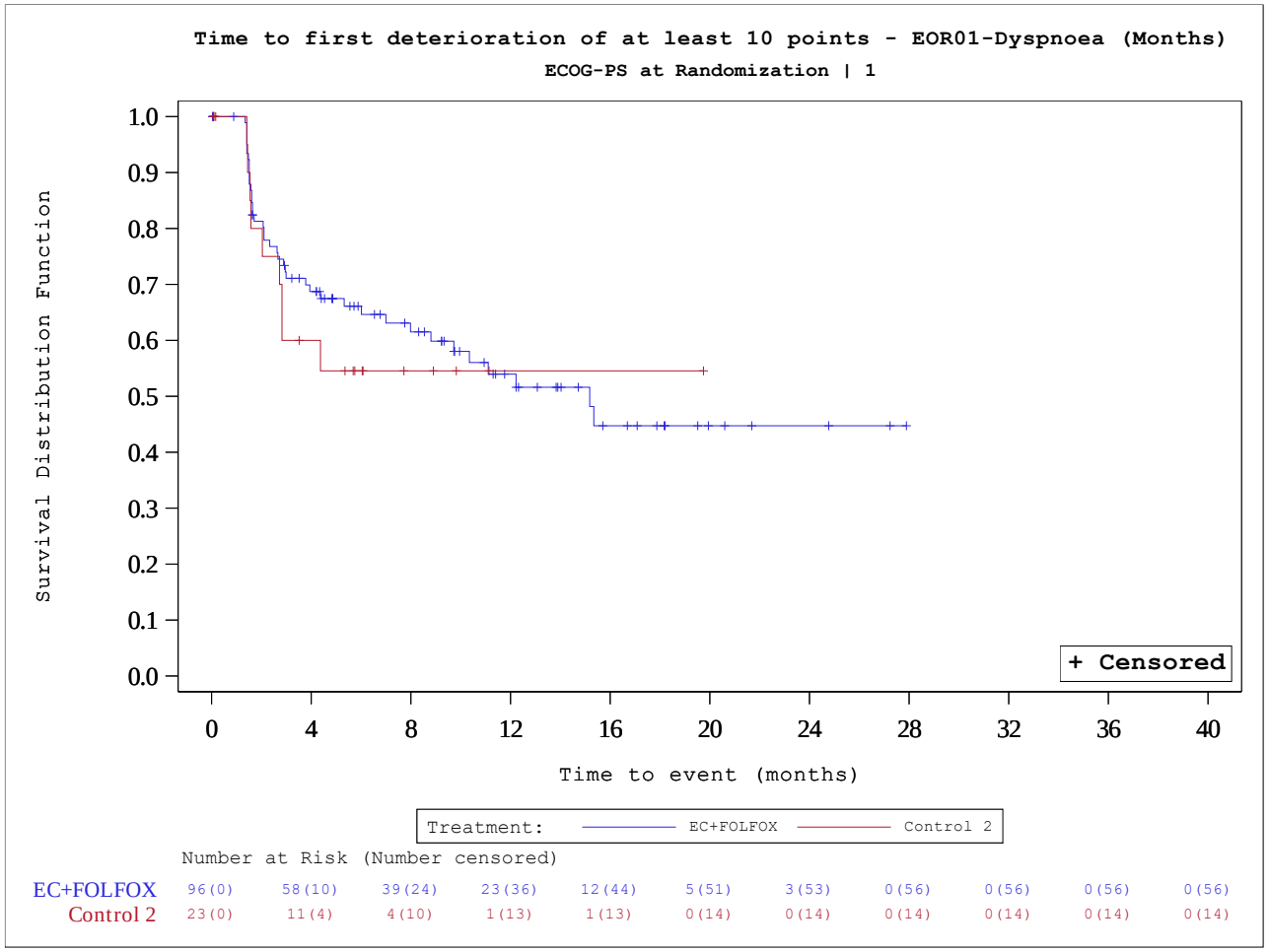
Full Analysis Set



Kaplan-Meier Plots for subgroups only created if p-value for interaction < 0.05.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Time to first improvement of at least 10 points - EOR01-Dyspnoea (Months)
Full Analysis Set

	EC+FOLFOX (N=219)	Control 2 (N=66)
Number of subjects with events, n (%)	47 (21.5)	9 (13.6)
Number of censored subjects, n (%)	172 (78.5)	57 (86.4)
Kaplan-Meier estimates of Time to Event (Months) [1]		
25%-ile (95% CI)	NE (4.9, NE)	NE (2.9, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
Stratified analysis [2]		
Hazard Ratio (95% CI) [3]	1.32 (0.64, 2.70)	
p-value [4]	0.4497	

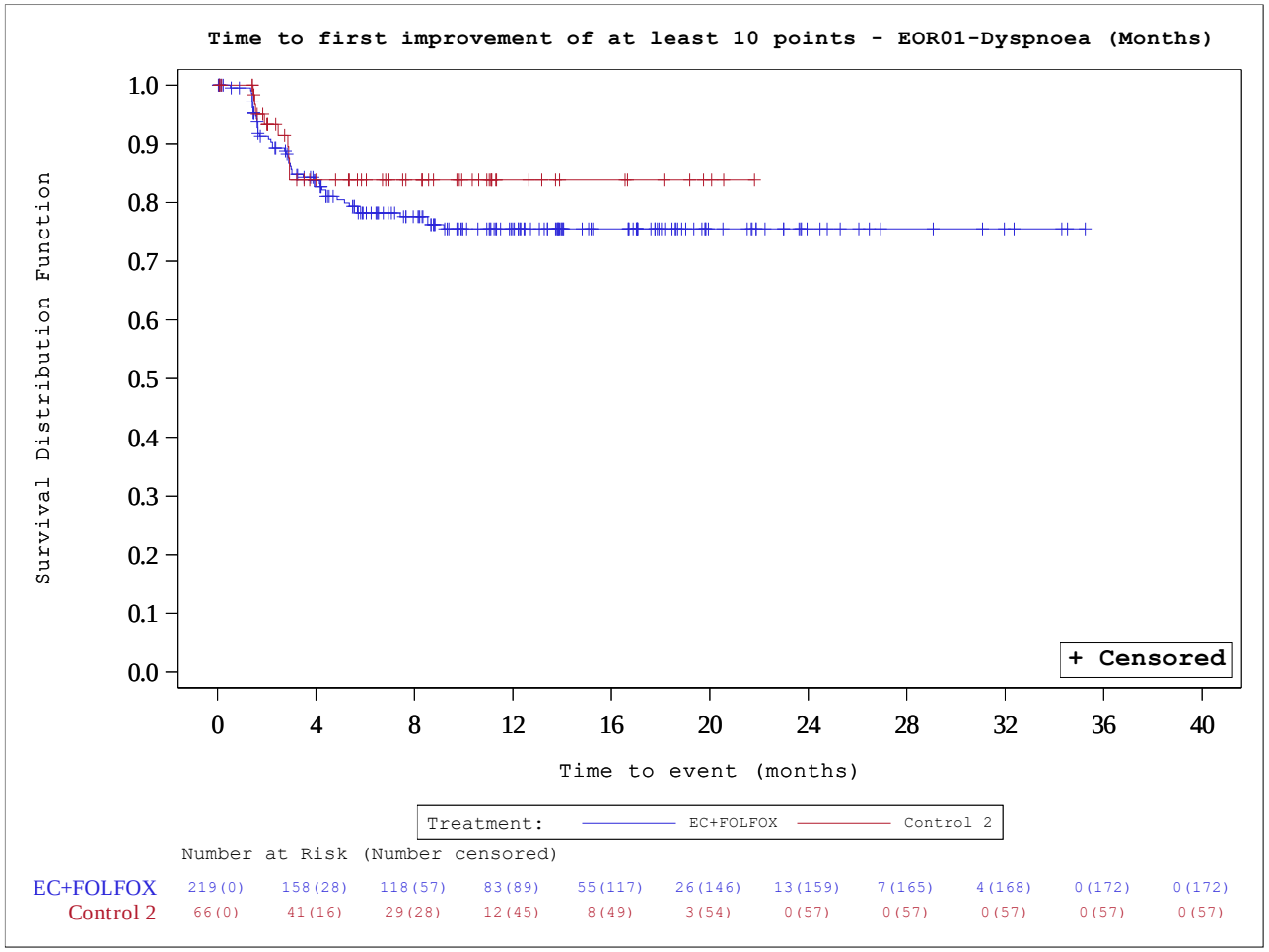
[1] Based on the Brookmeyer and Crowley method.
[2] Stratified by ECOG PS by Randomization.
[3] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio > 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[4] P-value from 2-sided log-rank test.
Including only patients from the full analysis set who completed a baseline (last PRO assessment prior to or on the first dose of study treatment) and at least 1 post-baseline PRO assessment.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Time to first improvement of at least 10 points - EOR01-Dyspnoea (Months) - Subgroup analysis
Full Analysis Set

Subgroup Level	EC+FOLFOX (N=219) n/ N (%)	EC+FOLFOX (N=219) Median (95% CI)[1]	Control 2 (N=66) n/ N (%)	Control 2 (N=66) Median (95% CI)[1]	Unstratified analysis Hazard Ratio (95% CI)[2]	Unstratified analysis p-Value[3]	Interaction p-Value[4]
Age (Years)							0.2088
< 65	33/ 139 (23.7)	NE (NE , NE)	8/ 41 (19.5)	NE (NE , NE)	1.08 (0.50, 2.34)	0.8459	
>= 65	14/ 80 (17.5)	NE (NE , NE)	1/ 25 (4.0)	NE (NE , NE)	4.26 (0.56, 32.44)	0.1256	
Sex							0.6643
Male	16/ 114 (14.0)	NE (NE , NE)	3/ 31 (9.7)	NE (NE , NE)	1.19 (0.35, 4.08)	0.7865	
Female	31/ 105 (29.5)	NE (NE , NE)	6/ 35 (17.1)	NE (NE , NE)	1.72 (0.72, 4.12)	0.2173	
Region							0.6738
Europe	24/ 104 (23.1)	NE (NE , NE)	4/ 38 (10.5)	NE (NE , NE)	1.88 (0.65, 5.43)	0.2333	
USA/Canada	1/ 8 (12.5)	NE (NE , NE)	1/ 6 (16.7)	NE (2.9, NE)	0.56 (0.03, 8.98)	0.6771	
Rest of World	22/ 107 (20.6)	NE (NE , NE)	4/ 22 (18.2)	NE (NE , NE)	1.12 (0.39, 3.26)	0.8322	
ECOG-PS at Randomization							0.7505
0	18/ 123 (14.6)	NE (NE , NE)	4/ 43 (9.3)	NE (NE , NE)	1.52 (0.51, 4.48)	0.4495	
1	29/ 96 (30.2)	NE (NE , NE)	5/ 23 (21.7)	NE (NE , NE)	1.17 (0.45, 3.03)	0.7437	
Number of Organs Involved							0.6070
<= 2	19/ 110 (17.3)	NE (NE , NE)	3/ 33 (9.1)	NE (NE , NE)	1.84 (0.55, 6.23)	0.3185	
>= 3	28/ 109 (25.7)	NE (NE , NE)	6/ 33 (18.2)	NE (NE , NE)	1.20 (0.50, 2.91)	0.6801	
Presence of Liver Metastases							0.6537
Yes	30/ 135 (22.2)	NE (NE , NE)	5/ 40 (12.5)	NE (NE , NE)	1.64 (0.64, 4.24)	0.2979	
No	17/ 84 (20.2)	NE (NE , NE)	4/ 26 (15.4)	NE (NE , NE)	1.20 (0.41, 3.58)	0.7378	
Side of Tumor							0.2410
Left	17/ 83 (20.5)	NE (NE , NE)	6/ 33 (18.2)	NE (NE , NE)	0.93 (0.37, 2.37)	0.8819	
Right	30/ 136 (22.1)	NE (NE , NE)	3/ 33 (9.1)	NE (NE , NE)	2.38 (0.73, 7.79)	0.1395	

[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio > 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.
[4] P-Value for interaction from Cox proportional hazards model using ties=exact option with treatment, subgroup and treatment*subgroup interaction as covariates.
Including only patients from the full analysis set who completed a baseline (last PRO assessment prior to or on the first dose of study treatment) and at least 1 post-baseline PRO assessment.
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Kaplan Meier Plot of Time to first improvement of at least 10 points - EOR01-Dyspnoea (Months)
Full Analysis Set



Kaplan-Meier Plots for subgroups only created if p-value for interaction < 0.05.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Time to first deterioration of at least 10 points - EOR01-Insomnia (Months)
Full Analysis Set

	EC+FOLFOX (N=219)	Control 2 (N=66)
Number of subjects with events, n (%)	97 (44.3)	23 (34.8)
Number of censored subjects, n (%)	122 (55.7)	43 (65.2)
Kaplan-Meier estimates of Time to Event (Months) [1]		
25%-ile (95% CI)	3.3 (2.8, 5.5)	2.9 (1.6, 9.8)
Median (95% CI)	17.1 (8.3, NE)	16.4 (6.7, NE)
75%-ile (95% CI)	29.8 (29.8, NE)	NE (NE, NE)
Stratified analysis [2]		
Hazard Ratio (95% CI) [3]	1.03 (0.65, 1.63)	
p-value [4]	0.8932	

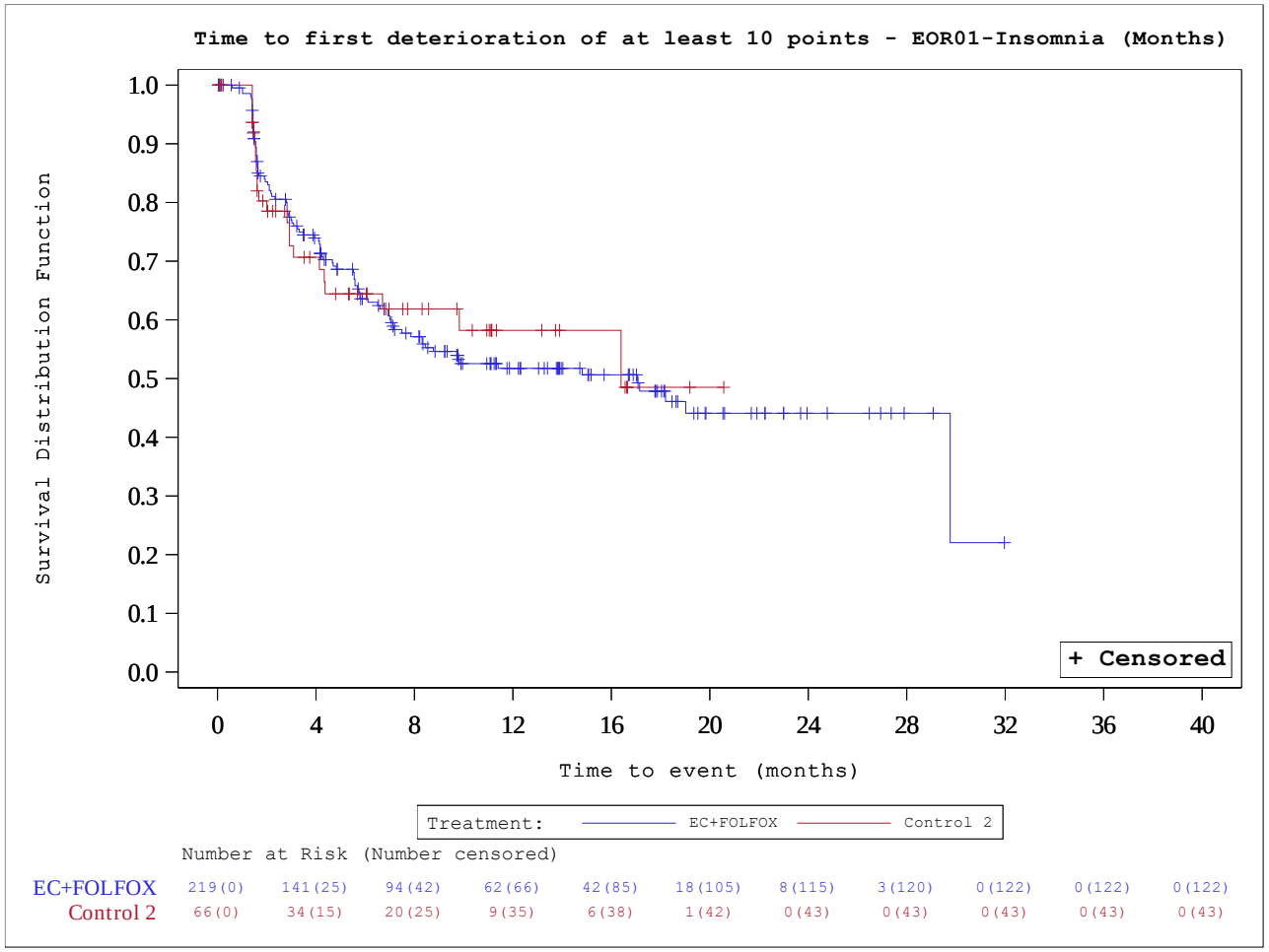
[1] Based on the Brookmeyer and Crowley method.
[2] Stratified by ECOG PS by Randomization.
[3] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[4] P-value from 2-sided log-rank test.
Including only patients from the full analysis set who completed a baseline (last PRO assessment prior to or on the first dose of study treatment) and at least 1 post-baseline PRO assessment.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Time to first deterioration of at least 10 points - EOR01-Insomnia (Months) - Subgroup analysis
Full Analysis Set

Subgroup Level	EC+FOLFOX (N=219) n/ N (%)	EC+FOLFOX (N=219) Median (95% CI)[1]	Control 2 (N=66) n/ N (%)	Control 2 (N=66) Median (95% CI)[1]	Unstratified analysis Hazard Ratio (95% CI)[2]	Unstratified analysis p-Value[3]	Interaction p-Value[4]
Age (Years)							0.2959
< 65	55/ 139 (39.6)	29.8 (9.8, NE)	14/ 41 (34.1)	16.4 (4.4, NE)	0.85 (0.47, 1.54)	0.5938	
>= 65	42/ 80 (52.5)	7.2 (4.2, 19.0)	9/ 25 (36.0)	NE (3.1, NE)	1.43 (0.70, 2.95)	0.3227	
Sex							0.4848
Male	56/ 114 (49.1)	7.5 (5.8, 29.8)	10/ 31 (32.3)	16.4 (2.8, NE)	1.24 (0.63, 2.44)	0.5242	
Female	41/ 105 (39.0)	19.0 (11.4, NE)	13/ 35 (37.1)	NE (4.4, NE)	0.86 (0.46, 1.60)	0.6280	
Region							0.8630
Europe	46/ 104 (44.2)	17.1 (8.3, NE)	13/ 38 (34.2)	NE (3.1, NE)	0.94 (0.51, 1.75)	0.8559	
USA/Canada	4/ 8 (50.0)	NE (1.6, NE)	2/ 6 (33.3)	NE (2.9, NE)	1.31 (0.24, 7.21)	0.7460	
Rest of World	47/ 107 (43.9)	9.8 (6.9, NE)	8/ 22 (36.4)	16.4 (4.4, NE)	1.06 (0.50, 2.26)	0.8784	
ECOG-PS at Randomization							0.7380
0	56/ 123 (45.5)	17.1 (8.3, NE)	15/ 43 (34.9)	NE (6.7, NE)	1.06 (0.60, 1.88)	0.8387	
1	41/ 96 (42.7)	NE (5.7, NE)	8/ 23 (34.8)	9.8 (4.3, NE)	0.98 (0.46, 2.09)	0.9604	
Number of Organs Involved							0.0324
<= 2	63/ 110 (57.3)	7.1 (5.6, 17.1)	11/ 33 (33.3)	NE (9.8, NE)	1.59 (0.83, 3.02)	0.1555	
>= 3	34/ 109 (31.2)	NE (14.8, NE)	12/ 33 (36.4)	6.7 (4.1, NE)	0.62 (0.32, 1.21)	0.1583	
Presence of Liver Metastases							0.4734
Yes	60/ 135 (44.4)	14.8 (7.0, 29.8)	15/ 40 (37.5)	NE (3.1, NE)	0.86 (0.49, 1.53)	0.6135	
No	37/ 84 (44.0)	18.2 (7.1, NE)	8/ 26 (30.8)	NE (6.7, NE)	1.32 (0.62, 2.84)	0.4689	
Side of Tumor							0.4479
Left	36/ 83 (43.4)	17.1 (7.1, NE)	9/ 33 (27.3)	NE (4.4, NE)	1.30 (0.62, 2.71)	0.4859	
Right	61/ 136 (44.9)	14.8 (7.0, NE)	14/ 33 (42.4)	16.4 (3.1, NE)	0.86 (0.48, 1.55)	0.6252	

[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.
[4] P-Value for interaction from Cox proportional hazards model using ties=exact option with treatment, subgroup and treatment*subgroup interaction as covariates.
Including only patients from the full analysis set who completed a baseline (last PRO assessment prior to or on the first dose of study treatment) and at least 1 post-baseline PRO assessment.
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Kaplan Meier Plot of Time to first deterioration of at least 10 points - EOR01-Insomnia (Months)
Full Analysis Set



Kaplan-Meier Plots for subgroups only created if p-value for interaction < 0.05.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
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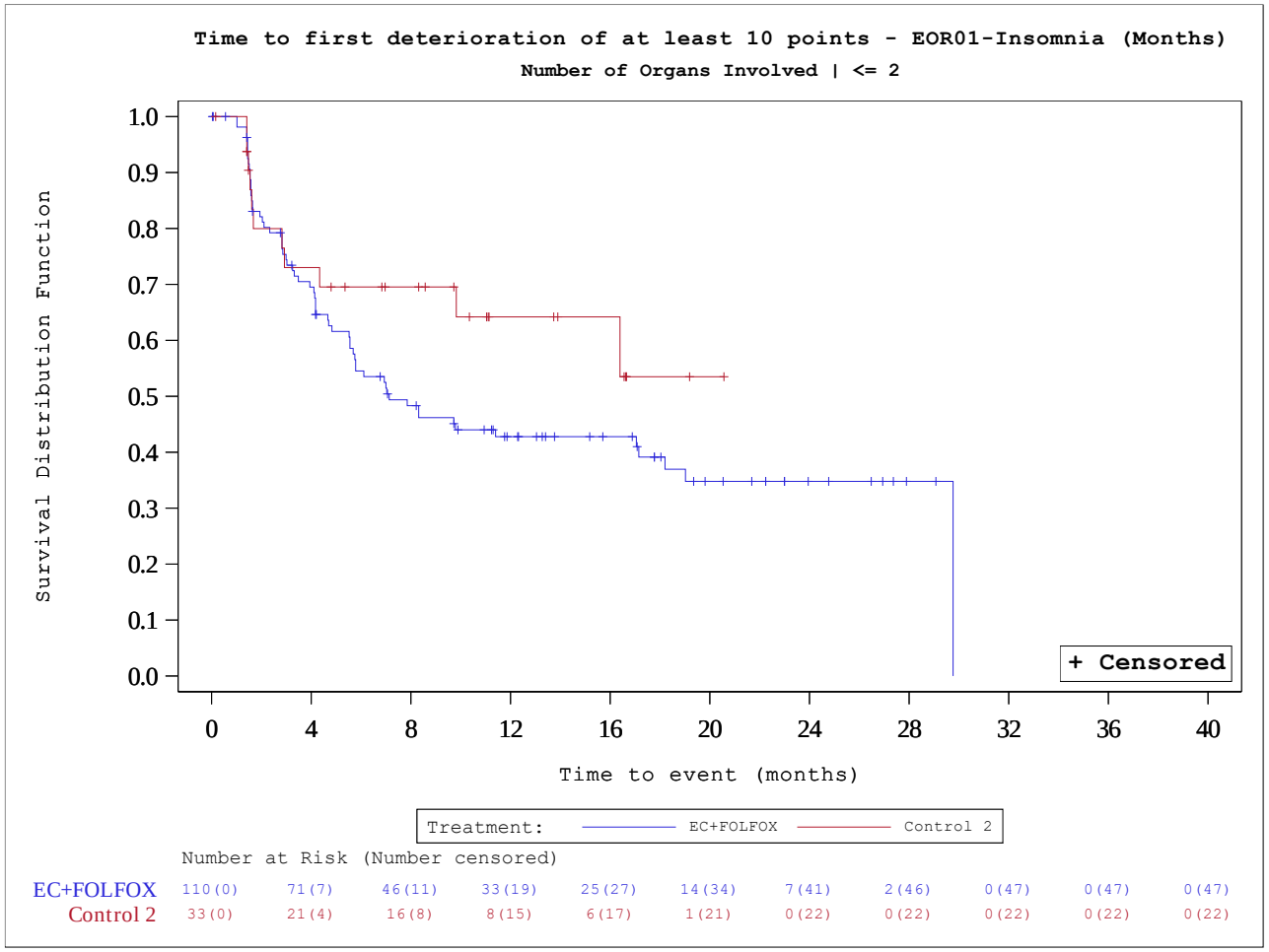

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Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
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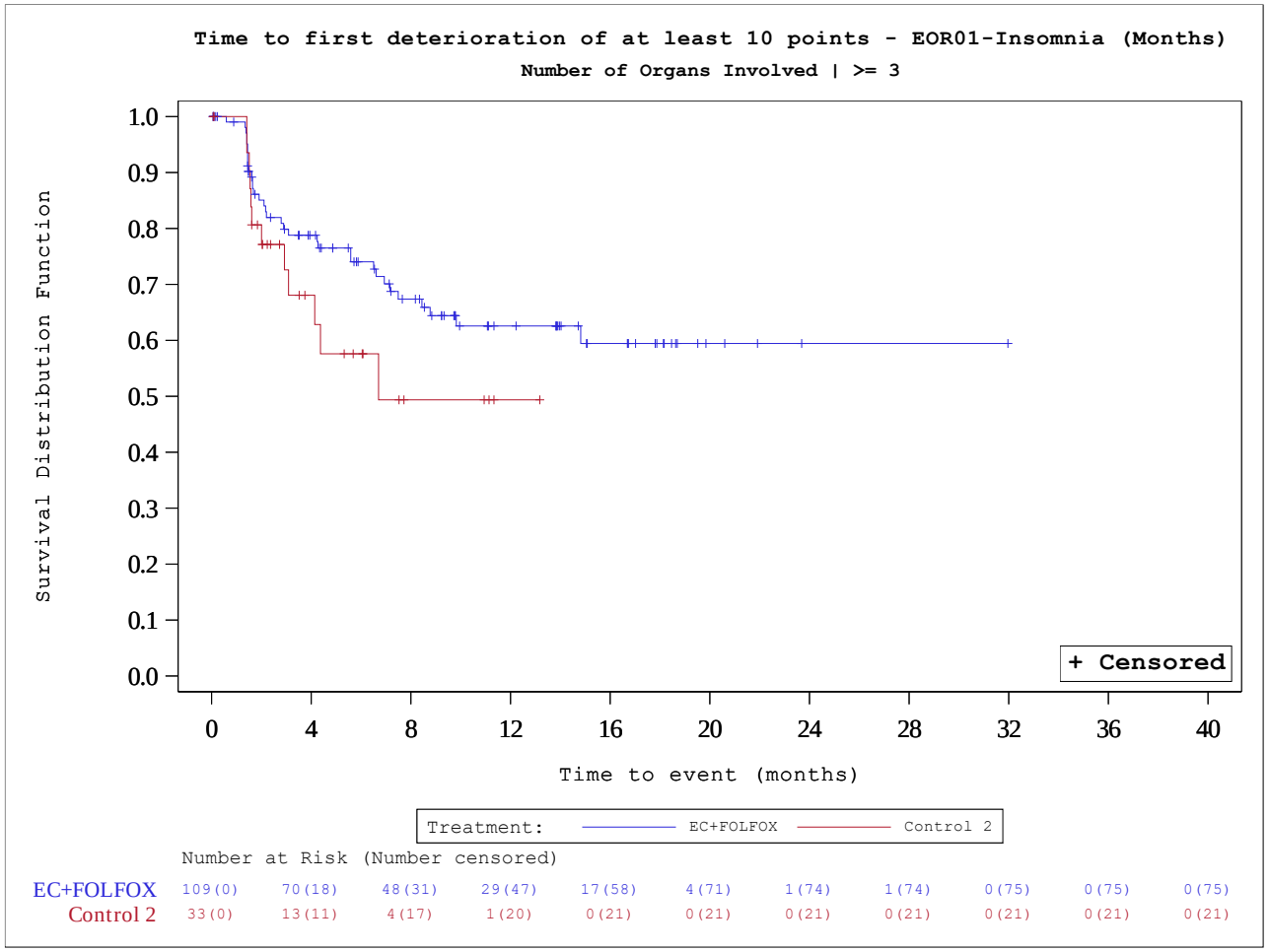
Full Analysis Set



Kaplan-Meier Plots for subgroups only created if p-value for interaction < 0.05.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Time to first improvement of at least 10 points - EOR01-Insomnia (Months)
Full Analysis Set

	EC+FOLFOX (N=219)	Control 2 (N=66)
Number of subjects with events, n (%)	97 (44.3)	18 (27.3)
Number of censored subjects, n (%)	122 (55.7)	48 (72.7)
Kaplan-Meier estimates of Time to Event (Months) [1]		
25%-ile (95% CI)	2.1 (1.6, 3.1)	5.5 (1.7, NE)
Median (95% CI)	16.9 (7.1, NE)	NE (15.3, NE)
75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
Stratified analysis [2]		
Hazard Ratio (95% CI) [3]	1.65 (0.99, 2.73)	
p-value [4]	0.0496	

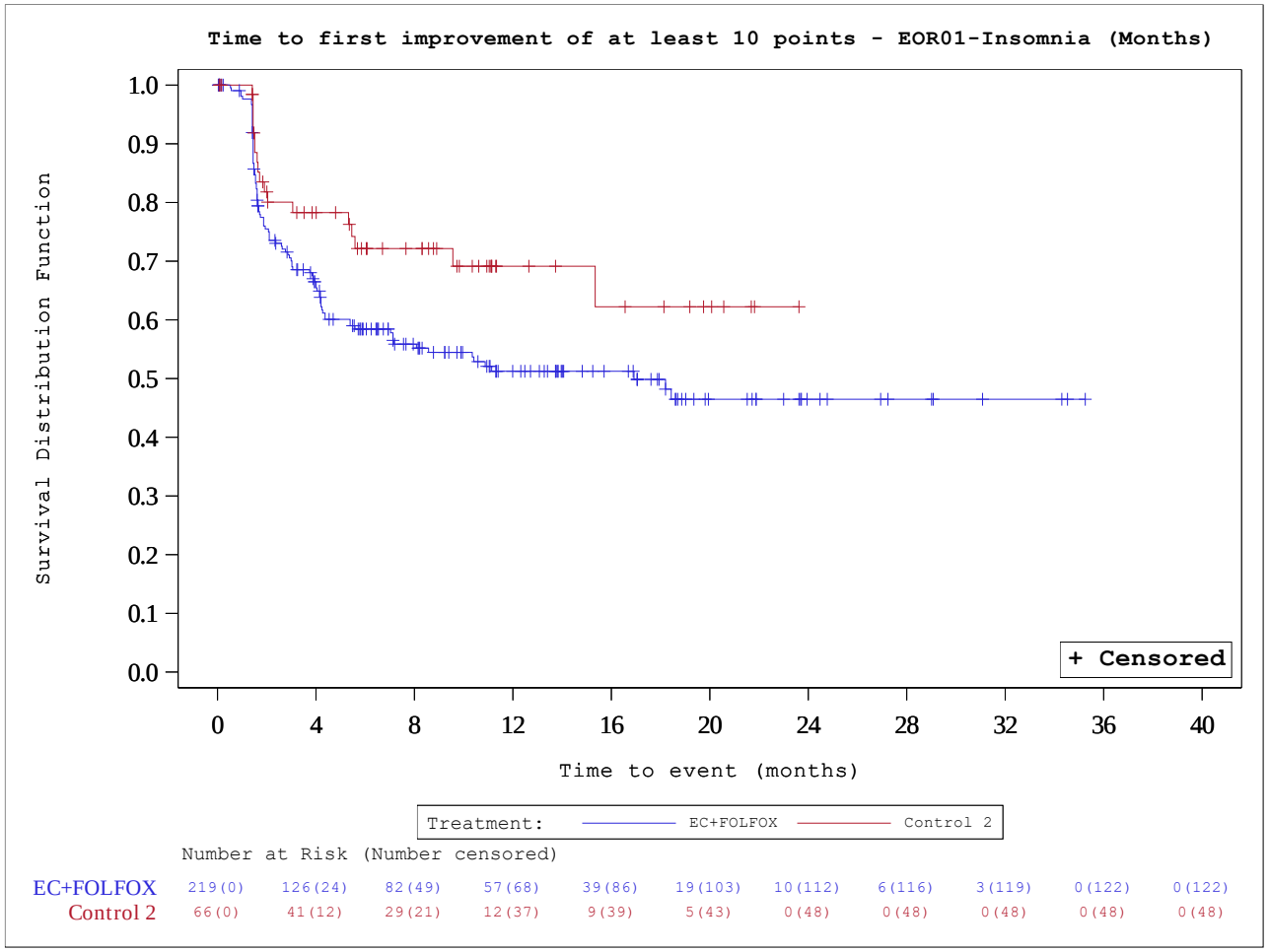
[1] Based on the Brookmeyer and Crowley method.
[2] Stratified by ECOG PS by Randomization.
[3] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio > 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[4] P-value from 2-sided log-rank test.
Including only patients from the full analysis set who completed a baseline (last PRO assessment prior to or on the first dose of study treatment) and at least 1 post-baseline PRO assessment.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Time to first improvement of at least 10 points - EOR01-Insomnia (Months) - Subgroup analysis
Full Analysis Set

Subgroup Level	EC+FOLFOX (N=219) n/ N (%)	EC+FOLFOX (N=219) Median (95% CI)[1]	Control 2 (N=66) n/ N (%)	Control 2 (N=66) Median (95% CI)[1]	Unstratified analysis Hazard Ratio (95% CI)[2]	Unstratified analysis p-Value[3]	Interaction p-Value[4]
Age (Years)							0.0760
< 65	71/ 139 (51.1)	7.1 (4.2, NE)	10/ 41 (24.4)	NE (NE , NE)	2.35 (1.21, 4.55)	0.0092	
>= 65	26/ 80 (32.5)	NE (18.4, NE)	8/ 25 (32.0)	15.3 (9.6, NE)	0.90 (0.41, 2.00)	0.8137	
Sex							0.1783
Male	42/ 114 (36.8)	NE (8.1, NE)	9/ 31 (29.0)	NE (5.6, NE)	1.19 (0.58, 2.44)	0.6326	
Female	55/ 105 (52.4)	8.6 (4.2, 18.2)	9/ 35 (25.7)	NE (15.3, NE)	2.34 (1.15, 4.73)	0.0148	
Region							0.2977
Europe	50/ 104 (48.1)	10.4 (4.2, NE)	9/ 38 (23.7)	15.3 (15.3, NE)	2.04 (1.00, 4.15)	0.0446	
USA/Canada	5/ 8 (62.5)	4.3 (3.0, NE)	1/ 6 (16.7)	NE (NE , NE)	4.27 (0.49, 36.84)	0.1512	
Rest of World	42/ 107 (39.3)	NE (8.1, NE)	8/ 22 (36.4)	NE (3.1, NE)	1.09 (0.51, 2.32)	0.8236	
ECOG-PS at Randomization							0.9455
0	51/ 123 (41.5)	NE (7.0, NE)	12/ 43 (27.9)	NE (15.3, NE)	1.63 (0.87, 3.07)	0.1220	
1	46/ 96 (47.9)	10.4 (4.2, NE)	6/ 23 (26.1)	NE (3.1, NE)	1.67 (0.71, 3.92)	0.2261	
Number of Organs Involved							0.7785
<= 2	38/ 110 (34.5)	NE (NE , NE)	6/ 33 (18.2)	NE (15.3, NE)	1.92 (0.81, 4.55)	0.1286	
>= 3	59/ 109 (54.1)	5.4 (3.0, 10.9)	12/ 33 (36.4)	NE (5.3, NE)	1.63 (0.88, 3.03)	0.1181	
Presence of Liver Metastases							0.0545
Yes	55/ 135 (40.7)	NE (7.1, NE)	14/ 40 (35.0)	15.3 (5.6, NE)	1.15 (0.64, 2.08)	0.6269	
No	42/ 84 (50.0)	10.9 (4.3, NE)	4/ 26 (15.4)	NE (NE , NE)	3.68 (1.32, 10.28)	0.0076	
Side of Tumor							0.9548
Left	42/ 83 (50.6)	7.0 (3.7, NE)	10/ 33 (30.3)	NE (5.3, NE)	1.74 (0.87, 3.46)	0.1103	
Right	55/ 136 (40.4)	18.2 (8.6, NE)	8/ 33 (24.2)	NE (15.3, NE)	1.78 (0.85, 3.73)	0.1223	

[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio > 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.
[4] P-Value for interaction from Cox proportional hazards model using ties=exact option with treatment, subgroup and treatment*subgroup interaction as covariates.
Including only patients from the full analysis set who completed a baseline (last PRO assessment prior to or on the first dose of study treatment) and at least 1 post-baseline PRO assessment.
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Kaplan Meier Plot of Time to first improvement of at least 10 points - EOR01-Insomnia (Months)
Full Analysis Set



Kaplan-Meier Plots for subgroups only created if p-value for interaction < 0.05.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Time to first deterioration of at least 10 points - EOR01-Appetite Loss (Months)
Full Analysis Set

	EC+FOLFOX (N=219)	Control 2 (N=66)
Number of subjects with events, n (%)	128 (58.4)	22 (33.3)
Number of censored subjects, n (%)	91 (41.6)	44 (66.7)
Kaplan-Meier estimates of Time to Event (Months) [1]		
25%-ile (95% CI)	1.6 (1.5, 2.0)	4.4 (2.9, 9.3)
Median (95% CI)	4.4 (3.2, 6.9)	NE (8.3, NE)
75%-ile (95% CI)	NE (18.1, NE)	NE (NE, NE)
Stratified analysis [2]		
Hazard Ratio (95% CI) [3]	2.03 (1.29, 3.20)	
p-value [4]	0.0019	

[1] Based on the Brookmeyer and Crowley method.
[2] Stratified by ECOG PS by Randomization.
[3] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[4] P-value from 2-sided log-rank test.
Including only patients from the full analysis set who completed a baseline (last PRO assessment prior to or on the first dose of study treatment) and at least 1 post-baseline PRO assessment.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Time to first deterioration of at least 10 points - EOR01-Appetite Loss (Months) - Subgroup analysis
Full Analysis Set

Subgroup Level	EC+FOLFOX (N=219) n/ N (%)	EC+FOLFOX (N=219) Median (95% CI)[1]	Control 2 (N=66) n/ N (%)	Control 2 (N=66) Median (95% CI)[1]	Unstratified analysis Hazard Ratio (95% CI)[2]	Unstratified analysis p-Value[3]	Interaction p-Value[4]
Age (Years)							0.9647
< 65	81/ 139 (58.3)	4.4 (2.9, 9.7)	14/ 41 (34.1)	NE (5.6, NE)	1.98 (1.12, 3.50)	0.0161	
>= 65	47/ 80 (58.8)	4.0 (2.9, 8.4)	8/ 25 (32.0)	NE (7.2, NE)	2.03 (0.96, 4.31)	0.0599	
Sex							0.1588
Male	65/ 114 (57.0)	4.4 (2.9, 9.7)	13/ 31 (41.9)	7.2 (4.4, NE)	1.47 (0.81, 2.67)	0.2020	
Female	63/ 105 (60.0)	4.4 (2.9, 8.5)	9/ 35 (25.7)	NE (9.3, NE)	2.84 (1.41, 5.71)	0.0022	
Region							0.5139
Europe	62/ 104 (59.6)	4.7 (3.0, 9.7)	10/ 38 (26.3)	NE (9.3, NE)	2.51 (1.28, 4.90)	0.0054	
USA/Canada	5/ 8 (62.5)	3.8 (1.6, NE)	2/ 6 (33.3)	NE (2.9, NE)	2.38 (0.46, 12.36)	0.2858	
Rest of World	61/ 107 (57.0)	4.0 (2.9, 9.7)	10/ 22 (45.5)	8.3 (3.0, NE)	1.46 (0.75, 2.86)	0.2645	
ECOG-PS at Randomization							0.4524
0	72/ 123 (58.5)	4.0 (2.8, 9.7)	17/ 43 (39.5)	NE (5.8, NE)	1.82 (1.07, 3.09)	0.0248	
1	56/ 96 (58.3)	4.5 (3.3, 9.7)	5/ 23 (21.7)	NE (9.7, NE)	2.68 (1.07, 6.70)	0.0278	
Number of Organs Involved							0.3468
<= 2	71/ 110 (64.5)	3.3 (2.9, 5.8)	11/ 33 (33.3)	NE (9.3, NE)	2.50 (1.32, 4.72)	0.0035	
>= 3	57/ 109 (52.3)	6.8 (3.3, 11.0)	11/ 33 (33.3)	NE (4.4, NE)	1.58 (0.83, 3.03)	0.1638	
Presence of Liver Metastases							0.0781
Yes	73/ 135 (54.1)	5.6 (2.9, 12.9)	16/ 40 (40.0)	8.3 (5.6, NE)	1.46 (0.85, 2.52)	0.1691	
No	55/ 84 (65.5)	4.0 (2.9, 6.1)	6/ 26 (23.1)	NE (9.7, NE)	3.61 (1.55, 8.40)	0.0014	
Side of Tumor							0.9768
Left	45/ 83 (54.2)	4.7 (2.9, NE)	10/ 33 (30.3)	NE (5.8, NE)	1.99 (1.00, 3.96)	0.0444	
Right	83/ 136 (61.0)	4.2 (2.9, 6.8)	12/ 33 (36.4)	9.7 (7.2, NE)	2.00 (1.09, 3.66)	0.0224	

[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.
[4] P-Value for interaction from Cox proportional hazards model using ties=exact option with treatment, subgroup and treatment*subgroup interaction as covariates.
Including only patients from the full analysis set who completed a baseline (last PRO assessment prior to or on the first dose of study treatment) and at least 1 post-baseline PRO assessment.
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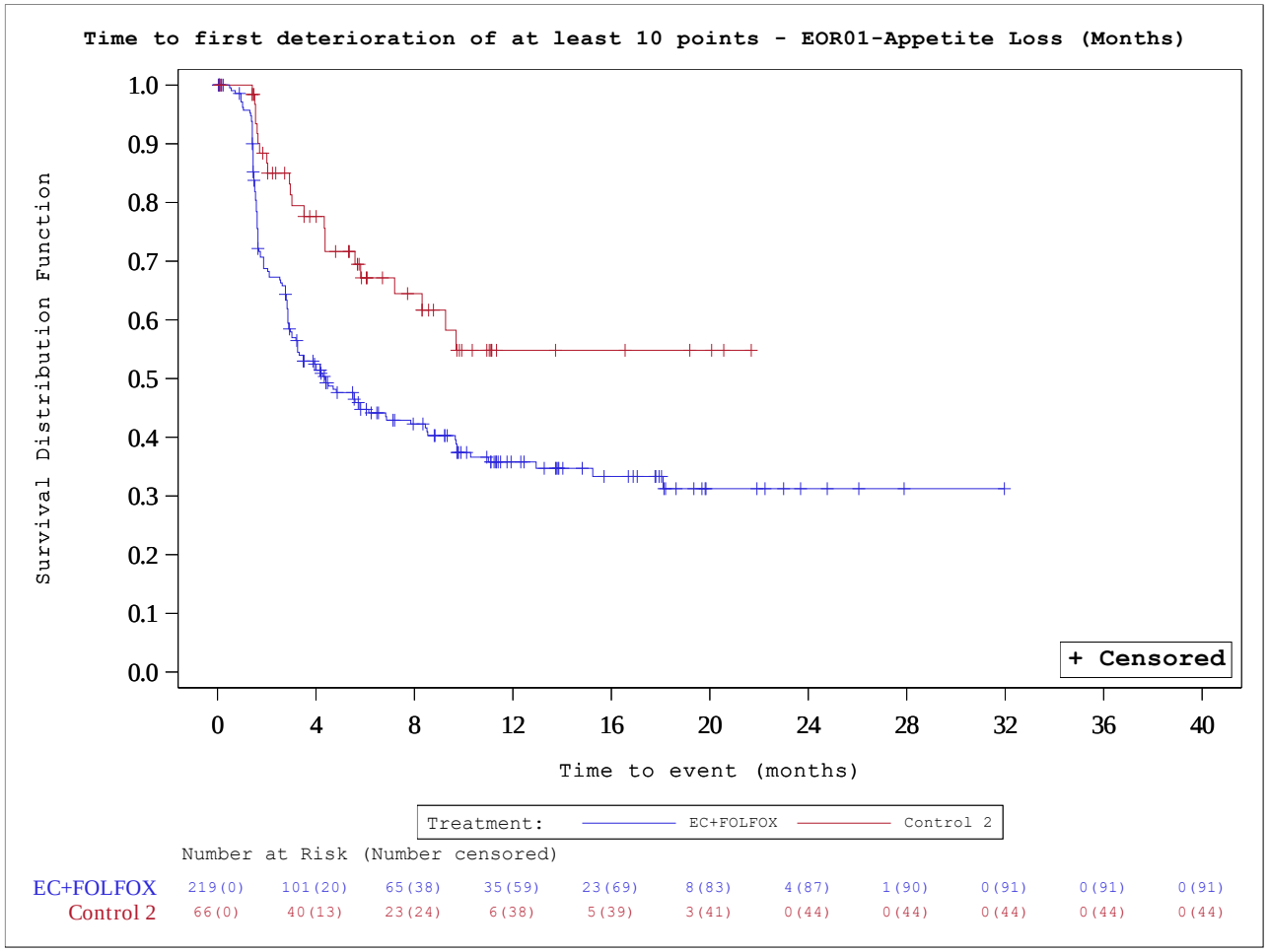
Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Kaplan Meier Plot of Time to first deterioration of at least 10 points - EOR01-Appetite Loss (Months)
Full Analysis Set



Kaplan-Meier Plots for subgroups only created if p-value for interaction < 0.05.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Time to first improvement of at least 10 points - EOR01-Appetite Loss (Months)
Full Analysis Set

	EC+FOLFOX (N=219)	Control 2 (N=66)
Number of subjects with events, n (%)	71 (32.4)	12 (18.2)
Number of censored subjects, n (%)	148 (67.6)	54 (81.8)
Kaplan-Meier estimates of Time to Event (Months) [1]		
25%-ile (95% CI)	4.4 (3.0, 8.3)	NE (4.7, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
Stratified analysis [2]		
Hazard Ratio (95% CI) [3]	1.66 (0.90, 3.07)	
p-value [4]	0.1030	

[1] Based on the Brookmeyer and Crowley method.
[2] Stratified by ECOG PS by Randomization.
[3] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio > 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[4] P-value from 2-sided log-rank test.
Including only patients from the full analysis set who completed a baseline (last PRO assessment prior to or on the first dose of study treatment) and at least 1 post-baseline PRO assessment.

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Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Time to first improvement of at least 10 points - EOR01-Appetite Loss (Months) - Subgroup analysis
Full Analysis Set

Subgroup Level	EC+FOLFOX (N=219) n/ N (%)	EC+FOLFOX (N=219) Median (95% CI)[1]	Control 2 (N=66) n/ N (%)	Control 2 (N=66) Median (95% CI)[1]	Unstratified analysis Hazard Ratio (95% CI)[2]	Unstratified analysis p-Value[3]	Interaction p-Value[4]
Age (Years)							0.8917
< 65	49/ 139 (35.3)	NE (NE , NE)	8/ 41 (19.5)	NE (NE , NE)	1.81 (0.86, 3.83)	0.1131	
>= 65	22/ 80 (27.5)	NE (NE , NE)	4/ 25 (16.0)	NE (NE , NE)	1.60 (0.55, 4.65)	0.3813	
Sex							0.8869
Male	30/ 114 (26.3)	NE (NE , NE)	4/ 31 (12.9)	NE (NE , NE)	1.96 (0.69, 5.57)	0.1964	
Female	41/ 105 (39.0)	NE (8.5, NE)	8/ 35 (22.9)	NE (NE , NE)	1.75 (0.82, 3.74)	0.1420	
Region							0.8866
Europe	33/ 104 (31.7)	NE (NE , NE)	6/ 38 (15.8)	NE (NE , NE)	1.81 (0.76, 4.32)	0.1737	
USA/Canada	3/ 8 (37.5)	NE (4.2, NE)	1/ 6 (16.7)	NE (NE , NE)	2.69 (0.28, 26.26)	0.3753	
Rest of World	35/ 107 (32.7)	NE (11.2, NE)	5/ 22 (22.7)	NE (NE , NE)	1.49 (0.58, 3.81)	0.4001	
ECOG-PS at Randomization							0.4526
0	34/ 123 (27.6)	NE (NE , NE)	6/ 43 (14.0)	NE (NE , NE)	2.08 (0.87, 4.94)	0.0913	
1	37/ 96 (38.5)	NE (8.5, NE)	6/ 23 (26.1)	NE (3.1, NE)	1.27 (0.54, 3.02)	0.5835	
Number of Organs Involved							0.2740
<= 2	29/ 110 (26.4)	NE (NE , NE)	3/ 33 (9.1)	NE (NE , NE)	2.90 (0.88, 9.54)	0.0649	
>= 3	42/ 109 (38.5)	NE (8.4, NE)	9/ 33 (27.3)	NE (5.3, NE)	1.33 (0.65, 2.74)	0.4318	
Presence of Liver Metastases							0.3143
Yes	50/ 135 (37.0)	NE (9.8, NE)	10/ 40 (25.0)	NE (NE , NE)	1.43 (0.73, 2.83)	0.2937	
No	21/ 84 (25.0)	NE (NE , NE)	2/ 26 (7.7)	NE (NE , NE)	3.33 (0.78, 14.22)	0.0840	
Side of Tumor							0.7778
Left	30/ 83 (36.1)	NE (9.8, NE)	6/ 33 (18.2)	NE (NE , NE)	1.94 (0.81, 4.67)	0.1280	
Right	41/ 136 (30.1)	NE (NE , NE)	6/ 33 (18.2)	NE (NE , NE)	1.63 (0.69, 3.85)	0.2581	

[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio > 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.
[4] P-Value for interaction from Cox proportional hazards model using ties=exact option with treatment, subgroup and treatment*subgroup interaction as covariates.
Including only patients from the full analysis set who completed a baseline (last PRO assessment prior to or on the first dose of study treatment) and at least 1 post-baseline PRO assessment.
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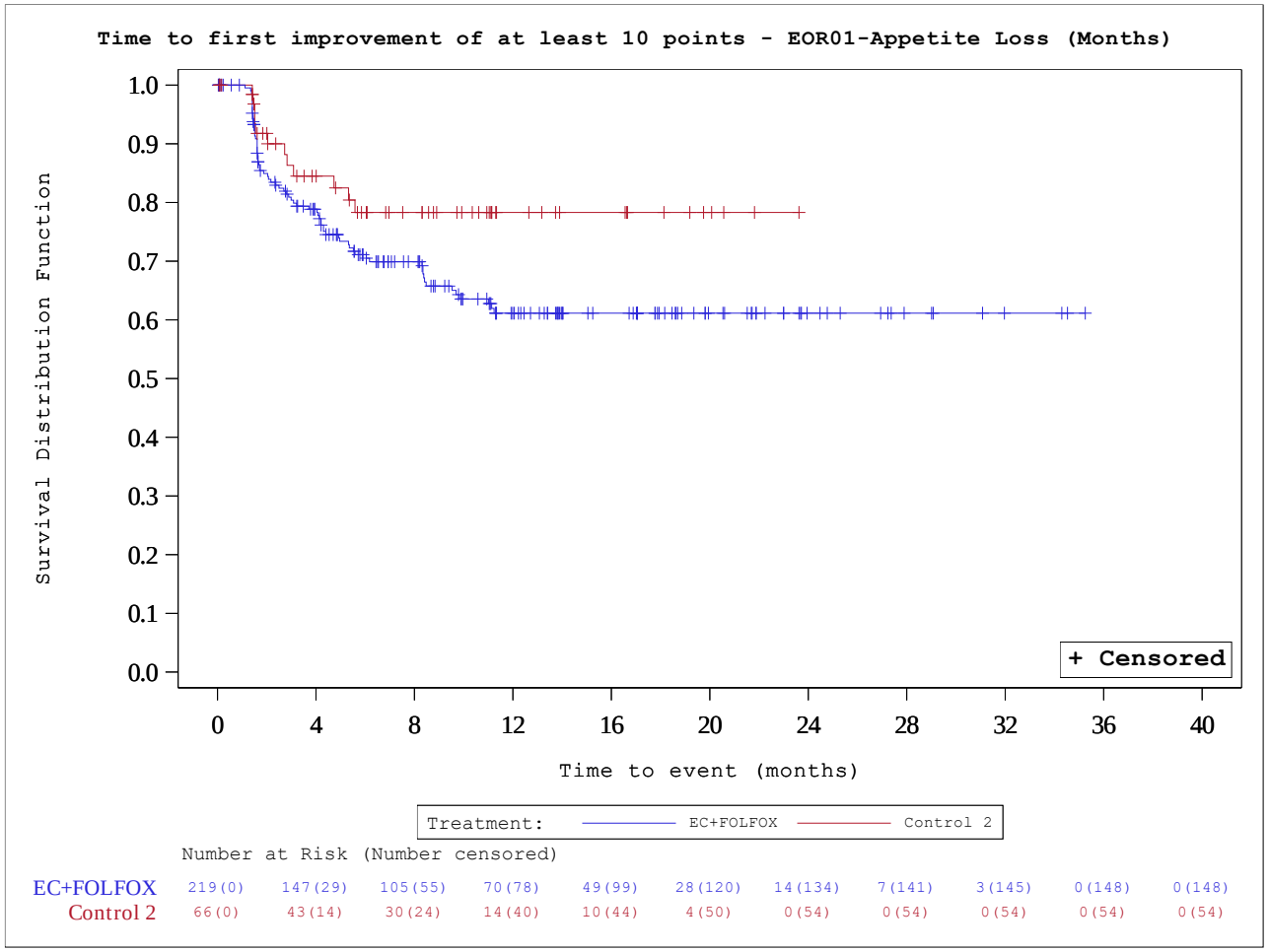
Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Kaplan Meier Plot of Time to first improvement of at least 10 points - EOR01-Appetite Loss (Months)
Full Analysis Set



Kaplan-Meier Plots for subgroups only created if p-value for interaction < 0.05.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Time to first deterioration of at least 10 points - EOR01-Constipation (Months)
Full Analysis Set

	EC+FOLFOX (N=219)	Control 2 (N=66)
Number of subjects with events, n (%)	96 (43.8)	20 (30.3)
Number of censored subjects, n (%)	123 (56.2)	46 (69.7)
Kaplan-Meier estimates of Time to Event (Months) [1]		
25%-ile (95% CI)	3.0 (2.2, 4.4)	7.1 (4.4, 12.6)
Median (95% CI)	16.7 (8.6, NE)	15.5 (9.7, NE)
75%-ile (95% CI)	NE (NE, NE)	NE (15.5, NE)
Stratified analysis [2]		
Hazard Ratio (95% CI) [3]	1.33 (0.82, 2.16)	
p-value [4]	0.2522	

[1] Based on the Brookmeyer and Crowley method.
[2] Stratified by ECOG PS by Randomization.
[3] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[4] P-value from 2-sided log-rank test.
Including only patients from the full analysis set who completed a baseline (last PRO assessment prior to or on the first dose of study treatment) and at least 1 post-baseline PRO assessment.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
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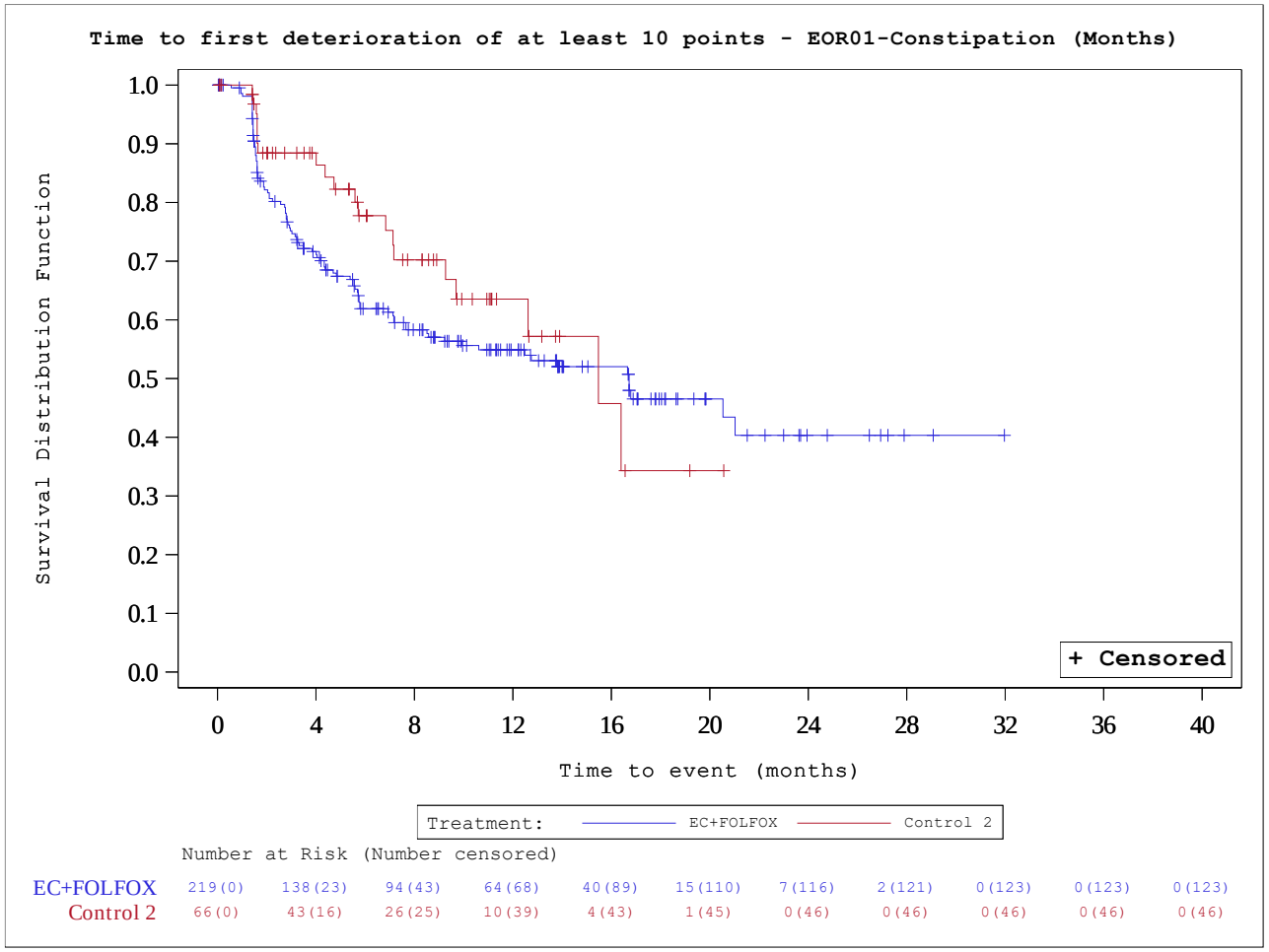
Time to first deterioration of at least 10 points - EOR01-Constipation (Months) - Subgroup analysis
Full Analysis Set

Subgroup Level	EC+FOLFOX (N=219) n/ N (%)	EC+FOLFOX (N=219) Median (95% CI)[1]	Control 2 (N=66) n/ N (%)	Control 2 (N=66) Median (95% CI)[1]	Unstratified analysis Hazard Ratio (95% CI)[2]	Unstratified analysis p-Value[3]	Interaction p-Value[4]
Age (Years)							0.4588
< 65	61/ 139 (43.9)	16.7 (9.2, NE)	14/ 41 (34.1)	15.5 (9.7, NE)	1.16 (0.64, 2.07)	0.6291	
>= 65	35/ 80 (43.8)	16.7 (5.6, NE)	6/ 25 (24.0)	NE (9.3, NE)	1.81 (0.76, 4.32)	0.1753	
Sex							0.9537
Male	49/ 114 (43.0)	16.7 (7.7, NE)	9/ 31 (29.0)	15.5 (12.6, NE)	1.33 (0.65, 2.71)	0.4332	
Female	47/ 105 (44.8)	16.7 (7.1, NE)	11/ 35 (31.4)	NE (7.2, NE)	1.37 (0.71, 2.66)	0.3416	
Region							0.2888
Europe	46/ 104 (44.2)	21.0 (7.7, NE)	8/ 38 (21.1)	15.5 (12.6, NE)	1.95 (0.92, 4.13)	0.0776	
USA/Canada	2/ 8 (25.0)	NE (5.6, NE)	2/ 6 (33.3)	NE (7.1, NE)	0.58 (0.08, 4.14)	0.5815	
Rest of World	48/ 107 (44.9)	16.7 (7.1, 20.5)	10/ 22 (45.5)	16.4 (4.7, NE)	0.89 (0.44, 1.77)	0.7300	
ECOG-PS at Randomization							0.5894
0	55/ 123 (44.7)	16.7 (8.5, NE)	15/ 43 (34.9)	15.5 (12.6, NE)	1.20 (0.67, 2.13)	0.5425	
1	41/ 96 (42.7)	12.7 (7.2, NE)	5/ 23 (21.7)	9.7 (9.3, NE)	1.69 (0.67, 4.30)	0.2632	
Number of Organs Involved							0.9423
<= 2	55/ 110 (50.0)	16.7 (5.6, NE)	12/ 33 (36.4)	15.5 (9.3, NE)	1.35 (0.72, 2.53)	0.3504	
>= 3	41/ 109 (37.6)	NE (9.2, NE)	8/ 33 (24.2)	12.6 (12.6, NE)	1.29 (0.60, 2.77)	0.5079	
Presence of Liver Metastases							0.7016
Yes	57/ 135 (42.2)	16.7 (8.5, NE)	12/ 40 (30.0)	12.6 (7.1, NE)	1.22 (0.65, 2.28)	0.5307	
No	39/ 84 (46.4)	16.7 (6.9, NE)	8/ 26 (30.8)	16.4 (9.7, NE)	1.53 (0.71, 3.30)	0.2693	
Side of Tumor							0.8324
Left	34/ 83 (41.0)	16.7 (7.7, NE)	9/ 33 (27.3)	15.5 (15.5, NE)	1.44 (0.69, 3.01)	0.3317	
Right	62/ 136 (45.6)	16.7 (7.2, 21.0)	11/ 33 (33.3)	12.6 (7.1, NE)	1.23 (0.65, 2.35)	0.5231	

[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.
[4] P-Value for interaction from Cox proportional hazards model using ties=exact option with treatment, subgroup and treatment*subgroup interaction as covariates.
Including only patients from the full analysis set who completed a baseline (last PRO assessment prior to or on the first dose of study treatment) and at least 1 post-baseline PRO assessment.
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Kaplan Meier Plot of Time to first deterioration of at least 10 points - EOR01-Constipation (Months)
Full Analysis Set



Kaplan-Meier Plots for subgroups only created if p-value for interaction < 0.05.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Time to first improvement of at least 10 points - EOR01-Constipation (Months)
Full Analysis Set

	EC+FOLFOX (N=219)	Control 2 (N=66)
Number of subjects with events, n (%)	52 (23.7)	14 (21.2)
Number of censored subjects, n (%)	167 (76.3)	52 (78.8)
Kaplan-Meier estimates of Time to Event (Months) [1]		
25%-ile (95% CI)	8.9 (2.8, NE)	9.3 (5.6, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
Stratified analysis [2]		
Hazard Ratio (95% CI) [3]	0.97 (0.53, 1.75)	
p-value [4]	0.9127	

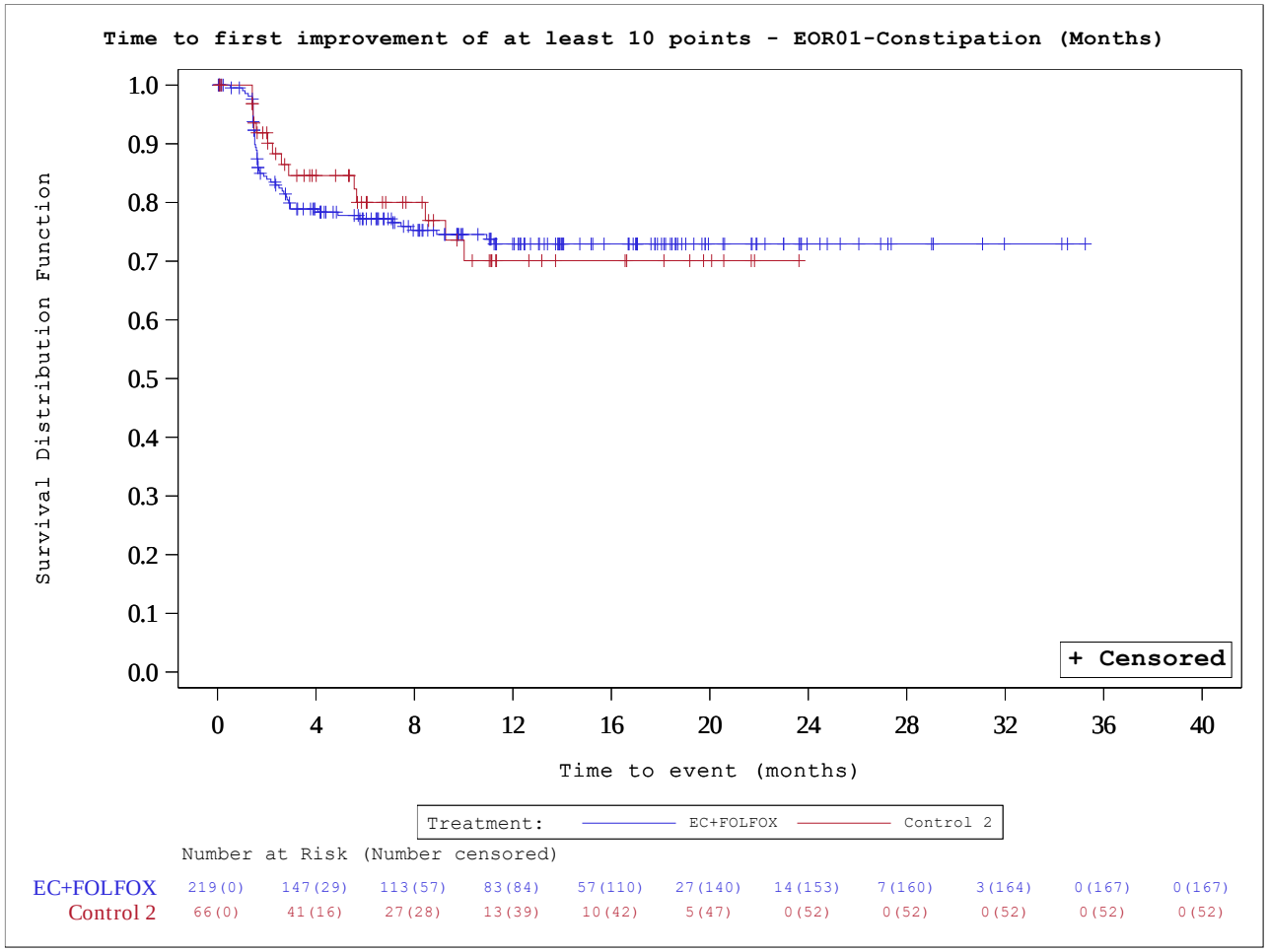
[1] Based on the Brookmeyer and Crowley method.
[2] Stratified by ECOG PS by Randomization.
[3] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio > 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[4] P-value from 2-sided log-rank test.
Including only patients from the full analysis set who completed a baseline (last PRO assessment prior to or on the first dose of study treatment) and at least 1 post-baseline PRO assessment.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Time to first improvement of at least 10 points - EOR01-Constipation (Months) - Subgroup analysis
Full Analysis Set

Subgroup Level	EC+FOLFOX (N=219) n/ N (%)	EC+FOLFOX (N=219) Median (95% CI)[1]	Control 2 (N=66) n/ N (%)	Control 2 (N=66) Median (95% CI)[1]	Unstratified analysis Hazard Ratio (95% CI)[2]	Unstratified analysis p-Value[3]	Interaction p-Value[4]
Age (Years)							0.3011
< 65	37/ 139 (26.6)	NE (NE , NE)	8/ 41 (19.5)	NE (NE , NE)	1.33 (0.62, 2.86)	0.4658	
>= 65	15/ 80 (18.8)	NE (NE , NE)	6/ 25 (24.0)	NE (9.3, NE)	0.70 (0.27, 1.82)	0.4674	
Sex							0.7489
Male	27/ 114 (23.7)	NE (NE , NE)	7/ 31 (22.6)	NE (10.0, NE)	0.98 (0.43, 2.24)	0.9555	
Female	25/ 105 (23.8)	NE (NE , NE)	7/ 35 (20.0)	NE (NE , NE)	1.14 (0.49, 2.64)	0.7621	
Region							0.6096
Europe	24/ 104 (23.1)	NE (NE , NE)	10/ 38 (26.3)	NE (9.3, NE)	0.73 (0.35, 1.53)	0.4052	
USA/Canada	3/ 8 (37.5)	NE (1.6, NE)	0/ 6 (0.0)	NE (NE , NE)	NE		
Rest of World	25/ 107 (23.4)	NE (NE , NE)	4/ 22 (18.2)	NE (10.0, NE)	1.38 (0.48, 3.96)	0.5551	
ECOG-PS at Randomization							0.7352
0	22/ 123 (17.9)	NE (NE , NE)	7/ 43 (16.3)	NE (NE , NE)	1.07 (0.46, 2.50)	0.8828	
1	30/ 96 (31.3)	NE (NE , NE)	7/ 23 (30.4)	NE (5.7, NE)	0.88 (0.38, 2.00)	0.7570	
Number of Organs Involved							0.6203
<= 2	22/ 110 (20.0)	NE (NE , NE)	7/ 33 (21.2)	NE (NE , NE)	0.88 (0.37, 2.06)	0.7626	
>= 3	30/ 109 (27.5)	NE (NE , NE)	7/ 33 (21.2)	NE (NE , NE)	1.22 (0.53, 2.77)	0.6445	
Presence of Liver Metastases							0.9883
Yes	37/ 135 (27.4)	NE (NE , NE)	10/ 40 (25.0)	NE (10.0, NE)	1.05 (0.52, 2.11)	0.8921	
No	15/ 84 (17.9)	NE (NE , NE)	4/ 26 (15.4)	NE (NE , NE)	1.08 (0.36, 3.26)	0.8945	
Side of Tumor							0.4643
Left	28/ 83 (33.7)	NE (10.9, NE)	8/ 33 (24.2)	NE (10.0, NE)	1.36 (0.62, 2.99)	0.4408	
Right	24/ 136 (17.6)	NE (NE , NE)	6/ 33 (18.2)	NE (NE , NE)	0.91 (0.37, 2.23)	0.8438	

[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio > 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.
[4] P-Value for interaction from Cox proportional hazards model using ties=exact option with treatment, subgroup and treatment*subgroup interaction as covariates.
Including only patients from the full analysis set who completed a baseline (last PRO assessment prior to or on the first dose of study treatment) and at least 1 post-baseline PRO assessment.
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Kaplan Meier Plot of Time to first improvement of at least 10 points - EOR01-Constipation (Months)
Full Analysis Set



Kaplan-Meier Plots for subgroups only created if p-value for interaction < 0.05.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Time to first deterioration of at least 10 points - EOR01-Diarrhea (Months)
Full Analysis Set

	EC+FOLFOX (N=219)	Control 2 (N=66)
Number of subjects with events, n (%)	88 (40.2)	25 (37.9)
Number of censored subjects, n (%)	131 (59.8)	41 (62.1)
Kaplan-Meier estimates of Time to Event (Months) [1]		
25%-ile (95% CI)	4.2 (2.8, 6.9)	4.0 (2.0, 5.8)
Median (95% CI)	22.2 (12.5, NE)	12.3 (5.8, NE)
75%-ile (95% CI)	NE (NE, NE)	NE (18.1, NE)
Stratified analysis [2]		
Hazard Ratio (95% CI) [3]	0.85 (0.54, 1.34)	
p-value [4]	0.4904	

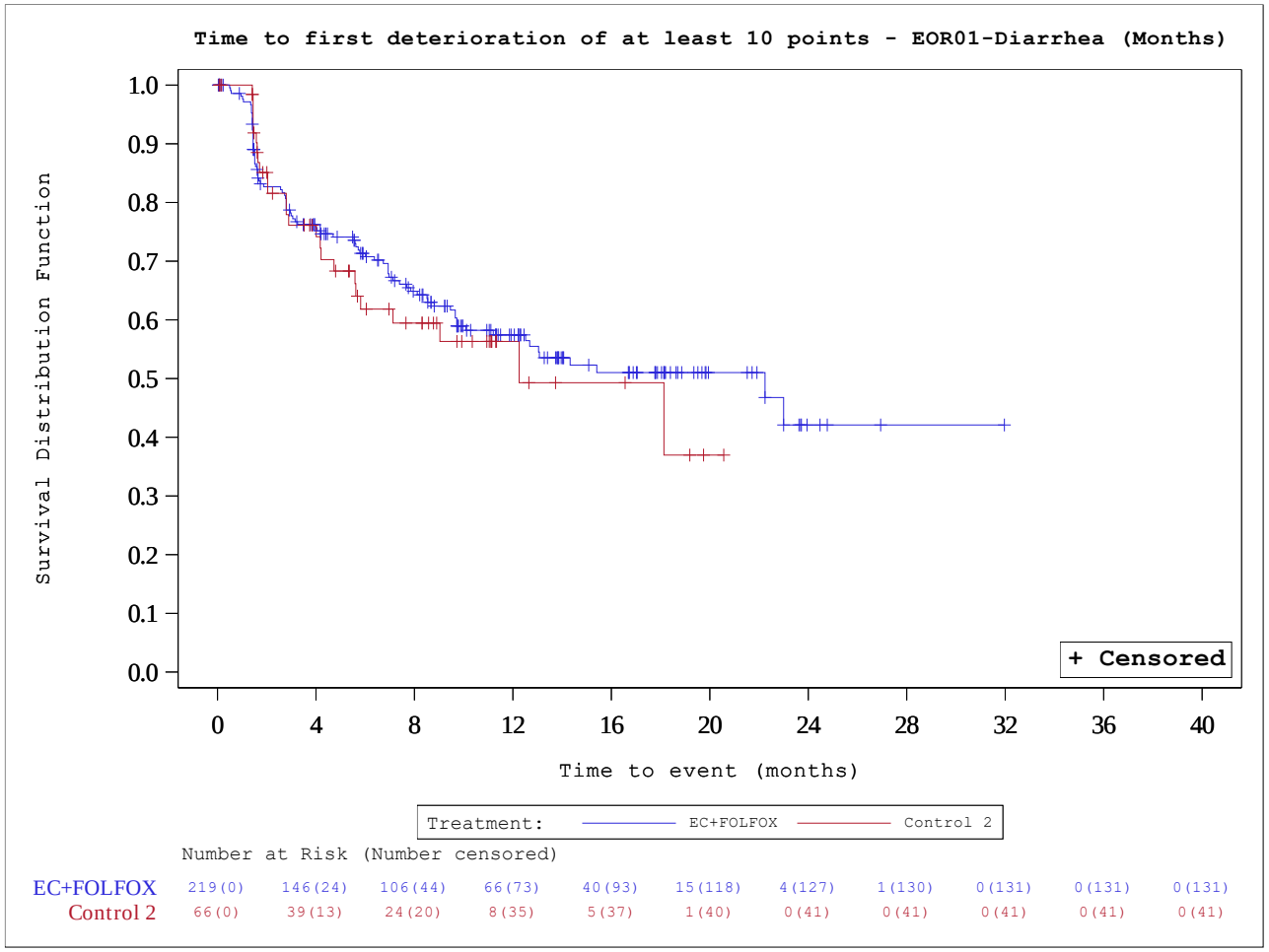
[1] Based on the Brookmeyer and Crowley method.
[2] Stratified by ECOG PS by Randomization.
[3] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[4] P-value from 2-sided log-rank test.
Including only patients from the full analysis set who completed a baseline (last PRO assessment prior to or on the first dose of study treatment) and at least 1 post-baseline PRO assessment.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Time to first deterioration of at least 10 points - EOR01-Diarrhea (Months) - Subgroup analysis
Full Analysis Set

Subgroup Level	EC+FOLFOX (N=219) n/ N (%)	EC+FOLFOX (N=219) Median (95% CI)[1]	Control 2 (N=66) n/ N (%)	Control 2 (N=66) Median (95% CI)[1]	Unstratified analysis Hazard Ratio (95% CI)[2]	Unstratified analysis p-Value[3]	Interaction p-Value[4]
Age (Years)							0.6181
< 65	55/ 139 (39.6)	22.2 (10.1, NE)	14/ 41 (34.1)	18.1 (5.6, NE)	0.98 (0.54, 1.77)	0.9461	
>= 65	33/ 80 (41.3)	13.1 (9.7, NE)	11/ 25 (44.0)	12.3 (2.8, NE)	0.77 (0.38, 1.53)	0.4557	
Sex							0.1391
Male	37/ 114 (32.5)	NE (13.1, NE)	12/ 31 (38.7)	9.0 (5.6, 18.1)	0.65 (0.34, 1.26)	0.1981	
Female	51/ 105 (48.6)	12.5 (7.7, 23.0)	13/ 35 (37.1)	12.3 (5.6, NE)	1.15 (0.62, 2.13)	0.6503	
Region							0.4841
Europe	43/ 104 (41.3)	22.2 (9.7, NE)	11/ 38 (28.9)	12.3 (9.0, NE)	1.11 (0.57, 2.16)	0.7576	
USA/Canada	3/ 8 (37.5)	NE (4.2, NE)	3/ 6 (50.0)	18.1 (7.1, NE)	0.75 (0.15, 3.77)	0.7306	
Rest of World	42/ 107 (39.3)	15.4 (8.8, NE)	11/ 22 (50.0)	5.6 (2.9, NE)	0.67 (0.34, 1.30)	0.2296	
ECOG-PS at Randomization							0.8842
0	48/ 123 (39.0)	22.2 (12.5, NE)	17/ 43 (39.5)	12.3 (5.8, NE)	0.83 (0.47, 1.45)	0.5103	
1	40/ 96 (41.7)	13.1 (8.1, NE)	8/ 23 (34.8)	NE (2.9, NE)	0.90 (0.42, 1.92)	0.7870	
Number of Organs Involved							0.0598
<= 2	53/ 110 (48.2)	13.1 (9.7, NE)	11/ 33 (33.3)	18.1 (9.0, NE)	1.28 (0.67, 2.46)	0.4492	
>= 3	35/ 109 (32.1)	NE (12.5, NE)	14/ 33 (42.4)	7.1 (4.2, NE)	0.58 (0.31, 1.09)	0.0873	
Presence of Liver Metastases							0.1809
Yes	49/ 135 (36.3)	NE (12.5, NE)	17/ 40 (42.5)	12.3 (4.2, 18.1)	0.69 (0.40, 1.21)	0.1972	
No	39/ 84 (46.4)	14.3 (8.5, NE)	8/ 26 (30.8)	NE (5.6, NE)	1.31 (0.61, 2.81)	0.4867	
Side of Tumor							0.5123
Left	26/ 83 (31.3)	NE (NE , NE)	9/ 33 (27.3)	NE (9.0, NE)	1.09 (0.51, 2.32)	0.8308	
Right	62/ 136 (45.6)	13.0 (9.7, 23.0)	16/ 33 (48.5)	7.1 (2.8, 18.1)	0.72 (0.41, 1.25)	0.2430	

[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.
[4] P-Value for interaction from Cox proportional hazards model using ties=exact option with treatment, subgroup and treatment*subgroup interaction as covariates.
Including only patients from the full analysis set who completed a baseline (last PRO assessment prior to or on the first dose of study treatment) and at least 1 post-baseline PRO assessment.
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Kaplan Meier Plot of Time to first deterioration of at least 10 points - EOR01-Diarrhea (Months)
Full Analysis Set



Kaplan-Meier Plots for subgroups only created if p-value for interaction < 0.05.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Time to first improvement of at least 10 points - EOR01-Diarrhea (Months)
Full Analysis Set

	EC+FOLFOX (N=219)	Control 2 (N=66)
Number of subjects with events, n (%)	54 (24.7)	12 (18.2)
Number of censored subjects, n (%)	165 (75.3)	54 (81.8)
Kaplan-Meier estimates of Time to Event (Months) [1]		
25%-ile (95% CI)	7.2 (3.0, NE)	NE (2.6, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
Stratified analysis [2]		
Hazard Ratio (95% CI) [3]	1.27 (0.68, 2.37)	
p-value [4]	0.4636	

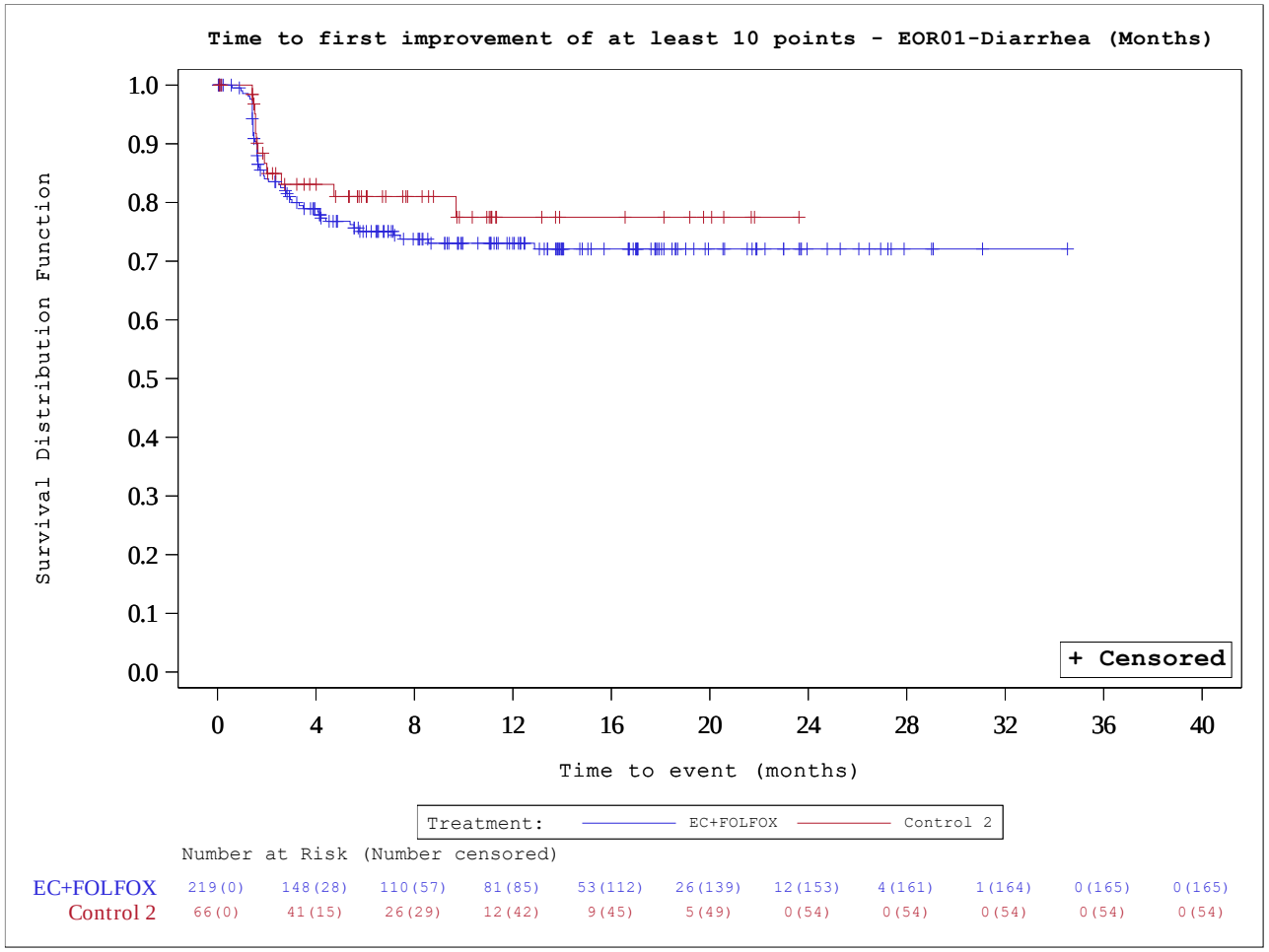
[1] Based on the Brookmeyer and Crowley method.
[2] Stratified by ECOG PS by Randomization.
[3] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio > 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[4] P-value from 2-sided log-rank test.
Including only patients from the full analysis set who completed a baseline (last PRO assessment prior to or on the first dose of study treatment) and at least 1 post-baseline PRO assessment.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Time to first improvement of at least 10 points - EOR01-Diarrhea (Months) - Subgroup analysis
Full Analysis Set

Subgroup Level	EC+FOLFOX (N=219) n/ N (%)	EC+FOLFOX (N=219) Median (95% CI)[1]	Control 2 (N=66) n/ N (%)	Control 2 (N=66) Median (95% CI)[1]	Unstratified analysis Hazard Ratio (95% CI)[2]	Unstratified analysis p-Value[3]	Interaction p-Value[4]
Age (Years)							0.4873
< 65	32/ 139 (23.0)	NE (NE , NE)	8/ 41 (19.5)	NE (NE , NE)	1.09 (0.50, 2.36)	0.8322	
>= 65	22/ 80 (27.5)	NE (NE , NE)	4/ 25 (16.0)	NE (NE , NE)	1.74 (0.60, 5.04)	0.3073	
Sex							0.8176
Male	32/ 114 (28.1)	NE (NE , NE)	6/ 31 (19.4)	NE (NE , NE)	1.35 (0.56, 3.22)	0.5000	
Female	22/ 105 (21.0)	NE (NE , NE)	6/ 35 (17.1)	NE (NE , NE)	1.18 (0.48, 2.92)	0.7203	
Region							0.3480
Europe	26/ 104 (25.0)	NE (NE , NE)	10/ 38 (26.3)	NE (9.7, NE)	0.80 (0.39, 1.66)	0.5514	
USA/Canada	4/ 8 (50.0)	NE (1.6, NE)	0/ 6 (0.0)	NE (NE , NE)	NE		
Rest of World	24/ 107 (22.4)	NE (NE , NE)	2/ 22 (9.1)	NE (NE , NE)	2.64 (0.62, 11.15)	0.1703	
ECOG-PS at Randomization							0.7238
0	28/ 123 (22.8)	NE (NE , NE)	8/ 43 (18.6)	NE (NE , NE)	1.15 (0.52, 2.53)	0.7222	
1	26/ 96 (27.1)	NE (NE , NE)	4/ 23 (17.4)	NE (9.7, NE)	1.48 (0.52, 4.23)	0.4694	
Number of Organs Involved							0.4819
<= 2	22/ 110 (20.0)	NE (NE , NE)	6/ 33 (18.2)	NE (NE , NE)	1.01 (0.41, 2.50)	0.9766	
>= 3	32/ 109 (29.4)	NE (NE , NE)	6/ 33 (18.2)	NE (NE , NE)	1.67 (0.70, 4.00)	0.2461	
Presence of Liver Metastases							0.0710
Yes	40/ 135 (29.6)	NE (NE , NE)	6/ 40 (15.0)	NE (NE , NE)	2.09 (0.89, 4.94)	0.0838	
No	14/ 84 (16.7)	NE (NE , NE)	6/ 26 (23.1)	NE (9.7, NE)	0.60 (0.23, 1.57)	0.2926	
Side of Tumor							0.9901
Left	25/ 83 (30.1)	NE (NE , NE)	7/ 33 (21.2)	NE (NE , NE)	1.40 (0.60, 3.23)	0.4348	
Right	29/ 136 (21.3)	NE (NE , NE)	5/ 33 (15.2)	NE (NE , NE)	1.35 (0.52, 3.48)	0.5379	

[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio > 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.
[4] P-Value for interaction from Cox proportional hazards model using ties=exact option with treatment, subgroup and treatment*subgroup interaction as covariates.
Including only patients from the full analysis set who completed a baseline (last PRO assessment prior to or on the first dose of study treatment) and at least 1 post-baseline PRO assessment.
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Kaplan Meier Plot of Time to first improvement of at least 10 points - EOR01-Diarrhea (Months)
Full Analysis Set



Kaplan-Meier Plots for subgroups only created if p-value for interaction < 0.05.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Time to first deterioration of at least 10 points - EOR01-Financial Difficulties (Months)
Full Analysis Set

	EC+FOLFOX (N=219)	Control 2 (N=66)
Number of subjects with events, n (%)	102 (46.6)	15 (22.7)
Number of censored subjects, n (%)	117 (53.4)	51 (77.3)
Kaplan-Meier estimates of Time to Event (Months) [1]		
25%-ile (95% CI)	3.5 (2.8, 4.7)	8.1 (3.7, NE)
Median (95% CI)	12.4 (8.3, 21.7)	NE (NE, NE)
75%-ile (95% CI)	NE (29.8, NE)	NE (NE, NE)
Stratified analysis [2]		
Hazard Ratio (95% CI) [3]	1.84 (1.06, 3.18)	
p-value [4]	0.0266	

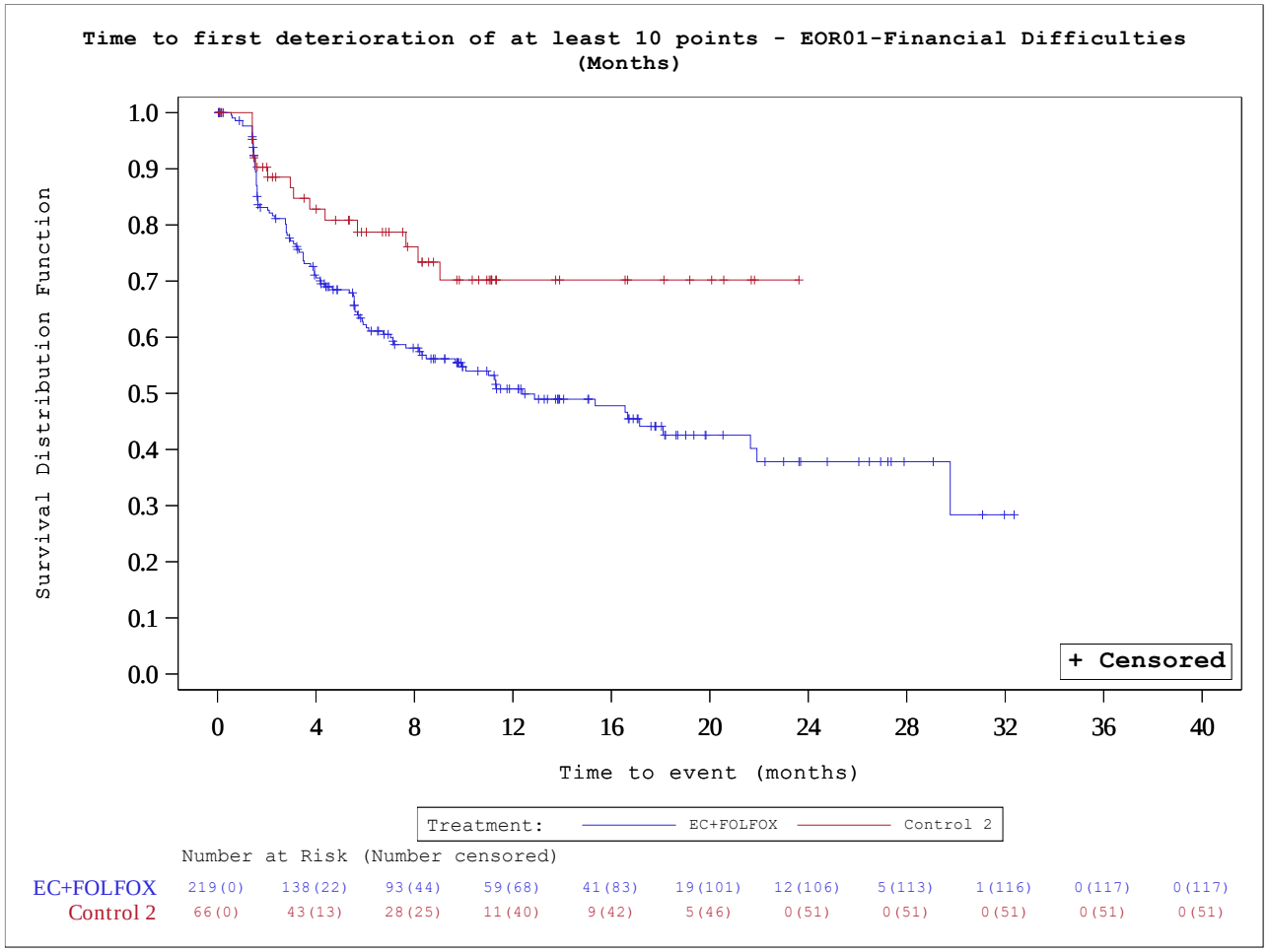
[1] Based on the Brookmeyer and Crowley method.
[2] Stratified by ECOG PS by Randomization.
[3] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[4] P-value from 2-sided log-rank test.
Including only patients from the full analysis set who completed a baseline (last PRO assessment prior to or on the first dose of study treatment) and at least 1 post-baseline PRO assessment.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Time to first deterioration of at least 10 points - EOR01-Financial Difficulties (Months) - Subgroup analysis
Full Analysis Set

Subgroup Level	EC+FOLFOX (N=219) n/ N (%)	EC+FOLFOX (N=219) Median (95% CI)[1]	Control 2 (N=66) n/ N (%)	Control 2 (N=66) Median (95% CI)[1]	Unstratified analysis Hazard Ratio (95% CI)[2]	Unstratified analysis p-Value[3]	Interaction p-Value[4]
Age (Years)							0.7090
< 65	67/ 139 (48.2)	12.9 (7.7, 21.9)	9/ 41 (22.0)	NE (NE , NE)	2.07 (1.03, 4.15)	0.0365	
>= 65	35/ 80 (43.8)	12.4 (6.0, NE)	6/ 25 (24.0)	NE (8.1, NE)	1.72 (0.72, 4.12)	0.2133	
Sex							0.4266
Male	52/ 114 (45.6)	12.4 (7.0, NE)	5/ 31 (16.1)	NE (NE , NE)	2.60 (1.04, 6.52)	0.0338	
Female	50/ 105 (47.6)	16.6 (7.1, 21.9)	10/ 35 (28.6)	NE (8.1, NE)	1.64 (0.83, 3.25)	0.1476	
Region							0.8185
Europe	52/ 104 (50.0)	11.0 (7.2, 21.7)	8/ 38 (21.1)	NE (9.0, NE)	2.08 (0.98, 4.39)	0.0492	
USA/Canada	3/ 8 (37.5)	NE (3.3, NE)	1/ 6 (16.7)	NE (NE , NE)	2.16 (0.22, 20.83)	0.4939	
Rest of World	47/ 107 (43.9)	16.6 (7.0, NE)	6/ 22 (27.3)	NE (3.7, NE)	1.54 (0.66, 3.61)	0.3157	
ECOG-PS at Randomization							0.1827
0	56/ 123 (45.5)	16.7 (8.2, NE)	8/ 43 (18.6)	NE (NE , NE)	2.51 (1.19, 5.27)	0.0118	
1	46/ 96 (47.9)	11.3 (7.0, 18.1)	7/ 23 (30.4)	NE (3.7, NE)	1.13 (0.51, 2.53)	0.7600	
Number of Organs Involved							0.0533
<= 2	56/ 110 (50.9)	12.4 (5.9, 29.8)	5/ 33 (15.2)	NE (NE , NE)	3.53 (1.41, 8.83)	0.0040	
>= 3	46/ 109 (42.2)	11.3 (7.7, NE)	10/ 33 (30.3)	NE (4.4, NE)	1.16 (0.58, 2.30)	0.6715	
Presence of Liver Metastases							0.7919
Yes	66/ 135 (48.9)	11.3 (6.7, 18.1)	9/ 40 (22.5)	NE (NE , NE)	2.03 (1.01, 4.08)	0.0413	
No	36/ 84 (42.9)	15.3 (8.5, NE)	6/ 26 (23.1)	NE (9.0, NE)	1.87 (0.79, 4.44)	0.1495	
Side of Tumor							0.8503
Left	39/ 83 (47.0)	15.3 (8.5, 29.8)	7/ 33 (21.2)	NE (9.0, NE)	2.00 (0.89, 4.49)	0.0893	
Right	63/ 136 (46.3)	11.3 (7.1, 21.9)	8/ 33 (24.2)	NE (NE , NE)	1.83 (0.88, 3.83)	0.0992	

[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.
[4] P-Value for interaction from Cox proportional hazards model using ties=exact option with treatment, subgroup and treatment*subgroup interaction as covariates.
Including only patients from the full analysis set who completed a baseline (last PRO assessment prior to or on the first dose of study treatment) and at least 1 post-baseline PRO assessment.
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Kaplan Meier Plot of Time to first deterioration of at least 10 points - EOR01-Financial Difficulties (Months)
Full Analysis Set



Kaplan-Meier Plots for subgroups only created if p-value for interaction < 0.05.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Time to first improvement of at least 10 points - EOR01-Financial Difficulties (Months)
Full Analysis Set

	EC+FOLFOX (N=219)	Control 2 (N=66)
Number of subjects with events, n (%)	52 (23.7)	7 (10.6)
Number of censored subjects, n (%)	167 (76.3)	59 (89.4)
Kaplan-Meier estimates of Time to Event (Months) [1]		
25%-ile (95% CI)	9.7 (4.8, NE)	NE (10.1, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
Stratified analysis [2]		
Hazard Ratio (95% CI) [3]	2.12 (0.96, 4.67)	
p-value [4]	0.0575	

[1] Based on the Brookmeyer and Crowley method.
[2] Stratified by ECOG PS by Randomization.
[3] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio > 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[4] P-value from 2-sided log-rank test.
Including only patients from the full analysis set who completed a baseline (last PRO assessment prior to or on the first dose of study treatment) and at least 1 post-baseline PRO assessment.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Time to first improvement of at least 10 points - EOR01-Financial Difficulties (Months) - Subgroup analysis
Full Analysis Set

Subgroup Level	EC+FOLFOX (N=219) n/ N (%)	EC+FOLFOX (N=219) Median (95% CI)[1]	Control 2 (N=66) n/ N (%)	Control 2 (N=66) Median (95% CI)[1]	Unstratified analysis Hazard Ratio (95% CI)[2]	Unstratified analysis p-Value[3]	Interaction p-Value[4]
Age (Years)							0.2378
< 65	34/ 139 (24.5)	NE (NE , NE)	6/ 41 (14.6)	NE (NE , NE)	1.55 (0.65, 3.69)	0.3198	
>= 65	18/ 80 (22.5)	NE (NE , NE)	1/ 25 (4.0)	NE (NE , NE)	6.07 (0.81, 45.44)	0.0453	
Sex							0.1725
Male	27/ 114 (23.7)	NE (NE , NE)	5/ 31 (16.1)	NE (NE , NE)	1.31 (0.51, 3.42)	0.5732	
Female	25/ 105 (23.8)	NE (NE , NE)	2/ 35 (5.7)	NE (NE , NE)	4.36 (1.03, 18.43)	0.0287	
Region							0.2539
Europe	19/ 104 (18.3)	NE (NE , NE)	3/ 38 (7.9)	NE (NE , NE)	2.05 (0.61, 6.93)	0.2389	
USA/Canada	1/ 8 (12.5)	NE (NE , NE)	2/ 6 (33.3)	NE (2.9, NE)	0.34 (0.03, 3.78)	0.3589	
Rest of World	32/ 107 (29.9)	NE (16.8, NE)	2/ 22 (9.1)	NE (NE , NE)	3.63 (0.87, 15.15)	0.0580	
ECOG-PS at Randomization							0.9864
0	22/ 123 (17.9)	NE (NE , NE)	7/ 43 (16.3)	NE (NE , NE)	1.05 (0.45, 2.46)	0.9164	
1	30/ 96 (31.3)	NE (NE , NE)	0/ 23 (0.0)	NE (NE , NE)	NE		
Number of Organs Involved							0.7167
<= 2	25/ 110 (22.7)	NE (NE , NE)	3/ 33 (9.1)	NE (NE , NE)	2.51 (0.76, 8.33)	0.1192	
>= 3	27/ 109 (24.8)	NE (NE , NE)	4/ 33 (12.1)	NE (NE , NE)	1.88 (0.66, 5.37)	0.2332	
Presence of Liver Metastases							0.4915
Yes	31/ 135 (23.0)	NE (NE , NE)	5/ 40 (12.5)	NE (NE , NE)	1.74 (0.67, 4.48)	0.2458	
No	21/ 84 (25.0)	NE (NE , NE)	2/ 26 (7.7)	NE (NE , NE)	3.30 (0.77, 14.08)	0.0873	
Side of Tumor							0.3190
Left	21/ 83 (25.3)	NE (NE , NE)	5/ 33 (15.2)	NE (NE , NE)	1.56 (0.58, 4.13)	0.3713	
Right	31/ 136 (22.8)	NE (NE , NE)	2/ 33 (6.1)	NE (NE , NE)	3.85 (0.92, 16.11)	0.0463	

[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio > 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.
[4] P-Value for interaction from Cox proportional hazards model using ties=exact option with treatment, subgroup and treatment*subgroup interaction as covariates.
Including only patients from the full analysis set who completed a baseline (last PRO assessment prior to or on the first dose of study treatment) and at least 1 post-baseline PRO assessment.
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

Pierre Fabre Pharma GmbH: Final
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Population: arm B vs. arm E
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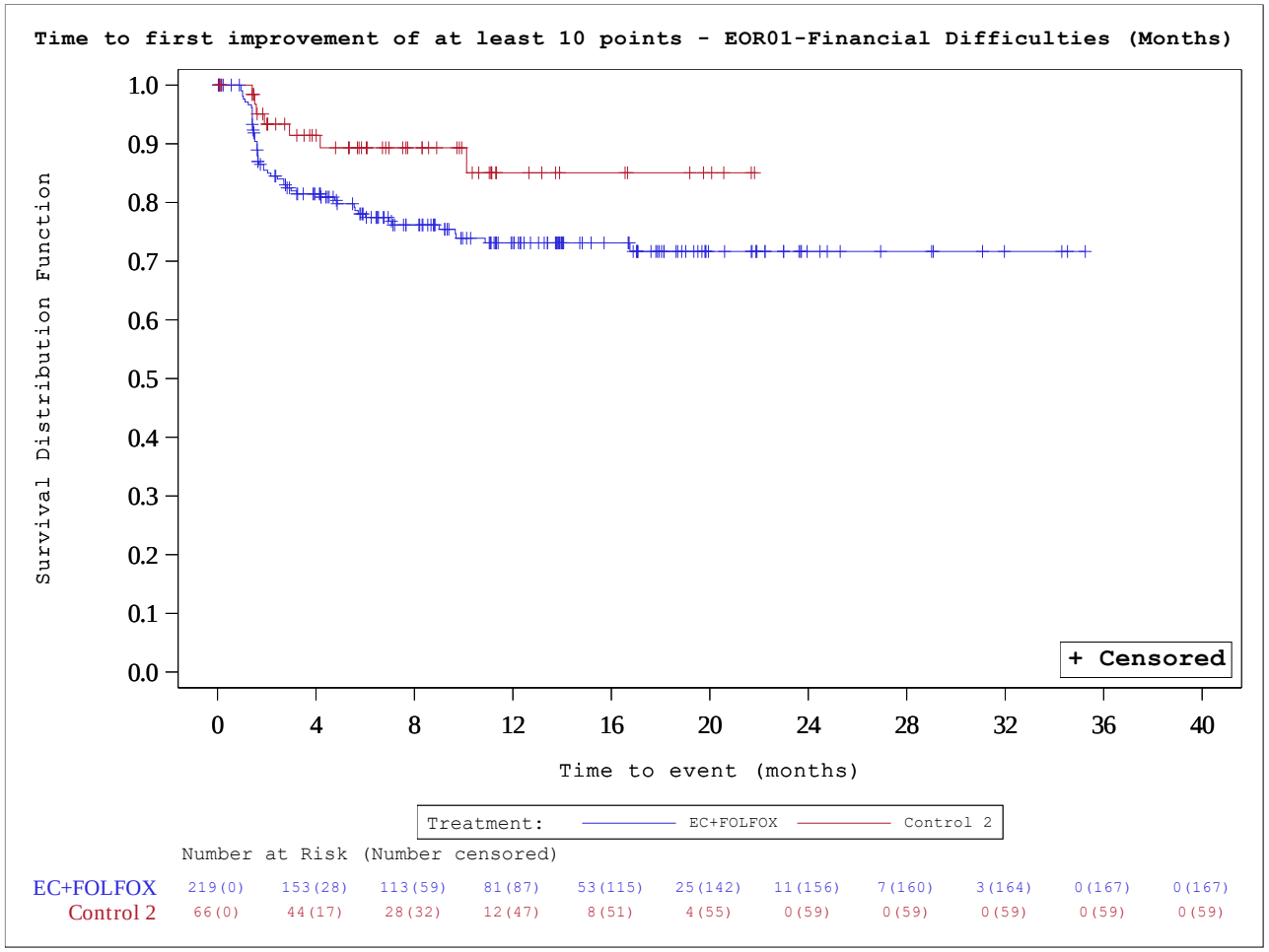
Kaplan Meier Plot of Time to first improvement of at least 10 points - EOR01-Financial Difficulties (Months)
Full Analysis Set



Kaplan-Meier Plots for subgroups only created if p-value for interaction < 0.05.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Time to first deterioration of at least 15 percent - EQ5D02-EQ-VAS Score (Months)
Full Analysis Set

	EC+FOLFOX (N=215)	Control 2 (N=65)
Number of subjects with events, n (%)	91 (42.3)	20 (30.8)
Number of censored subjects, n (%)	124 (57.7)	45 (69.2)
Kaplan-Meier estimates of Time to Event (Months) [1]		
25%-ile (95% CI)	4.1 (3.1, 5.5)	4.4 (2.0, NE)
Median (95% CI)	16.7 (10.2, NE)	NE (8.6, NE)
75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
Stratified analysis [2]		
Hazard Ratio (95% CI) [3]	1.18 (0.72, 1.92)	
p-value [4]	0.5135	

[1] Based on the Brookmeyer and Crowley method.
[2] Stratified by ECOG PS by Randomization.
[3] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[4] P-value from 2-sided log-rank test.
Including only patients from the full analysis set who completed a baseline (last PRO assessment prior to or on the first dose of study treatment) and at least 1 post-baseline PRO assessment.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Time to first deterioration of at least 15 percent - EQ5D02-EQ-VAS Score (Months) - Subgroup analysis
Full Analysis Set

Subgroup Level	EC+FOLFOX (N=215) n/ N (%)	EC+FOLFOX (N=215) Median (95% CI)[1]	Control 2 (N=65) n/ N (%)	Control 2 (N=65) Median (95% CI)[1]	Unstratified analysis Hazard Ratio (95% CI)[2]	Unstratified analysis p-Value[3]	Interaction p-Value[4]
Age (Years)							0.1684
< 65	57/ 136 (41.9)	16.7 (11.1, NE)	9/ 40 (22.5)	NE (NE , NE)	1.65 (0.82, 3.34)	0.1541	
>= 65	34/ 79 (43.0)	14.8 (7.2, NE)	11/ 25 (44.0)	8.6 (4.0, NE)	0.84 (0.42, 1.67)	0.6180	
Sex							0.5270
Male	46/ 112 (41.1)	16.7 (8.8, NE)	10/ 31 (32.3)	NE (5.6, NE)	1.04 (0.52, 2.07)	0.9057	
Female	45/ 103 (43.7)	18.4 (10.2, NE)	10/ 34 (29.4)	NE (6.7, NE)	1.41 (0.71, 2.80)	0.3193	
Region							0.3869
Europe	43/ 100 (43.0)	17.3 (9.6, NE)	10/ 37 (27.0)	NE (6.0, NE)	1.27 (0.63, 2.53)	0.5024	
USA/Canada	4/ 8 (50.0)	NE (1.6, NE)	1/ 6 (16.7)	NE (4.4, NE)	4.15 (0.46, 37.63)	0.1715	
Rest of World	44/ 107 (41.1)	15.3 (8.8, NE)	9/ 22 (40.9)	NE (4.4, NE)	0.91 (0.44, 1.87)	0.8052	
ECOG-PS at Randomization							0.9359
0	48/ 121 (39.7)	19.0 (9.6, NE)	14/ 43 (32.6)	NE (6.7, NE)	1.19 (0.66, 2.16)	0.5598	
1	43/ 94 (45.7)	13.9 (8.3, 20.4)	6/ 22 (27.3)	NE (4.4, NE)	1.14 (0.48, 2.70)	0.7598	
Number of Organs Involved							0.0018
<= 2	54/ 108 (50.0)	13.4 (5.7, NE)	6/ 32 (18.8)	NE (NE , NE)	2.99 (1.29, 6.95)	0.0074	
>= 3	37/ 107 (34.6)	20.4 (13.9, NE)	14/ 33 (42.4)	6.7 (2.9, NE)	0.55 (0.29, 1.02)	0.0531	
Presence of Liver Metastases							0.0666
Yes	49/ 132 (37.1)	19.0 (13.4, NE)	14/ 40 (35.0)	NE (5.3, NE)	0.84 (0.46, 1.54)	0.5836	
No	42/ 83 (50.6)	11.1 (5.4, 18.4)	6/ 25 (24.0)	NE (NE , NE)	2.24 (0.95, 5.28)	0.0576	
Side of Tumor							0.5541
Left	33/ 82 (40.2)	18.4 (8.8, NE)	10/ 32 (31.3)	NE (4.4, NE)	1.03 (0.51, 2.09)	0.9427	
Right	58/ 133 (43.6)	16.7 (8.3, NE)	10/ 33 (30.3)	NE (6.0, NE)	1.39 (0.71, 2.72)	0.3346	

[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.
[4] P-Value for interaction from Cox proportional hazards model using ties=exact option with treatment, subgroup and treatment*subgroup interaction as covariates.
Including only patients from the full analysis set who completed a baseline (last PRO assessment prior to or on the first dose of study treatment) and at least 1 post-baseline PRO assessment.
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Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
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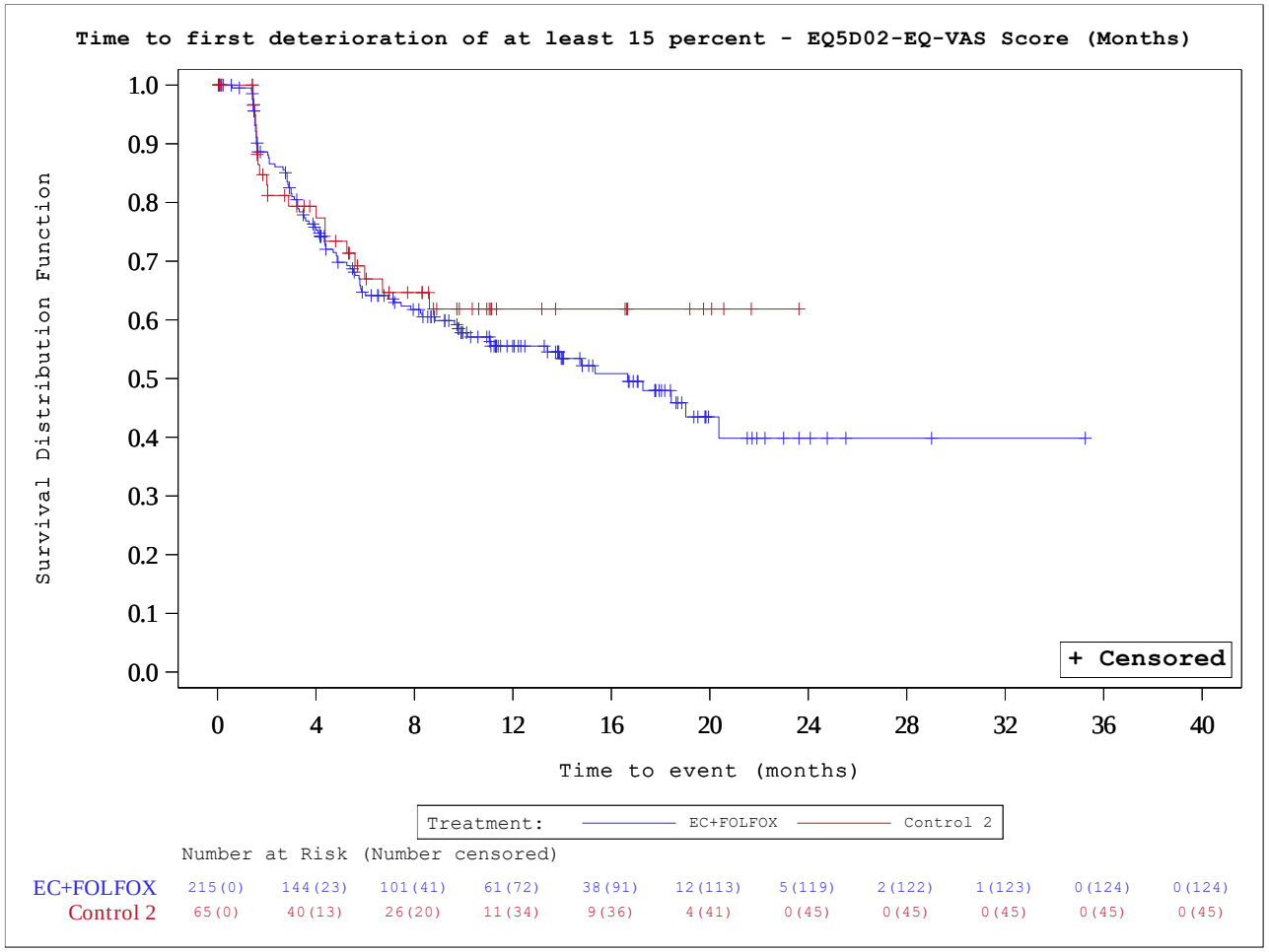
Kaplan Meier Plot of Time to first deterioration of at least 15 percent - EQ5D02-EQ-VAS Score (Months)
Full Analysis Set



Kaplan-Meier Plots for subgroups only created if p-value for interaction < 0.05.

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Encorafenib (PF-07263896) Protocol C4221015
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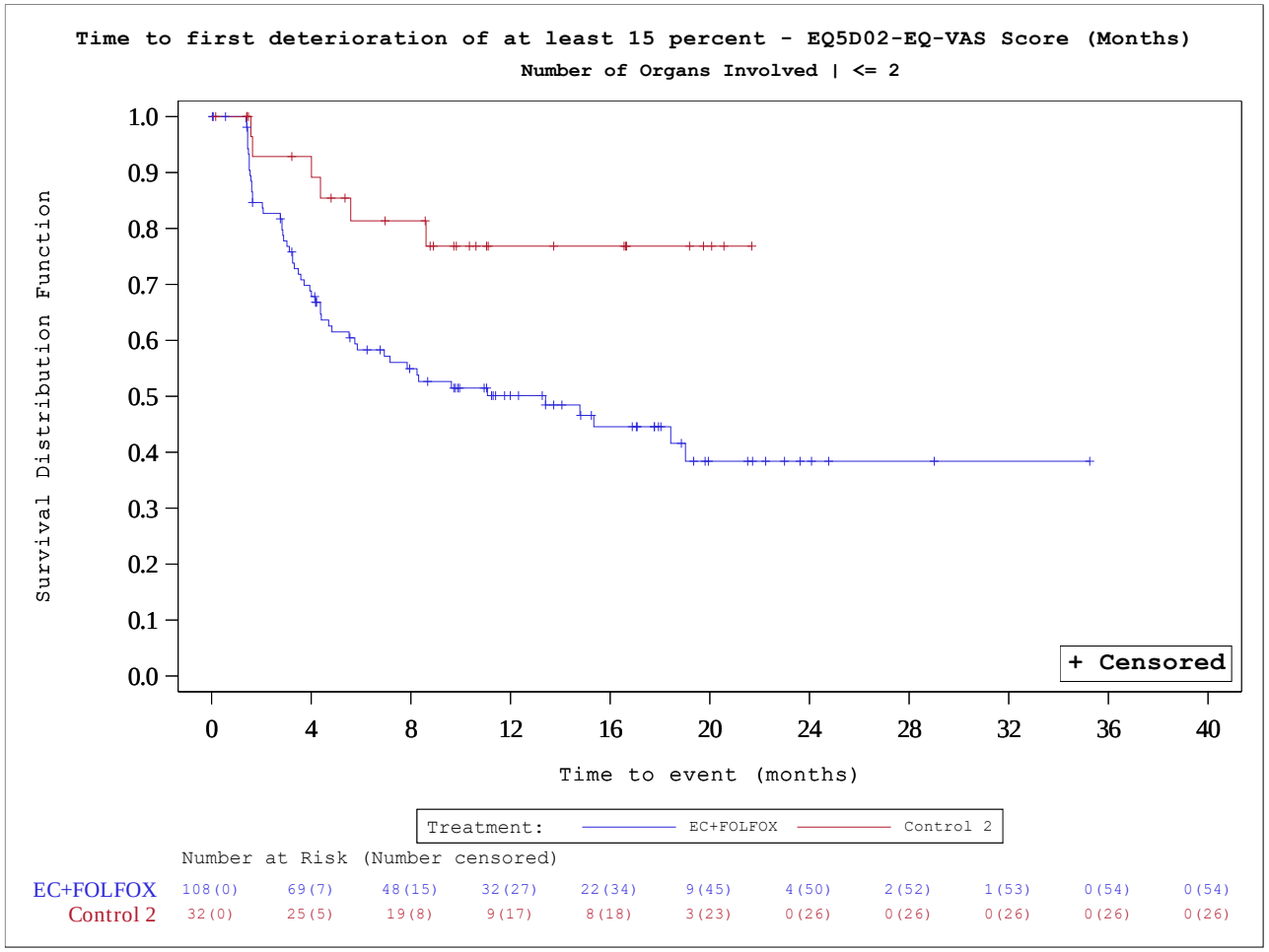

Kaplan-Meier Plots for subgroups only created if p-value for interaction < 0.05.

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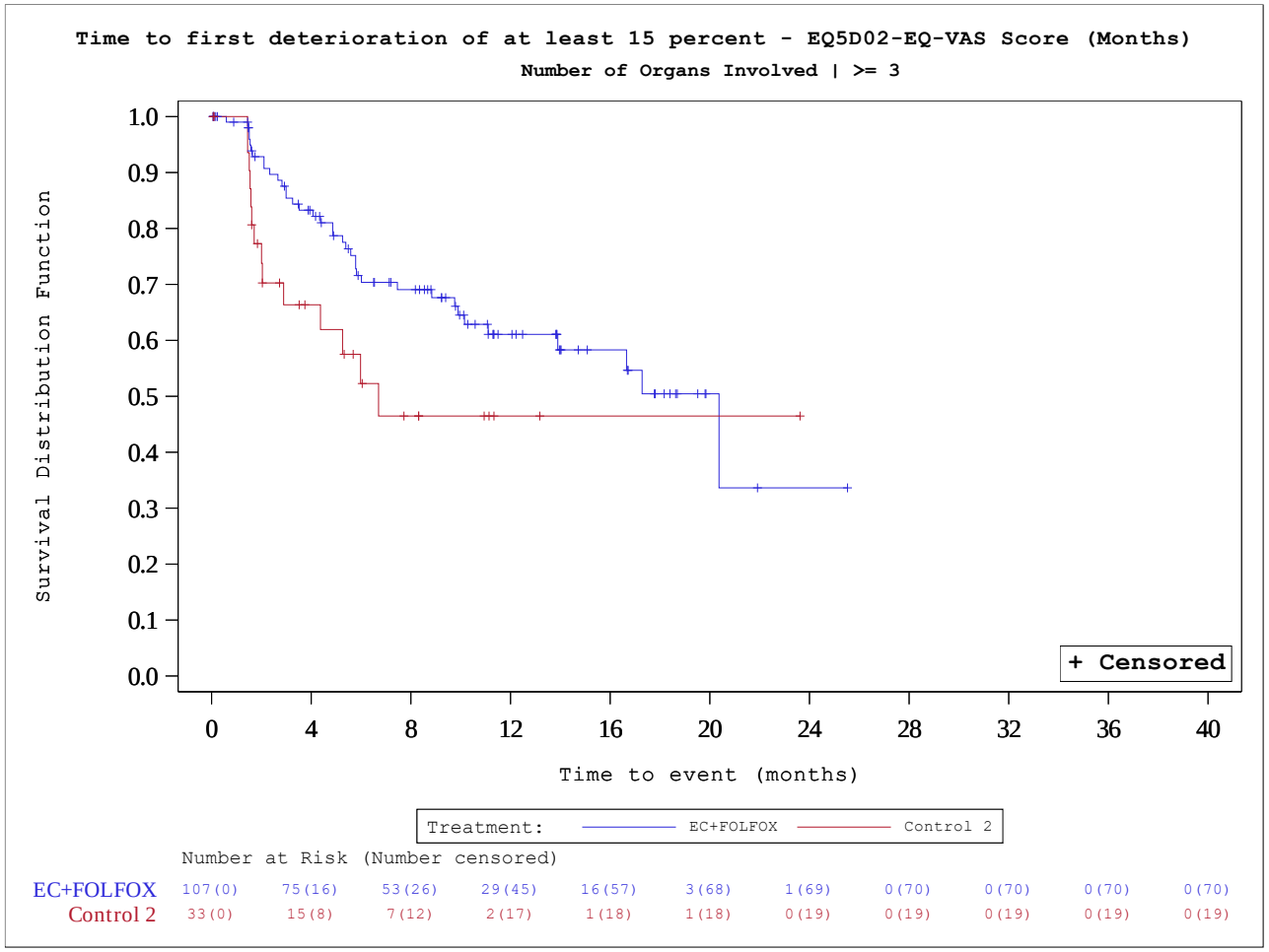

Kaplan-Meier Plots for subgroups only created if p-value for interaction < 0.05.

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Encorafenib (PF-07263896) Protocol C4221015
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Time to first improvement of at least 15 percent - EQ5D02-EQ-VAS Score (Months)
Full Analysis Set

	EC+FOLFOX (N=215)	Control 2 (N=65)
Number of subjects with events, n (%)	65 (30.2)	10 (15.4)
Number of censored subjects, n (%)	150 (69.8)	55 (84.6)
Kaplan-Meier estimates of Time to Event (Months) [1]		
25%-ile (95% CI)	6.0 (3.0, 11.3)	NE (5.6, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
Stratified analysis [2]		
Hazard Ratio (95% CI) [3]	1.78 (0.91, 3.47)	
p-value [4]	0.0875	

[1] Based on the Brookmeyer and Crowley method.
[2] Stratified by ECOG PS by Randomization.
[3] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio > 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[4] P-value from 2-sided log-rank test.
Including only patients from the full analysis set who completed a baseline (last PRO assessment prior to or on the first dose of study treatment) and at least 1 post-baseline PRO assessment.

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Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Time to first improvement of at least 15 percent - EQ5D02-EQ-VAS Score (Months) - Subgroup analysis
Full Analysis Set

Subgroup Level	EC+FOLFOX (N=215) n/ N (%)	EC+FOLFOX (N=215) Median (95% CI)[1]	Control 2 (N=65) n/ N (%)	Control 2 (N=65) Median (95% CI)[1]	Unstratified analysis Hazard Ratio (95% CI)[2]	Unstratified analysis p-Value[3]	Interaction p-Value[4]
Age (Years)							0.7551
< 65	43/ 136 (31.6)	NE (NE , NE)	6/ 40 (15.0)	NE (NE , NE)	2.03 (0.86, 4.77)	0.0977	
>= 65	22/ 79 (27.8)	NE (15.5, NE)	4/ 25 (16.0)	NE (NE , NE)	1.58 (0.54, 4.60)	0.3978	
Sex							0.6613
Male	29/ 112 (25.9)	NE (NE , NE)	3/ 31 (9.7)	NE (NE , NE)	2.33 (0.71, 7.68)	0.1502	
Female	36/ 103 (35.0)	NE (13.0, NE)	7/ 34 (20.6)	NE (NE , NE)	1.73 (0.77, 3.89)	0.1811	
Region							0.3155
Europe	37/ 100 (37.0)	NE (11.7, NE)	5/ 37 (13.5)	NE (NE , NE)	2.46 (0.97, 6.29)	0.0504	
USA/Canada	1/ 8 (12.5)	NE (NE , NE)	2/ 6 (33.3)	NE (2.9, NE)	0.39 (0.03, 4.26)	0.4192	
Rest of World	27/ 107 (25.2)	NE (NE , NE)	3/ 22 (13.6)	NE (NE , NE)	1.81 (0.55, 5.96)	0.3248	
ECOG-PS at Randomization							0.4572
0	33/ 121 (27.3)	NE (NE , NE)	5/ 43 (11.6)	NE (NE , NE)	2.18 (0.85, 5.60)	0.0957	
1	32/ 94 (34.0)	NE (10.9, NE)	5/ 22 (22.7)	NE (9.3, NE)	1.39 (0.54, 3.58)	0.4911	
Number of Organs Involved							0.9322
<= 2	25/ 108 (23.1)	NE (NE , NE)	4/ 32 (12.5)	NE (NE , NE)	1.81 (0.63, 5.20)	0.2635	
>= 3	40/ 107 (37.4)	16.8 (8.8, NE)	6/ 33 (18.2)	NE (NE , NE)	1.88 (0.79, 4.45)	0.1448	
Presence of Liver Metastases							0.4586
Yes	45/ 132 (34.1)	NE (11.7, NE)	6/ 40 (15.0)	NE (NE , NE)	2.28 (0.97, 5.34)	0.0514	
No	20/ 83 (24.1)	NE (NE , NE)	4/ 25 (16.0)	NE (NE , NE)	1.29 (0.44, 3.78)	0.6436	
Side of Tumor							0.2234
Left	32/ 82 (39.0)	NE (10.9, NE)	4/ 32 (12.5)	NE (NE , NE)	2.97 (1.05, 8.42)	0.0315	
Right	33/ 133 (24.8)	NE (NE , NE)	6/ 33 (18.2)	NE (NE , NE)	1.31 (0.55, 3.13)	0.5410	

[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio > 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.
[4] P-Value for interaction from Cox proportional hazards model using ties=exact option with treatment, subgroup and treatment*subgroup interaction as covariates.
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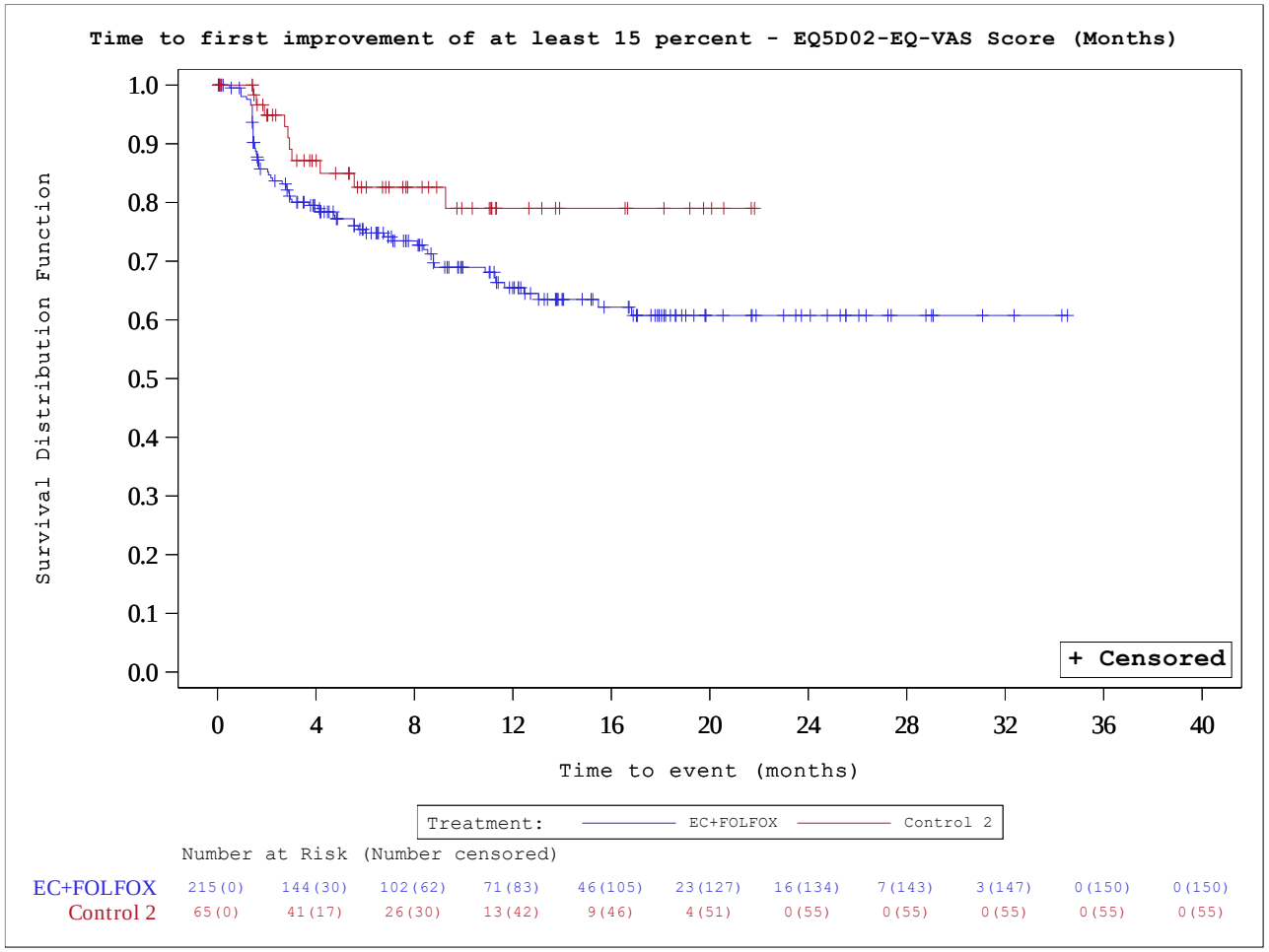
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Kaplan Meier Plot of Time to first improvement of at least 15 percent - EQ5D02-EQ-VAS Score (Months)
Full Analysis Set



Kaplan-Meier Plots for subgroups only created if p-value for interaction < 0.05.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Time to first deterioration of at least 15 percent - PGIS01 - Colorectal Cancer (Months)
Full Analysis Set

	EC+FOLFOX (N=219)	Control 2 (N=66)
Number of subjects with events, n (%)	85 (38.8)	18 (27.3)
Number of censored subjects, n (%)	134 (61.2)	48 (72.7)
Kaplan-Meier estimates of Time to Event (Months) [1]		
25%-ile (95% CI)	4.1 (2.9, 5.7)	5.6 (1.6, NE)
Median (95% CI)	23.4 (8.3, NE)	NE (11.3, NE)
75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
Stratified analysis [2]		
Hazard Ratio (95% CI) [3]	1.26 (0.76, 2.11)	
p-value [4]	0.3657	

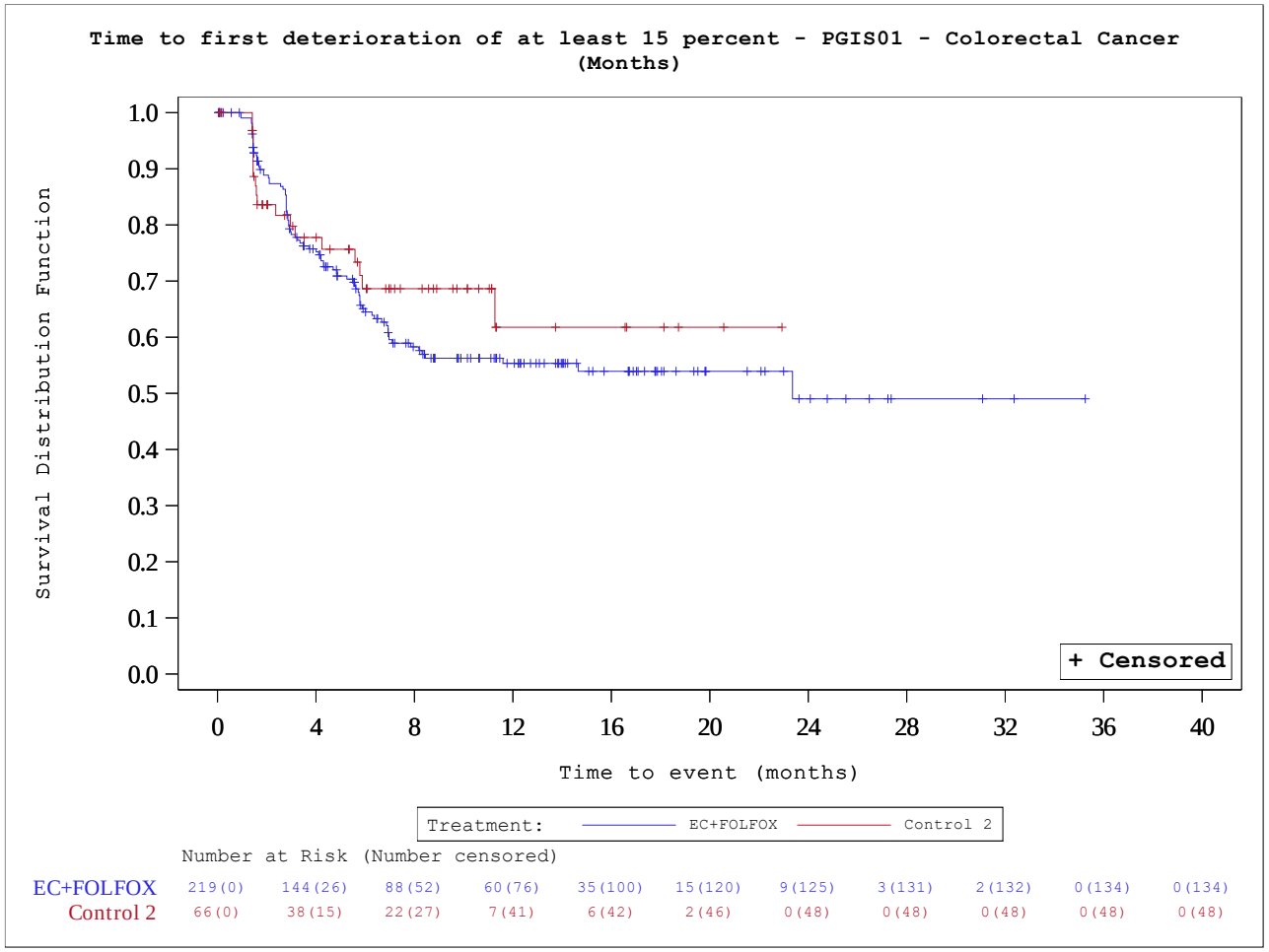
[1] Based on the Brookmeyer and Crowley method.
[2] Stratified by ECOG PS by Randomization.
[3] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[4] P-value from 2-sided log-rank test.
Including only patients from the full analysis set who completed a baseline (last PRO assessment prior to or on the first dose of study treatment) and at least 1 post-baseline PRO assessment.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Time to first deterioration of at least 15 percent - PGIS01 - Colorectal Cancer (Months) - Subgroup analysis
Full Analysis Set

Subgroup Level	EC+FOLFOX (N=219) n/ N (%)	EC+FOLFOX (N=219) Median (95% CI)[1]	Control 2 (N=66) n/ N (%)	Control 2 (N=66) Median (95% CI)[1]	Unstratified analysis Hazard Ratio (95% CI)[2]	Unstratified analysis p-Value[3]	Interaction p-Value[4]
Age (Years)							0.0410
< 65	57/ 139 (41.0)	23.4 (7.0, NE)	8/ 41 (19.5)	NE (NE , NE)	1.94 (0.93, 4.08)	0.0728	
>= 65	28/ 80 (35.0)	NE (7.1, NE)	10/ 25 (40.0)	11.3 (4.2, NE)	0.68 (0.33, 1.40)	0.3033	
Sex							0.6712
Male	49/ 114 (43.0)	11.6 (6.7, NE)	10/ 31 (32.3)	NE (4.2, NE)	1.08 (0.54, 2.12)	0.8325	
Female	36/ 105 (34.3)	NE (23.4, NE)	8/ 35 (22.9)	NE (11.3, NE)	1.35 (0.63, 2.91)	0.4351	
Region							0.7068
Europe	41/ 104 (39.4)	NE (7.9, NE)	10/ 38 (26.3)	NE (11.3, NE)	1.24 (0.62, 2.47)	0.5431	
USA/Canada	5/ 8 (62.5)	7.9 (1.6, NE)	0/ 6 (0.0)	NE (NE , NE)	NE		
Rest of World	39/ 107 (36.4)	23.4 (7.0, NE)	8/ 22 (36.4)	NE (3.2, NE)	0.81 (0.38, 1.74)	0.6015	
ECOG-PS at Randomization							0.5975
0	50/ 123 (40.7)	NE (6.9, NE)	14/ 43 (32.6)	NE (5.9, NE)	1.16 (0.64, 2.11)	0.6090	
1	35/ 96 (36.5)	23.4 (7.0, NE)	4/ 23 (17.4)	NE (NE , NE)	1.58 (0.56, 4.45)	0.3828	
Number of Organs Involved							0.0587
<= 2	48/ 110 (43.6)	14.7 (6.9, NE)	7/ 33 (21.2)	NE (NE , NE)	2.07 (0.94, 4.59)	0.0622	
>= 3	37/ 109 (33.9)	23.4 (8.3, NE)	11/ 33 (33.3)	11.3 (5.6, NE)	0.72 (0.37, 1.42)	0.3404	
Presence of Liver Metastases							0.0258
Yes	47/ 135 (34.8)	23.4 (23.4, NE)	14/ 40 (35.0)	NE (5.6, NE)	0.78 (0.43, 1.41)	0.4154	
No	38/ 84 (45.2)	11.6 (5.8, NE)	4/ 26 (15.4)	NE (NE , NE)	3.07 (1.09, 8.61)	0.0246	
Side of Tumor							0.5570
Left	28/ 83 (33.7)	NE (8.3, NE)	7/ 33 (21.2)	NE (11.3, NE)	1.45 (0.63, 3.32)	0.3779	
Right	57/ 136 (41.9)	14.7 (6.7, NE)	11/ 33 (33.3)	NE (3.2, NE)	1.03 (0.54, 1.96)	0.9215	

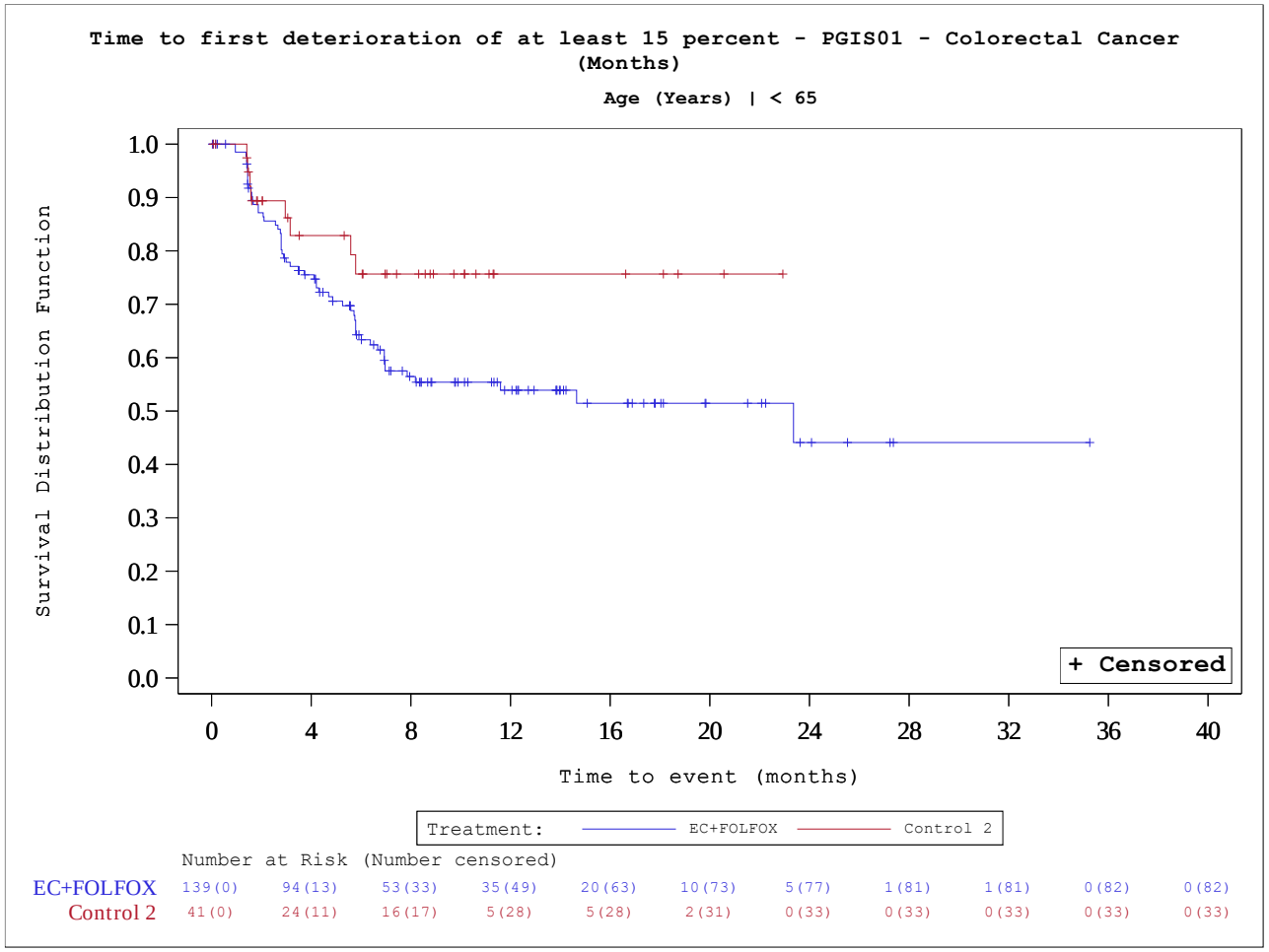
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.
[4] P-Value for interaction from Cox proportional hazards model using ties=exact option with treatment, subgroup and treatment*subgroup interaction as covariates.
Including only patients from the full analysis set who completed a baseline (last PRO assessment prior to or on the first dose of study treatment) and at least 1 post-baseline PRO assessment.
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Kaplan Meier Plot of Time to first deterioration of at least 15 percent - PGIS01 - Colorectal Cancer (Months)
Full Analysis Set



Kaplan-Meier Plots for subgroups only created if p-value for interaction < 0.05.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Kaplan Meier Plot of Time to first deterioration of at least 15 percent - PGIS01 - Colorectal Cancer (Months)
Full Analysis Set



Kaplan-Meier Plots for subgroups only created if p-value for interaction < 0.05.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
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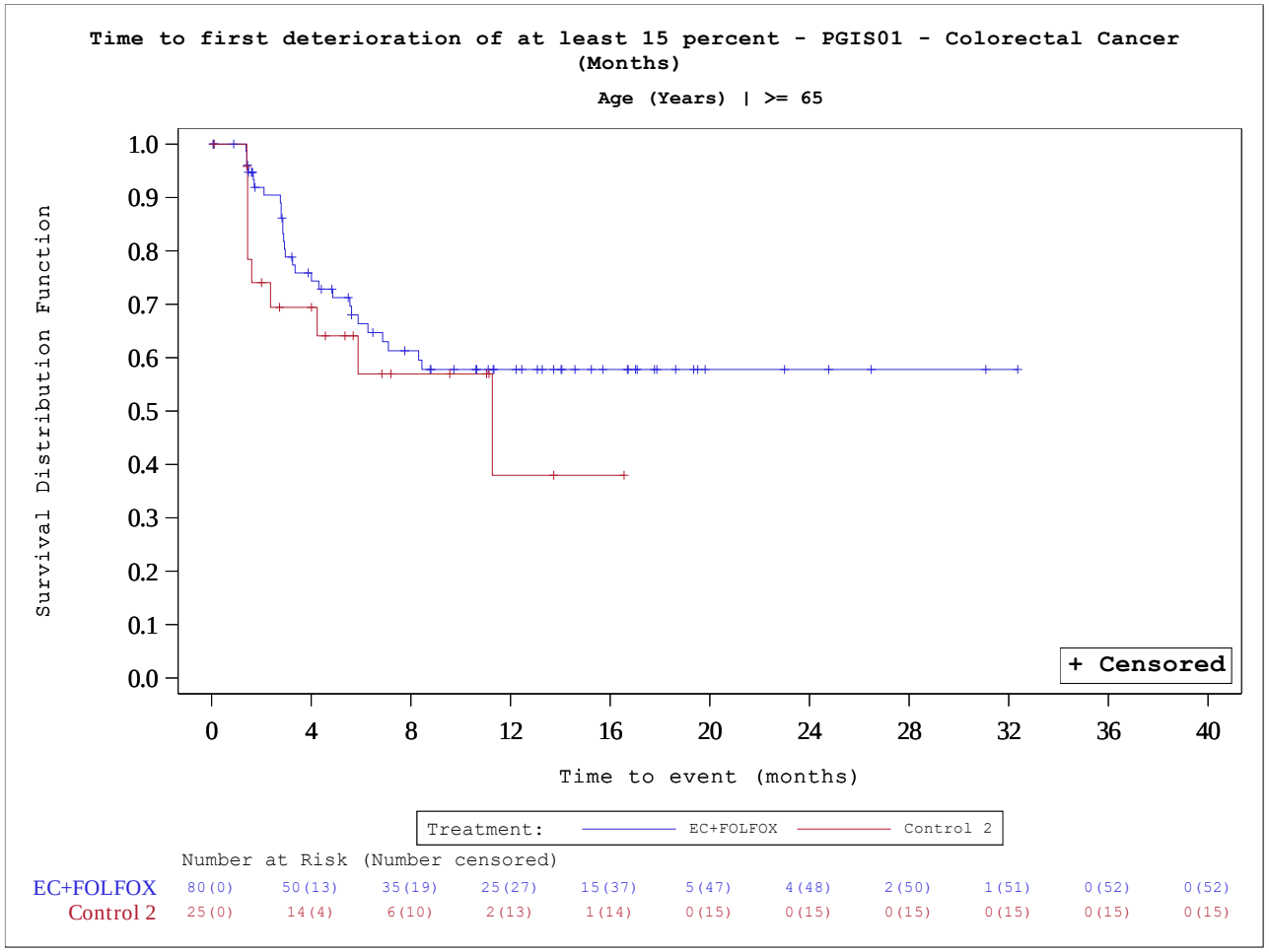
Kaplan Meier Plot of Time to first deterioration of at least 15 percent - PGIS01 - Colorectal Cancer (Months)
Full Analysis Set



Kaplan-Meier Plots for subgroups only created if p-value for interaction < 0.05.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
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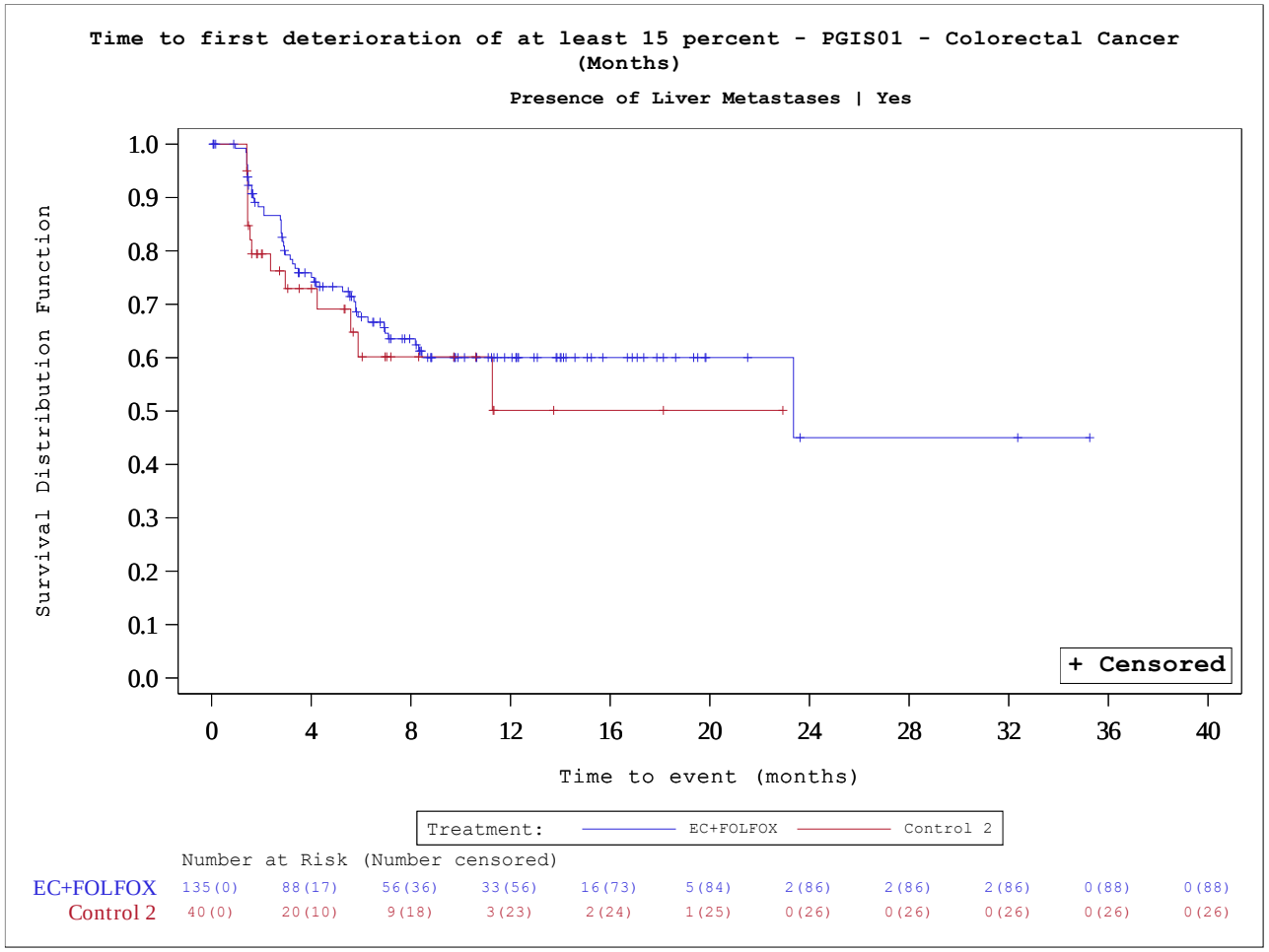

Kaplan-Meier Plots for subgroups only created if p-value for interaction < 0.05.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
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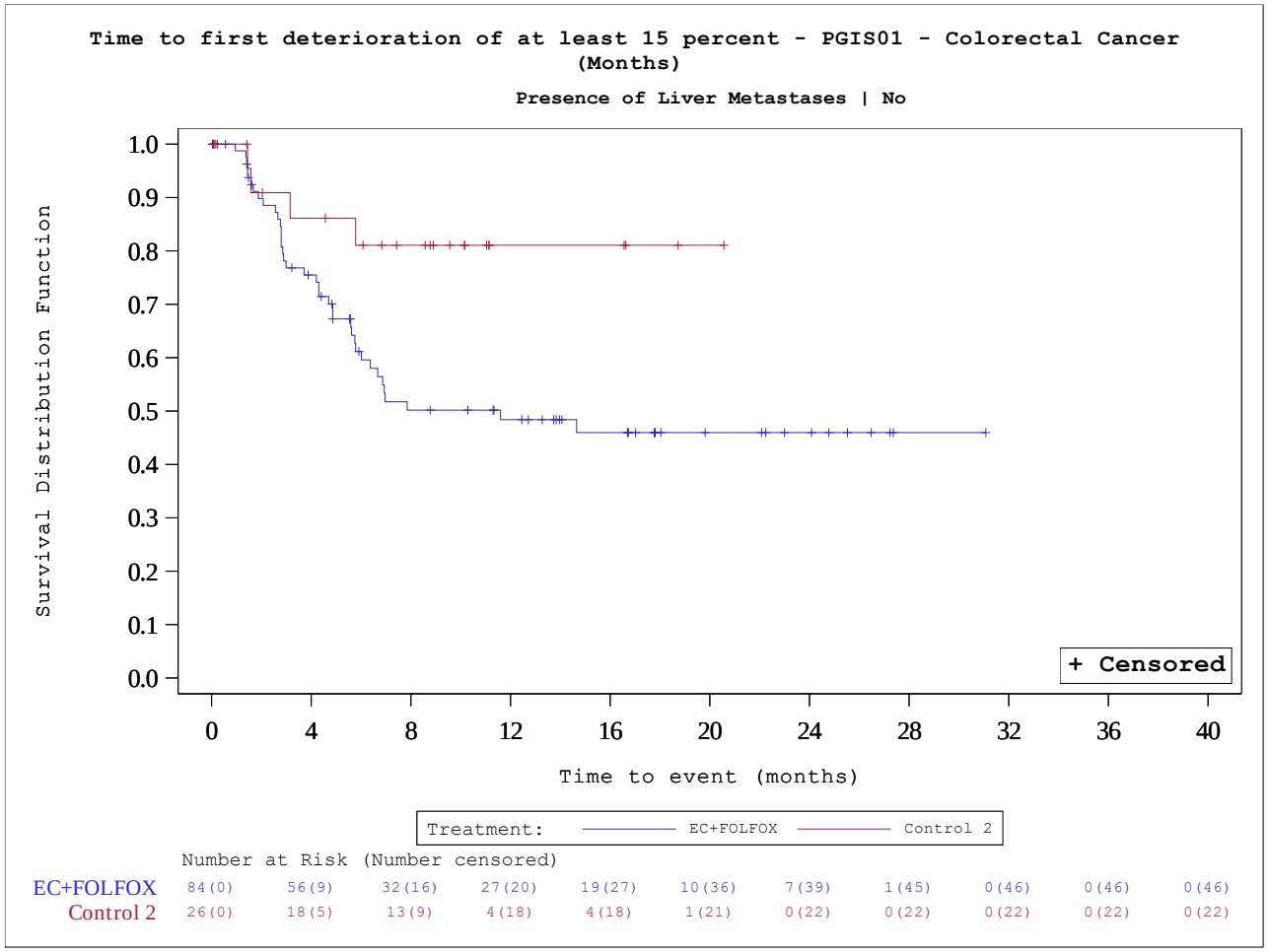
Full Analysis Set



Kaplan-Meier Plots for subgroups only created if p-value for interaction < 0.05.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Time to first improvement of at least 15 percent - PGIS01 - Colorectal Cancer (Months)
Full Analysis Set

	EC+FOLFOX (N=219)	Control 2 (N=66)
Number of subjects with events, n (%)	116 (53.0)	21 (31.8)
Number of censored subjects, n (%)	103 (47.0)	45 (68.2)
Kaplan-Meier estimates of Time to Event (Months) [1]		
25%-ile (95% CI)	1.6 (1.5, 2.1)	4.7 (1.6, 9.0)
Median (95% CI)	6.0 (3.9, 8.5)	NE (8.1, NE)
75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
Stratified analysis [2]		
Hazard Ratio (95% CI) [3]	1.74 (1.09, 2.78)	
p-value [4]	0.0191	

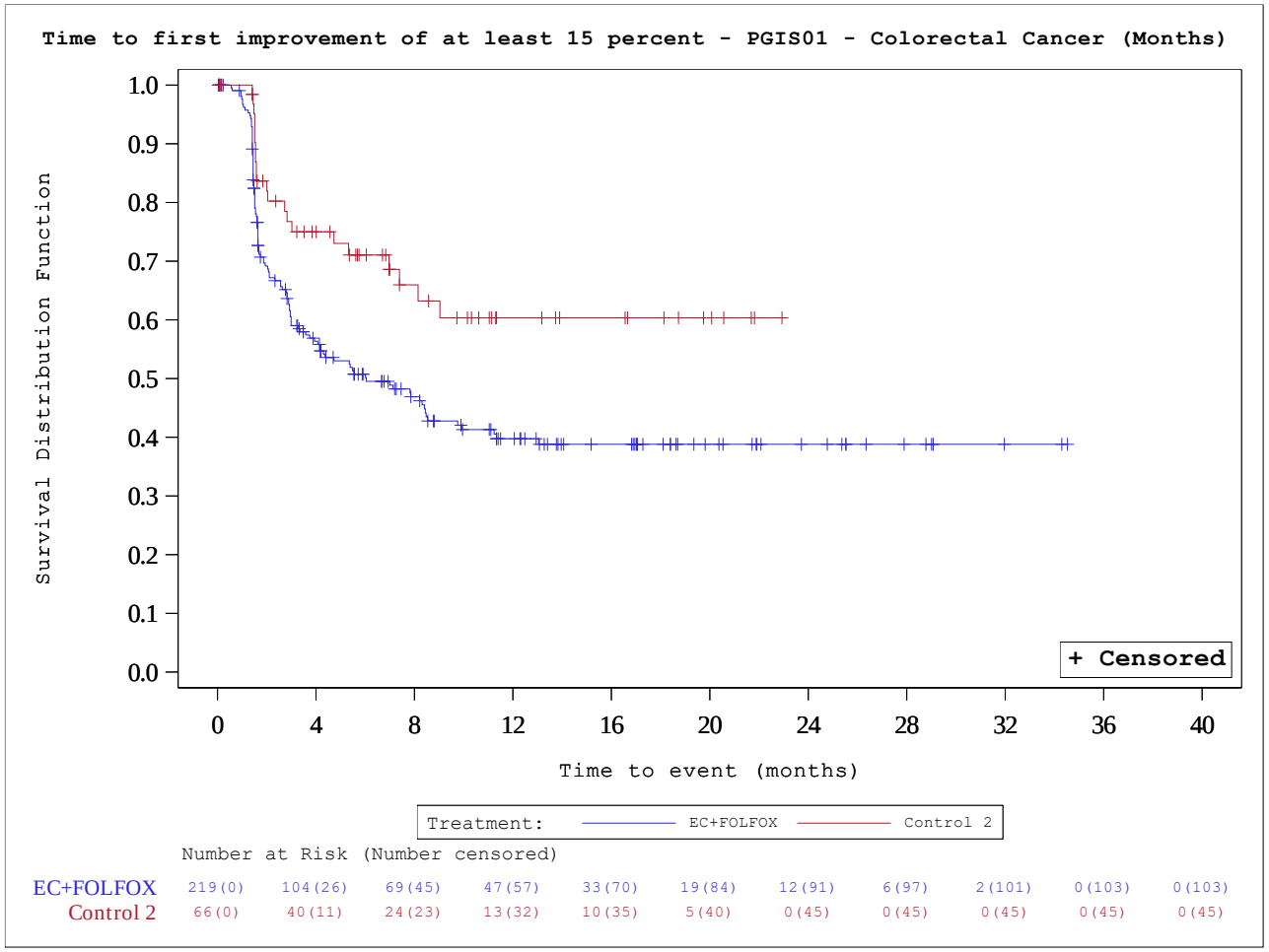
[1] Based on the Brookmeyer and Crowley method.
[2] Stratified by ECOG PS by Randomization.
[3] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio > 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[4] P-value from 2-sided log-rank test.
Including only patients from the full analysis set who completed a baseline (last PRO assessment prior to or on the first dose of study treatment) and at least 1 post-baseline PRO assessment.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Time to first improvement of at least 15 percent - PGIS01 - Colorectal Cancer (Months) - Subgroup analysis
Full Analysis Set

Subgroup Level	EC+FOLFOX (N=219) n/ N (%)	EC+FOLFOX (N=219) Median (95% CI)[1]	Control 2 (N=66) n/ N (%)	Control 2 (N=66) Median (95% CI)[1]	Unstratified analysis Hazard Ratio (95% CI)[2]	Unstratified analysis p-Value[3]	Interaction p-Value[4]
Age (Years)							0.4942
< 65	79/ 139 (56.8)	5.6 (3.4, 9.8)	15/ 41 (36.6)	NE (5.3, NE)	1.68 (0.97, 2.92)	0.0613	
>= 65	37/ 80 (46.3)	7.9 (3.0, NE)	6/ 25 (24.0)	NE (8.1, NE)	2.42 (1.02, 5.75)	0.0384	
Sex							0.5708
Male	56/ 114 (49.1)	5.6 (3.0, NE)	8/ 31 (25.8)	NE (9.0, NE)	2.20 (1.05, 4.61)	0.0320	
Female	60/ 105 (57.1)	7.0 (3.3, 8.5)	13/ 35 (37.1)	NE (5.3, NE)	1.69 (0.93, 3.07)	0.0848	
Region							0.8155
Europe	55/ 104 (52.9)	7.9 (3.0, NE)	13/ 38 (34.2)	NE (7.0, NE)	1.68 (0.92, 3.09)	0.0891	
USA/Canada	4/ 8 (50.0)	7.8 (3.0, NE)	1/ 6 (16.7)	NE (NE , NE)	3.35 (0.37, 30.38)	0.2551	
Rest of World	57/ 107 (53.3)	5.5 (3.0, 9.8)	7/ 22 (31.8)	NE (3.0, NE)	1.90 (0.86, 4.16)	0.1022	
ECOG-PS at Randomization							0.2639
0	57/ 123 (46.3)	8.5 (5.4, NE)	11/ 43 (25.6)	NE (NE , NE)	2.21 (1.16, 4.21)	0.0139	
1	59/ 96 (61.5)	3.9 (2.6, 7.9)	10/ 23 (43.5)	7.0 (1.6, NE)	1.28 (0.65, 2.50)	0.4754	
Number of Organs Involved							0.8440
<= 2	53/ 110 (48.2)	8.4 (5.6, NE)	9/ 33 (27.3)	NE (9.0, NE)	1.99 (0.98, 4.04)	0.0510	
>= 3	63/ 109 (57.8)	4.2 (2.6, 7.9)	12/ 33 (36.4)	NE (5.3, NE)	1.83 (0.99, 3.39)	0.0515	
Presence of Liver Metastases							0.6377
Yes	71/ 135 (52.6)	5.4 (3.0, 11.2)	12/ 40 (30.0)	NE (7.4, NE)	2.09 (1.13, 3.85)	0.0158	
No	45/ 84 (53.6)	7.8 (3.6, 13.0)	9/ 26 (34.6)	NE (4.7, NE)	1.65 (0.81, 3.38)	0.1658	
Side of Tumor							0.1314
Left	44/ 83 (53.0)	6.0 (2.8, NE)	14/ 33 (42.4)	9.0 (4.7, NE)	1.39 (0.76, 2.54)	0.2761	
Right	72/ 136 (52.9)	7.8 (3.6, 11.3)	7/ 33 (21.2)	NE (NE , NE)	2.97 (1.37, 6.45)	0.0039	

[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio > 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.
[4] P-Value for interaction from Cox proportional hazards model using ties=exact option with treatment, subgroup and treatment*subgroup interaction as covariates.
Including only patients from the full analysis set who completed a baseline (last PRO assessment prior to or on the first dose of study treatment) and at least 1 post-baseline PRO assessment.
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Kaplan Meier Plot of Time to first improvement of at least 15 percent - PGIS01 - Colorectal Cancer (Months)
Full Analysis Set



Kaplan-Meier Plots for subgroups only created if p-value for interaction < 0.05.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Time to first deterioration of at least 15 percent - PGI01-Change (Months)
Full Analysis Set

	EC+FOLFOX (N=212)	Control 2 (N=62)
Number of subjects with events, n (%)	136 (64.2)	43 (69.4)
Number of censored subjects, n (%)	76 (35.8)	19 (30.6)
Kaplan-Meier estimates of Time to Event (Months) [1]		
25%-ile (95% CI)	1.6 (1.5, 2.3)	1.5 (1.4, 1.8)
Median (95% CI)	6.4 (4.7, 7.7)	2.8 (1.9, 5.6)
75%-ile (95% CI)	22.1 (12.9, NE)	12.5 (5.6, NE)
Stratified analysis [2]		
Hazard Ratio (95% CI) [3]	0.77 (0.55, 1.09)	
p-value [4]	0.1450	

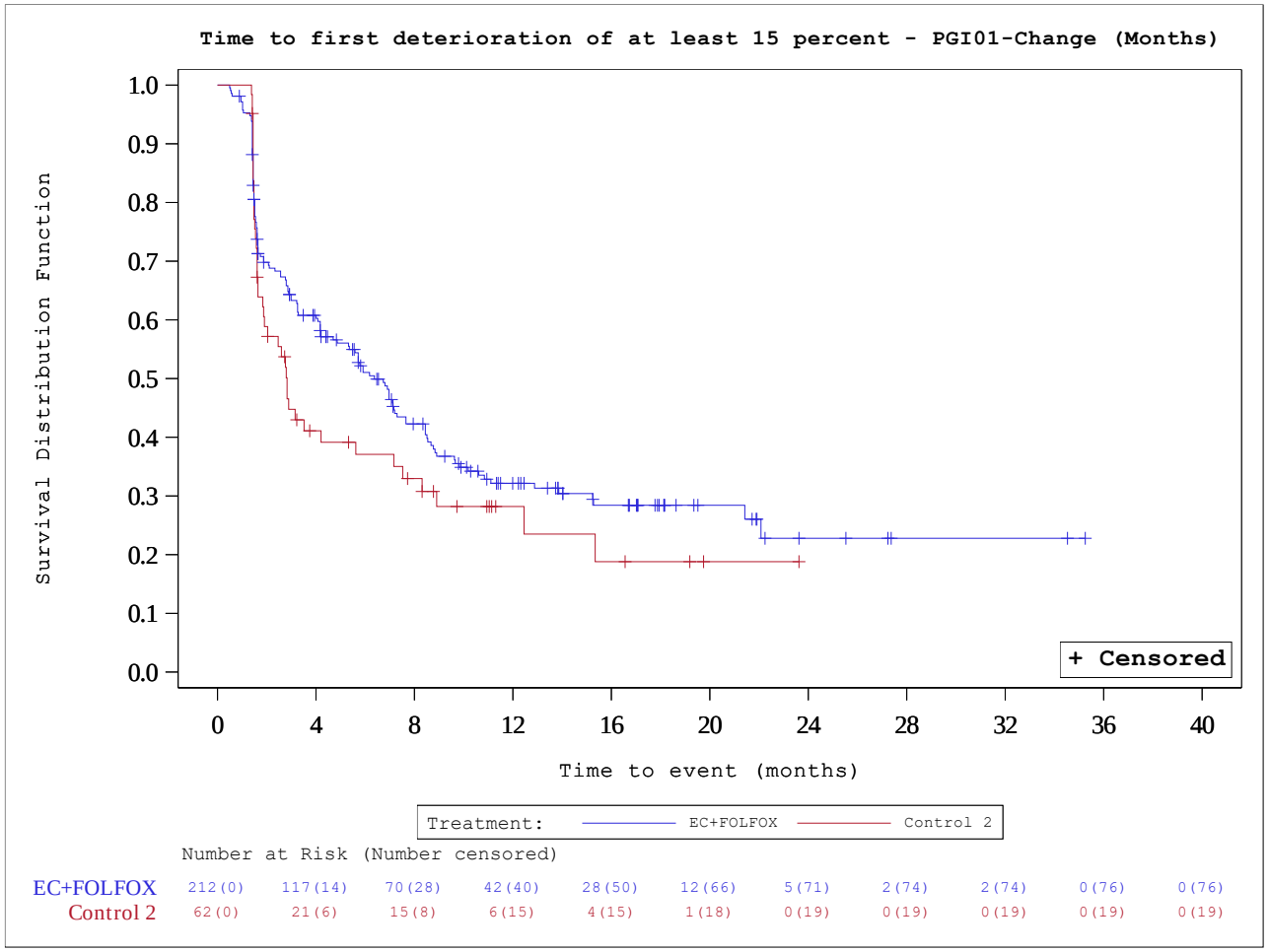
[1] Based on the Brookmeyer and Crowley method.
[2] Stratified by ECOG PS by Randomization.
[3] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[4] P-value from 2-sided log-rank test.
Including only patients from the full analysis set who completed at least 1 post-baseline PRO assessment.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Time to first deterioration of at least 15 percent - PGI01-Change (Months) - Subgroup analysis
Full Analysis Set

Subgroup Level	EC+FOLFOX (N=212) n/ N (%)	EC+FOLFOX (N=212) Median (95% CI)[1]	Control 2 (N=62) n/ N (%)	Control 2 (N=62) Median (95% CI)[1]	Unstratified analysis Hazard Ratio (95% CI)[2]	Unstratified analysis p-Value[3]	Interaction p-Value[4]
Age (Years)							0.6906
< 65	84/ 135 (62.2)	7.0 (5.7, 8.7)	25/ 39 (64.1)	3.2 (2.0, 8.3)	0.81 (0.52, 1.27)	0.3459	
>= 65	52/ 77 (67.5)	5.3 (2.9, 7.7)	18/ 23 (78.3)	1.9 (1.5, 7.5)	0.70 (0.41, 1.20)	0.2000	
Sex							0.0169
Male	70/ 109 (64.2)	5.8 (4.1, 7.1)	25/ 29 (86.2)	1.8 (1.6, 2.8)	0.48 (0.30, 0.76)	0.0015	
Female	66/ 103 (64.1)	7.2 (4.9, 9.6)	18/ 33 (54.5)	8.9 (2.9, 15.3)	1.11 (0.66, 1.88)	0.6841	
Region							0.0551
Europe	69/ 103 (67.0)	5.6 (2.9, 7.3)	30/ 35 (85.7)	2.5 (1.6, 2.8)	0.59 (0.38, 0.90)	0.0150	
USA/Canada	7/ 8 (87.5)	4.2 (1.6, 7.0)	2/ 6 (33.3)	NE (1.9, NE)	2.81 (0.58, 13.70)	0.1786	
Rest of World	60/ 101 (59.4)	7.7 (5.7, 10.2)	11/ 21 (52.4)	5.6 (1.6, NE)	0.97 (0.51, 1.85)	0.9268	
ECOG-PS at Randomization							0.5104
0	75/ 119 (63.0)	5.9 (3.3, 9.6)	30/ 42 (71.4)	2.6 (1.6, 7.2)	0.72 (0.47, 1.11)	0.1360	
1	61/ 93 (65.6)	6.8 (4.2, 7.7)	13/ 20 (65.0)	2.8 (2.0, NE)	0.88 (0.48, 1.61)	0.6647	
Number of Organs Involved							0.8151
<= 2	72/ 108 (66.7)	5.3 (3.2, 8.9)	22/ 32 (68.8)	1.9 (1.6, 8.9)	0.80 (0.50, 1.30)	0.3816	
>= 3	64/ 104 (61.5)	7.0 (5.7, 8.4)	21/ 30 (70.0)	3.2 (2.0, 7.5)	0.71 (0.43, 1.16)	0.1658	
Presence of Liver Metastases							0.1342
Yes	80/ 131 (61.1)	7.0 (4.2, 8.4)	29/ 39 (74.4)	2.0 (1.6, 7.2)	0.62 (0.40, 0.95)	0.0285	
No	56/ 81 (69.1)	5.9 (4.0, 8.5)	14/ 23 (60.9)	3.2 (2.6, NE)	1.04 (0.58, 1.87)	0.8925	
Side of Tumor							0.0452
Left	51/ 80 (63.8)	7.0 (4.9, 8.4)	19/ 32 (59.4)	7.5 (2.8, 12.5)	1.10 (0.65, 1.87)	0.7250	
Right	85/ 132 (64.4)	5.8 (4.1, 8.5)	24/ 30 (80.0)	1.9 (1.5, 2.8)	0.53 (0.33, 0.83)	0.0060	

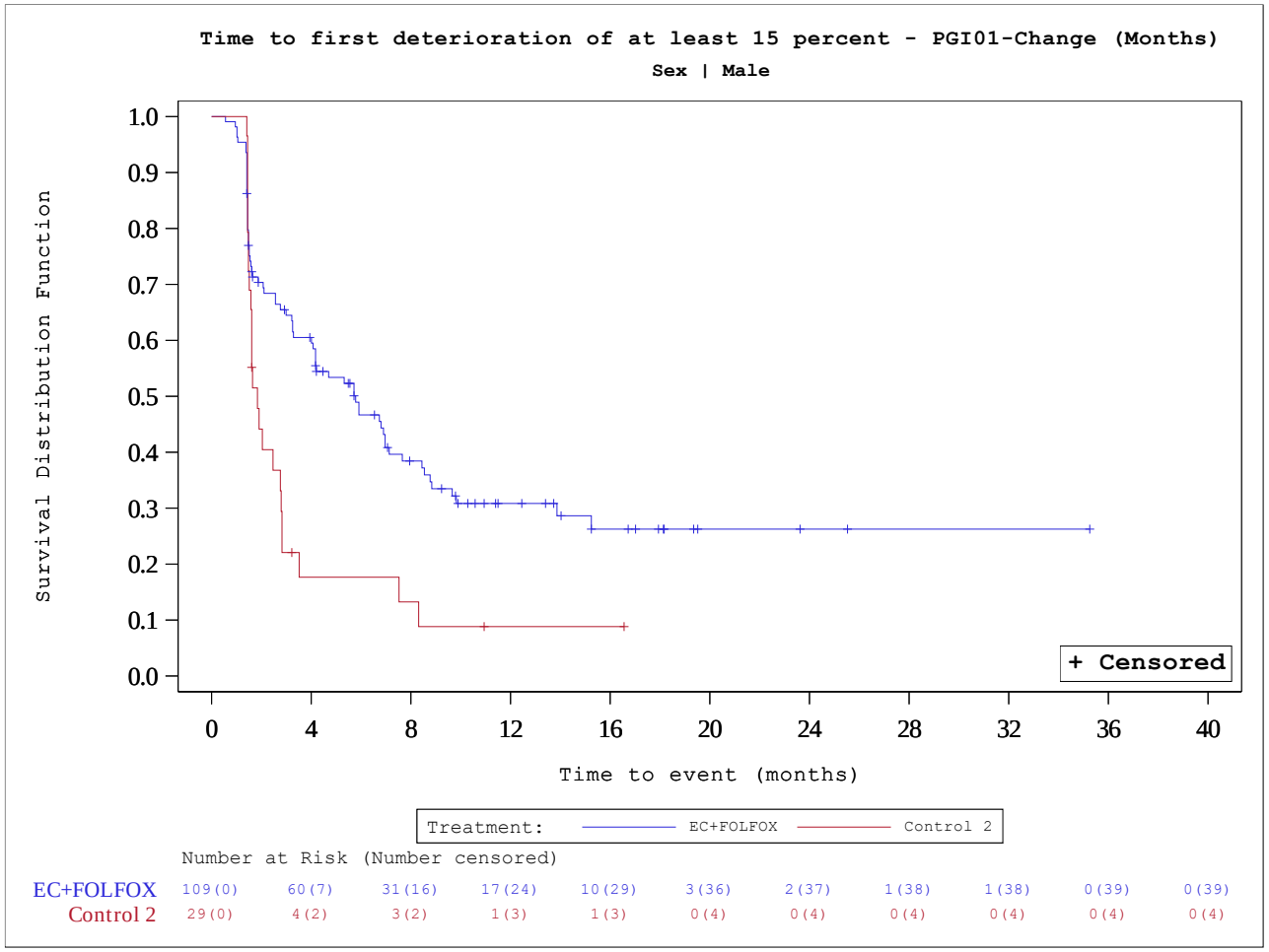
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.
[4] P-Value for interaction from Cox proportional hazards model using ties=exact option with treatment, subgroup and treatment*subgroup interaction as covariates.
Including only patients from the full analysis set who completed at least 1 post-baseline PRO assessment.
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Kaplan Meier Plot of Time to first deterioration of at least 15 percent - PGI01-Change (Months)
Full Analysis Set

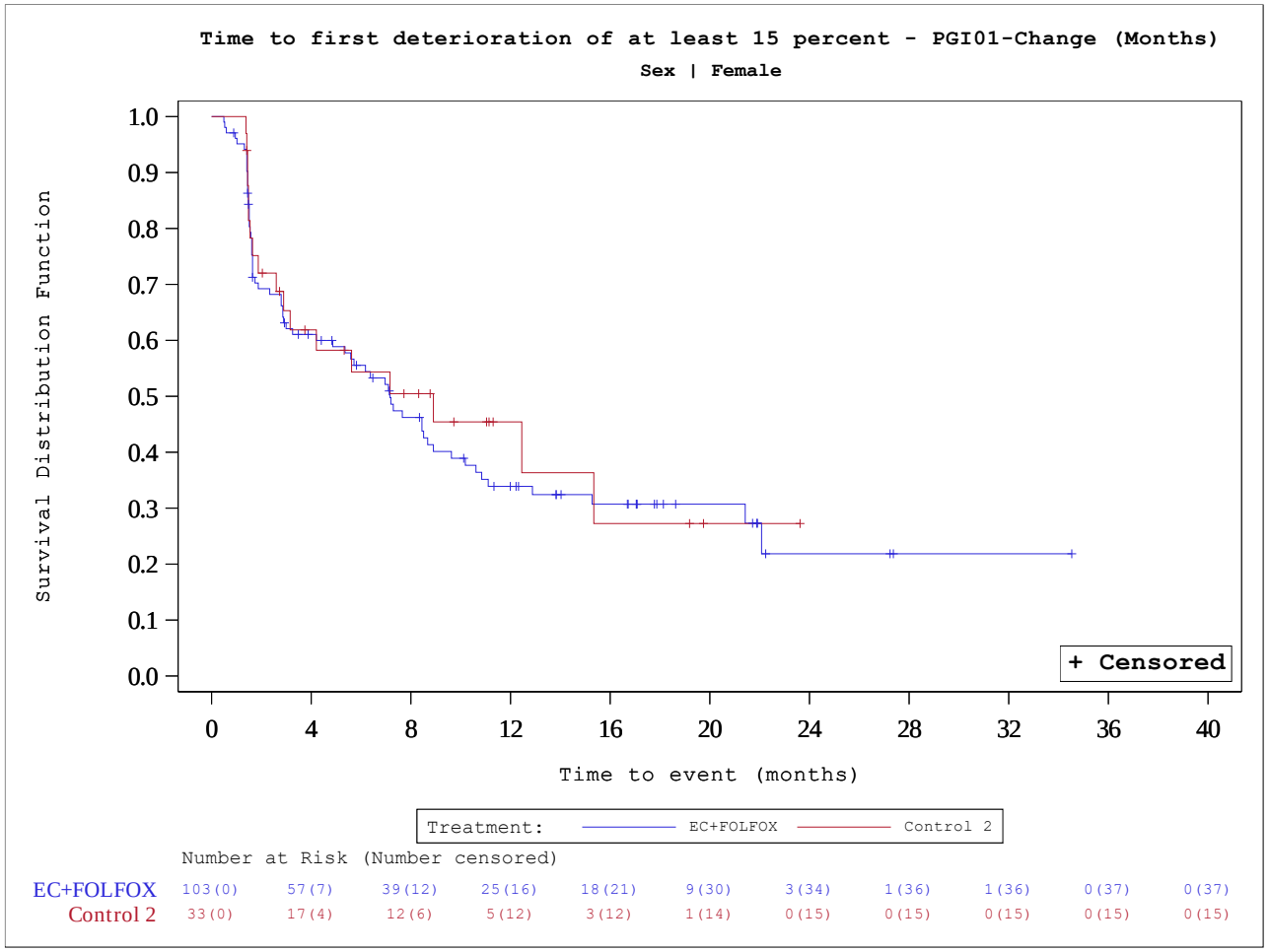


Kaplan-Meier Plots for subgroups only created if p-value for interaction < 0.05.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Kaplan Meier Plot of Time to first deterioration of at least 15 percent - PGI01-Change (Months)
Full Analysis Set



Kaplan-Meier Plots for subgroups only created if p-value for interaction < 0.05.



Kaplan-Meier Plots for subgroups only created if p-value for interaction < 0.05.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
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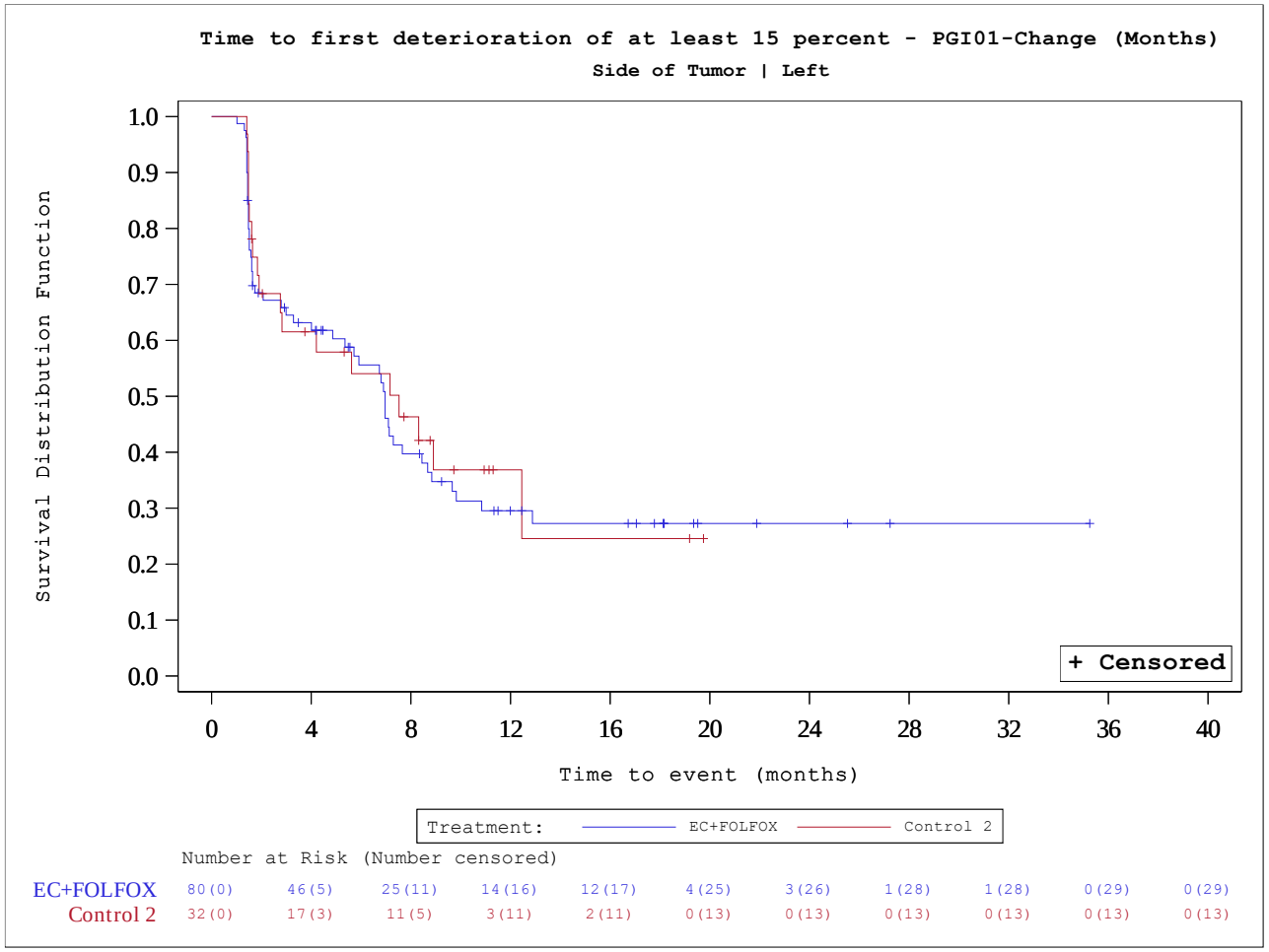
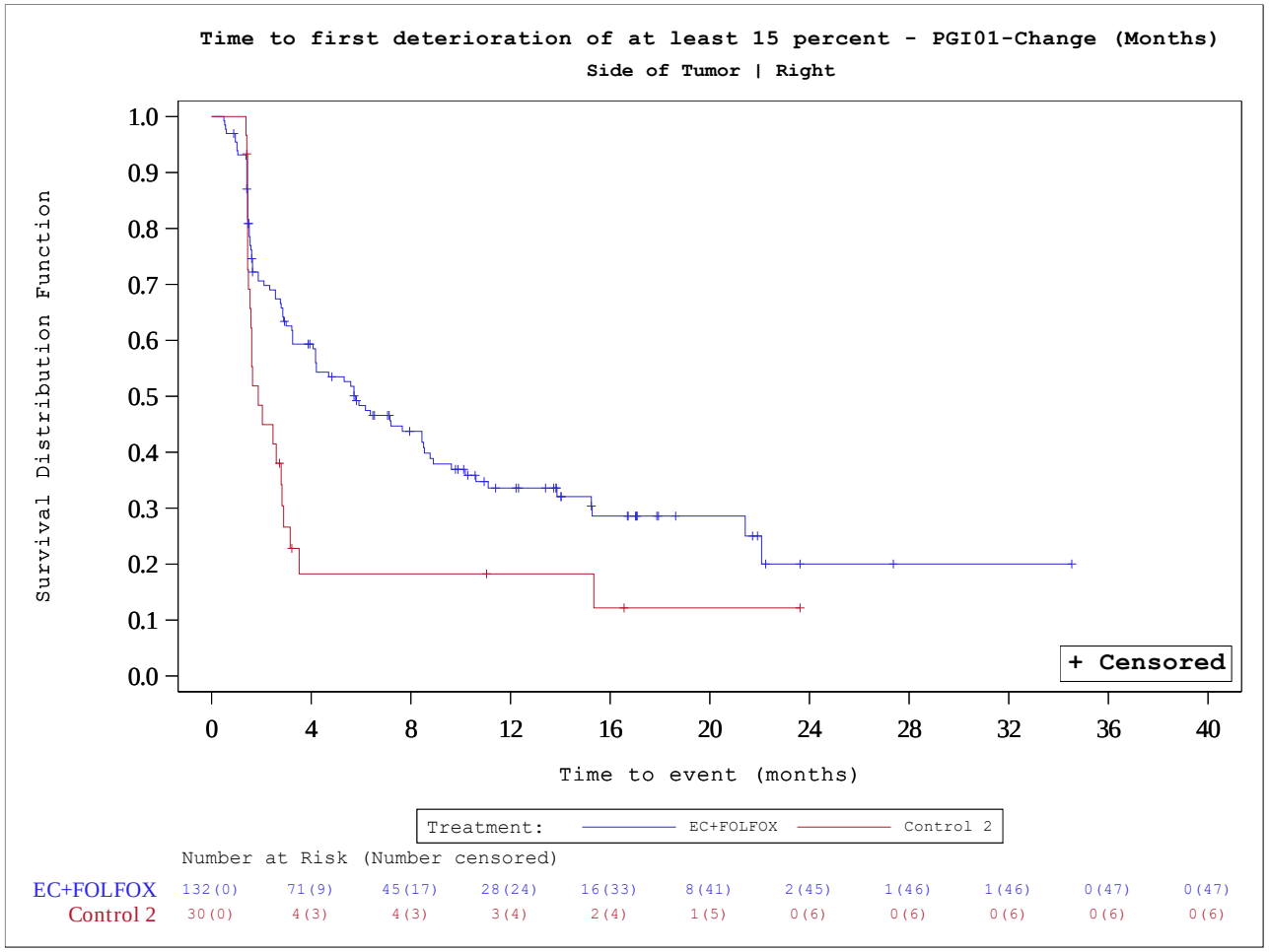
Kaplan Meier Plot of Time to first deterioration of at least 15 percent - PGI01-Change (Months)
Full Analysis Set



Kaplan-Meier Plots for subgroups only created if p-value for interaction < 0.05.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Kaplan Meier Plot of Time to first deterioration of at least 15 percent - PGI01-Change (Months)
Full Analysis Set



Kaplan-Meier Plots for subgroups only created if p-value for interaction < 0.05.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Time to first improvement of at least 15 percent - PGI01-Change (Months)
Full Analysis Set

	EC+FOLFOX (N=212)	Control 2 (N=62)
Number of subjects with events, n (%)	150 (70.8)	33 (53.2)
Number of censored subjects, n (%)	62 (29.2)	29 (46.8)
Kaplan-Meier estimates of Time to Event (Months) [1]		
25%-ile (95% CI)	2.6 (1.7, 2.8)	3.0 (1.7, 5.3)
Median (95% CI)	4.3 (3.4, 5.6)	7.2 (4.4, 10.1)
75%-ile (95% CI)	11.7 (9.0, 17.1)	NE (9.8, NE)
Stratified analysis [2]		
Hazard Ratio (95% CI) [3]	1.39 (0.95, 2.03)	
p-value [4]	0.0896	

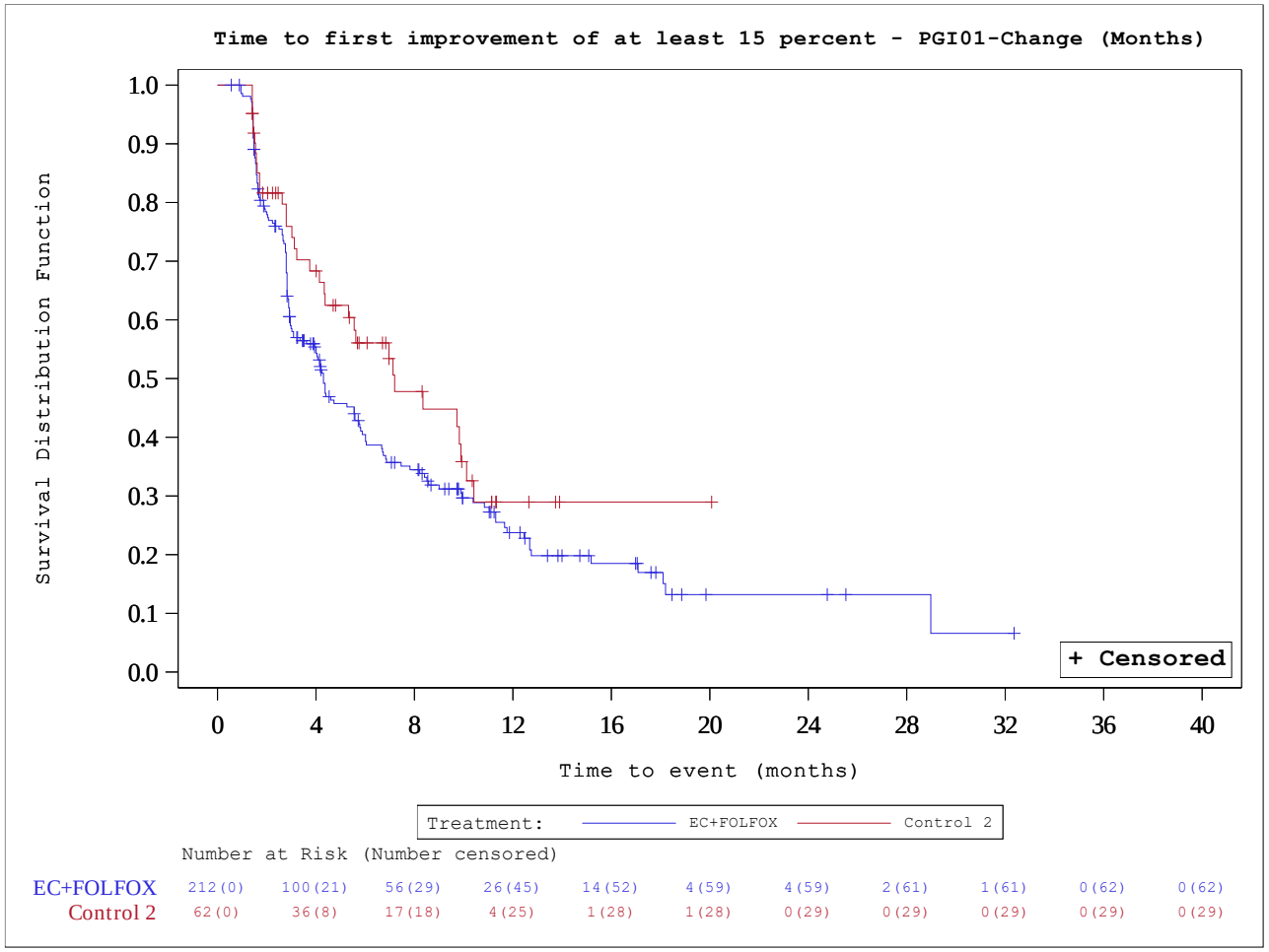
[1] Based on the Brookmeyer and Crowley method.
[2] Stratified by ECOG PS by Randomization.
[3] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio > 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[4] P-value from 2-sided log-rank test.
Including only patients from the full analysis set who completed at least 1 post-baseline PRO assessment.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Time to first improvement of at least 15 percent - PGI01-Change (Months) - Subgroup analysis
Full Analysis Set

Subgroup Level	EC+FOLFOX (N=212) n/ N (%)	EC+FOLFOX (N=212) Median (95% CI)[1]	Control 2 (N=62) n/ N (%)	Control 2 (N=62) Median (95% CI)[1]	Unstratified analysis Hazard Ratio (95% CI)[2]	Unstratified analysis p-Value[3]	Interaction p-Value[4]
Age (Years)							0.0855
< 65	92/ 135 (68.1)	4.4 (3.0, 6.0)	24/ 39 (61.5)	7.0 (4.1, 9.9)	1.05 (0.67, 1.65)	0.8335	
>= 65	58/ 77 (75.3)	4.2 (2.9, 5.9)	9/ 23 (39.1)	NE (4.4, NE)	2.17 (1.07, 4.39)	0.0279	
Sex							0.8117
Male	76/ 109 (69.7)	5.6 (3.4, 6.9)	14/ 29 (48.3)	7.0 (4.3, NE)	1.31 (0.74, 2.32)	0.3536	
Female	74/ 103 (71.8)	4.2 (2.9, 5.3)	19/ 33 (57.6)	7.2 (3.7, 9.9)	1.45 (0.87, 2.41)	0.1489	
Region							0.4651
Europe	68/ 103 (66.0)	5.3 (4.2, 6.8)	16/ 35 (45.7)	8.3 (5.3, NE)	1.31 (0.76, 2.27)	0.3294	
USA/Canada	6/ 8 (75.0)	4.4 (1.6, 7.5)	5/ 6 (83.3)	5.0 (2.6, 10.1)	0.88 (0.27, 2.90)	0.8330	
Rest of World	76/ 101 (75.2)	2.9 (2.8, 4.4)	12/ 21 (57.1)	9.8 (3.2, NE)	1.68 (0.91, 3.09)	0.0913	
ECOG-PS at Randomization							0.8607
0	88/ 119 (73.9)	4.3 (2.9, 6.7)	24/ 42 (57.1)	7.0 (4.3, 10.1)	1.39 (0.88, 2.18)	0.1551	
1	62/ 93 (66.7)	4.4 (4.0, 5.8)	9/ 20 (45.0)	9.9 (1.7, NE)	1.39 (0.69, 2.81)	0.3539	
Number of Organs Involved							0.9836
<= 2	83/ 108 (76.9)	4.3 (2.9, 6.0)	19/ 32 (59.4)	8.3 (4.1, 10.1)	1.35 (0.82, 2.23)	0.2360	
>= 3	67/ 104 (64.4)	4.4 (3.6, 6.0)	14/ 30 (46.7)	7.0 (3.7, NE)	1.44 (0.81, 2.56)	0.2172	
Presence of Liver Metastases							0.7169
Yes	94/ 131 (71.8)	4.2 (3.0, 5.7)	20/ 39 (51.3)	7.0 (4.3, 10.1)	1.46 (0.90, 2.37)	0.1223	
No	56/ 81 (69.1)	5.3 (2.9, 8.6)	13/ 23 (56.5)	9.8 (2.8, NE)	1.22 (0.67, 2.25)	0.5093	
Side of Tumor							0.2597
Left	53/ 80 (66.3)	4.6 (3.0, 9.9)	18/ 32 (56.3)	9.7 (3.1, 10.4)	1.07 (0.63, 1.84)	0.7988	
Right	97/ 132 (73.5)	4.2 (2.9, 5.6)	15/ 30 (50.0)	7.1 (4.3, 10.1)	1.64 (0.95, 2.83)	0.0718	

[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio > 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.
[4] P-Value for interaction from Cox proportional hazards model using ties=exact option with treatment, subgroup and treatment*subgroup interaction as covariates.
Including only patients from the full analysis set who completed at least 1 post-baseline PRO assessment.
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Kaplan Meier Plot of Time to first improvement of at least 15 percent - PGI01-Change (Months)
Full Analysis Set



Kaplan-Meier Plots for subgroups only created if p-value for interaction < 0.05.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Responder Analysis of Objective Response Rate based on BICR Assessment
Full Analysis Set

	EC+FOLFOX (N=236)	Control 2 (N=74)
Number of subjects with events, n (%)	155 (65.7)	30 (40.5)
Number of censored subjects, n (%)	81 (34.3)	44 (59.5)
Stratified analysis [1]		
Relative Risk (95% CI) [2]	1.51 (1.14, 2.01)	
p-value	0.0040	
Odds Ratio (95% CI) [2]	2.88 (1.65, 5.04)	
p-value	0.0002	
Risk Difference (95% CI) [2]	26.07 (13.46, 38.68)	
p-value	<.0001	

[1] Stratified by ECOG PS by Randomization.
[2] Calculated using normal approximation (Wald).
Risk ratio > 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Responder Analysis of Objective Response Rate based on BICR Assessment - Subgroup analysis
Full Analysis Set

Subgroup Level	EC+FOLFOX (N=236) n/ N (%)	Control 2 (N=74) n/ N (%)	Unstratified analysis Relative Risk (95% CI) [1]	p-Value [1]	Interaction p-Value [2]
Age (Years)					0.6610
< 65	100/ 150 (66.7)	18/ 46 (39.1)	1.70 (1.17, 2.49)	0.0057	
>= 65	55/ 86 (64.0)	12/ 28 (42.9)	1.49 (0.95, 2.35)	0.0855	
Sex					0.2826
Male	82/ 123 (66.7)	12/ 35 (34.3)	1.94 (1.21, 3.13)	0.0061	
Female	73/ 113 (64.6)	18/ 39 (46.2)	1.40 (0.97, 2.02)	0.0713	
Region					0.2740
Europe	76/ 109 (69.7)	15/ 43 (34.9)	2.00 (1.30, 3.06)	0.0015	
USA/Canada	8/ 15 (53.3)	4/ 8 (50.0)	1.07 (0.46, 2.47)	0.8802	
Rest of World	71/ 112 (63.4)	11/ 23 (47.8)	1.33 (0.85, 2.08)	0.2192	
ECOG-PS at Randomization					0.0804
0	89/ 131 (67.9)	24/ 48 (50.0)	1.36 (1.00, 1.85)	0.0498	
1	66/ 105 (62.9)	6/ 26 (23.1)	2.72 (1.33, 5.58)	0.0062	
Number of Organs Involved					0.0504
<= 2	77/ 119 (64.7)	18/ 34 (52.9)	1.22 (0.87, 1.72)	0.2523	
>= 3	78/ 117 (66.7)	12/ 40 (30.0)	2.22 (1.36, 3.63)	0.0014	
Presence of Liver Metastases					0.5366
Yes	100/ 147 (68.0)	18/ 46 (39.1)	1.74 (1.19, 2.53)	0.0040	
No	55/ 89 (61.8)	12/ 28 (42.9)	1.44 (0.91, 2.28)	0.1172	
Side of Tumor					0.7282
Left	60/ 90 (66.7)	14/ 36 (38.9)	1.71 (1.11, 2.65)	0.0151	
Right	95/ 146 (65.1)	16/ 38 (42.1)	1.55 (1.04, 2.29)	0.0292	

[1] Calculated using normal approximation (Wald).
[2] p-Value for interaction based on Cochran´s Q Test.
Risk ratio > 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Completion Rates of EORTC QLQ-C30
Full Analysis Set

	EC+FOLFOX (N=236)		Control 2 (N=74)	
Visit	Number of patients [1]	Completed (%)	Number of patients [1]	Completed (%)
BASELINE	201	201 (100.0)	44	44 (100.0)
WEEK6	194	190 (97.9)	58	56 (96.6)
WEEK12	187	182 (97.3)	41	41 (100.0)
WEEK18	180	179 (99.4)	41	40 (97.6)
WEEK24	163	161 (98.8)	36	35 (97.2)
WEEK30	144	140 (97.2)	28	28 (100.0)
WEEK36	140	139 (99.3)	23	23 (100.0)
WEEK42	123	123 (100.0)	20	20 (100.0)
WEEK48	112	106 (94.6)	14	14 (100.0)
WEEK54	98	93 (94.9)	11	11 (100.0)
WEEK60	82	79 (96.3)	11	11 (100.0)
WEEK66	71	67 (94.4)	8	8 (100.0)
WEEK72	63	59 (93.7)	9	9 (100.0)
WEEK78	50	49 (98.0)	6	6 (100.0)
WEEK86	37	35 (94.6)	6	6 (100.0)
WEEK94	34	33 (97.1)	3	3 (100.0)
WEEK102	22	21 (95.5)	0	
WEEK110	0		0	
WEEK118	13	12 (92.3)	0	
WEEK126	8	8 (100.0)	0	
WEEK134	8	7 (87.5)	0	
WEEK142	4	4 (100.0)	0	
WEEK150	2	2 (100.0)	0	
WEEK158	1	1 (100.0)	0	
WEEK166	0		0	
WEEK174	0		0	
WEEK182	0		0	
WEEK190	0		0	
WEEK198	0		0	
WEEK206	0		0	
WEEK214	0		0	
END OF TRT	79	77 (97.5)	39	39 (100.0)
FOLLOW UP	50	48 (96.0)	23	22 (95.7)

Baseline is the last non-missing measurement prior to first dose of study intervention.
[1] Defined as the number of patients who are eligible to complete the questionnaire at the respective visit.

	EC+FOLFOX (N=236)		Control 2 (N=74)	
Visit	Number of patients [1]	Completed (%)	Number of patients [1]	Completed (%)
BASELINE	197	197 (100.0)	42	42 (100.0)
WEEK6	192	188 (97.9)	56	54 (96.4)
WEEK12	185	180 (97.3)	40	40 (100.0)
WEEK18	177	175 (98.9)	40	39 (97.5)
WEEK24	161	159 (98.8)	35	34 (97.1)
WEEK30	136	136 (100.0)	28	28 (100.0)
WEEK36	136	136 (100.0)	23	23 (100.0)
WEEK42	121	121 (100.0)	20	20 (100.0)
WEEK48	110	104 (94.5)	14	14 (100.0)
WEEK54	96	91 (94.8)	11	11 (100.0)
WEEK60	81	78 (96.3)	11	11 (100.0)
WEEK66	70	66 (94.3)	8	8 (100.0)
WEEK72	62	58 (93.5)	9	9 (100.0)
WEEK78	49	48 (98.0)	6	6 (100.0)
WEEK86	36	34 (94.4)	6	6 (100.0)
WEEK94	33	32 (97.0)	3	3 (100.0)
WEEK102	22	20 (90.9)	0	
WEEK110	19	19 (100.0)	0	
WEEK118	12	11 (91.7)	0	
WEEK126	8	8 (100.0)	0	
WEEK134	7	6 (85.7)	0	
WEEK142	4	4 (100.0)	0	
WEEK150	2	2 (100.0)	0	
WEEK158	1	1 (100.0)	0	
WEEK166	0		0	
WEEK174	0		0	
WEEK182	0		0	
WEEK190	0		0	
WEEK198	0		0	
WEEK206	4	0 (0.0)	0	
WEEK214	2	0 (0.0)	0	
END OF TRT	75	75 (100.0)	39	38 (97.4)
FOLLOW UP	51	47 (92.2)	22	21 (95.5)

Baseline is the last non-missing measurement prior to first dose of study intervention.
[1] Defined as the number of patients who are eligible to complete the questionnaire at the respective visit.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Completion Rates of PGIS
Full Analysis Set

	EC+FOLFOX (N=236)		Control 2 (N=74)	
Visit	Number of patients [1]	Completed (%)	Number of patients [1]	Completed (%)
BASELINE	201	201 (100.0)	45	45 (100.0)
WEEK6	195	191 (97.9)	57	55 (96.5)
WEEK12	187	182 (97.3)	42	42 (100.0)
WEEK18	181	180 (99.4)	41	40 (97.6)
WEEK24	163	161 (98.8)	37	36 (97.3)
WEEK30	144	140 (97.2)	29	29 (100.0)
WEEK36	140	139 (99.3)	23	23 (100.0)
WEEK42	123	123 (100.0)	20	20 (100.0)
WEEK48	112	106 (94.6)	14	14 (100.0)
WEEK54	98	93 (94.9)	11	11 (100.0)
WEEK60	82	79 (96.3)	11	11 (100.0)
WEEK66	71	67 (94.4)	8	8 (100.0)
WEEK72	63	59 (93.7)	9	9 (100.0)
WEEK78	50	49 (98.0)	6	6 (100.0)
WEEK86	37	35 (94.6)	6	6 (100.0)
WEEK94	34	33 (97.1)	3	3 (100.0)
WEEK102	22	21 (95.5)	0	
WEEK110	20	20 (100.0)	0	
WEEK118	13	12 (92.3)	0	
WEEK126	8	8 (100.0)	0	
WEEK134	8	7 (87.5)	0	
WEEK142	4	4 (100.0)	0	
WEEK150	2	2 (100.0)	0	
WEEK158	1	1 (100.0)	0	
WEEK166	0		0	
WEEK174	0		0	
WEEK182	0		0	
WEEK190	0		0	
WEEK198	0		0	
WEEK206	0		0	
WEEK214	0		0	
END OF TRT	79	77 (97.5)	39	39 (100.0)
FOLLOW UP	2	0 (0.0)	7	4 (57.1)

Baseline is the last non-missing measurement prior to first dose of study intervention.
[1] Defined as the number of patients who are eligible to complete the questionnaire at the respective visit.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Completion Rates of PGIC
Full Analysis Set

	EC+FOLFOX (N=236)		Control 2 (N=74)	
Visit	Number of patients [1]	Completed (%)	Number of patients [1]	Completed (%)
WEEK6	195	190 (97.4)	55	51 (92.7)
WEEK12	187	181 (96.8)	42	42 (100.0)
WEEK18	181	180 (99.4)	41	38 (92.7)
WEEK24	163	156 (95.7)	36	34 (94.4)
WEEK30	144	140 (97.2)	29	29 (100.0)
WEEK36	140	138 (98.6)	23	23 (100.0)
WEEK42	123	123 (100.0)	20	20 (100.0)
WEEK48	112	105 (93.8)	14	14 (100.0)
WEEK54	98	91 (92.9)	11	11 (100.0)
WEEK60	82	79 (96.3)	11	11 (100.0)
WEEK66	71	67 (94.4)	8	7 (87.5)
WEEK72	63	59 (93.7)	9	9 (100.0)
WEEK78	50	49 (98.0)	6	6 (100.0)
WEEK86	37	35 (94.6)	6	6 (100.0)
WEEK94	34	32 (94.1)	3	3 (100.0)
WEEK102	22	21 (95.5)	0	
WEEK110	20	20 (100.0)	0	
WEEK118	13	12 (92.3)	0	
WEEK126	8	8 (100.0)	0	
WEEK134	8	7 (87.5)	0	
WEEK142	4	4 (100.0)	0	
WEEK150	2	2 (100.0)	0	
WEEK158	1	1 (100.0)	0	
WEEK166	0		0	
WEEK174	0		0	
WEEK182	0		0	
WEEK190	0		0	
WEEK198	0		0	
WEEK206	0		0	
WEEK214	0		0	
END OF TRT	79	75 (94.9)	39	36 (92.3)
FOLLOW UP	50	48 (96.0)	23	21 (91.3)

[1] Defined as the number of patients who are eligible to complete the questionnaire at the respective visit.

		EC+FOLFOX (N=236)	Control 2 (N=74)
EOR01-Global QOL	n (missing)	201 (35)	44 (30)
	Mean (SD)	67.12 (21.654)	67.23 (21.671)
	Median	66.67	66.67
	Q1, Q3	50.00, 83.33	50.00, 83.33
	Min, Max	0.0, 100.0	16.7, 100.0
EOR01-Physical Functioning	n (missing)	201 (35)	44 (30)
	Mean (SD)	82.92 (16.650)	85.76 (15.854)
	Median	86.67	93.33
	Q1, Q3	73.33, 93.33	80.00, 100.00
	Min, Max	13.3, 100.0	46.7, 100.0
EOR01-Role Functioning	n (missing)	201 (35)	44 (30)
	Mean (SD)	76.12 (24.982)	81.06 (27.040)
	Median	83.33	91.67
	Q1, Q3	66.67, 100.00	66.67, 100.00
	Min, Max	0.0, 100.0	0.0, 100.0
EOR01-Emotional Functioning	n (missing)	201 (35)	44 (30)
	Mean (SD)	73.71 (20.533)	75.57 (18.097)
	Median	75.00	75.00
	Q1, Q3	66.67, 83.33	62.50, 91.67
	Min, Max	0.0, 100.0	41.7, 100.0
EOR01-Cognitive Functioning	n (missing)	201 (35)	44 (30)
	Mean (SD)	87.73 (16.626)	89.39 (13.493)
	Median	100.00	100.00
	Q1, Q3	83.33, 100.00	83.33, 100.00
	Min, Max	16.7, 100.0	50.0, 100.0
EOR01-Social Functioning	n (missing)	201 (35)	44 (30)
	Mean (SD)	75.46 (24.384)	80.30 (24.714)
	Median	83.33	83.33
	Q1, Q3	66.67, 100.00	66.67, 100.00
	Min, Max	0.0, 100.0	16.7, 100.0
EOR01-Fatigue	n (missing)	201 (35)	44 (30)
	Mean (SD)	28.08 (21.944)	30.30 (22.526)
	Median	33.33	27.78
	Q1, Q3	11.11, 33.33	11.11, 33.33
	Min, Max	0.0, 88.9	0.0, 88.9
EOR01-Nausea and Vomiting	n (missing)	201 (35)	44 (30)
	Mean (SD)	4.81 (10.492)	6.44 (13.552)
	Median	0.00	0.00
	Q1, Q3	0.00, 0.00	0.00, 0.00
	Min, Max	0.0, 66.7	0.0, 50.0
EOR01-Pain	n (missing)	201 (35)	44 (30)
	Mean (SD)	25.54 (25.112)	20.83 (26.444)
	Median	16.67	16.67
	Q1, Q3	0.00, 33.33	0.00, 33.33
	Min, Max	0.0, 100.0	0.0, 100.0
EOR01-Dyspnoea	n (missing)	201 (35)	44 (30)
	Mean (SD)	13.60 (21.415)	12.12 (17.742)
	Median	0.00	0.00
	Q1, Q3	0.00, 33.33	0.00, 33.33
	Min, Max	0.0, 100.0	0.0, 66.7

		EC+FOLFOX (N=236)	Control 2 (N=74)
EOR01-Insomnia	n (missing)	201 (35)	44 (30)
	Mean (SD)	30.35 (28.905)	27.27 (28.999)
	Median	33.33	33.33
	Q1, Q3	0.00, 33.33	0.00, 33.33
	Min, Max	0.0, 100.0	0.0, 100.0
EOR01-Appetite Loss	n (missing)	201 (35)	44 (30)
	Mean (SD)	20.90 (26.354)	18.94 (29.111)
	Median	0.00	0.00
	Q1, Q3	0.00, 33.33	0.00, 33.33
	Min, Max	0.0, 100.0	0.0, 100.0
EOR01-Constipation	n (missing)	201 (35)	44 (30)
	Mean (SD)	14.10 (22.737)	15.91 (24.367)
	Median	0.00	0.00
	Q1, Q3	0.00, 33.33	0.00, 33.33
	Min, Max	0.0, 100.0	0.0, 100.0
EOR01-Diarrhea	n (missing)	201 (35)	44 (30)
	Mean (SD)	13.43 (23.376)	12.12 (22.836)
	Median	0.00	0.00
	Q1, Q3	0.00, 33.33	0.00, 33.33
	Min, Max	0.0, 100.0	0.0, 100.0
EOR01-Financial Difficulties	n (missing)	201 (35)	44 (30)
	Mean (SD)	17.41 (26.682)	16.67 (28.303)
	Median	0.00	0.00
	Q1, Q3	0.00, 33.33	0.00, 33.33
	Min, Max	0.0, 100.0	0.0, 100.0
EQ5D02-EQ-VAS Score	n (missing)	197 (39)	42 (32)
	Mean (SD)	70.85 (17.672)	74.71 (16.683)
	Median	70.00	79.00
	Q1, Q3	60.00, 83.00	65.00, 87.00
	Min, Max	16.0, 100.0	10.0, 100.0
PGIS01 - Colorectal Cancer	n (missing)	201 (35)	45 (29)
	Mean (SD)	1.31 (0.997)	1.20 (1.120)
	Median	1.00	1.00
	Q1, Q3	1.00, 2.00	0.00, 2.00
	Min, Max	0.0, 3.0	0.0, 3.0

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Summary over time - EOR01-Global QOL
Full Analysis Set

	EC+FOLFOX (N=236)				Control 2 (N=74)			
Visit	n	Median (Range)	Mean (SD)	95% CI [1]	n	Median (Range)	Mean (SD)	95% CI [1]
BASELINE	201	66.67 (0.0, 100.0)	67.12 (21.654)	[64.11, 70.13]	44	66.67 (16.7, 100.0)	67.23 (21.671)	[60.65, 73.82]
WEEK6	190	66.67 (0.0, 100.0)	64.74 (19.109)	[62.00, 67.47]	56	66.67 (16.7, 91.7)	62.95 (16.102)	[58.63, 67.26]
WEEK12	182	66.67 (0.0, 100.0)	66.35 (19.079)	[63.56, 69.14]	41	66.67 (0.0, 100.0)	64.94 (20.770)	[58.38, 71.49]
WEEK18	179	66.67 (0.0, 100.0)	66.90 (19.562)	[64.01, 69.78]	40	66.67 (16.7, 100.0)	67.29 (21.549)	[60.40, 74.18]
WEEK24	161	66.67 (0.0, 100.0)	63.82 (21.330)	[60.50, 67.14]	35	66.67 (0.0, 100.0)	70.12 (18.919)	[63.62, 76.62]
WEEK30	140	66.67 (0.0, 100.0)	66.13 (18.626)	[63.02, 69.24]	28	75.00 (16.7, 100.0)	71.73 (19.816)	[64.04, 79.41]
WEEK36	139	66.67 (0.0, 100.0)	67.69 (19.100)	[64.48, 70.89]	23	66.67 (0.0, 100.0)	67.75 (19.020)	[59.53, 75.98]
WEEK42	123	66.67 (0.0, 100.0)	70.05 (18.751)	[66.71, 73.40]	20	66.67 (50.0, 91.7)	72.50 (9.786)	[67.92, 77.08]
WEEK48	106	66.67 (0.0, 100.0)	69.18 (17.972)	[65.72, 72.64]	14	75.00 (50.0, 100.0)	73.21 (13.147)	[65.62, 80.81]
WEEK54	93	75.00 (16.7, 100.0)	70.88 (15.955)	[67.59, 74.16]	11	75.00 (58.3, 100.0)	75.00 (11.785)	[67.08, 82.92]
WEEK60	79	75.00 (16.7, 100.0)	71.52 (18.180)	[67.45, 75.59]	11	83.33 (50.0, 83.3)	72.73 (13.484)	[63.67, 81.79]
WEEK66	67	75.00 (0.0, 100.0)	69.03 (19.452)	[64.29, 73.77]	8	66.67 (8.3, 83.3)	64.58 (23.884)	[44.62, 84.55]
WEEK72	59	83.33 (25.0, 100.0)	71.33 (18.522)	[66.50, 76.15]	9	66.67 (66.7, 83.3)	73.15 (8.099)	[66.92, 79.37]
WEEK78	49	75.00 (33.3, 100.0)	73.13 (17.118)	[68.21, 78.05]	6	66.67 (58.3, 83.3)	70.83 (10.206)	[60.12, 81.54]
WEEK86	35	75.00 (33.3, 100.0)	71.67 (15.551)	[66.32, 77.01]	6	75.00 (33.3, 91.7)	69.44 (21.517)	[46.86, 92.02]
WEEK94	33	83.33 (33.3, 100.0)	74.75 (15.658)	[69.20, 80.30]	3	83.33 (66.7, 83.3)	77.78 (9.623)	[53.87, 101.68]
WEEK102	21	83.33 (50.0, 100.0)	76.98 (12.334)	[71.37, 82.60]	0	NE (NE, NE)	NE (NE)	[NE, NE]
WEEK118	12	83.33 (41.7, 100.0)	74.31 (16.460)	[63.85, 84.76]	0	NE (NE, NE)	NE (NE)	[NE, NE]
WEEK126	8	66.67 (33.3, 91.7)	65.62 (18.059)	[50.53, 80.72]	0	NE (NE, NE)	NE (NE)	[NE, NE]
WEEK134	7	75.00 (41.7, 100.0)	75.00 (19.245)	[57.20, 92.80]	0	NE (NE, NE)	NE (NE)	[NE, NE]
WEEK142	4	58.33 (33.3, 83.3)	58.33 (21.517)	[24.10, 92.57]	0	NE (NE, NE)	NE (NE)	[NE, NE]
WEEK150	2	66.67 (66.7, 66.7)	66.67 (0.000)	[NE, NE]	0	NE (NE, NE)	NE (NE)	[NE, NE]
WEEK158	1	50.00 (50.0, 50.0)	50.00 (NE)	[NE, NE]	0	NE (NE, NE)	NE (NE)	[NE, NE]
END OF TRT	77	58.33 (16.7, 100.0)	58.98 (22.327)	[53.92, 64.05]	39	66.67 (25.0, 83.3)	60.90 (19.790)	[54.48, 67.31]
FOLLOW UP	48	66.67 (0.0, 100.0)	65.28 (24.209)	[58.25, 72.31]	22	66.67 (8.3, 100.0)	66.67 (20.250)	[57.69, 75.64]

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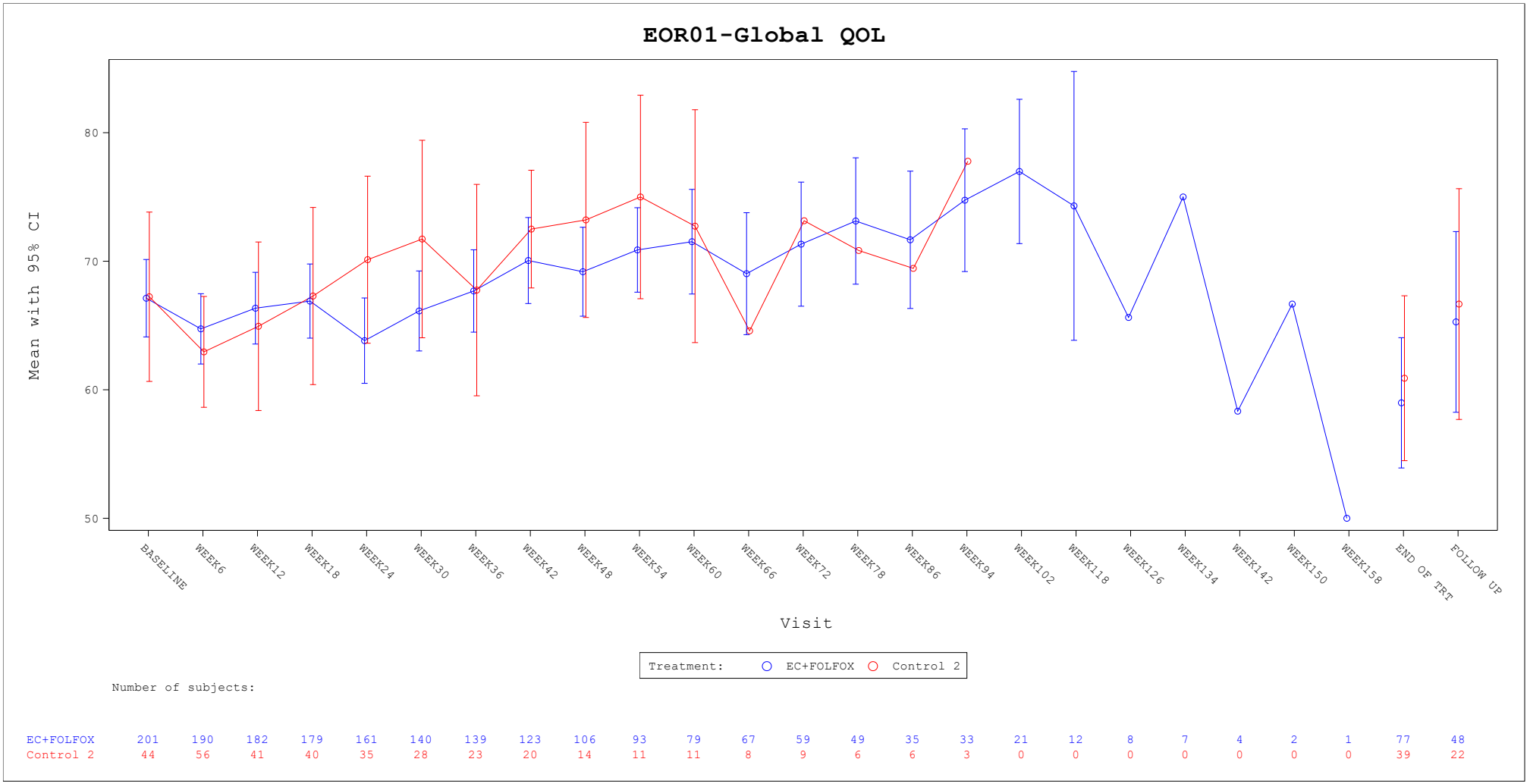
Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Plot over time - EOR01-Global QOL
Full Analysis Set



Number of subjects:

EC+FOLFOX	201	190	182	179	161	140	139	123	106	93	79	67	59	49	35	33	21	12	8	7	4	2	1	77	48
Control 2	44	56	41	40	35	28	23	20	14	11	11	8	9	6	6	3	0	0	0	0	0	0	0	39	22

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Encorafenib (PF-07263896) Protocol C4221015
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Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Summary over time - EOR01-Physical Functioning
Full Analysis Set

	EC+FOLFOX (N=236)				Control 2 (N=74)			
Visit	n	Median (Range)	Mean (SD)	95% CI [1]	n	Median (Range)	Mean (SD)	95% CI [1]
BASELINE	201	86.67 (13.3, 100.0)	82.92 (16.650)	[80.60, 85.23]	44	93.33 (46.7, 100.0)	85.76 (15.854)	[80.94, 90.58]
WEEK6	190	80.00 (20.0, 100.0)	77.51 (17.134)	[75.06, 79.96]	56	80.00 (0.0, 100.0)	79.11 (19.431)	[73.90, 84.31]
WEEK12	182	80.00 (26.7, 100.0)	78.90 (17.273)	[76.37, 81.43]	41	80.00 (20.0, 100.0)	78.29 (17.672)	[72.71, 83.87]
WEEK18	179	80.00 (26.7, 100.0)	78.85 (16.839)	[76.36, 81.33]	40	83.33 (40.0, 100.0)	79.83 (17.638)	[74.19, 85.47]
WEEK24	161	80.00 (0.0, 100.0)	76.27 (21.014)	[73.00, 79.54]	35	86.67 (0.0, 100.0)	81.14 (19.769)	[74.35, 87.93]
WEEK30	140	80.00 (6.7, 100.0)	77.90 (17.190)	[75.03, 80.78]	28	86.67 (6.7, 100.0)	79.88 (23.245)	[70.87, 88.89]
WEEK36	139	80.00 (0.0, 100.0)	77.27 (18.595)	[74.15, 80.38]	23	86.67 (53.3, 100.0)	84.06 (13.888)	[78.05, 90.06]
WEEK42	123	80.00 (13.3, 100.0)	79.19 (17.650)	[76.04, 82.34]	20	86.67 (33.3, 100.0)	86.00 (15.732)	[78.64, 93.36]
WEEK48	106	80.00 (0.0, 100.0)	79.94 (17.829)	[76.50, 83.37]	14	85.00 (33.3, 100.0)	83.10 (17.070)	[73.24, 92.95]
WEEK54	93	86.67 (20.0, 100.0)	80.72 (17.814)	[77.05, 84.39]	11	86.67 (46.7, 100.0)	87.27 (14.744)	[77.37, 97.18]
WEEK60	79	86.67 (20.0, 100.0)	82.78 (16.316)	[79.13, 86.44]	11	86.67 (33.3, 100.0)	81.82 (21.311)	[67.50, 96.13]
WEEK66	67	80.00 (33.3, 100.0)	82.29 (15.022)	[78.62, 85.95]	8	93.33 (6.7, 100.0)	79.17 (33.130)	[51.47, 106.86]
WEEK72	59	80.00 (26.7, 100.0)	80.34 (17.217)	[75.85, 84.83]	9	80.00 (66.7, 100.0)	85.19 (12.373)	[75.67, 94.70]
WEEK78	49	86.67 (26.7, 100.0)	82.72 (16.883)	[77.87, 87.57]	6	80.00 (60.0, 100.0)	82.22 (16.147)	[65.28, 99.17]
WEEK86	35	86.67 (46.7, 100.0)	84.38 (14.814)	[79.29, 89.47]	6	93.33 (33.3, 100.0)	83.33 (25.560)	[56.51, 110.16]
WEEK94	33	86.67 (40.0, 100.0)	84.65 (16.028)	[78.96, 90.33]	3	93.33 (86.7, 100.0)	93.33 (6.667)	[76.77, 109.89]
WEEK102	21	86.67 (40.0, 100.0)	83.17 (14.700)	[76.48, 89.87]	0	NE (NE, NE)	NE (NE)	[NE, NE]
WEEK118	12	90.00 (73.3, 100.0)	88.89 (9.983)	[82.55, 95.23]	0	NE (NE, NE)	NE (NE)	[NE, NE]
WEEK126	8	80.00 (60.0, 100.0)	81.67 (15.430)	[68.77, 94.57]	0	NE (NE, NE)	NE (NE)	[NE, NE]
WEEK134	7	93.33 (66.7, 100.0)	87.62 (14.105)	[74.57, 100.66]	0	NE (NE, NE)	NE (NE)	[NE, NE]
WEEK142	4	70.00 (60.0, 93.3)	73.33 (14.402)	[50.42, 96.25]	0	NE (NE, NE)	NE (NE)	[NE, NE]
WEEK150	2	73.33 (73.3, 73.3)	73.33 (0.000)	[NE, NE]	0	NE (NE, NE)	NE (NE)	[NE, NE]
WEEK158	1	86.67 (86.7, 86.7)	86.67 (NE)	[NE, NE]	0	NE (NE, NE)	NE (NE)	[NE, NE]
END OF TRT	77	80.00 (0.0, 100.0)	72.29 (22.661)	[67.15, 77.44]	39	73.33 (13.3, 100.0)	72.48 (21.476)	[65.52, 79.44]
FOLLOW UP	48	80.00 (6.7, 100.0)	75.28 (21.916)	[68.91, 81.64]	22	80.00 (13.3, 100.0)	73.94 (22.435)	[63.99, 83.89]

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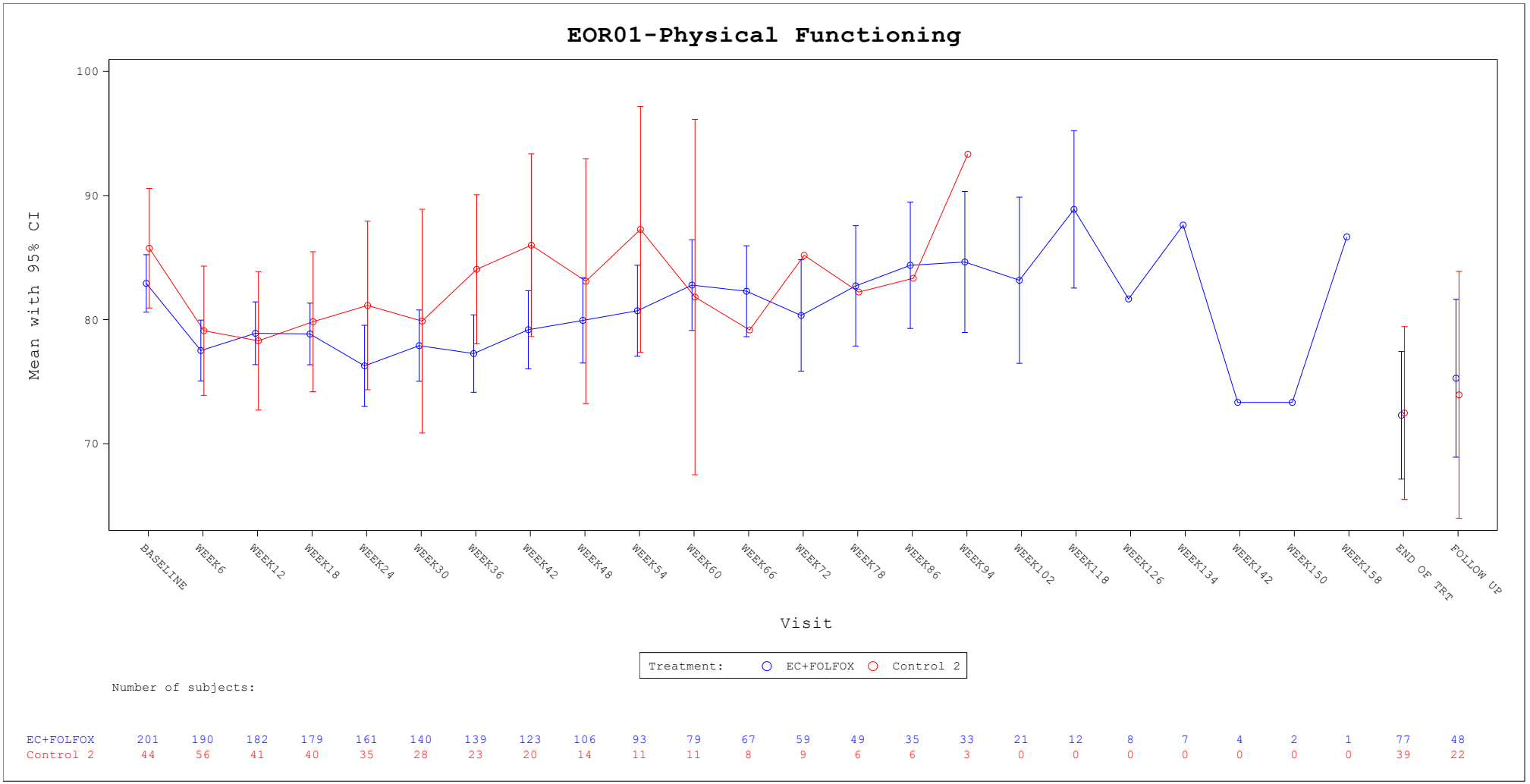
Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Plot over time - EOR01-Physical Functioning
Full Analysis Set



Number of subjects:

EC+FOLFOX	201	190	182	179	161	140	139	123	106	93	79	67	59	49	35	33	21	12	8	7	4	2	1	77	48
Control 2	44	56	41	40	35	28	23	20	14	11	11	8	9	6	6	3	0	0	0	0	0	0	0	39	22

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Summary over time - EOR01-Role Functioning
Full Analysis Set

	EC+FOLFOX (N=236)				Control 2 (N=74)			
Visit	n	Median (Range)	Mean (SD)	95% CI [1]	n	Median (Range)	Mean (SD)	95% CI [1]
BASELINE	201	83.33 (0.0, 100.0)	76.12 (24.982)	[72.64, 79.59]	44	91.67 (0.0, 100.0)	81.06 (27.040)	[72.84, 89.28]
WEEK6	190	66.67 (0.0, 100.0)	70.35 (24.866)	[66.79, 73.91]	56	66.67 (0.0, 100.0)	72.92 (24.580)	[66.33, 79.50]
WEEK12	182	66.67 (0.0, 100.0)	69.41 (25.899)	[65.63, 73.20]	41	66.67 (0.0, 100.0)	66.26 (30.616)	[56.60, 75.92]
WEEK18	179	66.67 (0.0, 100.0)	72.72 (24.396)	[69.12, 76.32]	40	66.67 (0.0, 100.0)	68.75 (29.281)	[59.39, 78.11]
WEEK24	161	66.67 (0.0, 100.0)	67.60 (30.233)	[62.89, 72.30]	35	66.67 (0.0, 100.0)	71.90 (23.836)	[63.72, 80.09]
WEEK30	140	66.67 (0.0, 100.0)	69.17 (25.830)	[64.85, 73.48]	28	66.67 (0.0, 100.0)	67.86 (29.720)	[56.33, 79.38]
WEEK36	139	66.67 (0.0, 100.0)	70.02 (26.556)	[65.57, 74.48]	23	83.33 (0.0, 100.0)	76.81 (22.885)	[66.92, 86.71]
WEEK42	123	66.67 (0.0, 100.0)	73.71 (24.795)	[69.29, 78.14]	20	83.33 (0.0, 100.0)	80.00 (25.131)	[68.24, 91.76]
WEEK48	106	66.67 (0.0, 100.0)	72.33 (25.186)	[67.48, 77.18]	14	83.33 (16.7, 100.0)	76.79 (26.989)	[61.20, 92.37]
WEEK54	93	66.67 (0.0, 100.0)	74.91 (24.527)	[69.86, 79.96]	11	83.33 (66.7, 100.0)	86.36 (14.564)	[76.58, 96.15]
WEEK60	79	83.33 (16.7, 100.0)	79.96 (21.579)	[75.12, 84.79]	11	66.67 (16.7, 100.0)	74.24 (26.208)	[56.64, 91.85]
WEEK66	67	66.67 (0.0, 100.0)	73.13 (22.087)	[67.75, 78.52]	8	91.67 (0.0, 100.0)	77.08 (34.431)	[48.30, 105.87]
WEEK72	59	66.67 (0.0, 100.0)	71.19 (27.304)	[64.07, 78.30]	9	66.67 (33.3, 100.0)	72.22 (20.412)	[56.53, 87.91]
WEEK78	49	66.67 (0.0, 100.0)	73.47 (23.550)	[66.70, 80.23]	6	75.00 (33.3, 100.0)	75.00 (25.276)	[48.47, 101.53]
WEEK86	35	66.67 (0.0, 100.0)	73.81 (26.595)	[64.67, 82.95]	6	87.50 (16.7, 100.0)	76.39 (31.805)	[43.01, 109.77]
WEEK94	33	83.33 (0.0, 100.0)	79.29 (23.581)	[70.93, 87.65]	3	100.00 (83.3, 100.0)	94.44 (9.623)	[70.54, 118.35]
WEEK102	21	83.33 (50.0, 100.0)	80.16 (15.473)	[73.12, 87.20]	0	NE (NE, NE)	NE (NE)	[NE, NE]
WEEK118	12	91.67 (66.7, 100.0)	86.11 (15.624)	[76.18, 96.04]	0	NE (NE, NE)	NE (NE)	[NE, NE]
WEEK126	8	66.67 (33.3, 100.0)	72.92 (25.099)	[51.93, 93.90]	0	NE (NE, NE)	NE (NE)	[NE, NE]
WEEK134	7	83.33 (50.0, 100.0)	83.33 (19.245)	[65.53, 101.13]	0	NE (NE, NE)	NE (NE)	[NE, NE]
WEEK142	4	66.67 (50.0, 100.0)	70.83 (20.972)	[37.46, 104.20]	0	NE (NE, NE)	NE (NE)	[NE, NE]
WEEK150	2	50.00 (33.3, 66.7)	50.00 (23.570)	[-161.77, 261.77]	0	NE (NE, NE)	NE (NE)	[NE, NE]
WEEK158	1	66.67 (66.7, 66.7)	66.67 (NE)	[NE, NE]	0	NE (NE, NE)	NE (NE)	[NE, NE]
END OF TRT	77	66.67 (0.0, 100.0)	66.02 (30.161)	[59.17, 72.86]	39	66.67 (0.0, 100.0)	58.55 (31.961)	[48.19, 68.91]
FOLLOW UP	48	66.67 (0.0, 100.0)	62.15 (31.273)	[53.07, 71.23]	22	75.00 (0.0, 100.0)	71.21 (28.257)	[58.68, 83.74]

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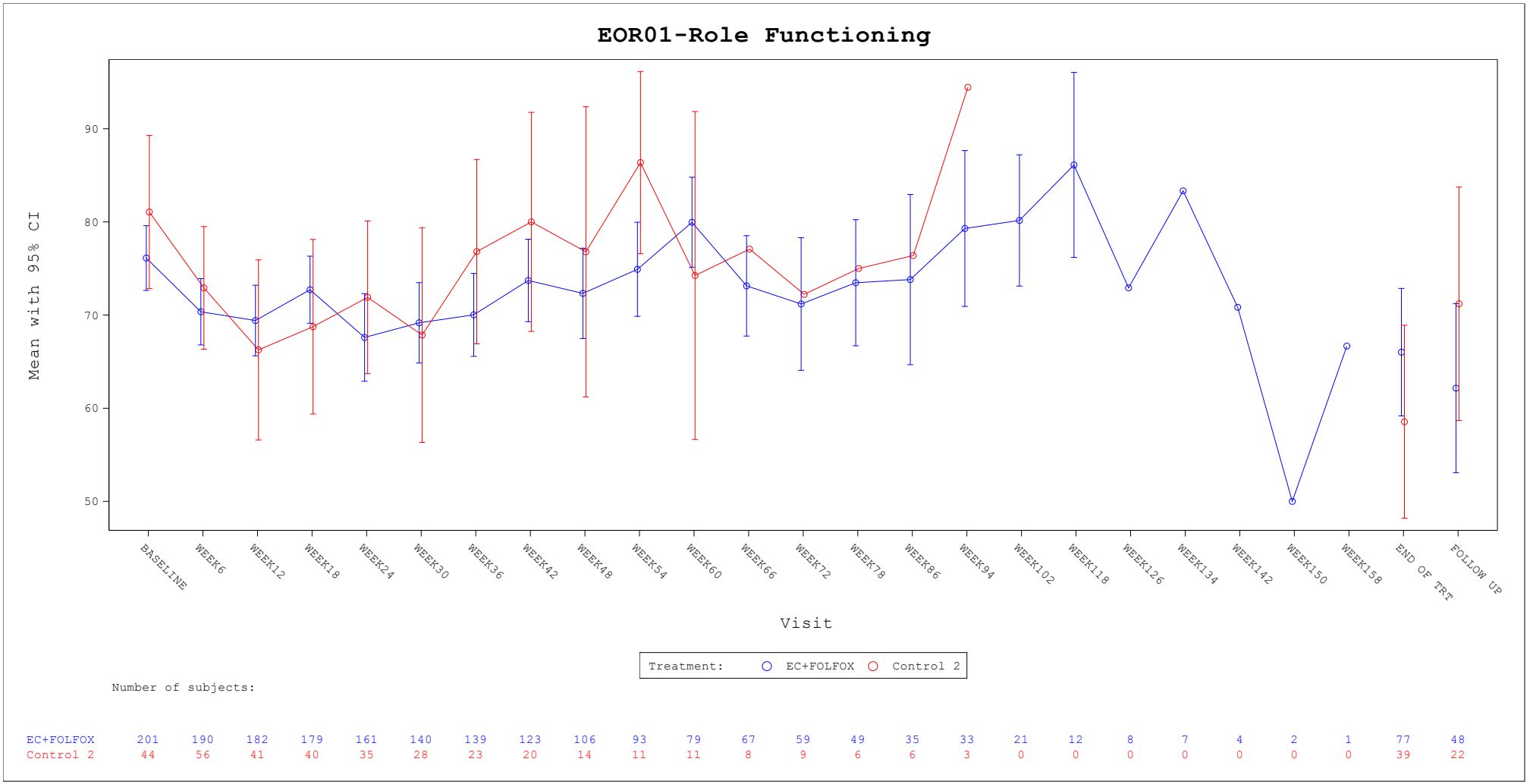
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Plot over time - EOR01-Role Functioning
Full Analysis Set



Number of subjects:

EC+FOLFOX	201	190	182	179	161	140	139	123	106	93	79	67	59	49	35	33	21	12	8	7	4	2	1	77	48
Control 2	44	56	41	40	35	28	23	20	14	11	11	8	9	6	6	3	0	0	0	0	0	0	0	39	22

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Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Summary over time - EOR01-Emotional Functioning
Full Analysis Set

	EC+FOLFOX (N=236)				Control 2 (N=74)			
Visit	n	Median (Range)	Mean (SD)	95% CI [1]	n	Median (Range)	Mean (SD)	95% CI [1]
BASELINE	201	75.00 (0.0, 100.0)	73.71 (20.533)	[70.86, 76.57]	44	75.00 (41.7, 100.0)	75.57 (18.097)	[70.07, 81.07]
WEEK6	190	83.33 (0.0, 100.0)	80.70 (18.555)	[78.05, 83.36]	56	75.00 (33.3, 100.0)	76.56 (18.302)	[71.66, 81.46]
WEEK12	182	83.33 (0.0, 100.0)	82.14 (18.104)	[79.49, 84.79]	41	83.33 (0.0, 100.0)	75.41 (26.283)	[67.11, 83.70]
WEEK18	179	83.33 (8.3, 100.0)	79.93 (20.194)	[76.96, 82.91]	40	79.17 (33.3, 100.0)	78.33 (20.307)	[71.84, 84.83]
WEEK24	161	83.33 (0.0, 100.0)	77.23 (22.836)	[73.67, 80.78]	35	83.33 (33.3, 100.0)	82.50 (18.185)	[76.25, 88.75]
WEEK30	140	83.33 (0.0, 100.0)	79.94 (20.039)	[76.59, 83.29]	28	83.33 (8.3, 100.0)	80.06 (21.676)	[71.65, 88.46]
WEEK36	139	83.33 (0.0, 100.0)	80.40 (20.111)	[77.02, 83.77]	23	91.67 (33.3, 100.0)	82.97 (20.486)	[74.11, 91.83]
WEEK42	123	83.33 (25.0, 100.0)	82.79 (17.973)	[79.58, 86.00]	20	83.33 (50.0, 100.0)	83.33 (15.294)	[76.18, 90.49]
WEEK48	106	91.67 (8.3, 100.0)	83.18 (19.787)	[79.37, 86.99]	14	91.67 (50.0, 100.0)	85.12 (15.393)	[76.23, 94.01]
WEEK54	93	91.67 (8.3, 100.0)	84.86 (17.590)	[81.23, 88.48]	11	83.33 (50.0, 100.0)	83.33 (14.434)	[73.64, 93.03]
WEEK60	79	91.67 (16.7, 100.0)	85.76 (16.940)	[81.97, 89.55]	11	83.33 (37.5, 100.0)	80.68 (17.704)	[68.79, 92.58]
WEEK66	67	83.33 (33.3, 100.0)	83.46 (16.823)	[79.35, 87.56]	8	91.67 (16.7, 100.0)	84.37 (27.973)	[60.99, 107.76]
WEEK72	59	91.67 (16.7, 100.0)	83.05 (19.326)	[78.01, 88.09]	9	91.67 (41.7, 100.0)	84.26 (21.018)	[68.10, 100.41]
WEEK78	49	91.67 (33.3, 100.0)	86.73 (15.675)	[82.23, 91.24]	6	91.67 (50.0, 100.0)	81.94 (22.618)	[58.21, 105.68]
WEEK86	35	91.67 (25.0, 100.0)	82.38 (20.884)	[75.21, 89.55]	6	97.92 (66.7, 100.0)	90.97 (13.544)	[76.76, 105.19]
WEEK94	33	91.67 (41.7, 100.0)	86.62 (16.789)	[80.66, 92.57]	3	91.67 (83.3, 100.0)	91.67 (8.333)	[70.97, 112.37]
WEEK102	21	83.33 (66.7, 100.0)	86.11 (12.454)	[80.44, 91.78]	0	NE (NE, NE)	NE (NE)	[NE, NE]
WEEK118	12	87.50 (58.3, 100.0)	86.11 (14.794)	[76.71, 95.51]	0	NE (NE, NE)	NE (NE)	[NE, NE]
WEEK126	8	75.00 (66.7, 100.0)	80.21 (14.731)	[67.89, 92.52]	0	NE (NE, NE)	NE (NE)	[NE, NE]
WEEK134	7	91.67 (41.7, 100.0)	83.33 (20.412)	[64.45, 102.21]	0	NE (NE, NE)	NE (NE)	[NE, NE]
WEEK142	4	79.17 (50.0, 91.7)	75.00 (18.002)	[46.35, 103.65]	0	NE (NE, NE)	NE (NE)	[NE, NE]
WEEK150	2	87.50 (75.0, 100.0)	87.50 (17.678)	[-71.33, 246.33]	0	NE (NE, NE)	NE (NE)	[NE, NE]
WEEK158	1	91.67 (91.7, 91.7)	91.67 (NE)	[NE, NE]	0	NE (NE, NE)	NE (NE)	[NE, NE]
END OF TRT	77	75.00 (0.0, 100.0)	68.07 (25.592)	[62.26, 73.88]	39	75.00 (33.3, 100.0)	72.86 (20.387)	[66.25, 79.47]
FOLLOW UP	48	75.00 (0.0, 100.0)	71.01 (25.147)	[63.71, 78.31]	22	75.00 (33.3, 100.0)	72.73 (22.739)	[62.65, 82.81]

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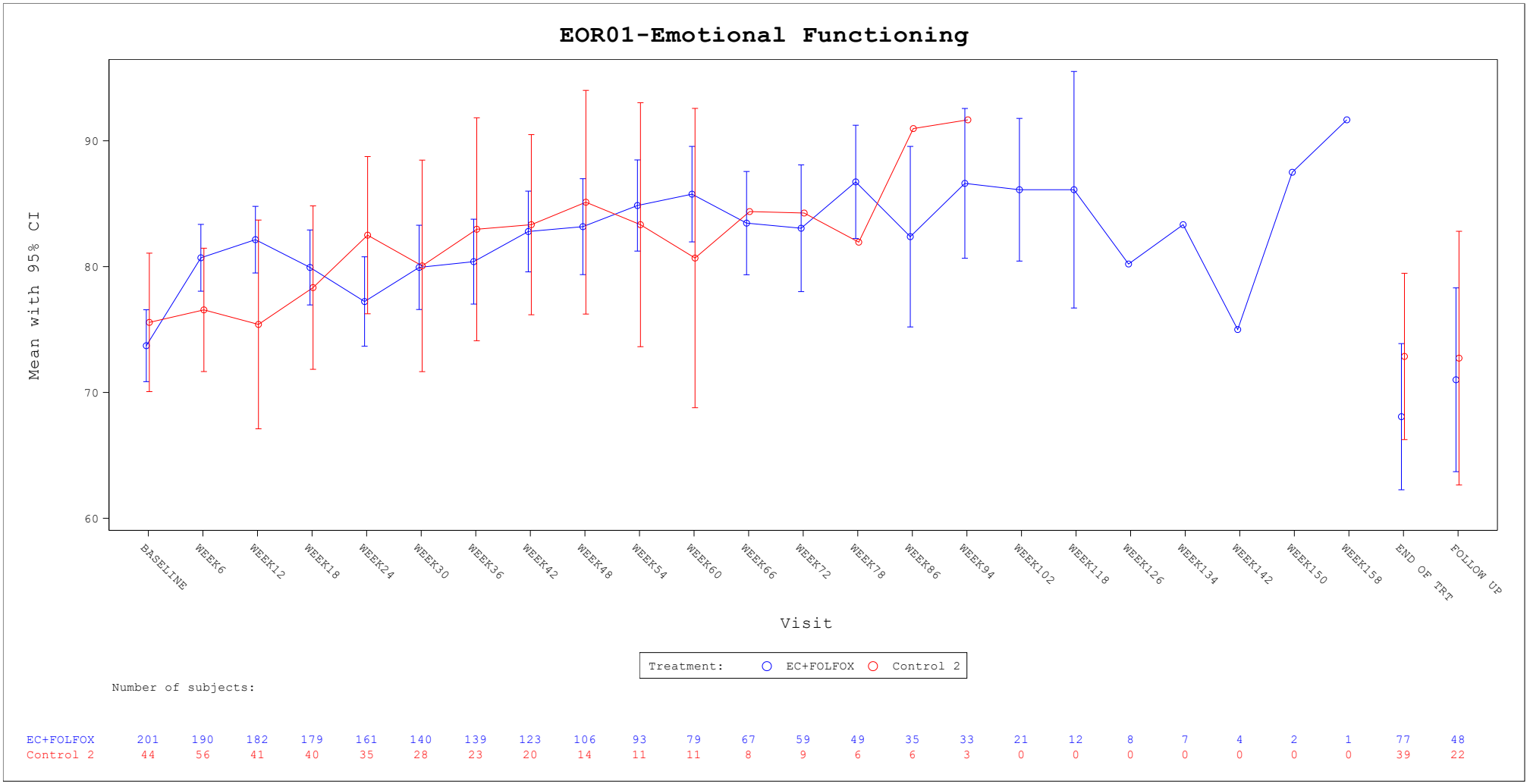
[1] Confidence interval based on the normal distribution.
For functional scales, higher scores represent a better level of functioning. For symptom-oriented scales, a higher score represents more severe symptoms.



Number of subjects:

EC+FOLFOX	201	190	182	179	161	140	139	123	106	93	79	67	59	49	35	33	21	12	8	7	4	2	1	77	48
Control 2	44	56	41	40	35	28	23	20	14	11	11	8	9	6	6	3	0	0	0	0	0	0	0	39	22

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Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Summary over time - EOR01-Cognitive Functioning
Full Analysis Set

	EC+FOLFOX (N=236)				Control 2 (N=74)			
Visit	n	Median (Range)	Mean (SD)	95% CI [1]	n	Median (Range)	Mean (SD)	95% CI [1]
BASELINE	201	100.00 (16.7, 100.0)	87.73 (16.626)	[85.42, 90.04]	44	100.00 (50.0, 100.0)	89.39 (13.493)	[85.29, 93.50]
WEEK6	190	100.00 (0.0, 100.0)	86.05 (18.622)	[83.39, 88.72]	56	83.33 (50.0, 100.0)	85.27 (14.650)	[81.34, 89.19]
WEEK12	182	83.33 (0.0, 100.0)	85.07 (18.910)	[82.31, 87.84]	41	83.33 (16.7, 100.0)	82.93 (20.493)	[76.46, 89.40]
WEEK18	179	100.00 (33.3, 100.0)	86.31 (17.232)	[83.77, 88.85]	40	83.33 (33.3, 100.0)	85.42 (17.373)	[79.86, 90.97]
WEEK24	161	83.33 (0.0, 100.0)	81.99 (20.067)	[78.86, 85.11]	35	83.33 (33.3, 100.0)	84.29 (18.052)	[78.08, 90.49]
WEEK30	140	83.33 (0.0, 100.0)	85.48 (17.864)	[82.49, 88.46]	28	83.33 (33.3, 100.0)	83.63 (17.928)	[76.68, 90.58]
WEEK36	139	83.33 (16.7, 100.0)	85.01 (16.459)	[82.25, 87.77]	23	83.33 (50.0, 100.0)	84.78 (17.345)	[77.28, 92.28]
WEEK42	123	83.33 (16.7, 100.0)	85.91 (17.730)	[82.74, 89.07]	20	100.00 (33.3, 100.0)	89.17 (16.468)	[81.46, 96.87]
WEEK48	106	100.00 (0.0, 100.0)	86.95 (17.367)	[83.61, 90.29]	14	95.83 (66.7, 100.0)	91.07 (10.573)	[84.97, 97.18]
WEEK54	93	83.33 (33.3, 100.0)	86.74 (15.650)	[83.52, 89.96]	11	100.00 (66.7, 100.0)	92.42 (11.459)	[84.73, 100.12]
WEEK60	79	100.00 (33.3, 100.0)	87.34 (15.837)	[83.79, 90.89]	11	83.33 (50.0, 100.0)	84.85 (17.408)	[73.15, 96.54]
WEEK66	67	83.33 (33.3, 100.0)	86.32 (16.899)	[82.20, 90.44]	8	91.67 (16.7, 100.0)	81.25 (28.781)	[57.19, 105.31]
WEEK72	59	83.33 (33.3, 100.0)	84.18 (17.349)	[79.66, 88.70]	9	100.00 (66.7, 100.0)	90.74 (12.108)	[81.43, 100.05]
WEEK78	49	100.00 (50.0, 100.0)	88.78 (13.345)	[84.94, 92.61]	6	83.33 (66.7, 100.0)	83.33 (18.257)	[64.17, 102.49]
WEEK86	35	83.33 (50.0, 100.0)	84.76 (17.326)	[78.81, 90.71]	6	100.00 (83.3, 100.0)	94.44 (8.607)	[85.41, 103.48]
WEEK94	33	100.00 (50.0, 100.0)	88.38 (15.301)	[82.96, 93.81]	3	100.00 (83.3, 100.0)	94.44 (9.623)	[70.54, 118.35]
WEEK102	21	100.00 (50.0, 100.0)	88.89 (15.215)	[81.96, 95.81]	0	NE (NE, NE)	NE (NE)	[NE, NE]
WEEK118	12	100.00 (50.0, 100.0)	87.50 (17.588)	[76.33, 98.67]	0	NE (NE, NE)	NE (NE)	[NE, NE]
WEEK126	8	100.00 (50.0, 100.0)	85.42 (22.603)	[66.52, 104.31]	0	NE (NE, NE)	NE (NE)	[NE, NE]
WEEK134	7	83.33 (33.3, 100.0)	83.33 (23.570)	[61.53, 105.13]	0	NE (NE, NE)	NE (NE)	[NE, NE]
WEEK142	4	75.00 (33.3, 100.0)	70.83 (28.464)	[25.54, 116.13]	0	NE (NE, NE)	NE (NE)	[NE, NE]
WEEK150	2	75.00 (66.7, 83.3)	75.00 (11.785)	[-30.89, 180.89]	0	NE (NE, NE)	NE (NE)	[NE, NE]
WEEK158	1	83.33 (83.3, 83.3)	83.33 (NE)	[NE, NE]	0	NE (NE, NE)	NE (NE)	[NE, NE]
END OF TRT	77	83.33 (0.0, 100.0)	78.35 (21.976)	[73.37, 83.34]	39	83.33 (50.0, 100.0)	80.34 (19.448)	[74.04, 86.65]
FOLLOW UP	48	83.33 (0.0, 100.0)	80.90 (22.803)	[74.28, 87.52]	22	75.00 (33.3, 100.0)	80.30 (18.993)	[71.88, 88.72]

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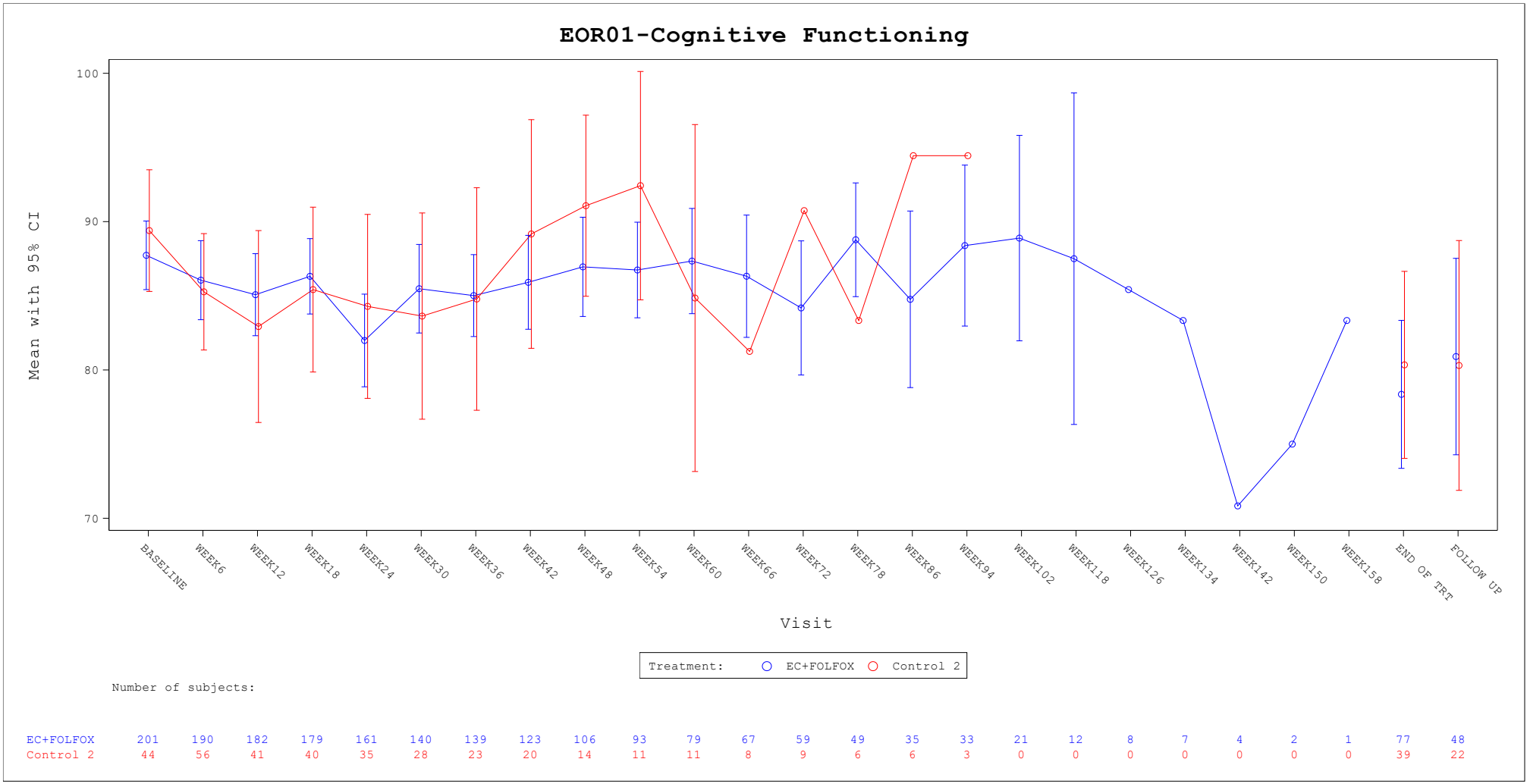
Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Plot over time - EOR01-Cognitive Functioning
Full Analysis Set



Number of subjects:

	BASELINE	WEEK6	WEEK12	WEEK18	WEEK24	WEEK30	WEEK36	WEEK42	WEEK48	WEEK54	WEEK60	WEEK66	WEEK72	WEEK78	WEEK86	WEEK94	WEEK102	WEEK118	WEEK126	WEEK134	WEEK142	WEEK150	WEEK158	END OF TRT	FOLLOW UP
EC+FOLFOX	201	190	182	179	161	140	139	123	106	93	79	67	59	49	35	33	21	12	8	7	4	2	1	77	48
Control 2	44	56	41	40	35	28	23	20	14	11	11	8	9	6	6	3	0	0	0	0	0	0	0	39	22

Baseline is the last non-missing measurement prior to first dose of study intervention.
No confidence intervalls are drawn, when there are less than 10 patients in treatment arm.
For functional scales, higher scores represent a better level of functioning. For symptom-oriented scales, a higher score represents more severe symptoms.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Summary over time - EOR01-Social Functioning
Full Analysis Set

	EC+FOLFOX (N=236)				Control 2 (N=74)			
Visit	n	Median (Range)	Mean (SD)	95% CI [1]	n	Median (Range)	Mean (SD)	95% CI [1]
BASELINE	201	83.33 (0.0, 100.0)	75.46 (24.384)	[72.06, 78.85]	44	83.33 (16.7, 100.0)	80.30 (24.714)	[72.79, 87.82]
WEEK6	190	66.67 (0.0, 100.0)	72.19 (24.789)	[68.65, 75.74]	56	79.17 (0.0, 100.0)	74.55 (24.589)	[67.97, 81.14]
WEEK12	182	66.67 (0.0, 100.0)	74.91 (24.260)	[71.36, 78.46]	41	83.33 (0.0, 100.0)	73.37 (28.088)	[64.51, 82.24]
WEEK18	179	66.67 (0.0, 100.0)	73.65 (23.088)	[70.24, 77.06]	40	66.67 (0.0, 100.0)	73.33 (24.979)	[65.34, 81.32]
WEEK24	161	66.67 (0.0, 100.0)	72.05 (26.654)	[67.90, 76.20]	35	83.33 (0.0, 100.0)	79.52 (22.897)	[71.66, 87.39]
WEEK30	140	66.67 (0.0, 100.0)	70.48 (25.077)	[66.29, 74.67]	28	66.67 (0.0, 100.0)	71.43 (24.367)	[61.98, 80.88]
WEEK36	139	66.67 (0.0, 100.0)	73.86 (25.064)	[69.66, 78.06]	23	66.67 (33.3, 100.0)	74.64 (18.715)	[66.54, 82.73]
WEEK42	123	66.67 (0.0, 100.0)	74.39 (25.004)	[69.93, 78.85]	20	83.33 (0.0, 100.0)	76.67 (22.556)	[66.11, 87.22]
WEEK48	106	66.67 (0.0, 100.0)	73.43 (26.204)	[68.38, 78.47]	14	66.67 (50.0, 100.0)	72.62 (12.416)	[65.45, 79.79]
WEEK54	93	83.33 (0.0, 100.0)	75.99 (24.874)	[70.86, 81.11]	11	66.67 (33.3, 100.0)	74.24 (18.803)	[61.61, 86.87]
WEEK60	79	83.33 (0.0, 100.0)	77.64 (25.302)	[71.97, 83.30]	11	83.33 (33.3, 100.0)	75.00 (17.873)	[62.99, 87.01]
WEEK66	67	66.67 (0.0, 100.0)	74.13 (23.080)	[68.50, 79.76]	8	83.33 (16.7, 100.0)	77.08 (29.463)	[52.45, 101.71]
WEEK72	59	83.33 (0.0, 100.0)	77.12 (22.722)	[71.20, 83.04]	9	66.67 (33.3, 100.0)	70.37 (20.031)	[54.97, 85.77]
WEEK78	49	66.67 (0.0, 100.0)	76.87 (22.520)	[70.40, 83.34]	6	66.67 (33.3, 100.0)	66.67 (21.082)	[44.54, 88.79]
WEEK86	35	83.33 (0.0, 100.0)	78.10 (24.843)	[69.56, 86.63]	6	75.00 (33.3, 83.3)	69.44 (19.484)	[49.00, 89.89]
WEEK94	33	83.33 (0.0, 100.0)	81.31 (20.732)	[73.96, 88.66]	3	66.67 (66.7, 83.3)	72.22 (9.623)	[48.32, 96.13]
WEEK102	21	66.67 (0.0, 100.0)	76.19 (23.905)	[65.31, 87.07]	0	NE (NE, NE)	NE (NE)	[NE, NE]
WEEK118	12	83.33 (50.0, 100.0)	83.33 (17.408)	[72.27, 94.39]	0	NE (NE, NE)	NE (NE)	[NE, NE]
WEEK126	8	75.00 (66.7, 100.0)	79.17 (14.773)	[66.82, 91.52]	0	NE (NE, NE)	NE (NE)	[NE, NE]
WEEK134	7	66.67 (50.0, 100.0)	78.57 (20.893)	[59.25, 97.89]	0	NE (NE, NE)	NE (NE)	[NE, NE]
WEEK142	4	83.33 (50.0, 100.0)	79.17 (25.000)	[39.39, 118.95]	0	NE (NE, NE)	NE (NE)	[NE, NE]
WEEK150	2	83.33 (66.7, 100.0)	83.33 (23.570)	[-128.44, 295.10]	0	NE (NE, NE)	NE (NE)	[NE, NE]
WEEK158	1	100.00 (100.0, 100.0)	100.00 (NE)	[NE, NE]	0	NE (NE, NE)	NE (NE)	[NE, NE]
END OF TRT	77	66.67 (0.0, 100.0)	64.72 (28.991)	[58.14, 71.30]	39	66.67 (0.0, 100.0)	67.95 (26.870)	[59.24, 76.66]
FOLLOW UP	48	66.67 (0.0, 100.0)	64.58 (30.486)	[55.73, 73.44]	22	66.67 (33.3, 100.0)	75.76 (19.739)	[67.01, 84.51]

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Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Plot over time - EOR01-Social Functioning
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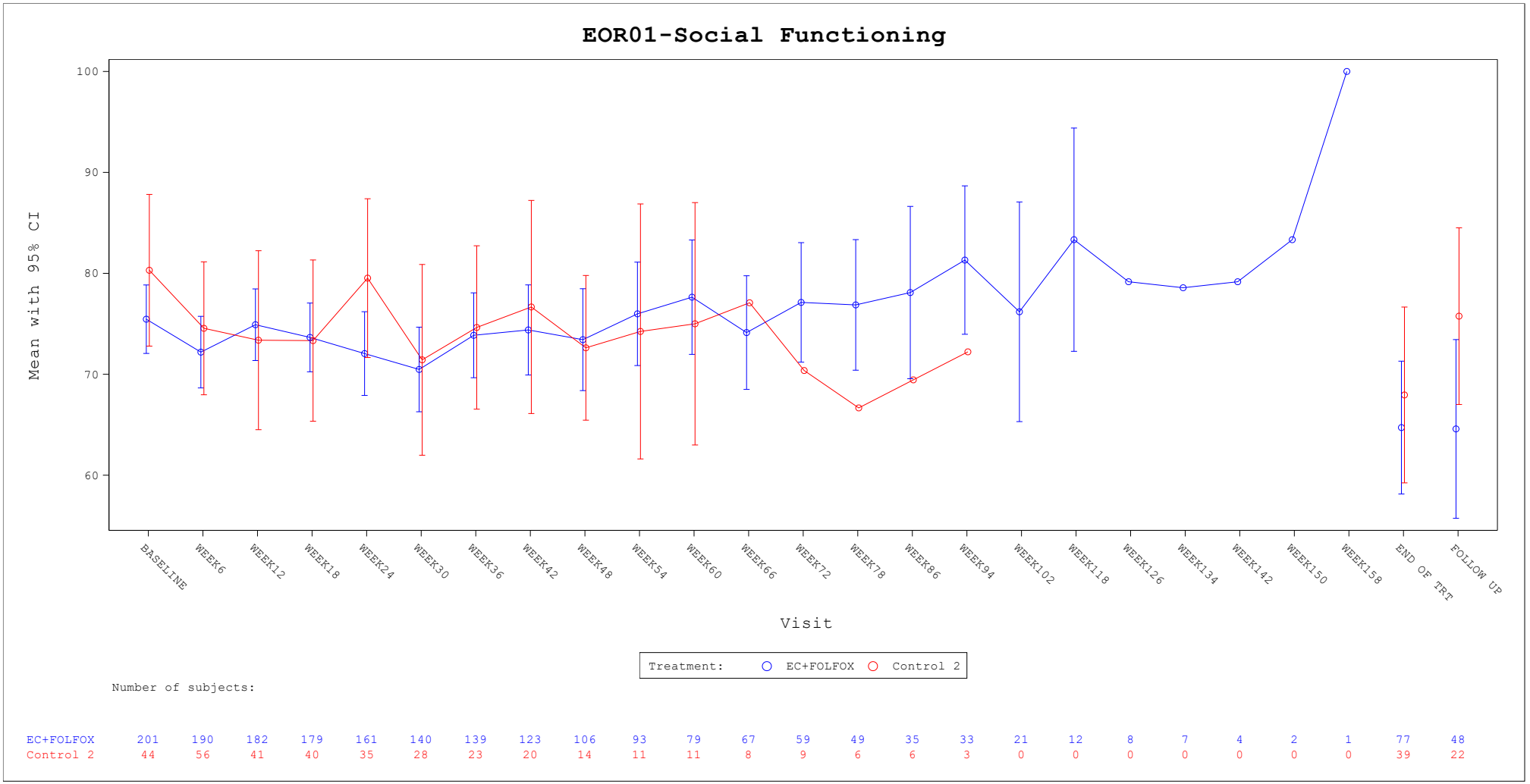

Number of subjects:

EC+FOLFOX	201	190	182	179	161	140	139	123	106	93	79	67	59	49	35	33	21	12	8	7	4	2	1	77	48
Control 2	44	56	41	40	35	28	23	20	14	11	11	8	9	6	6	3	0	0	0	0	0	0	0	39	22

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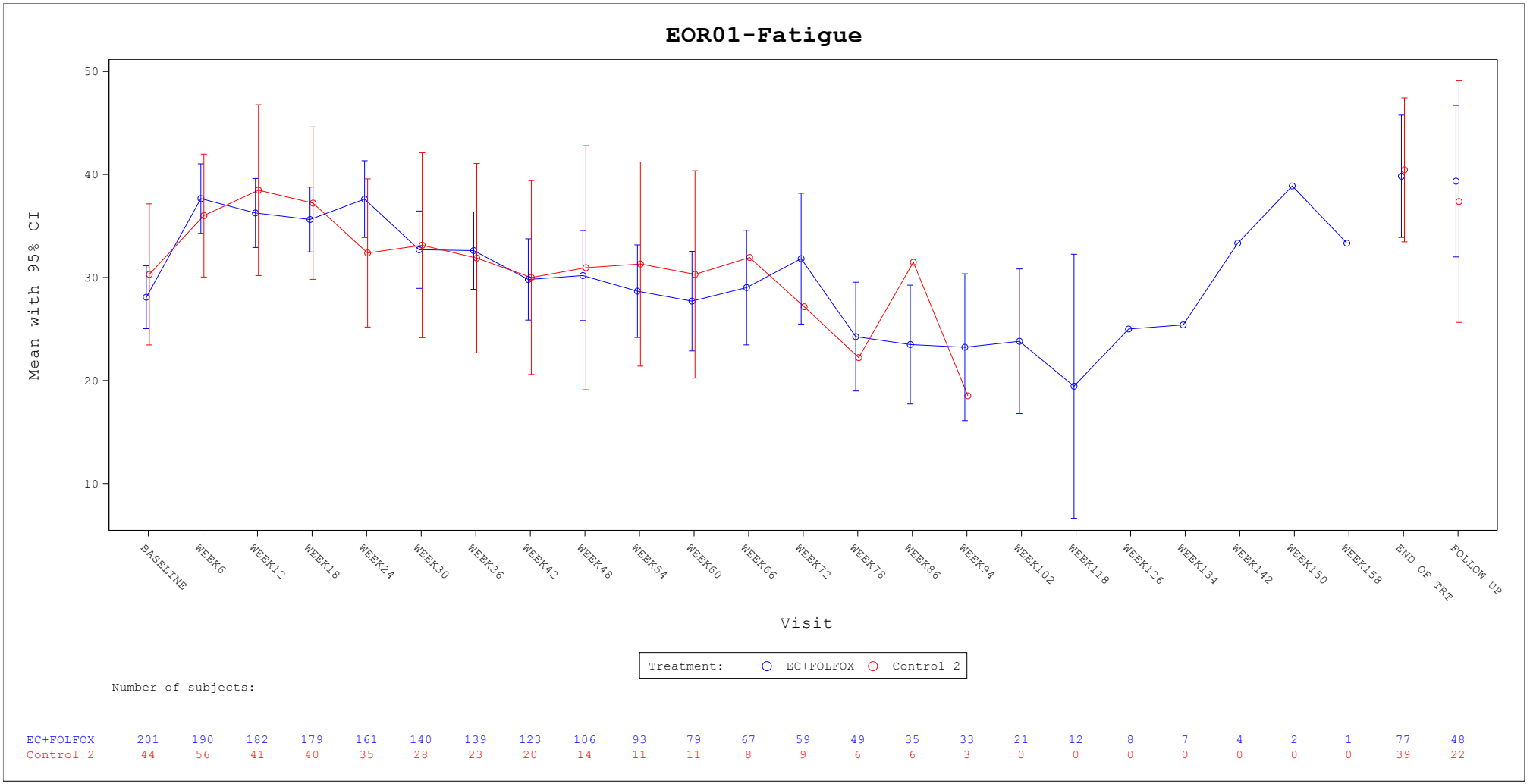
Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Summary over time - EOR01-Fatigue
Full Analysis Set

	EC+FOLFOX (N=236)				Control 2 (N=74)			
Visit	n	Median (Range)	Mean (SD)	95% CI [1]	n	Median (Range)	Mean (SD)	95% CI [1]
BASELINE	201	33.33 (0.0, 88.9)	28.08 (21.944)	[25.03, 31.13]	44	27.78 (0.0, 88.9)	30.30 (22.526)	[23.45, 37.15]
WEEK6	190	33.33 (0.0, 100.0)	37.66 (23.607)	[34.28, 41.04]	56	33.33 (0.0, 88.9)	36.01 (22.272)	[30.05, 41.98]
WEEK12	182	33.33 (0.0, 100.0)	36.26 (22.907)	[32.91, 39.61]	41	33.33 (0.0, 100.0)	38.48 (26.276)	[30.19, 46.78]
WEEK18	179	33.33 (0.0, 88.9)	35.63 (21.352)	[32.48, 38.78]	40	33.33 (0.0, 100.0)	37.22 (23.136)	[29.82, 44.62]
WEEK24	161	33.33 (0.0, 100.0)	37.61 (23.930)	[33.89, 41.34]	35	33.33 (0.0, 100.0)	32.38 (20.939)	[25.19, 39.57]
WEEK30	140	33.33 (0.0, 100.0)	32.70 (22.452)	[28.95, 36.45]	28	33.33 (0.0, 100.0)	33.13 (23.153)	[24.16, 42.11]
WEEK36	139	33.33 (0.0, 100.0)	32.61 (22.391)	[28.86, 36.37]	23	22.22 (0.0, 100.0)	31.88 (21.269)	[22.69, 41.08]
WEEK42	123	33.33 (0.0, 100.0)	29.81 (22.100)	[25.87, 33.75]	20	33.33 (0.0, 100.0)	30.00 (20.104)	[20.59, 39.41]
WEEK48	106	33.33 (0.0, 100.0)	30.19 (22.681)	[25.82, 34.56]	14	33.33 (0.0, 88.9)	30.95 (20.524)	[19.10, 42.80]
WEEK54	93	33.33 (0.0, 88.9)	28.67 (21.815)	[24.18, 33.17]	11	33.33 (11.1, 66.7)	31.31 (14.756)	[21.40, 41.23]
WEEK60	79	33.33 (0.0, 77.8)	27.71 (21.562)	[22.88, 32.54]	11	22.22 (11.1, 66.7)	30.30 (14.982)	[20.24, 40.37]
WEEK66	67	33.33 (0.0, 100.0)	29.02 (22.800)	[23.46, 34.58]	8	33.33 (0.0, 100.0)	31.94 (30.538)	[6.41, 57.47]
WEEK72	59	33.33 (0.0, 100.0)	31.83 (24.366)	[25.48, 38.18]	9	33.33 (11.1, 44.4)	27.16 (11.264)	[18.50, 35.82]
WEEK78	49	33.33 (0.0, 66.7)	24.26 (18.380)	[18.98, 29.54]	6	27.78 (0.0, 33.3)	22.22 (14.055)	[7.47, 36.97]
WEEK86	35	33.33 (0.0, 55.6)	23.49 (16.780)	[17.73, 29.26]	6	33.33 (11.1, 55.6)	31.48 (14.768)	[15.98, 46.98]
WEEK94	33	33.33 (0.0, 66.7)	23.23 (20.101)	[16.10, 30.36]	3	11.11 (11.1, 33.3)	18.52 (12.830)	[-13.35, 50.39]
WEEK102	21	33.33 (0.0, 44.4)	23.81 (15.430)	[16.79, 30.83]	0	NE (NE, NE)	NE (NE)	[NE, NE]
WEEK118	12	16.67 (0.0, 55.6)	19.44 (20.170)	[6.63, 32.26]	0	NE (NE, NE)	NE (NE)	[NE, NE]
WEEK126	8	27.78 (0.0, 66.7)	25.00 (22.023)	[6.59, 43.41]	0	NE (NE, NE)	NE (NE)	[NE, NE]
WEEK134	7	33.33 (0.0, 66.7)	25.40 (26.227)	[1.14, 49.65]	0	NE (NE, NE)	NE (NE)	[NE, NE]
WEEK142	4	33.33 (0.0, 66.7)	33.33 (27.217)	[-9.97, 76.64]	0	NE (NE, NE)	NE (NE)	[NE, NE]
WEEK150	2	38.89 (33.3, 44.4)	38.89 (7.857)	[-31.70, 109.48]	0	NE (NE, NE)	NE (NE)	[NE, NE]
WEEK158	1	33.33 (33.3, 33.3)	33.33 (NE)	[NE, NE]	0	NE (NE, NE)	NE (NE)	[NE, NE]
END OF TRT	77	33.33 (0.0, 100.0)	39.83 (26.142)	[33.89, 45.76]	39	33.33 (0.0, 77.8)	40.46 (21.552)	[33.47, 47.44]
FOLLOW UP	48	33.33 (0.0, 100.0)	39.35 (25.312)	[32.00, 46.70]	22	33.33 (0.0, 100.0)	37.37 (26.460)	[25.64, 49.11]

Baseline is the last non-missing measurement prior to first dose of study intervention.
[1] Confidence interval based on the normal distribution.
For functional scales, higher scores represent a better level of functioning. For symptom-oriented scales, a higher score represents more severe symptoms.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Plot over time - EOR01-Fatigue
Full Analysis Set



Number of subjects:

EC+FOLFOX	201	190	182	179	161	140	139	123	106	93	79	67	59	49	35	33	21	12	8	7	4	2	1	77	48
Control 2	44	56	41	40	35	28	23	20	14	11	11	8	9	6	6	3	0	0	0	0	0	0	0	39	22

Baseline is the last non-missing measurement prior to first dose of study intervention.
No confidence intervalls are drawn, when there are less than 10 patients in treatment arm.
For functional scales, higher scores represent a better level of functioning. For symptom-oriented scales, a higher score represents more severe symptoms.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Summary over time - EOR01-Nausea and Vomiting
Full Analysis Set

	EC+FOLFOX (N=236)				Control 2 (N=74)			
Visit	n	Median (Range)	Mean (SD)	95% CI [1]	n	Median (Range)	Mean (SD)	95% CI [1]
BASELINE	201	0.00 (0.0, 66.7)	4.81 (10.492)	[3.35, 6.27]	44	0.00 (0.0, 50.0)	6.44 (13.552)	[2.32, 10.56]
WEEK6	190	0.00 (0.0, 100.0)	13.16 (20.772)	[10.19, 16.13]	56	0.00 (0.0, 83.3)	13.24 (19.577)	[8.00, 18.49]
WEEK12	182	0.00 (0.0, 100.0)	11.54 (17.900)	[8.92, 14.16]	41	0.00 (0.0, 100.0)	11.79 (19.718)	[5.56, 18.01]
WEEK18	179	0.00 (0.0, 100.0)	10.34 (18.536)	[7.60, 13.07]	40	0.00 (0.0, 83.3)	11.67 (17.783)	[5.98, 17.35]
WEEK24	161	0.00 (0.0, 100.0)	7.66 (16.351)	[5.12, 10.21]	35	0.00 (0.0, 66.7)	10.48 (16.212)	[4.91, 16.05]
WEEK30	140	0.00 (0.0, 50.0)	5.95 (11.669)	[4.00, 7.90]	28	0.00 (0.0, 50.0)	9.23 (14.931)	[3.44, 15.02]
WEEK36	139	0.00 (0.0, 50.0)	6.12 (11.895)	[4.12, 8.11]	23	0.00 (0.0, 83.3)	10.87 (18.538)	[2.85, 18.89]
WEEK42	123	0.00 (0.0, 50.0)	4.88 (10.825)	[2.95, 6.81]	20	0.00 (0.0, 50.0)	10.00 (14.710)	[3.12, 16.88]
WEEK48	106	0.00 (0.0, 66.7)	5.82 (11.511)	[3.60, 8.03]	14	0.00 (0.0, 50.0)	7.74 (15.492)	[-1.21, 16.68]
WEEK54	93	0.00 (0.0, 66.7)	6.27 (12.983)	[3.60, 8.95]	11	0.00 (0.0, 50.0)	10.61 (15.407)	[0.26, 20.96]
WEEK60	79	0.00 (0.0, 50.0)	4.85 (11.053)	[2.38, 7.33]	11	8.33 (0.0, 33.3)	11.36 (13.056)	[2.59, 20.13]
WEEK66	67	0.00 (0.0, 33.3)	5.97 (11.124)	[3.26, 8.68]	8	0.00 (0.0, 100.0)	12.50 (35.355)	[-17.06, 42.06]
WEEK72	59	0.00 (0.0, 66.7)	4.52 (11.919)	[1.41, 7.63]	9	0.00 (0.0, 33.3)	11.11 (14.434)	[0.02, 22.21]
WEEK78	49	0.00 (0.0, 33.3)	3.74 (8.516)	[1.30, 6.19]	6	0.00 (0.0, 0.0)	0.00 (0.000)	[NE, NE]
WEEK86	35	0.00 (0.0, 33.3)	3.81 (9.116)	[0.68, 6.94]	6	8.33 (0.0, 33.3)	12.50 (14.672)	[-2.90, 27.90]
WEEK94	33	0.00 (0.0, 50.0)	4.04 (10.232)	[0.41, 7.67]	3	0.00 (0.0, 33.3)	11.11 (19.245)	[-36.70, 58.92]
WEEK102	21	0.00 (0.0, 33.3)	4.76 (9.344)	[0.51, 9.02]	0	NE (NE, NE)	NE (NE)	[NE, NE]
WEEK118	12	0.00 (0.0, 16.7)	1.39 (4.811)	[-1.67, 4.45]	0	NE (NE, NE)	NE (NE)	[NE, NE]
WEEK126	8	0.00 (0.0, 0.0)	0.00 (0.000)	[NE, NE]	0	NE (NE, NE)	NE (NE)	[NE, NE]
WEEK134	7	0.00 (0.0, 16.7)	2.38 (6.299)	[-3.45, 8.21]	0	NE (NE, NE)	NE (NE)	[NE, NE]
WEEK142	4	0.00 (0.0, 0.0)	0.00 (0.000)	[NE, NE]	0	NE (NE, NE)	NE (NE)	[NE, NE]
WEEK150	2	0.00 (0.0, 0.0)	0.00 (0.000)	[NE, NE]	0	NE (NE, NE)	NE (NE)	[NE, NE]
WEEK158	1	0.00 (0.0, 0.0)	0.00 (NE)	[NE, NE]	0	NE (NE, NE)	NE (NE)	[NE, NE]
END OF TRT	77	0.00 (0.0, 100.0)	10.17 (18.168)	[6.05, 14.30]	39	0.00 (0.0, 66.7)	10.68 (18.531)	[4.68, 16.69]
FOLLOW UP	48	0.00 (0.0, 66.7)	5.90 (12.150)	[2.37, 9.43]	22	0.00 (0.0, 66.7)	9.09 (16.846)	[1.62, 16.56]

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[1] Confidence interval based on the normal distribution.
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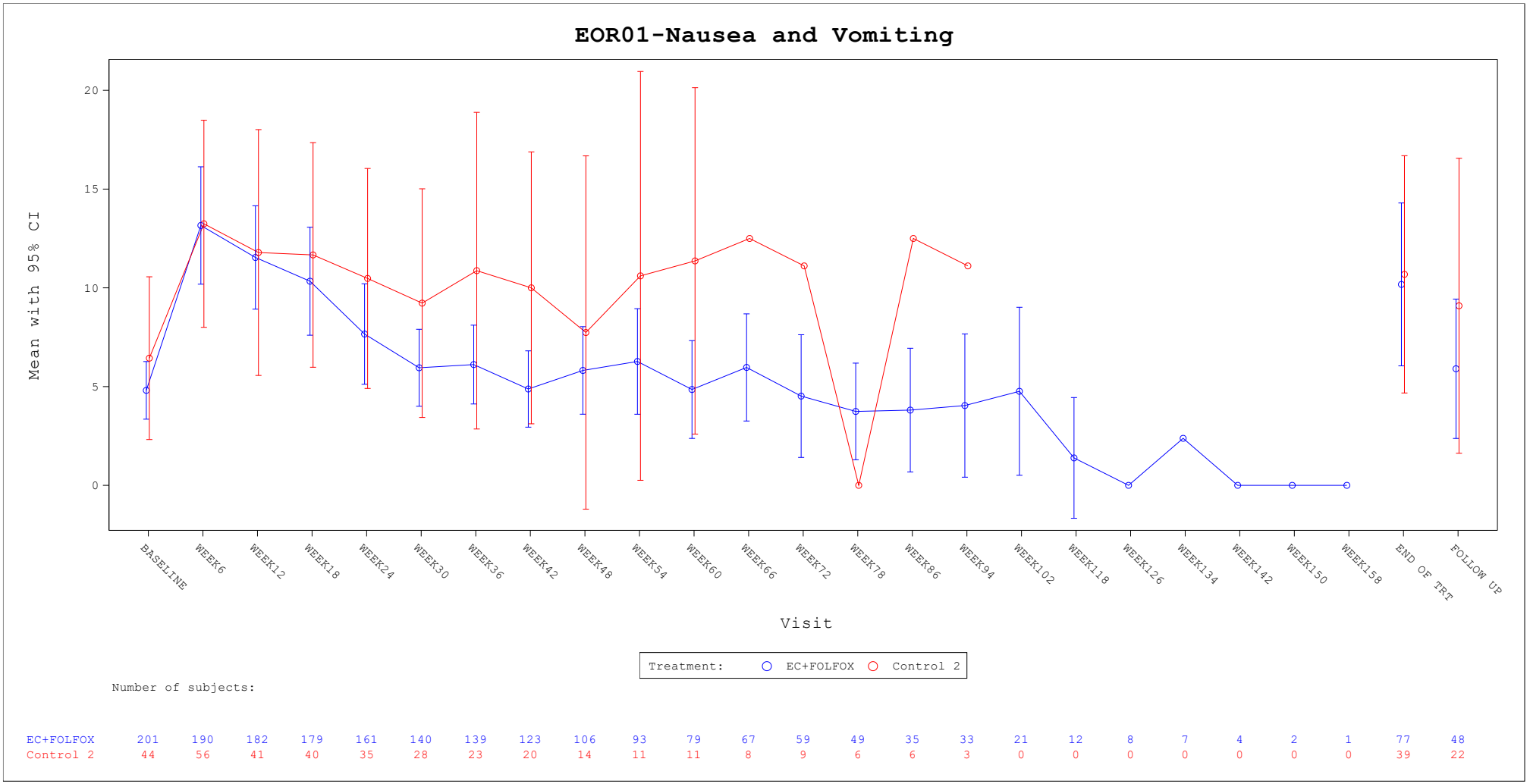

Number of subjects:

EC+FOLFOX	201	190	182	179	161	140	139	123	106	93	79	67	59	49	35	33	21	12	8	7	4	2	1	77	48
Control 2	44	56	41	40	35	28	23	20	14	11	11	8	9	6	6	3	0	0	0	0	0	0	0	39	22

Baseline is the last non-missing measurement prior to first dose of study intervention.
No confidence intervalls are drawn, when there are less than 10 patients in treatment arm.
For functional scales, higher scores represent a better level of functioning. For symptom-oriented scales, a higher score represents more severe symptoms.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Summary over time - EOR01-Pain
Full Analysis Set

	EC+FOLFOX (N=236)				Control 2 (N=74)			
Visit	n	Median (Range)	Mean (SD)	95% CI [1]	n	Median (Range)	Mean (SD)	95% CI [1]
BASELINE	201	16.67 (0.0, 100.0)	25.54 (25.112)	[22.05, 29.03]	44	16.67 (0.0, 100.0)	20.83 (26.444)	[12.79, 28.87]
WEEK6	190	16.67 (0.0, 100.0)	19.56 (22.979)	[16.27, 22.85]	56	0.00 (0.0, 83.3)	15.77 (23.499)	[9.48, 22.07]
WEEK12	182	16.67 (0.0, 100.0)	17.58 (21.149)	[14.49, 20.68]	41	0.00 (0.0, 100.0)	19.11 (30.348)	[9.53, 28.68]
WEEK18	179	16.67 (0.0, 100.0)	18.16 (22.575)	[14.83, 21.49]	40	0.00 (0.0, 100.0)	20.42 (27.344)	[11.67, 29.16]
WEEK24	161	16.67 (0.0, 100.0)	23.91 (26.795)	[19.74, 28.08]	35	0.00 (0.0, 66.7)	12.14 (16.338)	[6.53, 17.76]
WEEK30	140	16.67 (0.0, 100.0)	22.98 (24.442)	[18.89, 27.06]	28	0.00 (0.0, 100.0)	19.35 (25.363)	[9.51, 29.18]
WEEK36	139	16.67 (0.0, 100.0)	18.82 (21.123)	[15.28, 22.37]	23	0.00 (0.0, 100.0)	15.94 (25.365)	[4.97, 26.91]
WEEK42	123	16.67 (0.0, 83.3)	19.51 (21.415)	[15.69, 23.33]	20	16.67 (0.0, 50.0)	15.00 (15.198)	[7.89, 22.11]
WEEK48	106	16.67 (0.0, 100.0)	19.50 (22.826)	[15.10, 23.89]	14	0.00 (0.0, 33.3)	5.95 (10.555)	[-0.14, 12.05]
WEEK54	93	16.67 (0.0, 100.0)	16.67 (19.812)	[12.59, 20.75]	11	0.00 (0.0, 50.0)	9.09 (15.570)	[-1.37, 19.55]
WEEK60	79	16.67 (0.0, 100.0)	17.72 (21.240)	[12.96, 22.48]	11	0.00 (0.0, 83.3)	16.67 (25.820)	[-0.68, 34.01]
WEEK66	67	16.67 (0.0, 100.0)	18.66 (23.124)	[13.02, 24.30]	8	25.00 (0.0, 100.0)	27.08 (33.259)	[-0.72, 54.89]
WEEK72	59	0.00 (0.0, 83.3)	17.80 (22.714)	[11.88, 23.72]	9	0.00 (0.0, 33.3)	9.26 (14.699)	[-2.04, 20.56]
WEEK78	49	0.00 (0.0, 83.3)	13.95 (19.048)	[8.47, 19.42]	6	0.00 (0.0, 33.3)	8.33 (13.944)	[-6.30, 22.97]
WEEK86	35	16.67 (0.0, 66.7)	16.67 (18.078)	[10.46, 22.88]	6	0.00 (0.0, 33.3)	5.56 (13.608)	[-8.73, 19.84]
WEEK94	33	0.00 (0.0, 66.7)	12.63 (18.648)	[6.01, 19.24]	3	0.00 (0.0, 33.3)	11.11 (19.245)	[-36.70, 58.92]
WEEK102	21	0.00 (0.0, 33.3)	12.70 (14.818)	[5.95, 19.44]	0	NE (NE, NE)	NE (NE)	[NE, NE]
WEEK118	12	0.00 (0.0, 50.0)	12.50 (17.588)	[1.33, 23.67]	0	NE (NE, NE)	NE (NE)	[NE, NE]
WEEK126	8	0.00 (0.0, 50.0)	12.50 (19.416)	[-3.73, 28.73]	0	NE (NE, NE)	NE (NE)	[NE, NE]
WEEK134	7	0.00 (0.0, 66.7)	11.90 (24.934)	[-11.16, 34.96]	0	NE (NE, NE)	NE (NE)	[NE, NE]
WEEK142	4	16.67 (0.0, 66.7)	25.00 (31.914)	[-25.78, 75.78]	0	NE (NE, NE)	NE (NE)	[NE, NE]
WEEK150	2	8.33 (0.0, 16.7)	8.33 (11.785)	[-97.55, 114.22]	0	NE (NE, NE)	NE (NE)	[NE, NE]
WEEK158	1	0.00 (0.0, 0.0)	0.00 (NE)	[NE, NE]	0	NE (NE, NE)	NE (NE)	[NE, NE]
END OF TRT	77	33.33 (0.0, 100.0)	29.65 (29.571)	[22.94, 36.37]	39	16.67 (0.0, 100.0)	27.35 (29.491)	[17.79, 36.91]
FOLLOW UP	48	33.33 (0.0, 100.0)	27.43 (28.865)	[19.05, 35.81]	22	16.67 (0.0, 100.0)	26.52 (28.480)	[13.89, 39.14]

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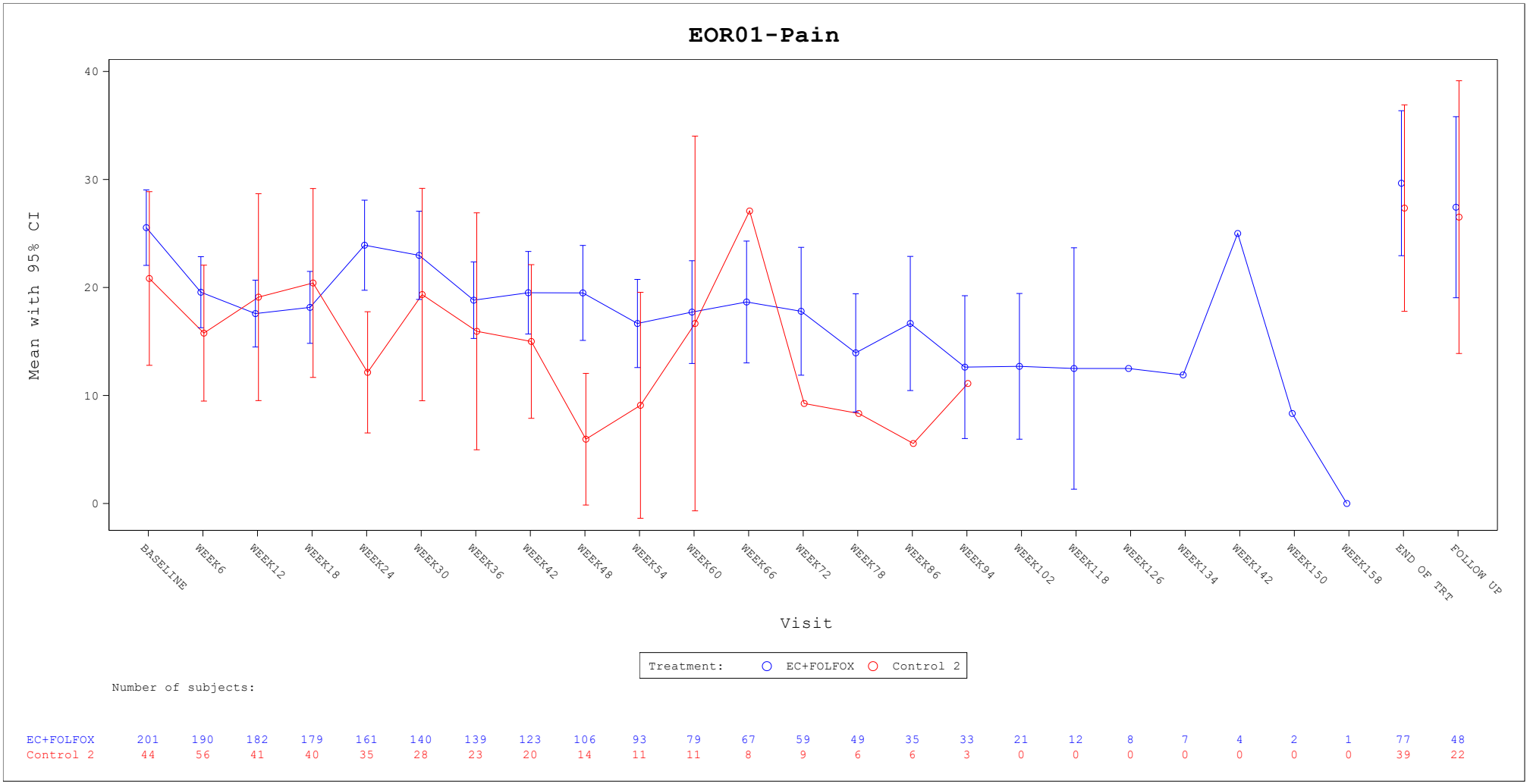
Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Plot over time - EOR01-Pain
Full Analysis Set



Number of subjects:

EC+FOLFOX	201	190	182	179	161	140	139	123	106	93	79	67	59	49	35	33	21	12	8	7	4	2	1	77	48
Control 2	44	56	41	40	35	28	23	20	14	11	11	8	9	6	6	3	0	0	0	0	0	0	0	39	22

Baseline is the last non-missing measurement prior to first dose of study intervention.
No confidence intervalls are drawn, when there are less than 10 patients in treatment arm.
For functional scales, higher scores represent a better level of functioning. For symptom-oriented scales, a higher score represents more severe symptoms.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Summary over time - EOR01-Dyspnoea
Full Analysis Set

	EC+FOLFOX (N=236)				Control 2 (N=74)			
Visit	n	Median (Range)	Mean (SD)	95% CI [1]	n	Median (Range)	Mean (SD)	95% CI [1]
BASELINE	201	0.00 (0.0, 100.0)	13.60 (21.415)	[10.62, 16.58]	44	0.00 (0.0, 66.7)	12.12 (17.742)	[6.73, 17.52]
WEEK6	190	0.00 (0.0, 100.0)	19.47 (24.265)	[16.00, 22.95]	56	0.00 (0.0, 100.0)	14.58 (21.335)	[8.87, 20.30]
WEEK12	182	0.00 (0.0, 100.0)	18.86 (26.069)	[15.05, 22.68]	41	0.00 (0.0, 100.0)	19.11 (24.597)	[11.34, 26.87]
WEEK18	179	0.00 (0.0, 100.0)	16.76 (22.727)	[13.41, 20.11]	40	0.00 (0.0, 100.0)	16.67 (26.149)	[8.30, 25.03]
WEEK24	161	0.00 (0.0, 100.0)	18.01 (24.719)	[14.17, 21.86]	35	0.00 (0.0, 66.7)	14.76 (19.289)	[8.14, 21.39]
WEEK30	140	0.00 (0.0, 100.0)	14.29 (20.831)	[10.80, 17.77]	28	8.33 (0.0, 100.0)	19.64 (24.450)	[10.16, 29.12]
WEEK36	139	0.00 (0.0, 100.0)	13.19 (22.205)	[9.47, 16.91]	23	0.00 (0.0, 66.7)	18.84 (22.079)	[9.29, 28.39]
WEEK42	123	0.00 (0.0, 100.0)	11.38 (21.266)	[7.59, 15.18]	20	0.00 (0.0, 100.0)	18.33 (27.519)	[5.45, 31.21]
WEEK48	106	0.00 (0.0, 100.0)	10.69 (20.340)	[6.77, 14.61]	14	0.00 (0.0, 66.7)	11.90 (21.111)	[-0.28, 24.09]
WEEK54	93	0.00 (0.0, 100.0)	14.34 (21.646)	[9.88, 18.79]	11	0.00 (0.0, 33.3)	6.06 (13.484)	[-3.00, 15.12]
WEEK60	79	0.00 (0.0, 66.7)	15.61 (21.240)	[10.85, 20.37]	11	0.00 (0.0, 66.7)	22.73 (28.159)	[3.81, 41.64]
WEEK66	67	0.00 (0.0, 66.7)	14.43 (19.440)	[9.69, 19.17]	8	0.00 (0.0, 66.7)	16.67 (25.198)	[-4.40, 37.73]
WEEK72	59	0.00 (0.0, 100.0)	15.82 (23.453)	[9.71, 21.93]	9	33.33 (0.0, 100.0)	25.93 (32.394)	[1.03, 50.83]
WEEK78	49	0.00 (0.0, 66.7)	13.61 (19.147)	[8.11, 19.10]	6	16.67 (0.0, 100.0)	27.78 (38.968)	[-13.12, 68.67]
WEEK86	35	0.00 (0.0, 33.3)	7.62 (14.201)	[2.74, 12.50]	6	16.67 (0.0, 100.0)	27.78 (38.968)	[-13.12, 68.67]
WEEK94	33	0.00 (0.0, 33.3)	8.08 (14.506)	[2.94, 13.22]	3	0.00 (0.0, 33.3)	11.11 (19.245)	[-36.70, 58.92]
WEEK102	21	0.00 (0.0, 33.3)	9.52 (15.430)	[2.50, 16.55]	0	NE (NE, NE)	NE (NE)	[NE, NE]
WEEK118	12	0.00 (0.0, 66.7)	11.11 (21.711)	[-2.68, 24.91]	0	NE (NE, NE)	NE (NE)	[NE, NE]
WEEK126	8	0.00 (0.0, 66.7)	16.67 (25.198)	[-4.40, 37.73]	0	NE (NE, NE)	NE (NE)	[NE, NE]
WEEK134	7	0.00 (0.0, 66.7)	14.29 (26.227)	[-9.97, 38.54]	0	NE (NE, NE)	NE (NE)	[NE, NE]
WEEK142	4	16.67 (0.0, 66.7)	25.00 (31.914)	[-25.78, 75.78]	0	NE (NE, NE)	NE (NE)	[NE, NE]
WEEK150	2	16.67 (0.0, 33.3)	16.67 (23.570)	[-195.10, 228.44]	0	NE (NE, NE)	NE (NE)	[NE, NE]
WEEK158	1	0.00 (0.0, 0.0)	0.00 (NE)	[NE, NE]	0	NE (NE, NE)	NE (NE)	[NE, NE]
END OF TRT	77	33.33 (0.0, 100.0)	22.08 (26.825)	[15.99, 28.17]	39	33.33 (0.0, 100.0)	23.08 (24.368)	[15.18, 30.98]
FOLLOW UP	48	0.00 (0.0, 100.0)	18.06 (22.762)	[11.45, 24.67]	22	16.67 (0.0, 66.7)	19.70 (22.204)	[9.85, 29.54]

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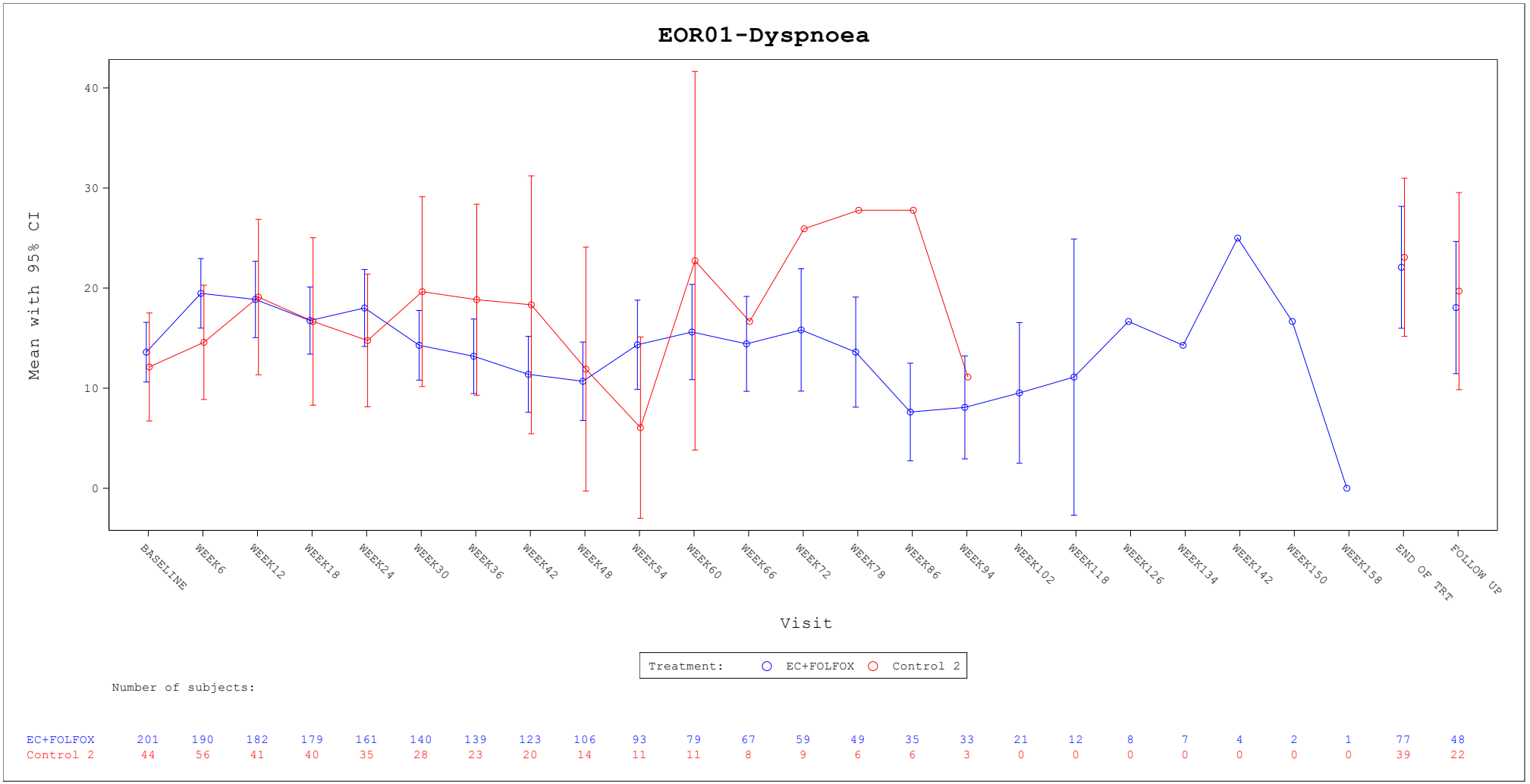
Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Plot over time - EOR01-Dyspnoea
Full Analysis Set



Number of subjects:

EC+FOLFOX	201	190	182	179	161	140	139	123	106	93	79	67	59	49	35	33	21	12	8	7	4	2	1	77	48
Control 2	44	56	41	40	35	28	23	20	14	11	11	8	9	6	6	3	0	0	0	0	0	0	0	39	22

Baseline is the last non-missing measurement prior to first dose of study intervention.
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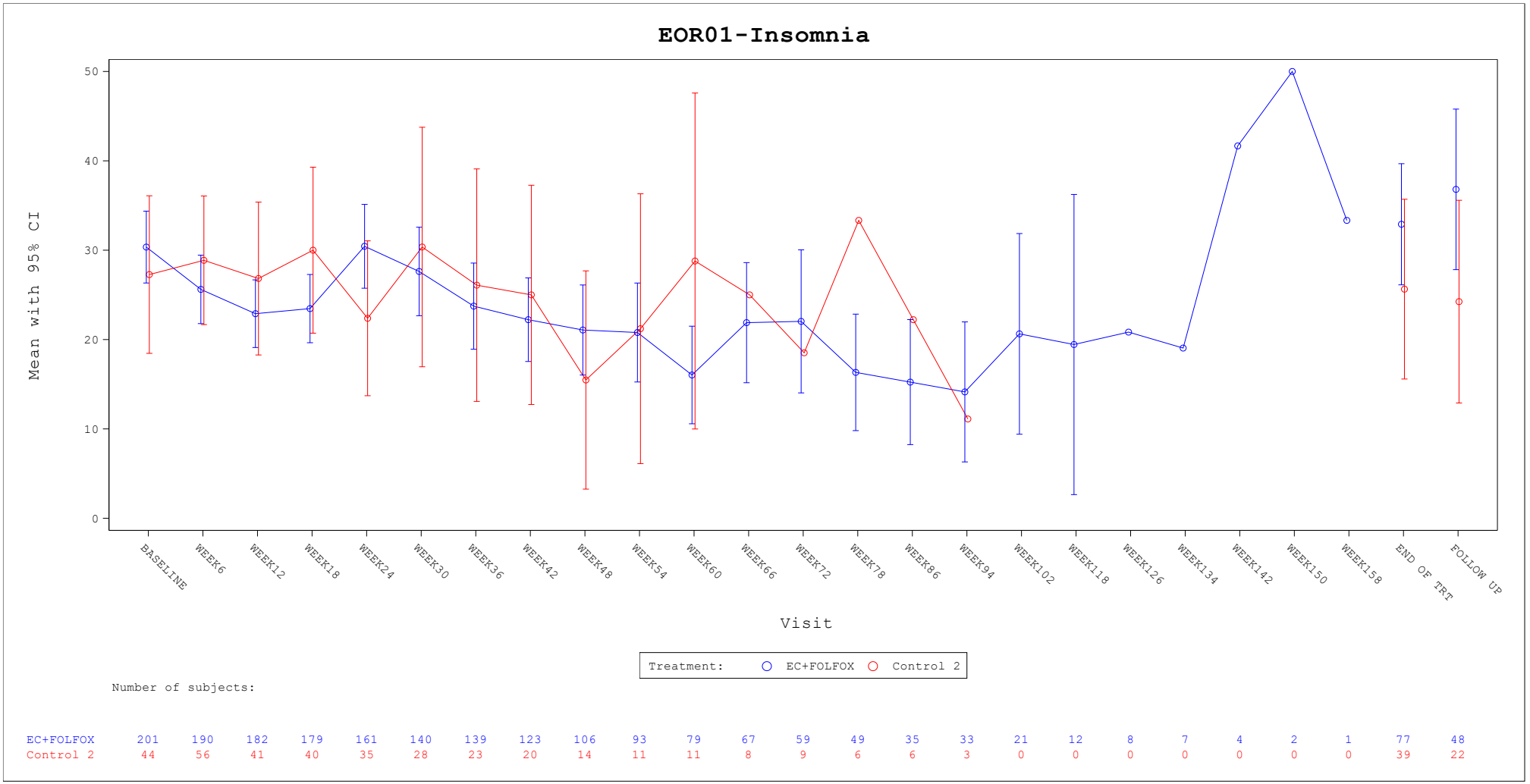
Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Summary over time - EOR01-Insomnia
Full Analysis Set

	EC+FOLFOX (N=236)				Control 2 (N=74)			
Visit	n	Median (Range)	Mean (SD)	95% CI [1]	n	Median (Range)	Mean (SD)	95% CI [1]
BASELINE	201	33.33 (0.0, 100.0)	30.35 (28.905)	[26.33, 34.37]	44	33.33 (0.0, 100.0)	27.27 (28.999)	[18.46, 36.09]
WEEK6	190	33.33 (0.0, 100.0)	25.61 (26.760)	[21.78, 29.44]	56	33.33 (0.0, 100.0)	28.87 (26.873)	[21.67, 36.07]
WEEK12	182	33.33 (0.0, 100.0)	22.89 (25.885)	[19.11, 26.68]	41	33.33 (0.0, 100.0)	26.83 (27.100)	[18.28, 35.38]
WEEK18	179	33.33 (0.0, 100.0)	23.46 (25.881)	[19.65, 27.28]	40	33.33 (0.0, 100.0)	30.00 (29.040)	[20.71, 39.29]
WEEK24	161	33.33 (0.0, 100.0)	30.43 (30.137)	[25.74, 35.13]	35	33.33 (0.0, 100.0)	22.38 (25.225)	[13.72, 31.05]
WEEK30	140	33.33 (0.0, 100.0)	27.62 (29.638)	[22.67, 32.57]	28	33.33 (0.0, 100.0)	30.36 (34.562)	[16.96, 43.76]
WEEK36	139	0.00 (0.0, 100.0)	23.74 (28.726)	[18.92, 28.56]	23	33.33 (0.0, 100.0)	26.09 (30.078)	[13.08, 39.09]
WEEK42	123	0.00 (0.0, 100.0)	22.22 (26.193)	[17.55, 26.90]	20	33.33 (0.0, 100.0)	25.00 (26.213)	[12.73, 37.27]
WEEK48	106	0.00 (0.0, 100.0)	21.07 (26.156)	[16.03, 26.11]	14	0.00 (0.0, 66.7)	15.48 (21.147)	[3.27, 27.69]
WEEK54	93	0.00 (0.0, 100.0)	20.79 (26.880)	[15.25, 26.32]	11	33.33 (0.0, 66.7)	21.21 (22.473)	[6.11, 36.31]
WEEK60	79	0.00 (0.0, 100.0)	16.03 (24.379)	[10.57, 21.49]	11	33.33 (0.0, 100.0)	28.79 (27.979)	[9.99, 47.58]
WEEK66	67	0.00 (0.0, 100.0)	21.89 (27.556)	[15.17, 28.61]	8	33.33 (0.0, 66.7)	25.00 (23.570)	[5.29, 44.71]
WEEK72	59	0.00 (0.0, 100.0)	22.03 (30.707)	[14.03, 30.04]	9	33.33 (0.0, 33.3)	18.52 (17.568)	[5.01, 32.02]
WEEK78	49	0.00 (0.0, 100.0)	16.33 (22.692)	[9.81, 22.84]	6	33.33 (0.0, 66.7)	33.33 (29.814)	[2.05, 64.62]
WEEK86	35	0.00 (0.0, 66.7)	15.24 (20.361)	[8.24, 22.23]	6	16.67 (0.0, 66.7)	22.22 (27.217)	[-6.34, 50.78]
WEEK94	33	0.00 (0.0, 66.7)	14.14 (22.096)	[6.31, 21.98]	3	0.00 (0.0, 33.3)	11.11 (19.245)	[-36.70, 58.92]
WEEK102	21	0.00 (0.0, 66.7)	20.63 (24.667)	[9.41, 31.86]	0	NE (NE, NE)	NE (NE)	[NE, NE]
WEEK118	12	0.00 (0.0, 66.7)	19.44 (26.432)	[2.65, 36.24]	0	NE (NE, NE)	NE (NE)	[NE, NE]
WEEK126	8	16.67 (0.0, 66.7)	20.83 (24.801)	[0.10, 41.57]	0	NE (NE, NE)	NE (NE)	[NE, NE]
WEEK134	7	0.00 (0.0, 66.7)	19.05 (26.227)	[-5.21, 43.30]	0	NE (NE, NE)	NE (NE)	[NE, NE]
WEEK142	4	50.00 (0.0, 66.7)	41.67 (31.914)	[-9.12, 92.45]	0	NE (NE, NE)	NE (NE)	[NE, NE]
WEEK150	2	50.00 (33.3, 66.7)	50.00 (23.570)	[-161.77, 261.77]	0	NE (NE, NE)	NE (NE)	[NE, NE]
WEEK158	1	33.33 (33.3, 33.3)	33.33 (NE)	[NE, NE]	0	NE (NE, NE)	NE (NE)	[NE, NE]
END OF TRT	77	33.33 (0.0, 100.0)	32.90 (29.860)	[26.12, 39.68]	39	0.00 (0.0, 100.0)	25.64 (31.027)	[15.58, 35.70]
FOLLOW UP	48	33.33 (0.0, 100.0)	36.81 (30.935)	[27.82, 45.79]	22	33.33 (0.0, 66.7)	24.24 (25.577)	[12.90, 35.58]

Baseline is the last non-missing measurement prior to first dose of study intervention.
[1] Confidence interval based on the normal distribution.
For functional scales, higher scores represent a better level of functioning. For symptom-oriented scales, a higher score represents more severe symptoms.



Number of subjects:

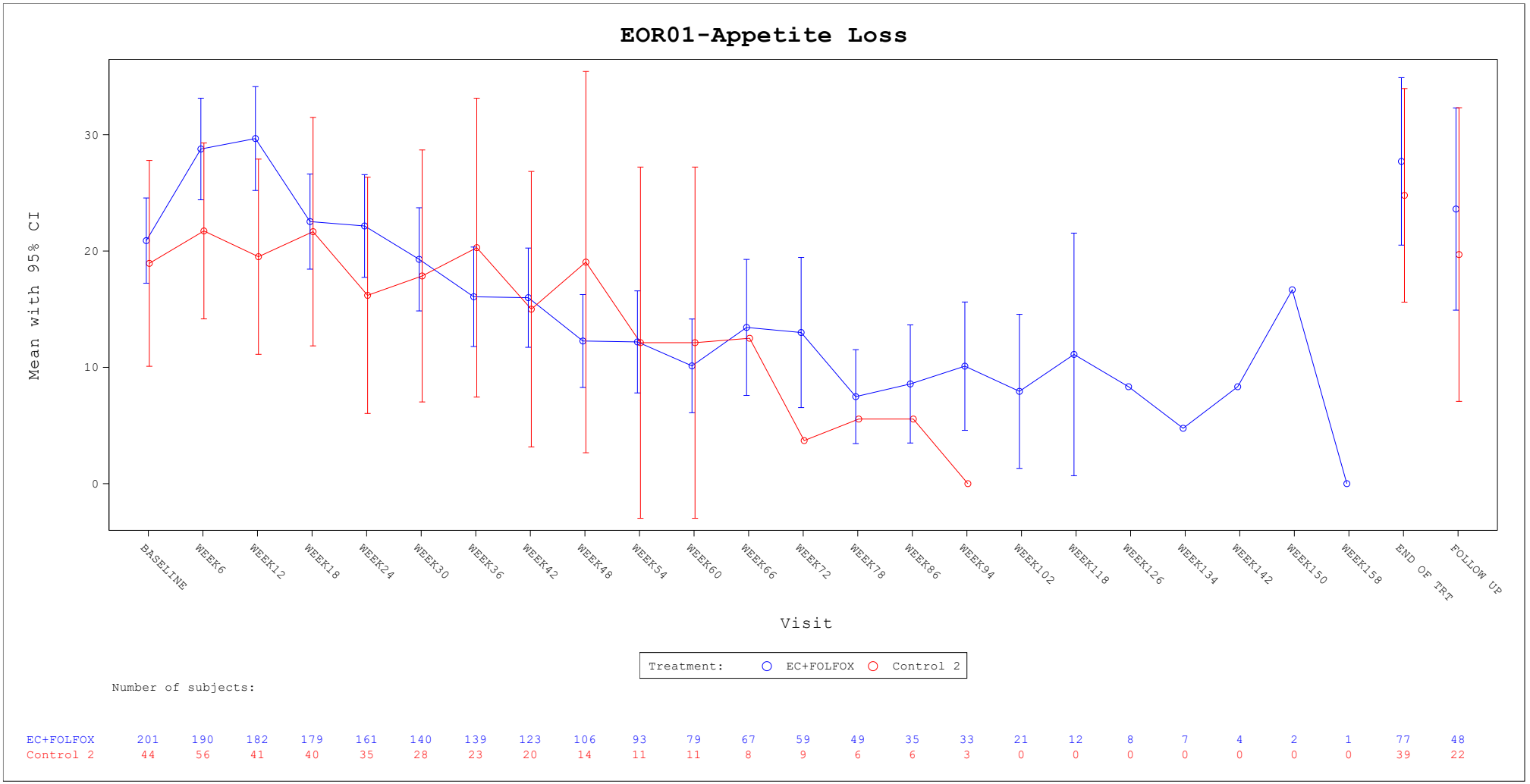
EC+FOLFOX	201	190	182	179	161	140	139	123	106	93	79	67	59	49	35	33	21	12	8	7	4	2	1	77	48
Control 2	44	56	41	40	35	28	23	20	14	11	11	8	9	6	6	3	0	0	0	0	0	0	0	39	22

Baseline is the last non-missing measurement prior to first dose of study intervention.
No confidence intervalls are drawn, when there are less than 10 patients in treatment arm.
For functional scales, higher scores represent a better level of functioning. For symptom-oriented scales, a higher score represents more severe symptoms.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Summary over time - EOR01-Appetite Loss
Full Analysis Set

	EC+FOLFOX (N=236)				Control 2 (N=74)			
Visit	n	Median (Range)	Mean (SD)	95% CI [1]	n	Median (Range)	Mean (SD)	95% CI [1]
BASELINE	201	0.00 (0.0, 100.0)	20.90 (26.354)	[17.23, 24.56]	44	0.00 (0.0, 100.0)	18.94 (29.111)	[10.09, 27.79]
WEEK6	190	33.33 (0.0, 100.0)	28.77 (30.520)	[24.40, 33.14]	56	0.00 (0.0, 100.0)	21.73 (28.234)	[14.17, 29.29]
WEEK12	182	33.33 (0.0, 100.0)	29.67 (30.527)	[25.21, 34.14]	41	0.00 (0.0, 100.0)	19.51 (26.589)	[11.12, 27.90]
WEEK18	179	0.00 (0.0, 100.0)	22.53 (27.732)	[18.44, 26.62]	40	0.00 (0.0, 100.0)	21.67 (30.709)	[11.85, 31.49]
WEEK24	161	0.00 (0.0, 100.0)	22.15 (28.369)	[17.74, 26.57]	35	0.00 (0.0, 100.0)	16.19 (29.563)	[6.04, 26.35]
WEEK30	140	0.00 (0.0, 100.0)	19.29 (26.543)	[14.85, 23.72]	28	0.00 (0.0, 100.0)	17.86 (27.936)	[7.02, 28.69]
WEEK36	139	0.00 (0.0, 100.0)	16.07 (25.491)	[11.79, 20.34]	23	0.00 (0.0, 100.0)	20.29 (29.711)	[7.44, 33.14]
WEEK42	123	0.00 (0.0, 100.0)	15.99 (23.896)	[11.72, 20.25]	20	0.00 (0.0, 100.0)	15.00 (25.305)	[3.16, 26.84]
WEEK48	106	0.00 (0.0, 100.0)	12.26 (20.741)	[8.27, 16.26]	14	0.00 (0.0, 66.7)	19.05 (28.388)	[2.66, 35.44]
WEEK54	93	0.00 (0.0, 100.0)	12.19 (21.301)	[7.80, 16.57]	11	0.00 (0.0, 66.7)	12.12 (22.473)	[-2.98, 27.22]
WEEK60	79	0.00 (0.0, 66.7)	10.13 (17.986)	[6.10, 14.16]	11	0.00 (0.0, 66.7)	12.12 (22.473)	[-2.98, 27.22]
WEEK66	67	0.00 (0.0, 100.0)	13.43 (23.967)	[7.59, 19.28]	8	0.00 (0.0, 100.0)	12.50 (35.355)	[-17.06, 42.06]
WEEK72	59	0.00 (0.0, 100.0)	12.99 (24.772)	[6.54, 19.45]	9	0.00 (0.0, 33.3)	3.70 (11.111)	[-4.84, 12.24]
WEEK78	49	0.00 (0.0, 33.3)	7.48 (14.052)	[3.45, 11.52]	6	0.00 (0.0, 33.3)	5.56 (13.608)	[-8.73, 19.84]
WEEK86	35	0.00 (0.0, 33.3)	8.57 (14.781)	[3.49, 13.65]	6	0.00 (0.0, 33.3)	5.56 (13.608)	[-8.73, 19.84]
WEEK94	33	0.00 (0.0, 33.3)	10.10 (15.556)	[4.58, 15.62]	3	0.00 (0.0, 0.0)	0.00 (0.000)	[NE, NE]
WEEK102	21	0.00 (0.0, 33.3)	7.94 (14.548)	[1.31, 14.56]	0	NE (NE, NE)	NE (NE)	[NE, NE]
WEEK118	12	0.00 (0.0, 33.3)	11.11 (16.412)	[0.68, 21.54]	0	NE (NE, NE)	NE (NE)	[NE, NE]
WEEK126	8	0.00 (0.0, 33.3)	8.33 (15.430)	[-4.57, 21.23]	0	NE (NE, NE)	NE (NE)	[NE, NE]
WEEK134	7	0.00 (0.0, 33.3)	4.76 (12.599)	[-6.89, 16.41]	0	NE (NE, NE)	NE (NE)	[NE, NE]
WEEK142	4	0.00 (0.0, 33.3)	8.33 (16.667)	[-18.19, 34.85]	0	NE (NE, NE)	NE (NE)	[NE, NE]
WEEK150	2	16.67 (0.0, 33.3)	16.67 (23.570)	[-195.10, 228.44]	0	NE (NE, NE)	NE (NE)	[NE, NE]
WEEK158	1	0.00 (0.0, 0.0)	0.00 (NE)	[NE, NE]	0	NE (NE, NE)	NE (NE)	[NE, NE]
END OF TRT	77	33.33 (0.0, 100.0)	27.71 (31.716)	[20.51, 34.90]	39	33.33 (0.0, 100.0)	24.79 (28.323)	[15.60, 33.97]
FOLLOW UP	48	0.00 (0.0, 100.0)	23.61 (29.940)	[14.92, 32.30]	22	0.00 (0.0, 100.0)	19.70 (28.469)	[7.07, 32.32]

Baseline is the last non-missing measurement prior to first dose of study intervention.
[1] Confidence interval based on the normal distribution.
For functional scales, higher scores represent a better level of functioning. For symptom-oriented scales, a higher score represents more severe symptoms.



Number of subjects:

EC+FOLFOX	201	190	182	179	161	140	139	123	106	93	79	67	59	49	35	33	21	12	8	7	4	2	1	77	48
Control 2	44	56	41	40	35	28	23	20	14	11	11	8	9	6	6	3	0	0	0	0	0	0	0	39	22

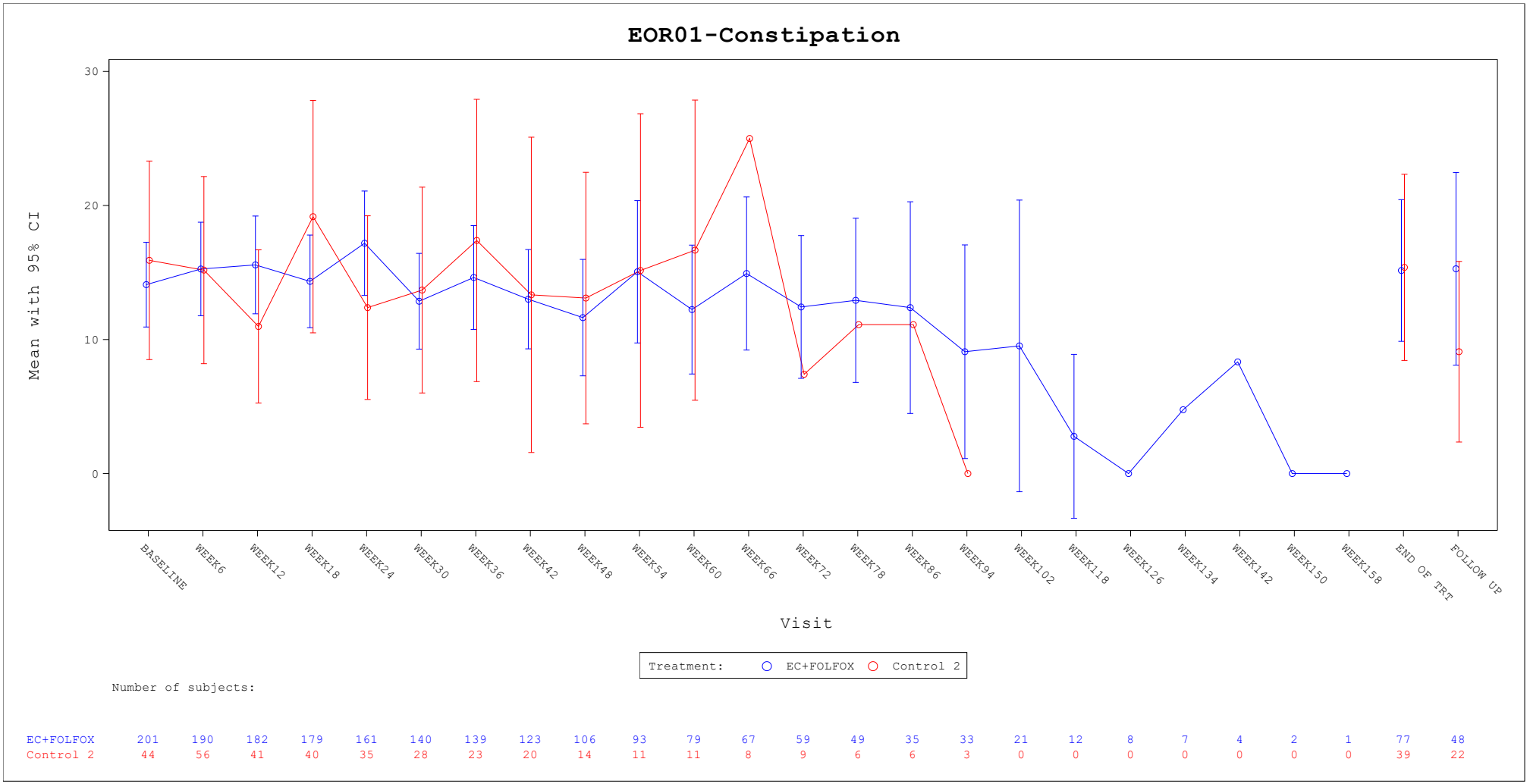
Baseline is the last non-missing measurement prior to first dose of study intervention.
No confidence intervalls are drawn, when there are less than 10 patients in treatment arm.
For functional scales, higher scores represent a better level of functioning. For symptom-oriented scales, a higher score represents more severe symptoms.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Summary over time - EOR01-Constipation
Full Analysis Set

	EC+FOLFOX (N=236)				Control 2 (N=74)			
Visit	n	Median (Range)	Mean (SD)	95% CI [1]	n	Median (Range)	Mean (SD)	95% CI [1]
BASELINE	201	0.00 (0.0, 100.0)	14.10 (22.737)	[10.93, 17.26]	44	0.00 (0.0, 100.0)	15.91 (24.367)	[8.50, 23.32]
WEEK6	190	0.00 (0.0, 100.0)	15.26 (24.387)	[11.77, 18.75]	56	0.00 (0.0, 100.0)	15.18 (26.068)	[8.20, 22.16]
WEEK12	182	0.00 (0.0, 100.0)	15.57 (24.937)	[11.92, 19.22]	41	0.00 (0.0, 66.7)	10.98 (18.108)	[5.26, 16.69]
WEEK18	179	0.00 (0.0, 100.0)	14.34 (23.421)	[10.88, 17.79]	40	0.00 (0.0, 100.0)	19.17 (27.099)	[10.50, 27.83]
WEEK24	161	0.00 (0.0, 100.0)	17.18 (25.029)	[13.29, 21.08]	35	0.00 (0.0, 66.7)	12.38 (19.944)	[5.53, 19.23]
WEEK30	140	0.00 (0.0, 100.0)	12.86 (21.378)	[9.28, 16.43]	28	0.00 (0.0, 66.7)	13.69 (19.800)	[6.01, 21.37]
WEEK36	139	0.00 (0.0, 100.0)	14.63 (23.092)	[10.76, 18.50]	23	0.00 (0.0, 66.7)	17.39 (24.349)	[6.86, 27.92]
WEEK42	123	0.00 (0.0, 100.0)	13.01 (20.748)	[9.30, 16.71]	20	0.00 (0.0, 100.0)	13.33 (25.131)	[1.57, 25.10]
WEEK48	106	0.00 (0.0, 100.0)	11.64 (22.557)	[7.29, 15.98]	14	0.00 (0.0, 33.3)	13.10 (16.249)	[3.71, 22.48]
WEEK54	93	0.00 (0.0, 100.0)	15.05 (25.781)	[9.74, 20.36]	11	0.00 (0.0, 33.3)	15.15 (17.408)	[3.46, 26.85]
WEEK60	79	0.00 (0.0, 100.0)	12.24 (21.468)	[7.43, 17.04]	11	16.67 (0.0, 33.3)	16.67 (16.667)	[5.47, 27.86]
WEEK66	67	0.00 (0.0, 100.0)	14.93 (23.415)	[9.21, 20.64]	8	16.67 (0.0, 100.0)	25.00 (34.503)	[-3.85, 53.85]
WEEK72	59	0.00 (0.0, 100.0)	12.43 (20.434)	[7.10, 17.75]	9	0.00 (0.0, 33.3)	7.41 (14.699)	[-3.89, 18.71]
WEEK78	49	0.00 (0.0, 100.0)	12.93 (21.318)	[6.80, 19.05]	6	0.00 (0.0, 33.3)	11.11 (17.213)	[-6.95, 29.18]
WEEK86	35	0.00 (0.0, 100.0)	12.38 (22.989)	[4.48, 20.28]	6	0.00 (0.0, 33.3)	11.11 (17.213)	[-6.95, 29.18]
WEEK94	33	0.00 (0.0, 100.0)	9.09 (22.473)	[1.12, 17.06]	3	0.00 (0.0, 0.0)	0.00 (0.000)	[NE, NE]
WEEK102	21	0.00 (0.0, 100.0)	9.52 (23.905)	[-1.36, 20.41]	0	NE (NE, NE)	NE (NE)	[NE, NE]
WEEK118	12	0.00 (0.0, 33.3)	2.78 (9.623)	[-3.34, 8.89]	0	NE (NE, NE)	NE (NE)	[NE, NE]
WEEK126	8	0.00 (0.0, 0.0)	0.00 (0.000)	[NE, NE]	0	NE (NE, NE)	NE (NE)	[NE, NE]
WEEK134	7	0.00 (0.0, 33.3)	4.76 (12.599)	[-6.89, 16.41]	0	NE (NE, NE)	NE (NE)	[NE, NE]
WEEK142	4	0.00 (0.0, 33.3)	8.33 (16.667)	[-18.19, 34.85]	0	NE (NE, NE)	NE (NE)	[NE, NE]
WEEK150	2	0.00 (0.0, 0.0)	0.00 (0.000)	[NE, NE]	0	NE (NE, NE)	NE (NE)	[NE, NE]
WEEK158	1	0.00 (0.0, 0.0)	0.00 (NE)	[NE, NE]	0	NE (NE, NE)	NE (NE)	[NE, NE]
END OF TRT	77	0.00 (0.0, 100.0)	15.15 (23.287)	[9.87, 20.44]	39	0.00 (0.0, 66.7)	15.38 (21.421)	[8.44, 22.33]
FOLLOW UP	48	0.00 (0.0, 100.0)	15.28 (24.753)	[8.09, 22.47]	22	0.00 (0.0, 33.3)	9.09 (15.195)	[2.35, 15.83]

Baseline is the last non-missing measurement prior to first dose of study intervention.
[1] Confidence interval based on the normal distribution.
For functional scales, higher scores represent a better level of functioning. For symptom-oriented scales, a higher score represents more severe symptoms.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Plot over time - EOR01-Constipation
Full Analysis Set



Number of subjects:

EC+FOLFOX	201	190	182	179	161	140	139	123	106	93	79	67	59	49	35	33	21	12	8	7	4	2	1	77	48
Control 2	44	56	41	40	35	28	23	20	14	11	11	8	9	6	6	3	0	0	0	0	0	0	0	39	22

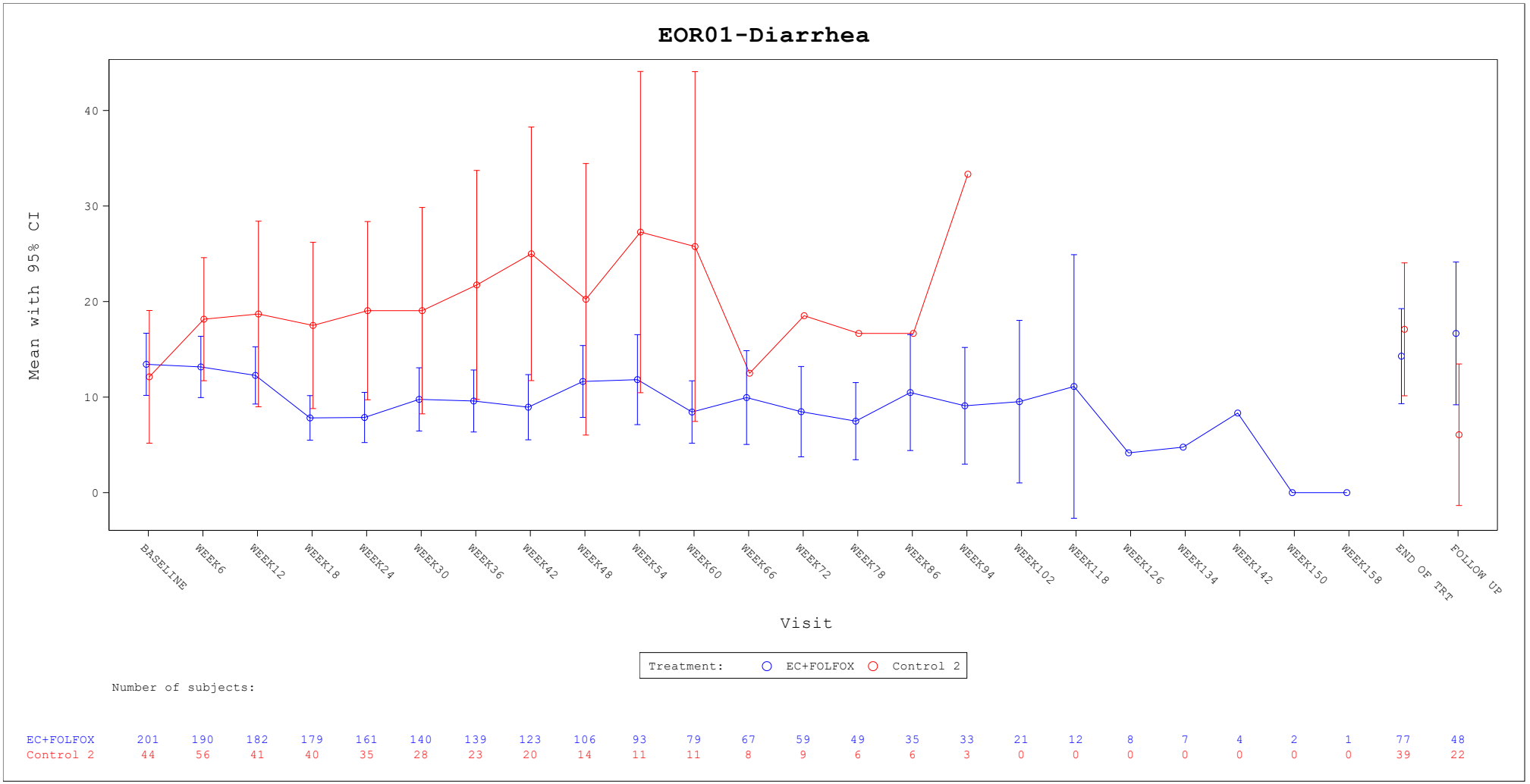
Baseline is the last non-missing measurement prior to first dose of study intervention.
No confidence intervalls are drawn, when there are less than 10 patients in treatment arm.
For functional scales, higher scores represent a better level of functioning. For symptom-oriented scales, a higher score represents more severe symptoms.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Summary over time - EOR01-Diarrhea
Full Analysis Set

	EC+FOLFOX (N=236)				Control 2 (N=74)			
Visit	n	Median (Range)	Mean (SD)	95% CI [1]	n	Median (Range)	Mean (SD)	95% CI [1]
BASELINE	201	0.00 (0.0, 100.0)	13.43 (23.376)	[10.18, 16.68]	44	0.00 (0.0, 100.0)	12.12 (22.836)	[5.18, 19.06]
WEEK6	190	0.00 (0.0, 100.0)	13.16 (22.406)	[9.95, 16.36]	56	0.00 (0.0, 100.0)	18.15 (24.053)	[11.71, 24.60]
WEEK12	182	0.00 (0.0, 100.0)	12.27 (20.481)	[9.28, 15.27]	41	0.00 (0.0, 100.0)	18.70 (30.776)	[8.99, 28.41]
WEEK18	179	0.00 (0.0, 66.7)	7.82 (15.830)	[5.49, 10.16]	40	0.00 (0.0, 100.0)	17.50 (27.203)	[8.80, 26.20]
WEEK24	161	0.00 (0.0, 100.0)	7.87 (16.880)	[5.24, 10.49]	35	0.00 (0.0, 100.0)	19.05 (27.159)	[9.72, 28.38]
WEEK30	140	0.00 (0.0, 66.7)	9.76 (19.790)	[6.46, 13.07]	28	0.00 (0.0, 100.0)	19.05 (27.857)	[8.25, 29.85]
WEEK36	139	0.00 (0.0, 100.0)	9.59 (19.347)	[6.35, 12.84]	23	0.00 (0.0, 100.0)	21.74 (27.723)	[9.75, 33.73]
WEEK42	123	0.00 (0.0, 100.0)	8.94 (19.121)	[5.53, 12.36]	20	33.33 (0.0, 100.0)	25.00 (28.357)	[11.73, 38.27]
WEEK48	106	0.00 (0.0, 100.0)	11.64 (19.541)	[7.87, 15.40]	14	8.33 (0.0, 66.7)	20.24 (24.615)	[6.03, 34.45]
WEEK54	93	0.00 (0.0, 100.0)	11.83 (22.865)	[7.12, 16.54]	11	33.33 (0.0, 66.7)	27.27 (25.025)	[10.46, 44.08]
WEEK60	79	0.00 (0.0, 33.3)	8.44 (14.587)	[5.17, 11.71]	11	33.33 (0.0, 66.7)	25.76 (27.247)	[7.45, 44.06]
WEEK66	67	0.00 (0.0, 100.0)	9.95 (20.113)	[5.04, 14.86]	8	0.00 (0.0, 33.3)	12.50 (17.252)	[-1.92, 26.92]
WEEK72	59	0.00 (0.0, 66.7)	8.47 (18.145)	[3.75, 13.20]	9	0.00 (0.0, 66.7)	18.52 (29.397)	[-4.08, 41.12]
WEEK78	49	0.00 (0.0, 33.3)	7.48 (14.052)	[3.45, 11.52]	6	16.67 (0.0, 33.3)	16.67 (18.257)	[-2.49, 35.83]
WEEK86	35	0.00 (0.0, 66.7)	10.48 (17.660)	[4.41, 16.54]	6	16.67 (0.0, 33.3)	16.67 (18.257)	[-2.49, 35.83]
WEEK94	33	0.00 (0.0, 66.7)	9.09 (17.225)	[2.98, 15.20]	3	33.33 (0.0, 66.7)	33.33 (33.333)	[-49.47, 116.14]
WEEK102	21	0.00 (0.0, 66.7)	9.52 (18.687)	[1.02, 18.03]	0	NE (NE, NE)	NE (NE)	[NE, NE]
WEEK118	12	0.00 (0.0, 66.7)	11.11 (21.711)	[-2.68, 24.91]	0	NE (NE, NE)	NE (NE)	[NE, NE]
WEEK126	8	0.00 (0.0, 33.3)	4.17 (11.785)	[-5.69, 14.02]	0	NE (NE, NE)	NE (NE)	[NE, NE]
WEEK134	7	0.00 (0.0, 33.3)	4.76 (12.599)	[-6.89, 16.41]	0	NE (NE, NE)	NE (NE)	[NE, NE]
WEEK142	4	0.00 (0.0, 33.3)	8.33 (16.667)	[-18.19, 34.85]	0	NE (NE, NE)	NE (NE)	[NE, NE]
WEEK150	2	0.00 (0.0, 0.0)	0.00 (0.000)	[NE, NE]	0	NE (NE, NE)	NE (NE)	[NE, NE]
WEEK158	1	0.00 (0.0, 0.0)	0.00 (NE)	[NE, NE]	0	NE (NE, NE)	NE (NE)	[NE, NE]
END OF TRT	77	0.00 (0.0, 100.0)	14.29 (21.917)	[9.31, 19.26]	39	0.00 (0.0, 66.7)	17.09 (21.456)	[10.14, 24.05]
FOLLOW UP	48	0.00 (0.0, 100.0)	16.67 (25.728)	[9.20, 24.14]	22	0.00 (0.0, 66.7)	6.06 (16.703)	[-1.34, 13.47]

Baseline is the last non-missing measurement prior to first dose of study intervention.
[1] Confidence interval based on the normal distribution.
For functional scales, higher scores represent a better level of functioning. For symptom-oriented scales, a higher score represents more severe symptoms.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Plot over time - EOR01-Diarrhea
Full Analysis Set



Number of subjects:

EC+FOLFOX	201	190	182	179	161	140	139	123	106	93	79	67	59	49	35	33	21	12	8	7	4	2	1	77	48
Control 2	44	56	41	40	35	28	23	20	14	11	11	8	9	6	6	3	0	0	0	0	0	0	0	39	22

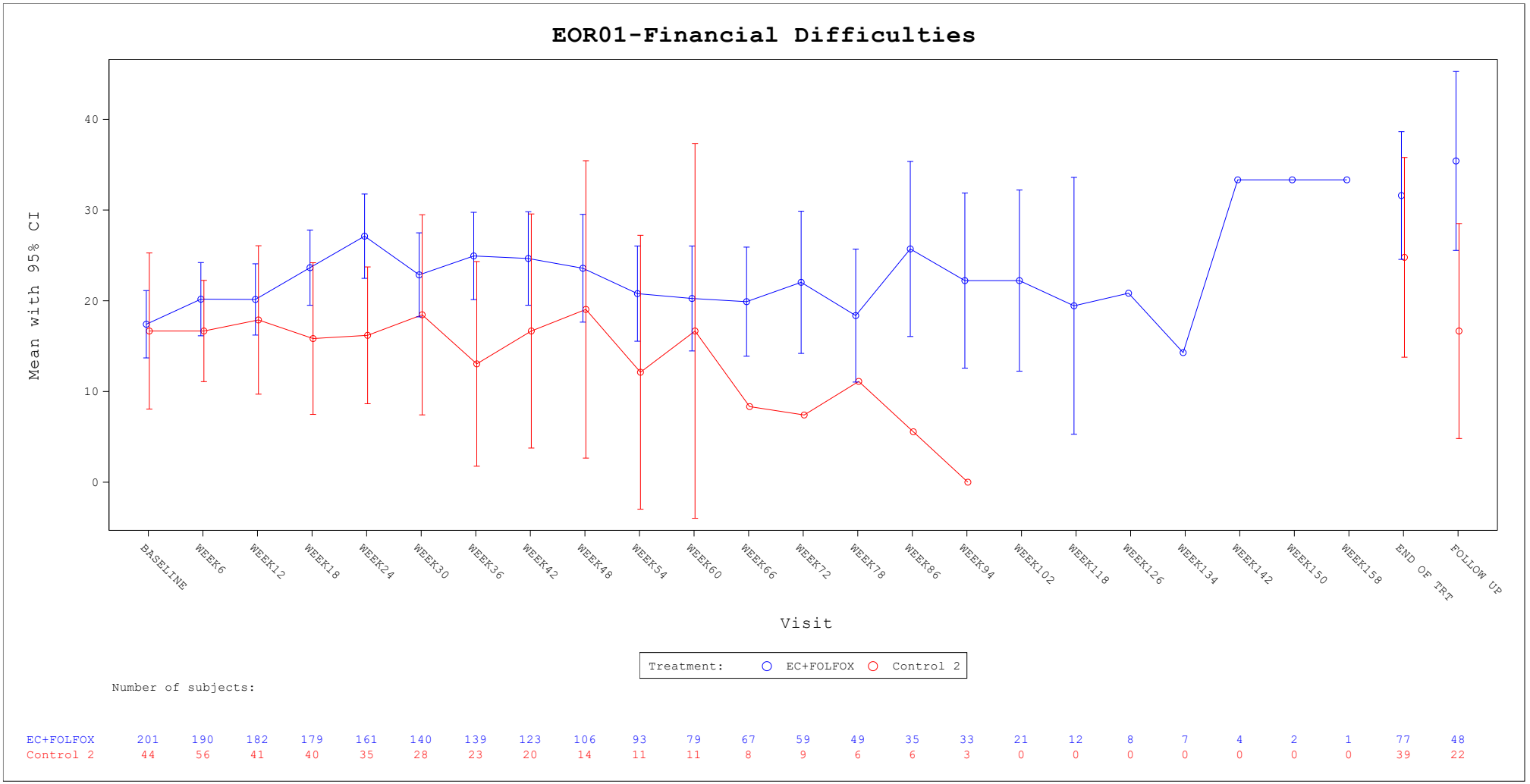
Baseline is the last non-missing measurement prior to first dose of study intervention.
No confidence intervalls are drawn, when there are less than 10 patients in treatment arm.
For functional scales, higher scores represent a better level of functioning. For symptom-oriented scales, a higher score represents more severe symptoms.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Summary over time - EOR01-Financial Difficulties
Full Analysis Set

	EC+FOLFOX (N=236)				Control 2 (N=74)			
Visit	n	Median (Range)	Mean (SD)	95% CI [1]	n	Median (Range)	Mean (SD)	95% CI [1]
BASELINE	201	0.00 (0.0, 100.0)	17.41 (26.682)	[13.70, 21.12]	44	0.00 (0.0, 100.0)	16.67 (28.303)	[8.06, 25.27]
WEEK6	190	0.00 (0.0, 100.0)	20.18 (28.213)	[16.14, 24.21]	56	0.00 (0.0, 100.0)	16.67 (20.841)	[11.09, 22.25]
WEEK12	182	0.00 (0.0, 100.0)	20.15 (26.859)	[16.22, 24.07]	41	0.00 (0.0, 100.0)	17.89 (25.925)	[9.70, 26.07]
WEEK18	179	33.33 (0.0, 100.0)	23.65 (28.144)	[19.50, 27.80]	40	0.00 (0.0, 100.0)	15.83 (26.135)	[7.47, 24.19]
WEEK24	161	33.33 (0.0, 100.0)	27.12 (29.862)	[22.47, 31.77]	35	0.00 (0.0, 66.7)	16.19 (21.950)	[8.65, 23.73]
WEEK30	140	33.33 (0.0, 100.0)	22.86 (27.726)	[18.22, 27.49]	28	0.00 (0.0, 100.0)	18.45 (28.451)	[7.42, 29.48]
WEEK36	139	33.33 (0.0, 100.0)	24.94 (28.684)	[20.13, 29.75]	23	0.00 (0.0, 100.0)	13.04 (26.091)	[1.76, 24.33]
WEEK42	123	33.33 (0.0, 100.0)	24.66 (28.895)	[19.50, 29.82]	20	0.00 (0.0, 100.0)	16.67 (27.572)	[3.76, 29.57]
WEEK48	106	0.00 (0.0, 100.0)	23.58 (30.849)	[17.64, 29.53]	14	0.00 (0.0, 100.0)	19.05 (28.388)	[2.66, 35.44]
WEEK54	93	0.00 (0.0, 100.0)	20.79 (25.497)	[15.54, 26.04]	11	0.00 (0.0, 66.7)	12.12 (22.473)	[-2.98, 27.22]
WEEK60	79	0.00 (0.0, 100.0)	20.25 (25.830)	[14.47, 26.04]	11	0.00 (0.0, 83.3)	16.67 (30.732)	[-3.98, 37.31]
WEEK66	67	0.00 (0.0, 100.0)	19.90 (24.659)	[13.89, 25.92]	8	0.00 (0.0, 66.7)	8.33 (23.570)	[-11.37, 28.04]
WEEK72	59	0.00 (0.0, 100.0)	22.03 (30.077)	[14.20, 29.87]	9	0.00 (0.0, 33.3)	7.41 (14.699)	[-3.89, 18.71]
WEEK78	49	0.00 (0.0, 100.0)	18.37 (25.514)	[11.04, 25.70]	6	0.00 (0.0, 66.7)	11.11 (27.217)	[-17.45, 39.67]
WEEK86	35	33.33 (0.0, 100.0)	25.71 (28.105)	[16.06, 35.37]	6	0.00 (0.0, 33.3)	5.56 (13.608)	[-8.73, 19.84]
WEEK94	33	0.00 (0.0, 100.0)	22.22 (27.217)	[12.57, 31.87]	3	0.00 (0.0, 0.0)	0.00 (0.000)	[NE, NE]
WEEK102	21	33.33 (0.0, 66.7)	22.22 (21.943)	[12.23, 32.21]	0	NE (NE, NE)	NE (NE)	[NE, NE]
WEEK118	12	16.67 (0.0, 66.7)	19.44 (22.285)	[5.29, 33.60]	0	NE (NE, NE)	NE (NE)	[NE, NE]
WEEK126	8	16.67 (0.0, 66.7)	20.83 (24.801)	[0.10, 41.57]	0	NE (NE, NE)	NE (NE)	[NE, NE]
WEEK134	7	0.00 (0.0, 33.3)	14.29 (17.817)	[-2.19, 30.76]	0	NE (NE, NE)	NE (NE)	[NE, NE]
WEEK142	4	33.33 (0.0, 66.7)	33.33 (27.217)	[-9.97, 76.64]	0	NE (NE, NE)	NE (NE)	[NE, NE]
WEEK150	2	33.33 (0.0, 66.7)	33.33 (47.140)	[-390.21, 456.87]	0	NE (NE, NE)	NE (NE)	[NE, NE]
WEEK158	1	33.33 (33.3, 33.3)	33.33 (NE)	[NE, NE]	0	NE (NE, NE)	NE (NE)	[NE, NE]
END OF TRT	77	33.33 (0.0, 100.0)	31.60 (31.014)	[24.56, 38.64]	39	0.00 (0.0, 100.0)	24.79 (33.957)	[13.78, 35.79]
FOLLOW UP	48	33.33 (0.0, 100.0)	35.42 (33.970)	[25.55, 45.28]	22	0.00 (0.0, 100.0)	16.67 (26.726)	[4.82, 28.52]

Baseline is the last non-missing measurement prior to first dose of study intervention.
[1] Confidence interval based on the normal distribution.
For functional scales, higher scores represent a better level of functioning. For symptom-oriented scales, a higher score represents more severe symptoms.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Plot over time - EOR01-Financial Difficulties
Full Analysis Set



Number of subjects:

EC+FOLFOX	201	190	182	179	161	140	139	123	106	93	79	67	59	49	35	33	21	12	8	7	4	2	1	77	48
Control 2	44	56	41	40	35	28	23	20	14	11	11	8	9	6	6	3	0	0	0	0	0	0	0	39	22

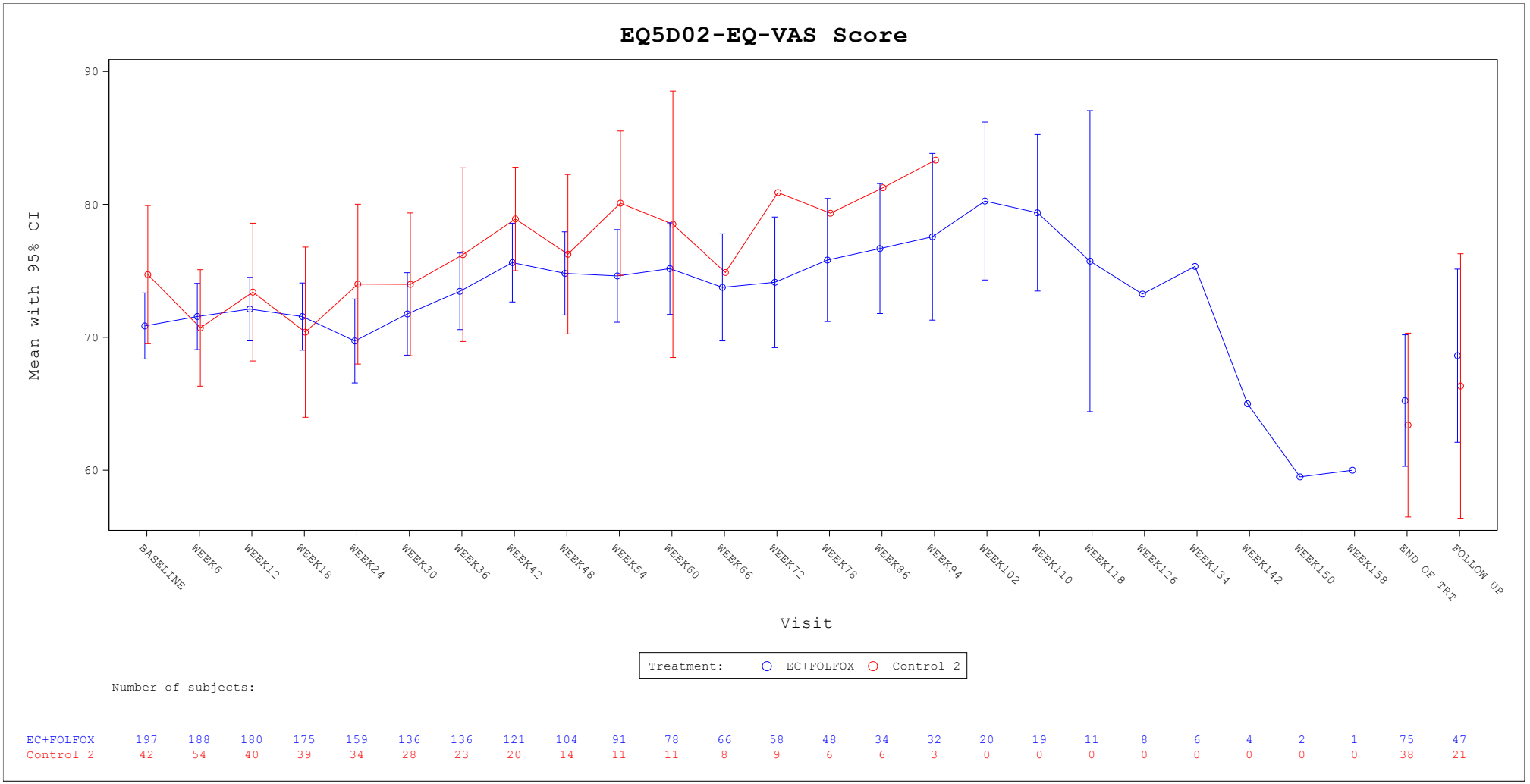
Baseline is the last non-missing measurement prior to first dose of study intervention.
No confidence intervalls are drawn, when there are less than 10 patients in treatment arm.
For functional scales, higher scores represent a better level of functioning. For symptom-oriented scales, a higher score represents more severe symptoms.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Summary over time - EQ5D02-EQ-VAS Score
Full Analysis Set

	EC+FOLFOX (N=236)				Control 2 (N=74)			
Visit	n	Median (Range)	Mean (SD)	95% CI [1]	n	Median (Range)	Mean (SD)	95% CI [1]
BASELINE	197	70.00 (16.0, 100.0)	70.85 (17.672)	[68.37, 73.34]	42	79.00 (10.0, 100.0)	74.71 (16.683)	[69.52, 79.91]
WEEK6	188	75.00 (15.0, 100.0)	71.56 (17.330)	[69.07, 74.06]	54	73.00 (20.0, 93.0)	70.70 (16.051)	[66.32, 75.08]
WEEK12	180	75.00 (20.0, 100.0)	72.12 (16.233)	[69.73, 74.51]	40	77.50 (30.0, 100.0)	73.40 (16.202)	[68.22, 78.58]
WEEK18	175	71.00 (20.0, 99.0)	71.56 (16.937)	[69.03, 74.09]	39	75.00 (17.0, 99.0)	70.38 (19.747)	[63.98, 76.79]
WEEK24	159	72.00 (0.0, 99.0)	69.72 (20.162)	[66.57, 72.88]	34	76.50 (5.0, 100.0)	74.00 (17.231)	[67.99, 80.01]
WEEK30	136	79.00 (25.0, 100.0)	71.76 (18.290)	[68.66, 74.86]	28	79.50 (47.0, 94.0)	73.98 (13.853)	[68.61, 79.35]
WEEK36	136	79.00 (14.0, 99.0)	73.46 (16.987)	[70.58, 76.34]	23	80.00 (30.0, 98.0)	76.22 (15.109)	[69.68, 82.75]
WEEK42	121	80.00 (30.0, 100.0)	75.62 (16.465)	[72.66, 78.58]	20	79.00 (61.0, 90.0)	78.90 (8.322)	[75.01, 82.79]
WEEK48	104	80.00 (30.0, 100.0)	74.81 (16.079)	[71.68, 77.93]	14	76.75 (50.0, 89.0)	76.25 (10.383)	[70.26, 82.24]
WEEK54	91	80.00 (20.0, 100.0)	74.62 (16.736)	[71.13, 78.10]	11	79.00 (64.0, 92.0)	80.09 (8.080)	[74.66, 85.52]
WEEK60	78	78.00 (40.0, 98.0)	75.17 (15.273)	[71.72, 78.61]	11	85.00 (49.5, 94.0)	78.50 (14.918)	[68.48, 88.52]
WEEK66	66	79.00 (9.0, 98.0)	73.76 (16.378)	[69.73, 77.78]	8	81.50 (10.0, 95.0)	74.88 (26.707)	[52.55, 97.20]
WEEK72	58	80.00 (20.0, 100.0)	74.14 (18.670)	[69.23, 79.05]	9	82.00 (65.0, 92.0)	80.89 (9.320)	[73.72, 88.05]
WEEK78	48	80.00 (36.0, 100.0)	75.81 (15.952)	[71.18, 80.44]	6	85.00 (64.0, 89.0)	79.33 (12.028)	[66.71, 91.96]
WEEK86	34	80.00 (39.0, 99.0)	76.68 (14.006)	[71.79, 81.56]	6	85.75 (69.0, 89.0)	81.25 (9.196)	[71.60, 90.90]
WEEK94	32	83.00 (30.0, 99.0)	77.56 (17.391)	[71.29, 83.83]	3	89.00 (70.0, 91.0)	83.33 (11.590)	[54.54, 112.13]
WEEK102	20	80.00 (55.0, 98.0)	80.25 (12.690)	[74.31, 86.19]	0	NE (NE, NE)	NE (NE)	[NE, NE]
WEEK110	19	80.00 (51.0, 97.0)	79.37 (12.217)	[73.48, 85.26]	0	NE (NE, NE)	NE (NE)	[NE, NE]
WEEK118	11	80.00 (45.0, 94.0)	75.73 (16.853)	[64.41, 87.05]	0	NE (NE, NE)	NE (NE)	[NE, NE]
WEEK126	8	77.50 (51.0, 90.0)	73.25 (16.799)	[59.21, 87.29]	0	NE (NE, NE)	NE (NE)	[NE, NE]
WEEK134	6	77.50 (50.0, 93.0)	75.33 (14.692)	[59.91, 90.75]	0	NE (NE, NE)	NE (NE)	[NE, NE]
WEEK142	4	60.50 (50.0, 89.0)	65.00 (18.129)	[36.15, 93.85]	0	NE (NE, NE)	NE (NE)	[NE, NE]
WEEK150	2	59.50 (50.0, 69.0)	59.50 (13.435)	[-61.21, 180.21]	0	NE (NE, NE)	NE (NE)	[NE, NE]
WEEK158	1	60.00 (60.0, 60.0)	60.00 (NE)	[NE, NE]	0	NE (NE, NE)	NE (NE)	[NE, NE]
END OF TRT	75	70.00 (19.0, 100.0)	65.24 (21.498)	[60.29, 70.19]	38	70.00 (19.0, 95.0)	63.39 (21.041)	[56.48, 70.31]
FOLLOW UP	47	73.00 (1.0, 100.0)	68.62 (22.183)	[62.10, 75.13]	21	70.00 (0.0, 100.0)	66.33 (21.859)	[56.38, 76.28]

Baseline is the last non-missing measurement prior to first dose of study intervention.
[1] Confidence interval based on the normal distribution.
Higher score means better health state.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Plot over time - EQ5D02-EQ-VAS Score
Full Analysis Set



Number of subjects:

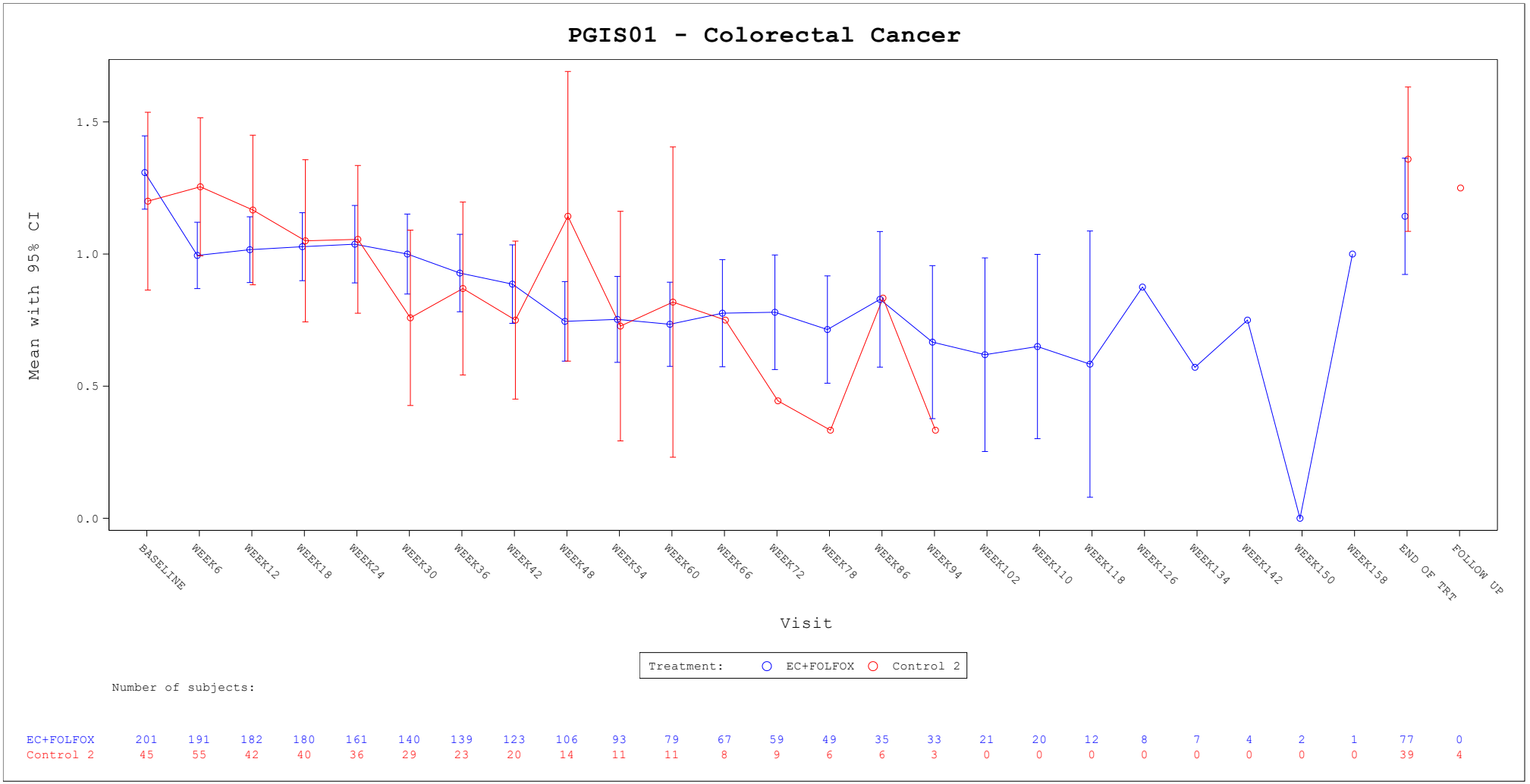
EC+FOLFOX	197	188	180	175	159	136	136	121	104	91	78	66	58	48	34	32	20	19	11	8	6	4	2	1	75	47
Control 2	42	54	40	39	34	28	23	20	14	11	11	8	9	6	6	3	0	0	0	0	0	0	0	0	38	21

Baseline is the last non-missing measurement prior to first dose of study intervention.
No confidence intervalls are drawn, when there are less than 10 patients in treatment arm.
Higher score means better health state.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Summary over time - PGIS01 - Colorectal Cancer
Full Analysis Set

	EC+FOLFOX (N=236)				Control 2 (N=74)			
Visit	n	Median (Range)	Mean (SD)	95% CI [1]	n	Median (Range)	Mean (SD)	95% CI [1]
BASELINE	201	1.00 (0.0, 3.0)	1.31 (0.997)	[1.17, 1.45]	45	1.00 (0.0, 3.0)	1.20 (1.120)	[0.86, 1.54]
WEEK6	191	1.00 (0.0, 3.0)	0.99 (0.880)	[0.87, 1.12]	55	1.00 (0.0, 3.0)	1.25 (0.966)	[0.99, 1.52]
WEEK12	182	1.00 (0.0, 3.0)	1.02 (0.851)	[0.89, 1.14]	42	1.00 (0.0, 3.0)	1.17 (0.908)	[0.88, 1.45]
WEEK18	180	1.00 (0.0, 3.0)	1.03 (0.874)	[0.90, 1.16]	40	1.00 (0.0, 3.0)	1.05 (0.959)	[0.74, 1.36]
WEEK24	161	1.00 (0.0, 3.0)	1.04 (0.941)	[0.89, 1.18]	36	1.00 (0.0, 3.0)	1.06 (0.826)	[0.78, 1.34]
WEEK30	140	1.00 (0.0, 3.0)	1.00 (0.906)	[0.85, 1.15]	29	1.00 (0.0, 3.0)	0.76 (0.872)	[0.43, 1.09]
WEEK36	139	1.00 (0.0, 3.0)	0.93 (0.873)	[0.78, 1.07]	23	1.00 (0.0, 3.0)	0.87 (0.757)	[0.54, 1.20]
WEEK42	123	1.00 (0.0, 3.0)	0.89 (0.832)	[0.74, 1.03]	20	1.00 (0.0, 2.0)	0.75 (0.639)	[0.45, 1.05]
WEEK48	106	1.00 (0.0, 3.0)	0.75 (0.781)	[0.59, 0.90]	14	1.00 (0.0, 3.0)	1.14 (0.949)	[0.59, 1.69]
WEEK54	93	1.00 (0.0, 3.0)	0.75 (0.789)	[0.59, 0.92]	11	1.00 (0.0, 2.0)	0.73 (0.647)	[0.29, 1.16]
WEEK60	79	1.00 (0.0, 3.0)	0.73 (0.711)	[0.57, 0.89]	11	1.00 (0.0, 3.0)	0.82 (0.874)	[0.23, 1.41]
WEEK66	67	1.00 (0.0, 3.0)	0.78 (0.832)	[0.57, 0.98]	8	0.50 (0.0, 3.0)	0.75 (1.035)	[-0.12, 1.62]
WEEK72	59	1.00 (0.0, 3.0)	0.78 (0.832)	[0.56, 1.00]	9	0.00 (0.0, 1.0)	0.44 (0.527)	[0.04, 0.85]
WEEK78	49	1.00 (0.0, 2.0)	0.71 (0.707)	[0.51, 0.92]	6	0.00 (0.0, 1.0)	0.33 (0.516)	[-0.21, 0.88]
WEEK86	35	1.00 (0.0, 3.0)	0.83 (0.747)	[0.57, 1.09]	6	1.00 (0.0, 2.0)	0.83 (0.753)	[0.04, 1.62]
WEEK94	33	0.00 (0.0, 3.0)	0.67 (0.816)	[0.38, 0.96]	3	0.00 (0.0, 1.0)	0.33 (0.577)	[-1.10, 1.77]
WEEK102	21	0.00 (0.0, 3.0)	0.62 (0.805)	[0.25, 0.99]	0	NE (NE, NE)	NE (NE)	[NE, NE]
WEEK110	20	0.50 (0.0, 2.0)	0.65 (0.745)	[0.30, 1.00]	0	NE (NE, NE)	NE (NE)	[NE, NE]
WEEK118	12	0.00 (0.0, 2.0)	0.58 (0.793)	[0.08, 1.09]	0	NE (NE, NE)	NE (NE)	[NE, NE]
WEEK126	8	0.00 (0.0, 3.0)	0.88 (1.246)	[-0.17, 1.92]	0	NE (NE, NE)	NE (NE)	[NE, NE]
WEEK134	7	0.00 (0.0, 2.0)	0.57 (0.787)	[-0.16, 1.30]	0	NE (NE, NE)	NE (NE)	[NE, NE]
WEEK142	4	0.00 (0.0, 3.0)	0.75 (1.500)	[-1.64, 3.14]	0	NE (NE, NE)	NE (NE)	[NE, NE]
WEEK150	2	0.00 (0.0, 0.0)	0.00 (0.000)	[NE, NE]	0	NE (NE, NE)	NE (NE)	[NE, NE]
WEEK158	1	1.00 (1.0, 1.0)	1.00 (NE)	[NE, NE]	0	NE (NE, NE)	NE (NE)	[NE, NE]
END OF TRT	77	1.00 (0.0, 3.0)	1.14 (0.969)	[0.92, 1.36]	39	1.00 (0.0, 3.0)	1.36 (0.843)	[1.09, 1.63]
FOLLOW UP	0	NE (NE, NE)	NE (NE)	[NE, NE]	4	1.50 (0.0, 2.0)	1.25 (0.957)	[-0.27, 2.77]

Baseline is the last non-missing measurement prior to first dose of study intervention.
[1] Confidence interval based on the normal distribution.
Higher score means worse impression of severity.



Number of subjects:

EC+FOLFOX	201	191	182	180	161	140	139	123	106	93	79	67	59	49	35	33	21	20	12	8	7	4	2	1	77	0
Control 2	45	55	42	40	36	29	23	20	14	11	11	8	9	6	6	3	0	0	0	0	0	0	0	0	39	4

Baseline is the last non-missing measurement prior to first dose of study intervention.
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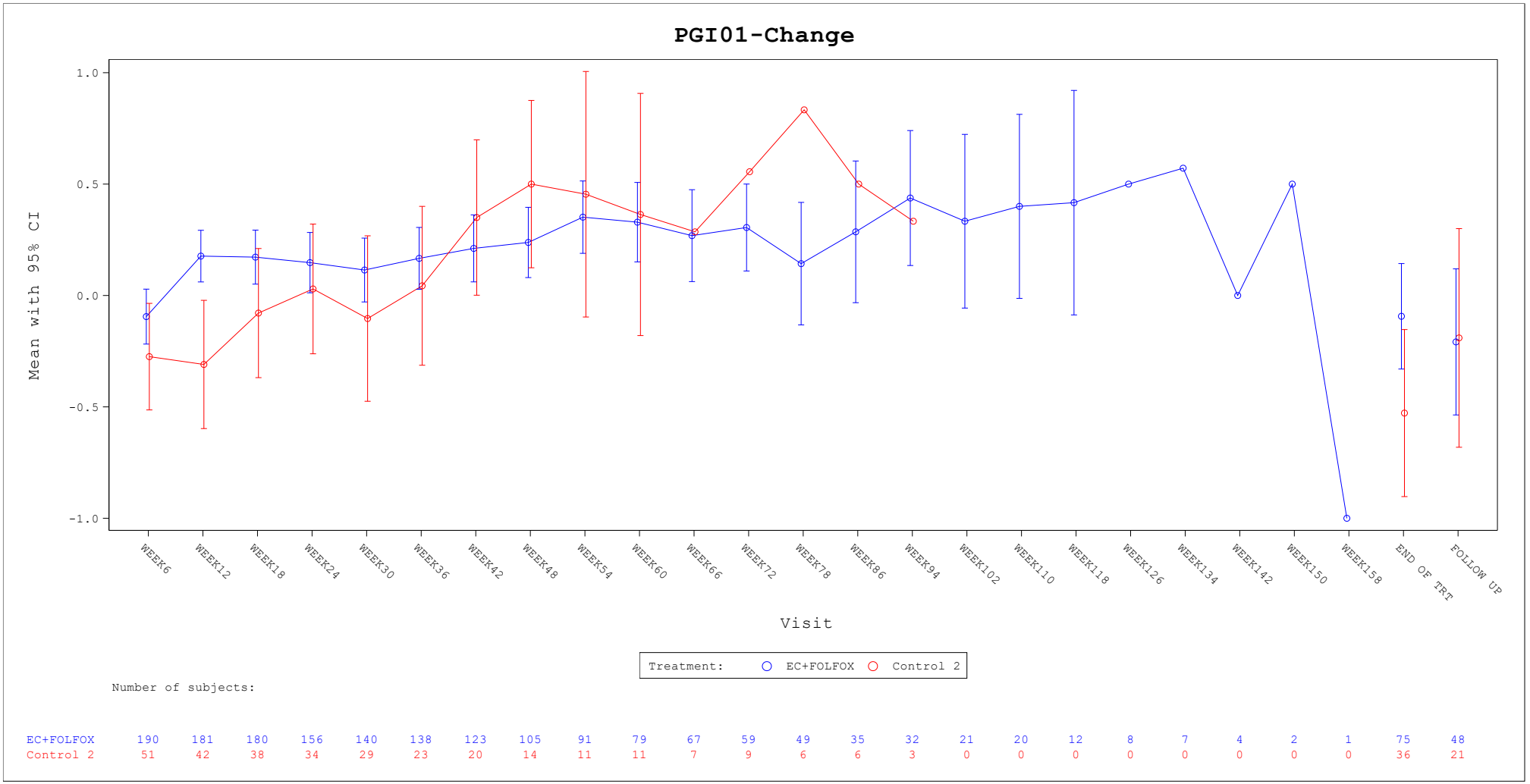
Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Summary over time - PGI01-Change
Full Analysis Set

	EC+FOLFOX (N=236)				Control 2 (N=74)			
Visit	n	Median (Range)	Mean (SD)	95% CI [1]	n	Median (Range)	Mean (SD)	95% CI [1]
WEEK6	190	0.00 (-2.0, 1.0)	-0.09 (0.862)	[-0.22, 0.03]	51	0.00 (-2.0, 1.0)	-0.27 (0.850)	[-0.51, -0.04]
WEEK12	181	0.00 (-2.0, 1.0)	0.18 (0.790)	[0.06, 0.29]	42	0.00 (-2.0, 1.0)	-0.31 (0.924)	[-0.60, -0.02]
WEEK18	180	0.00 (-2.0, 1.0)	0.17 (0.824)	[0.05, 0.29]	38	0.00 (-2.0, 1.0)	-0.08 (0.882)	[-0.37, 0.21]
WEEK24	156	0.00 (-2.0, 1.0)	0.15 (0.856)	[0.01, 0.28]	34	0.00 (-2.0, 1.0)	0.03 (0.834)	[-0.26, 0.32]
WEEK30	140	0.00 (-2.0, 1.0)	0.11 (0.857)	[-0.03, 0.26]	29	0.00 (-2.0, 1.0)	-0.10 (0.976)	[-0.47, 0.27]
WEEK36	138	0.00 (-2.0, 1.0)	0.17 (0.825)	[0.03, 0.31]	23	0.00 (-2.0, 1.0)	0.04 (0.825)	[-0.31, 0.40]
WEEK42	123	0.00 (-2.0, 1.0)	0.21 (0.842)	[0.06, 0.36]	20	0.50 (-1.0, 1.0)	0.35 (0.745)	[0.00, 0.70]
WEEK48	105	0.00 (-2.0, 1.0)	0.24 (0.815)	[0.08, 0.40]	14	1.00 (-1.0, 1.0)	0.50 (0.650)	[0.12, 0.88]
WEEK54	91	1.00 (-2.0, 1.0)	0.35 (0.780)	[0.19, 0.51]	11	1.00 (-1.0, 1.0)	0.45 (0.820)	[-0.10, 1.01]
WEEK60	79	1.00 (-2.0, 1.0)	0.33 (0.796)	[0.15, 0.51]	11	1.00 (-1.0, 1.0)	0.36 (0.809)	[-0.18, 0.91]
WEEK66	67	0.00 (-2.0, 1.0)	0.27 (0.845)	[0.06, 0.47]	7	1.00 (-1.0, 1.0)	0.29 (0.951)	[-0.59, 1.17]
WEEK72	59	0.00 (-1.0, 1.0)	0.31 (0.749)	[0.11, 0.50]	9	1.00 (0.0, 1.0)	0.56 (0.527)	[0.15, 0.96]
WEEK78	49	0.00 (-2.0, 1.0)	0.14 (0.957)	[-0.13, 0.42]	6	1.00 (0.0, 1.0)	0.83 (0.408)	[0.40, 1.26]
WEEK86	35	1.00 (-2.0, 1.0)	0.29 (0.926)	[-0.03, 0.60]	6	1.00 (-1.0, 1.0)	0.50 (0.837)	[-0.38, 1.38]
WEEK94	32	1.00 (-2.0, 1.0)	0.44 (0.840)	[0.13, 0.74]	3	1.00 (-1.0, 1.0)	0.33 (1.155)	[-2.54, 3.20]
WEEK102	21	1.00 (-2.0, 1.0)	0.33 (0.856)	[-0.06, 0.72]	0	NE (NE, NE)	NE (NE)	[NE, NE]
WEEK110	20	1.00 (-2.0, 1.0)	0.40 (0.883)	[-0.01, 0.81]	0	NE (NE, NE)	NE (NE)	[NE, NE]
WEEK118	12	1.00 (-1.0, 1.0)	0.42 (0.793)	[-0.09, 0.92]	0	NE (NE, NE)	NE (NE)	[NE, NE]
WEEK126	8	1.00 (-1.0, 1.0)	0.50 (0.926)	[-0.27, 1.27]	0	NE (NE, NE)	NE (NE)	[NE, NE]
WEEK134	7	1.00 (-1.0, 1.0)	0.57 (0.787)	[-0.16, 1.30]	0	NE (NE, NE)	NE (NE)	[NE, NE]
WEEK142	4	0.50 (-2.0, 1.0)	0.00 (1.414)	[-2.25, 2.25]	0	NE (NE, NE)	NE (NE)	[NE, NE]
WEEK150	2	0.50 (0.0, 1.0)	0.50 (0.707)	[-5.85, 6.85]	0	NE (NE, NE)	NE (NE)	[NE, NE]
WEEK158	1	-1.00 (-1.0, -1.0)	-1.00 (NE)	[NE, NE]	0	NE (NE, NE)	NE (NE)	[NE, NE]
END OF TRT	75	0.00 (-2.0, 1.0)	-0.09 (1.029)	[-0.33, 0.14]	36	-1.00 (-2.0, 1.0)	-0.53 (1.108)	[-0.90, -0.15]
FOLLOW UP	48	0.00 (-2.0, 1.0)	-0.21 (1.129)	[-0.54, 0.12]	21	0.00 (-2.0, 1.0)	-0.19 (1.078)	[-0.68, 0.30]

Baseline is the last non-missing measurement prior to first dose of study intervention.
[1] Confidence interval based on the normal distribution.
Categories were transformed to ordinal scale: 2=MUCH BETTER, 1=A LITTLE BETTER, 0=NO CHANGE, -1=A LITTLE WORSE, -2=MUCH WORSE.
Higher score means better impression of change.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Plot over time - PGI01-Change
Full Analysis Set



Number of subjects:

EC+FOLFOX	190	181	180	156	140	138	123	105	91	79	67	59	49	35	32	21	20	12	8	7	4	2	1	75	48
Control 2	51	42	38	34	29	23	20	14	11	11	7	9	6	6	3	0	0	0	0	0	0	0	0	36	21

Baseline is the last non-missing measurement prior to first dose of study intervention.
No confidence intervalls are drawn, when there are less than 10 patients in treatment arm.
Categories were transformed to ordinal scale: 2=MUCH BETTER, 1=A LITTLE BETTER, 0=NO CHANGE, -1=A LITTLE WORSE, -2=MUCH WORSE.
Higher score means better impression of change.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Any AE
Safety Analysis Set

	EC+FOLFOX (N=232)	Control 2 (N=68)
Number of subjects with events, n (%)	232 (100.0)	67 (98.5)
Number of censored subjects, n (%)	0 (0.0)	1 (1.5)
Kaplan-Meier estimates of Time to Event (months) [1]		
25%-ile (95% CI)	0.0 (NE, NE)	0.0 (0.0, 0.1)
Median (95% CI)	0.1 (0.1, 0.1)	0.1 (0.1, 0.1)
75%-ile (95% CI)	0.3 (0.2, 0.5)	0.3 (0.1, 0.5)
Unstratified analysis		
Hazard Ratio (95% CI) [2]	1.20 (0.91, 1.59)	
p-value [3]	0.1599	

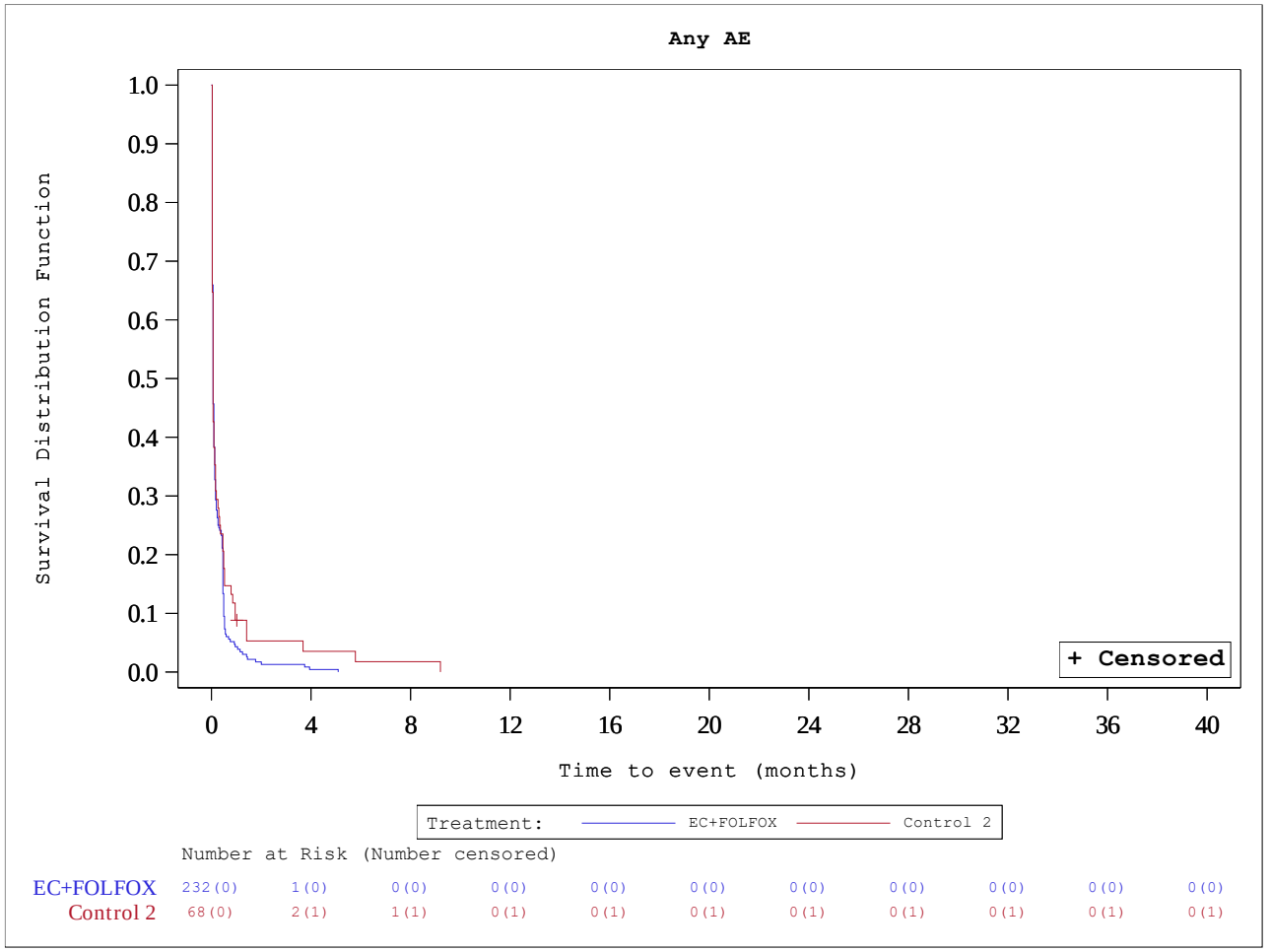
Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Any AE - Subgroup analysis
Safety Analysis Set

Subgroup Level	EC+FOLFOX (N=232) n/ N (%)	EC+FOLFOX (N=232) Median (95% CI)[1]	Control 2 (N=68) n/ N (%)	Control 2 (N=68) Median (95% CI)[1]	Unstratified analysis Hazard Ratio (95% CI)[2]	Unstratified analysis p-Value[3]	Interaction p-Value[4]
Age (Years)							0.7504
< 65	148/ 148 (100.0)	0.1 (0.1, 0.1)	41/ 42 (97.6)	0.1 (0.0, 0.1)	1.15 (0.80, 1.64)	0.3842	
>= 65	84/ 84 (100.0)	0.1 (0.1, 0.1)	26/ 26 (100.0)	0.1 (0.1, 0.3)	1.23 (0.79, 1.93)	0.3559	
Sex							0.5535
Male	121/ 121 (100.0)	0.1 (0.1, 0.1)	32/ 32 (100.0)	0.1 (0.1, 0.3)	1.30 (0.87, 1.94)	0.1883	
Female	111/ 111 (100.0)	0.1 (0.1, 0.1)	35/ 36 (97.2)	0.1 (0.0, 0.1)	1.09 (0.73, 1.60)	0.5750	
Region							0.7079
Europe	108/ 108 (100.0)	0.1 (0.1, 0.1)	37/ 38 (97.4)	0.1 (0.1, 0.4)	1.29 (0.88, 1.88)	0.1888	
USA/Canada	15/ 15 (100.0)	0.1 (0.0, 0.2)	7/ 7 (100.0)	0.1 (0.0, 0.1)	0.68 (0.26, 1.78)	0.3617	
Rest of World	109/ 109 (100.0)	0.1 (0.1, 0.1)	23/ 23 (100.0)	0.1 (0.0, 0.1)	1.04 (0.65, 1.66)	0.7694	
ECOG-PS at Randomization							0.2641
0	130/ 130 (100.0)	0.1 (0.1, 0.1)	44/ 44 (100.0)	0.1 (0.0, 0.2)	1.30 (0.91, 1.85)	0.1206	
1	102/ 102 (100.0)	0.1 (0.1, 0.1)	23/ 24 (95.8)	0.1 (0.1, 0.1)	0.95 (0.60, 1.51)	0.8263	
Number of Organs Involved							0.4307
<= 2	116/ 116 (100.0)	0.1 (0.1, 0.1)	32/ 33 (97.0)	0.1 (0.0, 0.1)	1.30 (0.86, 1.96)	0.1657	
>= 3	116/ 116 (100.0)	0.1 (0.1, 0.1)	35/ 35 (100.0)	0.1 (0.1, 0.3)	1.07 (0.73, 1.57)	0.7534	
Presence of Liver Metastases							0.3540
Yes	146/ 146 (100.0)	0.1 (0.1, 0.1)	42/ 42 (100.0)	0.1 (0.1, 0.2)	1.09 (0.77, 1.55)	0.6104	
No	86/ 86 (100.0)	0.1 (0.1, 0.1)	25/ 26 (96.2)	0.1 (0.0, 0.2)	1.34 (0.84, 2.14)	0.1763	
Side of Tumor							0.2344
Left	88/ 88 (100.0)	0.1 (0.1, 0.1)	33/ 33 (100.0)	0.1 (0.0, 0.1)	1.03 (0.68, 1.56)	0.8409	
Right	144/ 144 (100.0)	0.1 (0.1, 0.1)	34/ 35 (97.1)	0.1 (0.1, 0.2)	1.38 (0.94, 2.03)	0.0927	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.
[4] P-Value for interaction from Cox proportional hazards model using ties=exact option with treatment, subgroup and treatment*subgroup interaction as covariates.
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Kaplan Meier Plot of Any AE
Safety Analysis Set



Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
Kaplan-Meier Plots for subgroups only created if p-value for interaction < 0.05.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Any AE excluding events related to underlying disease progression
Safety Analysis Set

	EC+FOLFOX (N=232)	Control 2 (N=68)
Number of subjects with events, n (%)	231 (99.6)	64 (94.1)
Number of censored subjects, n (%)	1 (0.4)	4 (5.9)
Kaplan-Meier estimates of Time to Event (months) [1]		
25%-ile (95% CI)	0.0 (0.0, 0.1)	0.1 (0.0, 0.1)
Median (95% CI)	0.1 (0.1, 0.2)	0.3 (0.1, 0.5)
75%-ile (95% CI)	0.5 (0.5, 0.6)	1.5 (0.6, 2.1)
Unstratified analysis		
Hazard Ratio (95% CI) [2]	1.57 (1.19, 2.08)	
p-value [3]	0.0015	

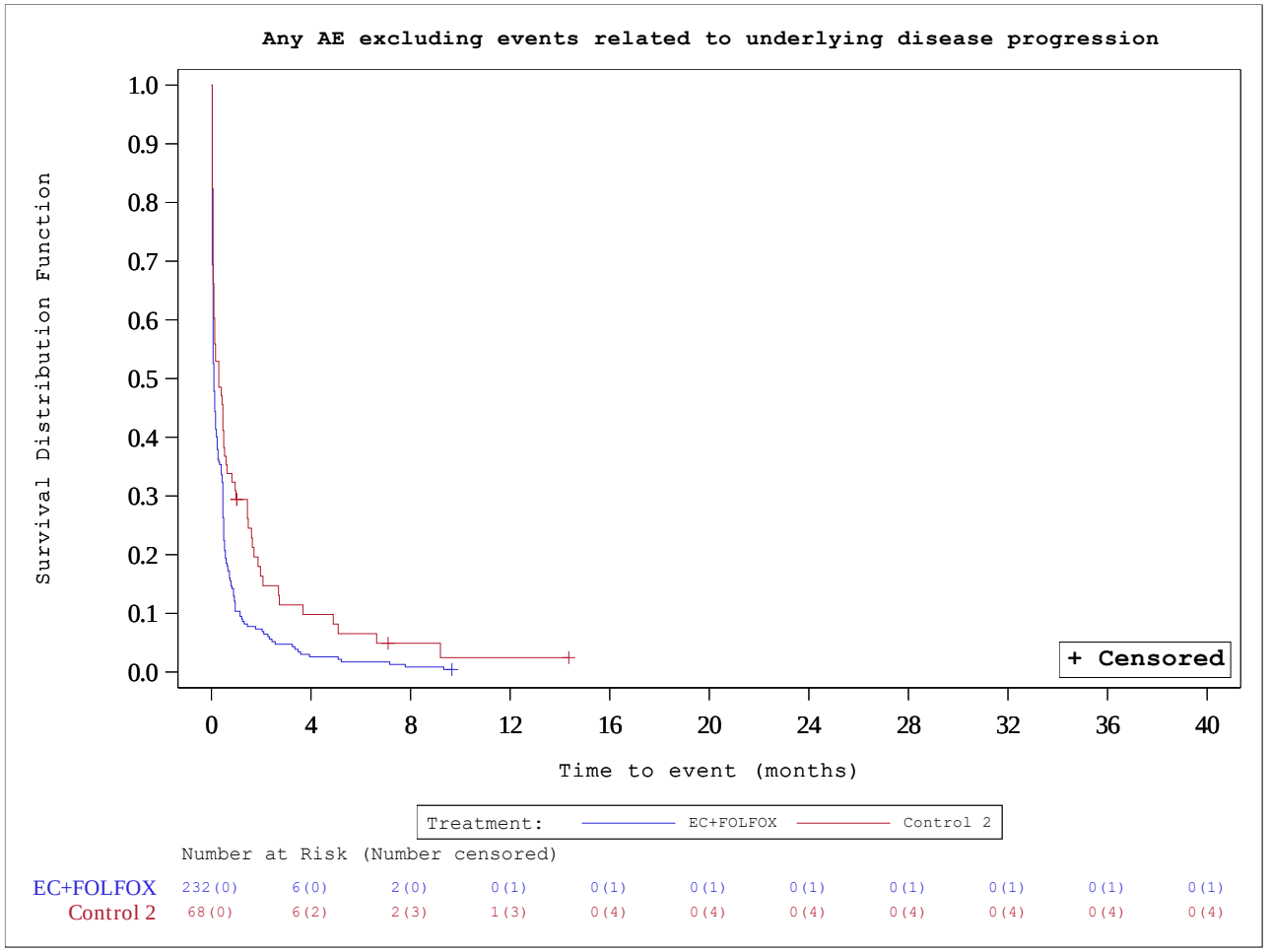
Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Any AE excluding events related to underlying disease progression - Subgroup analysis
Safety Analysis Set

Subgroup Level	EC+FOLFOX (N=232) n/ N (%)	EC+FOLFOX (N=232) Median (95% CI)[1]	Control 2 (N=68) n/ N (%)	Control 2 (N=68) Median (95% CI)[1]	Unstratified analysis Hazard Ratio (95% CI)[2]	Unstratified analysis p-Value[3]	Interaction p-Value[4]
Age (Years)							0.4222
< 65	147/ 148 (99.3)	0.1 (0.1, 0.1)	39/ 42 (92.9)	0.1 (0.1, 0.5)	1.36 (0.95, 1.94)	0.0803	
>= 65	84/ 84 (100.0)	0.1 (0.1, 0.4)	25/ 26 (96.2)	0.5 (0.2, 1.4)	1.97 (1.24, 3.13)	0.0039	
Sex							0.3257
Male	120/ 121 (99.2)	0.1 (0.1, 0.2)	30/ 32 (93.8)	0.5 (0.2, 1.7)	1.85 (1.23, 2.78)	0.0027	
Female	111/ 111 (100.0)	0.1 (0.1, 0.2)	34/ 36 (94.4)	0.1 (0.1, 0.5)	1.36 (0.92, 2.00)	0.1123	
Region							0.9178
Europe	107/ 108 (99.1)	0.2 (0.1, 0.5)	36/ 38 (94.7)	0.5 (0.2, 1.4)	1.66 (1.13, 2.43)	0.0112	
USA/Canada	15/ 15 (100.0)	0.1 (0.1, 0.2)	6/ 7 (85.7)	0.1 (0.0, 0.8)	1.62 (0.58, 4.56)	0.3314	
Rest of World	109/ 109 (100.0)	0.1 (0.1, 0.1)	22/ 23 (95.7)	0.1 (0.1, 0.5)	1.43 (0.89, 2.30)	0.1152	
ECOG-PS at Randomization							0.2525
0	130/ 130 (100.0)	0.1 (0.1, 0.2)	41/ 44 (93.2)	0.2 (0.1, 0.6)	1.77 (1.23, 2.54)	0.0015	
1	101/ 102 (99.0)	0.1 (0.1, 0.4)	23/ 24 (95.8)	0.4 (0.1, 0.8)	1.29 (0.82, 2.03)	0.3126	
Number of Organs Involved							0.8232
<= 2	116/ 116 (100.0)	0.1 (0.1, 0.2)	31/ 33 (93.9)	0.2 (0.1, 0.6)	1.60 (1.07, 2.39)	0.0210	
>= 3	115/ 116 (99.1)	0.1 (0.1, 0.2)	33/ 35 (94.3)	0.4 (0.1, 1.0)	1.51 (1.02, 2.23)	0.0381	
Presence of Liver Metastases							0.5442
Yes	145/ 146 (99.3)	0.1 (0.1, 0.2)	40/ 42 (95.2)	0.3 (0.1, 1.0)	1.46 (1.02, 2.08)	0.0372	
No	86/ 86 (100.0)	0.1 (0.1, 0.2)	24/ 26 (92.3)	0.3 (0.1, 0.6)	1.73 (1.08, 2.76)	0.0194	
Side of Tumor							0.2053
Left	88/ 88 (100.0)	0.1 (0.1, 0.2)	32/ 33 (97.0)	0.1 (0.1, 0.5)	1.26 (0.84, 1.91)	0.2317	
Right	143/ 144 (99.3)	0.1 (0.1, 0.2)	32/ 35 (91.4)	0.5 (0.1, 1.5)	1.84 (1.25, 2.72)	0.0019	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.
[4] P-Value for interaction from Cox proportional hazards model using ties=exact option with treatment, subgroup and treatment*subgroup interaction as covariates.
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Kaplan Meier Plot of Any AE excluding events related to underlying disease progression
Safety Analysis Set



Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
Kaplan-Meier Plots for subgroups only created if p-value for interaction < 0.05.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Serious AE
Safety Analysis Set

	EC+FOLFOX (N=232)	Control 2 (N=68)
Number of subjects with events, n (%)	107 (46.1)	30 (44.1)
Number of censored subjects, n (%)	125 (53.9)	38 (55.9)
Kaplan-Meier estimates of Time to Event (months) [1]		
25%-ile (95% CI)	3.1 (1.5, 5.0)	2.7 (1.6, 5.6)
Median (95% CI)	15.4 (10.7, NE)	11.9 (7.5, NE)
75%-ile (95% CI)	NE (NE, NE)	NE (14.5, NE)
Unstratified analysis		
Hazard Ratio (95% CI) [2]	0.92 (0.61, 1.37)	
p-value [3]	0.6692	

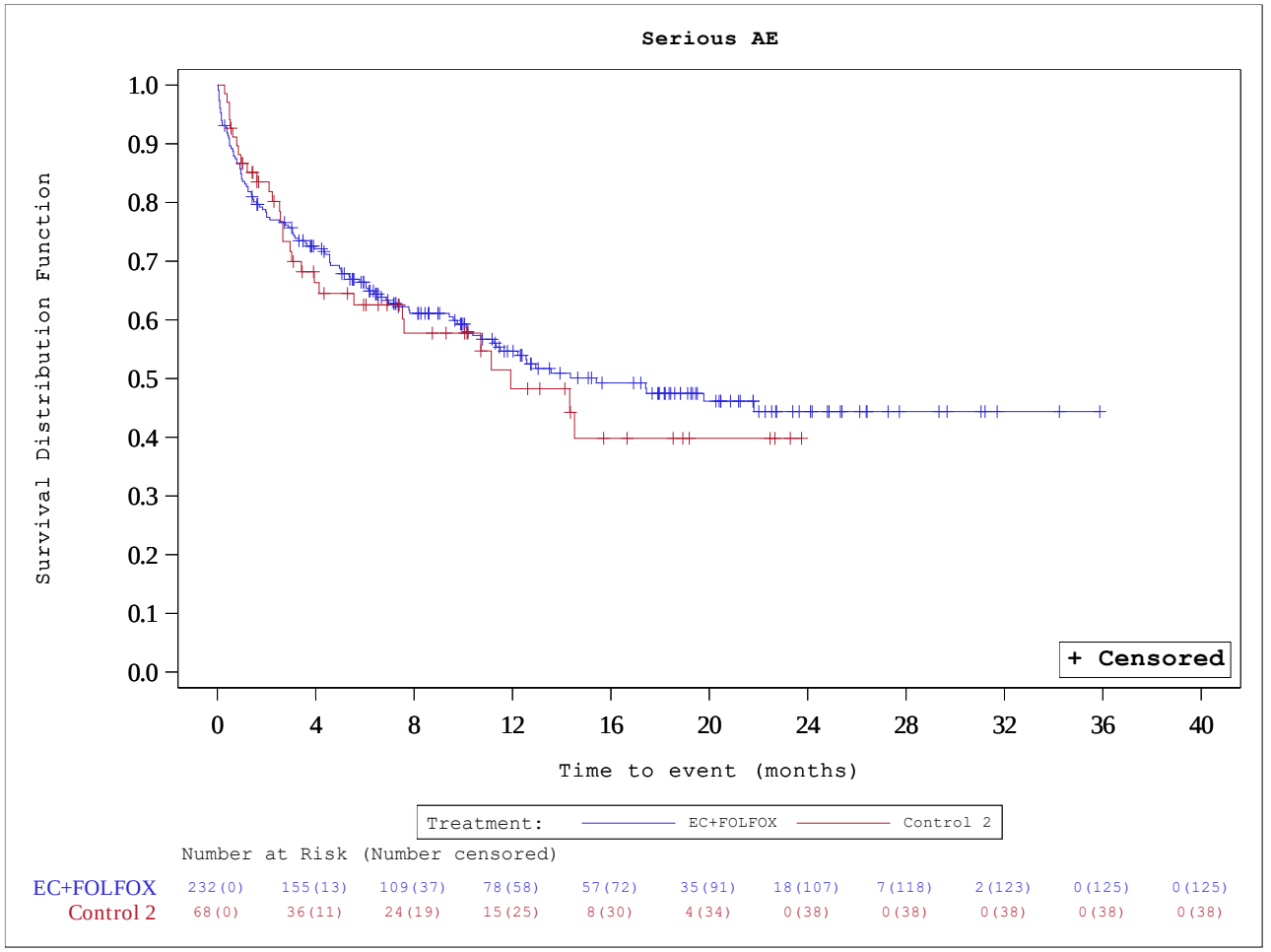
Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Serious AE - Subgroup analysis
Safety Analysis Set

Subgroup Level	EC+FOLFOX (N=232) n/ N (%)	EC+FOLFOX (N=232) Median (95% CI)[1]	Control 2 (N=68) n/ N (%)	Control 2 (N=68) Median (95% CI)[1]	Unstratified analysis Hazard Ratio (95% CI)[2]	Unstratified analysis p-Value[3]	Interaction p-Value[4]
Age (Years)							0.1778
< 65	59/ 148 (39.9)	NE (12.9, NE)	19/ 42 (45.2)	11.1 (4.1, NE)	0.74 (0.44, 1.25)	0.2550	
>= 65	48/ 84 (57.1)	10.1 (4.6, 17.4)	11/ 26 (42.3)	14.3 (3.9, NE)	1.25 (0.65, 2.41)	0.5117	
Sex							0.1104
Male	47/ 121 (38.8)	21.8 (13.6, NE)	15/ 32 (46.9)	11.1 (5.6, 14.5)	0.62 (0.35, 1.12)	0.1093	
Female	60/ 111 (54.1)	10.7 (6.0, 15.4)	15/ 36 (41.7)	11.9 (3.4, NE)	1.28 (0.73, 2.26)	0.3866	
Region							0.6610
Europe	50/ 108 (46.3)	17.4 (10.2, NE)	15/ 38 (39.5)	11.1 (4.1, NE)	0.96 (0.54, 1.72)	0.8943	
USA/Canada	7/ 15 (46.7)	15.4 (1.5, NE)	3/ 7 (42.9)	NE (3.4, NE)	1.32 (0.34, 5.16)	0.6805	
Rest of World	50/ 109 (45.9)	13.6 (7.0, NE)	12/ 23 (52.2)	7.6 (3.0, 14.5)	0.73 (0.39, 1.38)	0.3353	
ECOG-PS at Randomization							0.9395
0	50/ 130 (38.5)	NE (17.4, NE)	18/ 44 (40.9)	14.5 (7.6, NE)	0.84 (0.49, 1.44)	0.5291	
1	57/ 102 (55.9)	10.1 (5.0, 14.4)	12/ 24 (50.0)	5.6 (3.0, NE)	0.85 (0.46, 1.60)	0.6204	
Number of Organs Involved							0.8921
<= 2	44/ 116 (37.9)	NE (17.4, NE)	13/ 33 (39.4)	14.5 (11.1, NE)	0.87 (0.47, 1.61)	0.6534	
>= 3	63/ 116 (54.3)	10.1 (5.4, 13.6)	17/ 35 (48.6)	5.6 (2.6, NE)	0.95 (0.55, 1.63)	0.8447	
Presence of Liver Metastases							0.8653
Yes	71/ 146 (48.6)	12.6 (9.4, NE)	20/ 42 (47.6)	10.7 (3.0, NE)	0.90 (0.54, 1.47)	0.6647	
No	36/ 86 (41.9)	NE (11.2, NE)	10/ 26 (38.5)	14.5 (7.6, NE)	0.95 (0.47, 1.93)	0.8963	
Side of Tumor							0.0967
Left	37/ 88 (42.0)	19.8 (10.1, NE)	17/ 33 (51.5)	10.7 (2.5, NE)	0.62 (0.35, 1.10)	0.0979	
Right	70/ 144 (48.6)	12.9 (9.8, NE)	13/ 35 (37.1)	NE (4.1, NE)	1.28 (0.71, 2.31)	0.4168	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.
[4] P-Value for interaction from Cox proportional hazards model using ties=exact option with treatment, subgroup and treatment*subgroup interaction as covariates.
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Kaplan Meier Plot of Serious AE
Safety Analysis Set



Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
Kaplan-Meier Plots for subgroups only created if p-value for interaction < 0.05.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Serious AE excluding events related to underlying disease progression
Safety Analysis Set

	EC+FOLFOX (N=232)	Control 2 (N=68)
Number of subjects with events, n (%)	72 (31.0)	16 (23.5)
Number of censored subjects, n (%)	160 (69.0)	52 (76.5)
Kaplan-Meier estimates of Time to Event (months) [1]		
25%-ile (95% CI)	7.3 (5.0, 11.5)	10.7 (5.6, NE)
Median (95% CI)	NE (NE, NE)	NE (13.8, NE)
75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
Unstratified analysis		
Hazard Ratio (95% CI) [2]	1.17 (0.68, 2.01)	
p-value [3]	0.5713	

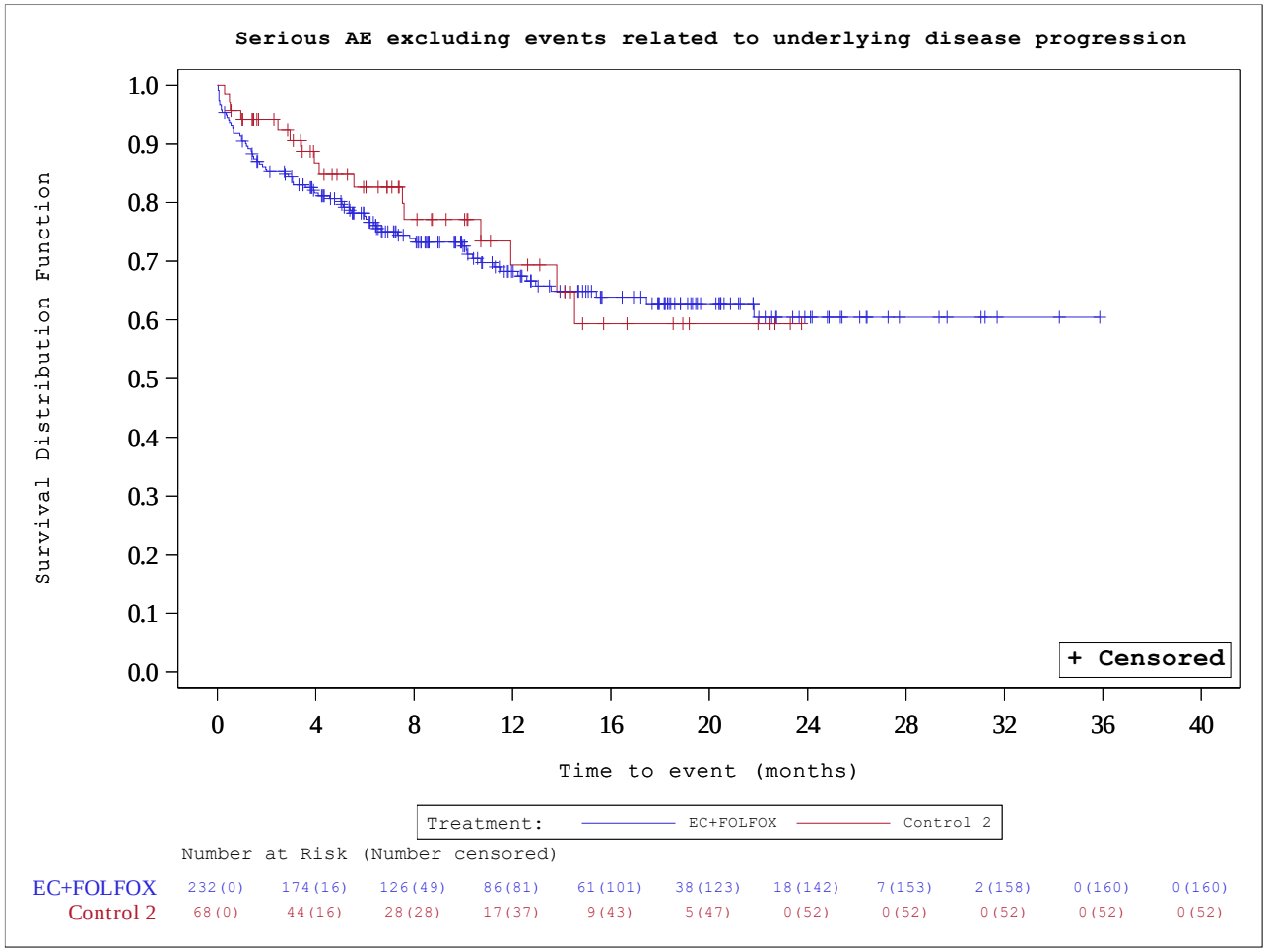
Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Serious AE excluding events related to underlying disease progression - Subgroup analysis
Safety Analysis Set

Subgroup Level	EC+FOLFOX (N=232) n/ N (%)	EC+FOLFOX (N=232) Median (95% CI)[1]	Control 2 (N=68) n/ N (%)	Control 2 (N=68) Median (95% CI)[1]	Unstratified analysis Hazard Ratio (95% CI)[2]	Unstratified analysis p-Value[3]	Interaction p-Value[4]
Age (Years)							0.4695
< 65	40/ 148 (27.0)	NE (NE , NE)	10/ 42 (23.8)	NE (11.9, NE)	0.99 (0.50, 1.99)	0.9826	
>= 65	32/ 84 (38.1)	21.8 (10.7, NE)	6/ 26 (23.1)	NE (14.5, NE)	1.45 (0.60, 3.48)	0.4033	
Sex							0.1203
Male	32/ 121 (26.4)	NE (21.8, NE)	9/ 32 (28.1)	14.5 (7.6, NE)	0.72 (0.34, 1.52)	0.3913	
Female	40/ 111 (36.0)	NE (12.9, NE)	7/ 36 (19.4)	NE (NE , NE)	1.78 (0.80, 3.98)	0.1520	
Region							0.7888
Europe	31/ 108 (28.7)	NE (21.8, NE)	9/ 38 (23.7)	NE (13.8, NE)	1.02 (0.49, 2.16)	0.9488	
USA/Canada	6/ 15 (40.0)	15.4 (5.5, NE)	2/ 7 (28.6)	NE (3.9, NE)	1.58 (0.32, 7.95)	0.5725	
Rest of World	35/ 109 (32.1)	NE (17.4, NE)	5/ 23 (21.7)	14.5 (11.9, NE)	1.32 (0.52, 3.38)	0.5621	
ECOG-PS at Randomization							0.3820
0	34/ 130 (26.2)	NE (NE , NE)	8/ 44 (18.2)	NE (14.5, NE)	1.32 (0.61, 2.86)	0.4747	
1	38/ 102 (37.3)	NE (12.2, NE)	8/ 24 (33.3)	11.9 (5.6, NE)	0.80 (0.37, 1.73)	0.5639	
Number of Organs Involved							0.4445
<= 2	27/ 116 (23.3)	NE (NE , NE)	8/ 33 (24.2)	NE (14.5, NE)	0.90 (0.41, 1.98)	0.7871	
>= 3	45/ 116 (38.8)	NE (11.2, NE)	8/ 35 (22.9)	NE (10.7, NE)	1.40 (0.66, 2.98)	0.3837	
Presence of Liver Metastases							0.3990
Yes	50/ 146 (34.2)	NE (13.6, NE)	9/ 42 (21.4)	NE (NE , NE)	1.41 (0.69, 2.86)	0.3452	
No	22/ 86 (25.6)	NE (NE , NE)	7/ 26 (26.9)	NE (11.9, NE)	0.84 (0.36, 1.98)	0.6912	
Side of Tumor							0.7548
Left	27/ 88 (30.7)	NE (NE , NE)	8/ 33 (24.2)	NE (11.9, NE)	1.05 (0.47, 2.31)	0.9087	
Right	45/ 144 (31.3)	NE (21.8, NE)	8/ 35 (22.9)	NE (14.5, NE)	1.28 (0.60, 2.72)	0.5193	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.
[4] P-Value for interaction from Cox proportional hazards model using ties=exact option with treatment, subgroup and treatment*subgroup interaction as covariates.
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Kaplan Meier Plot of Serious AE excluding events related to underlying disease progression
Safety Analysis Set



Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
Kaplan-Meier Plots for subgroups only created if p-value for interaction < 0.05.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Severe AE
Safety Analysis Set

	EC+FOLFOX (N=232)	Control 2 (N=68)
Number of subjects with events, n (%)	199 (85.8)	56 (82.4)
Number of censored subjects, n (%)	33 (14.2)	12 (17.6)
Kaplan-Meier estimates of Time to Event (months) [1]		
25%-ile (95% CI)	0.5 (0.5, 0.5)	0.6 (0.5, 1.3)
Median (95% CI)	1.5 (1.0, 1.9)	2.5 (1.4, 3.8)
75%-ile (95% CI)	5.1 (3.6, 6.7)	8.0 (3.8, 11.8)
Unstratified analysis		
Hazard Ratio (95% CI) [2]	1.18 (0.88, 1.59)	
p-value [3]	0.2860	

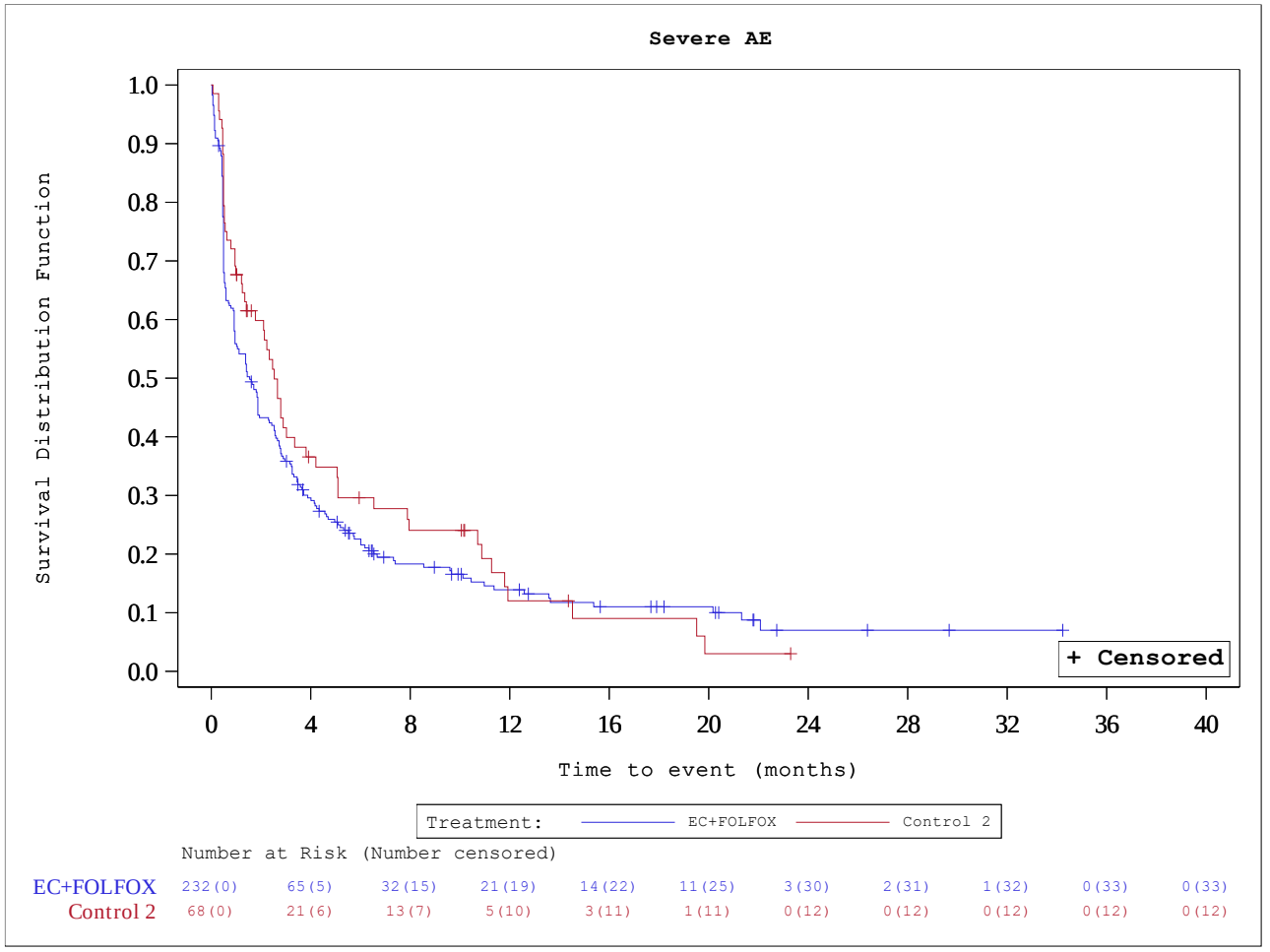
Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Severe AE - Subgroup analysis
Safety Analysis Set

Subgroup Level	EC+FOLFOX (N=232) n/ N (%)	EC+FOLFOX (N=232) Median (95% CI)[1]	Control 2 (N=68) n/ N (%)	Control 2 (N=68) Median (95% CI)[1]	Unstratified analysis Hazard Ratio (95% CI)[2]	Unstratified analysis p-Value[3]	Interaction p-Value[4]
Age (Years)							0.6918
< 65	124/ 148 (83.8)	1.8 (1.4, 2.7)	35/ 42 (83.3)	2.5 (1.2, 3.8)	1.13 (0.78, 1.64)	0.5357	
>= 65	75/ 84 (89.3)	1.0 (0.6, 1.9)	21/ 26 (80.8)	2.7 (0.8, 5.1)	1.28 (0.79, 2.08)	0.3228	
Sex							0.0903
Male	98/ 121 (81.0)	2.3 (1.7, 3.2)	27/ 32 (84.4)	2.5 (1.4, 4.2)	0.91 (0.59, 1.39)	0.6551	
Female	101/ 111 (91.0)	0.6 (0.5, 1.4)	29/ 36 (80.6)	2.7 (1.2, 5.1)	1.56 (1.03, 2.37)	0.0360	
Region							0.2568
Europe	90/ 108 (83.3)	1.9 (1.0, 2.8)	29/ 38 (76.3)	2.7 (2.1, 5.1)	1.28 (0.84, 1.95)	0.2492	
USA/Canada	14/ 15 (93.3)	0.5 (0.3, 0.9)	6/ 7 (85.7)	3.8 (0.3, 6.5)	1.92 (0.72, 5.11)	0.1980	
Rest of World	95/ 109 (87.2)	1.4 (1.0, 2.6)	21/ 23 (91.3)	1.3 (0.8, 5.1)	0.94 (0.58, 1.50)	0.7794	
ECOG-PS at Randomization							0.8477
0	108/ 130 (83.1)	2.6 (1.6, 3.4)	35/ 44 (79.5)	2.8 (2.2, 6.5)	1.15 (0.79, 1.68)	0.4733	
1	91/ 102 (89.2)	0.8 (0.5, 1.4)	21/ 24 (87.5)	1.2 (0.5, 3.0)	1.09 (0.68, 1.76)	0.7405	
Number of Organs Involved							0.2810
<= 2	103/ 116 (88.8)	1.8 (1.0, 2.7)	26/ 33 (78.8)	4.2 (2.5, 8.0)	1.37 (0.89, 2.11)	0.1532	
>= 3	96/ 116 (82.8)	1.4 (0.9, 2.3)	30/ 35 (85.7)	1.8 (1.0, 2.8)	1.00 (0.66, 1.51)	0.9792	
Presence of Liver Metastases							0.4204
Yes	125/ 146 (85.6)	1.4 (0.9, 1.9)	37/ 42 (88.1)	2.1 (1.0, 2.8)	1.07 (0.74, 1.55)	0.7275	
No	74/ 86 (86.0)	2.3 (1.0, 3.6)	19/ 26 (73.1)	6.5 (2.5, 11.3)	1.41 (0.85, 2.35)	0.1866	
Side of Tumor							0.0807
Left	76/ 88 (86.4)	2.6 (1.6, 3.3)	29/ 33 (87.9)	2.1 (1.0, 3.8)	0.87 (0.56, 1.33)	0.5035	
Right	123/ 144 (85.4)	1.0 (0.7, 1.8)	27/ 35 (77.1)	2.8 (2.1, 5.1)	1.48 (0.97, 2.24)	0.0647	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.
[4] P-Value for interaction from Cox proportional hazards model using ties=exact option with treatment, subgroup and treatment*subgroup interaction as covariates.
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Kaplan Meier Plot of Severe AE
Safety Analysis Set



Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
Kaplan-Meier Plots for subgroups only created if p-value for interaction < 0.05.

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Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Severe AE excluding events related to underlying disease progression
Safety Analysis Set

	EC+FOLFOX (N=232)	Control 2 (N=68)
Number of subjects with events, n (%)	139 (59.9)	31 (45.6)
Number of censored subjects, n (%)	93 (40.1)	37 (54.4)
Kaplan-Meier estimates of Time to Event (months) [1]		
25%-ile (95% CI)	2.6 (1.7, 3.5)	3.4 (2.5, 5.3)
Median (95% CI)	6.2 (5.4, 10.1)	10.7 (5.3, 19.8)
75%-ile (95% CI)	28.8 (20.2, NE)	NE (14.5, NE)
Unstratified analysis		
Hazard Ratio (95% CI) [2]	1.20 (0.82, 1.78)	
p-value [3]	0.3495	

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[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Severe AE excluding events related to underlying disease progression - Subgroup analysis
Safety Analysis Set

Subgroup Level	EC+FOLFOX (N=232) n/ N (%)	EC+FOLFOX (N=232) Median (95% CI)[1]	Control 2 (N=68) n/ N (%)	Control 2 (N=68) Median (95% CI)[1]	Unstratified analysis Hazard Ratio (95% CI)[2]	Unstratified analysis p-Value[3]	Interaction p-Value[4]
Age (Years)							0.4320
< 65	88/ 148 (59.5)	6.2 (5.2, 11.0)	21/ 42 (50.0)	7.0 (4.1, 19.8)	1.05 (0.65, 1.70)	0.8256	
>= 65	51/ 84 (60.7)	5.8 (4.7, 11.5)	10/ 26 (38.5)	14.5 (5.1, NE)	1.46 (0.74, 2.89)	0.2727	
Sex							0.1507
Male	64/ 121 (52.9)	7.3 (6.1, 21.3)	15/ 32 (46.9)	7.0 (4.1, 19.8)	0.87 (0.49, 1.54)	0.6355	
Female	75/ 111 (67.6)	5.1 (4.4, 9.1)	16/ 36 (44.4)	10.7 (5.1, NE)	1.59 (0.93, 2.73)	0.0881	
Region							0.8979
Europe	66/ 108 (61.1)	6.1 (4.7, 10.0)	17/ 38 (44.7)	10.7 (4.1, NE)	1.19 (0.70, 2.03)	0.5279	
USA/Canada	10/ 15 (66.7)	3.0 (1.9, NE)	5/ 7 (71.4)	6.5 (3.4, 7.0)	1.17 (0.39, 3.47)	0.7807	
Rest of World	63/ 109 (57.8)	6.9 (5.6, 15.4)	9/ 23 (39.1)	11.9 (5.6, NE)	1.45 (0.72, 2.91)	0.2972	
ECOG-PS at Randomization							0.1780
0	76/ 130 (58.5)	6.7 (5.2, 15.0)	17/ 44 (38.6)	14.5 (6.5, NE)	1.42 (0.84, 2.40)	0.1910	
1	63/ 102 (61.8)	6.0 (4.6, 10.0)	14/ 24 (58.3)	5.3 (3.4, 11.9)	0.82 (0.46, 1.47)	0.5049	
Number of Organs Involved							0.5957
<= 2	64/ 116 (55.2)	11.0 (5.6, 20.2)	16/ 33 (48.5)	11.9 (5.1, NE)	1.07 (0.62, 1.85)	0.8197	
>= 3	75/ 116 (64.7)	5.8 (4.6, 6.9)	15/ 35 (42.9)	7.0 (4.1, 19.8)	1.33 (0.76, 2.32)	0.3145	
Presence of Liver Metastases							0.2053
Yes	83/ 146 (56.8)	7.1 (5.4, 12.6)	20/ 42 (47.6)	7.0 (4.1, 19.8)	0.97 (0.59, 1.58)	0.9001	
No	56/ 86 (65.1)	5.5 (4.2, 7.3)	11/ 26 (42.3)	14.5 (5.6, NE)	1.69 (0.88, 3.22)	0.1103	
Side of Tumor							0.8885
Left	50/ 88 (56.8)	7.3 (5.4, 22.1)	13/ 33 (39.4)	10.7 (5.3, NE)	1.15 (0.62, 2.13)	0.6512	
Right	89/ 144 (61.8)	6.0 (5.0, 9.1)	18/ 35 (51.4)	6.5 (4.1, NE)	1.22 (0.74, 2.03)	0.4313	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.
[4] P-Value for interaction from Cox proportional hazards model using ties=exact option with treatment, subgroup and treatment*subgroup interaction as covariates.
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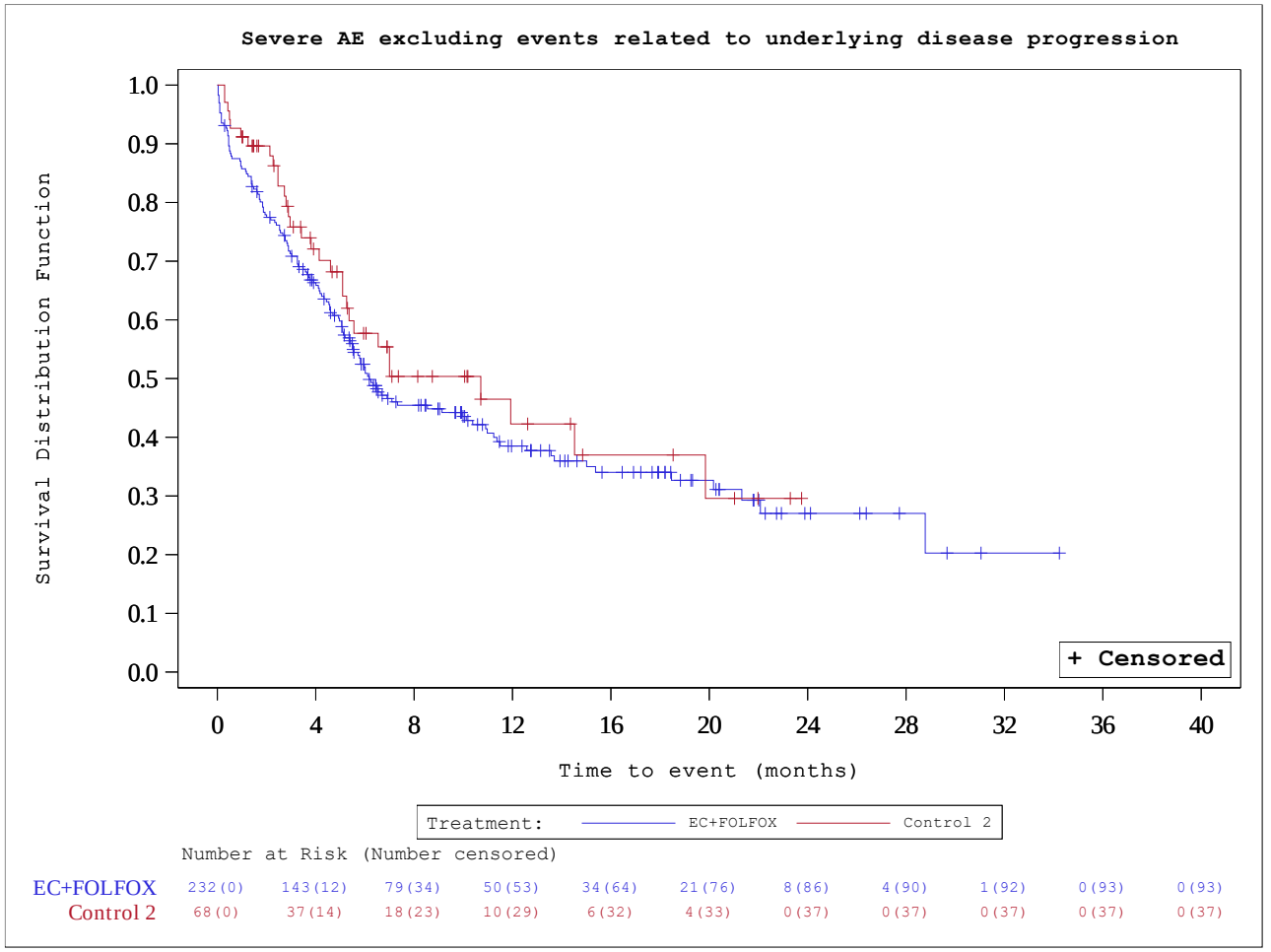
Kaplan Meier Plot of Severe AE excluding events related to underlying disease progression
Safety Analysis Set



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Kaplan-Meier Plots for subgroups only created if p-value for interaction < 0.05.

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Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
AE leading to discontinuation of Encorafenib
Safety Analysis Set

	EC+FOLFOX (N=232)	Control 2 (N=68)
Number of subjects with events, n (%)	32 (13.8)	0 (0.0)
Number of censored subjects, n (%)	200 (86.2)	68 (100.0)
Kaplan-Meier estimates of Time to Event (months) [1]		
25%-ile (95% CI)	NE (30.8, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
Unstratified analysis		
Hazard Ratio (95% CI) [2]	NE	
p-value [3]		

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
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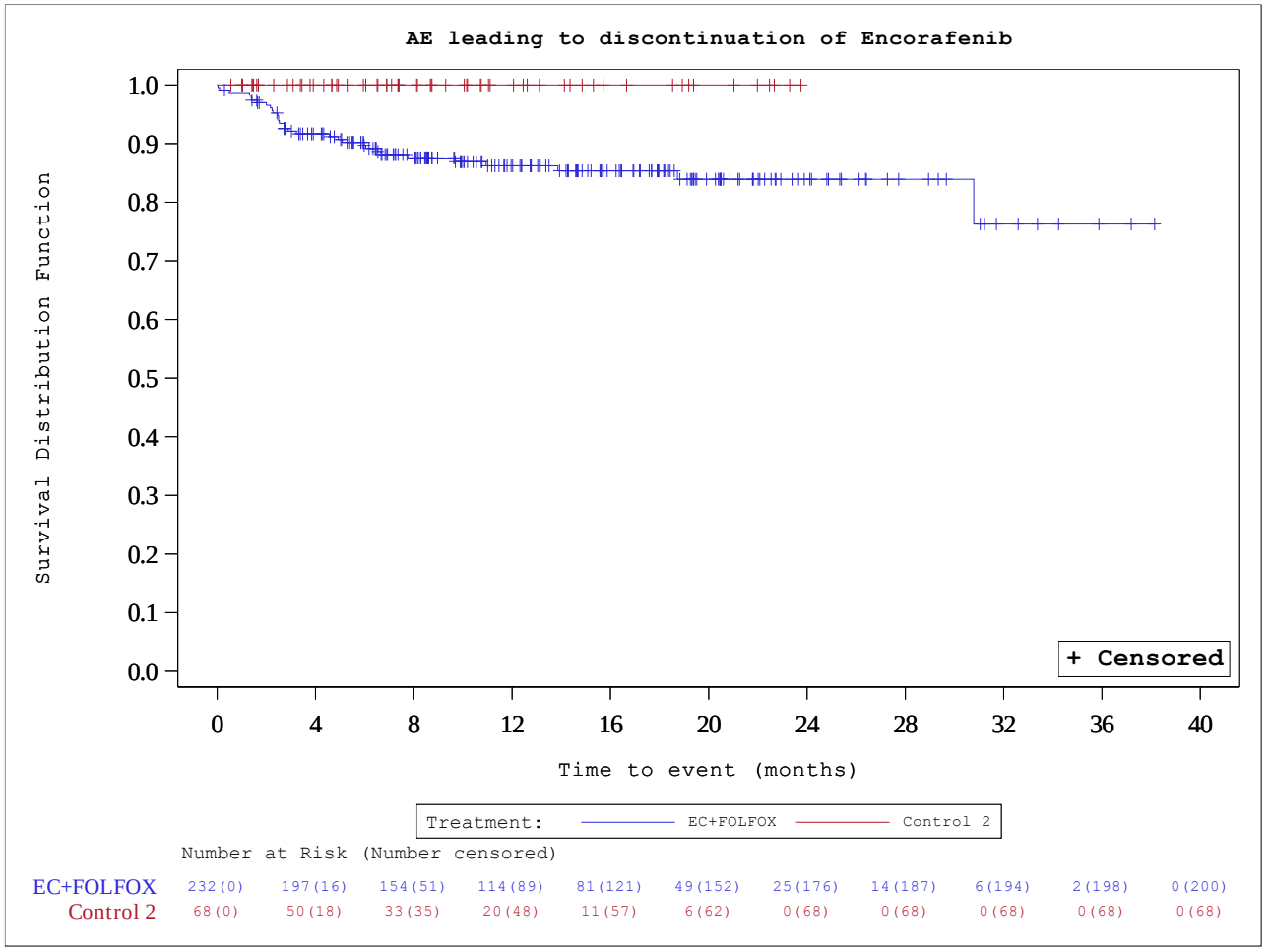
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
AE leading to discontinuation of Encorafenib - Subgroup analysis
Safety Analysis Set

Subgroup Level	EC+FOLFOX (N=232) n/ N (%)	EC+FOLFOX (N=232) Median (95% CI)[1]	Control 2 (N=68) n/ N (%)	Control 2 (N=68) Median (95% CI)[1]	Unstratified analysis Hazard Ratio (95% CI)[2]	Unstratified analysis p-Value[3]	Interaction p-Value[4]
Age (Years)							0.9998
< 65	17/ 148 (11.5)	NE (NE , NE)	0/ 42 (0.0)	NE (NE , NE)	NE		
>= 65	15/ 84 (17.9)	NE (30.8, NE)	0/ 26 (0.0)	NE (NE , NE)	NE		
Sex							1.0000
Male	16/ 121 (13.2)	NE (NE , NE)	0/ 32 (0.0)	NE (NE , NE)	NE		
Female	16/ 111 (14.4)	NE (NE , NE)	0/ 36 (0.0)	NE (NE , NE)	NE		
Region							1.0000
Europe	12/ 108 (11.1)	NE (NE , NE)	0/ 38 (0.0)	NE (NE , NE)	NE		
USA/Canada	1/ 15 (6.7)	NE (NE , NE)	0/ 7 (0.0)	NE (NE , NE)	NE		
Rest of World	19/ 109 (17.4)	NE (NE , NE)	0/ 23 (0.0)	NE (NE , NE)	NE		
ECOG-PS at Randomization							0.9998
0	15/ 130 (11.5)	NE (NE , NE)	0/ 44 (0.0)	NE (NE , NE)	NE		
1	17/ 102 (16.7)	NE (NE , NE)	0/ 24 (0.0)	NE (NE , NE)	NE		
Number of Organs Involved							0.9997
<= 2	12/ 116 (10.3)	NE (NE , NE)	0/ 33 (0.0)	NE (NE , NE)	NE		
>= 3	20/ 116 (17.2)	NE (NE , NE)	0/ 35 (0.0)	NE (NE , NE)	NE		
Presence of Liver Metastases							0.9995
Yes	26/ 146 (17.8)	NE (NE , NE)	0/ 42 (0.0)	NE (NE , NE)	NE		
No	6/ 86 (7.0)	NE (30.8, NE)	0/ 26 (0.0)	NE (NE , NE)	NE		
Side of Tumor							0.9999
Left	14/ 88 (15.9)	NE (NE , NE)	0/ 33 (0.0)	NE (NE , NE)	NE		
Right	18/ 144 (12.5)	NE (30.8, NE)	0/ 35 (0.0)	NE (NE , NE)	NE		

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.
[4] P-Value for interaction from Cox proportional hazards model using ties=exact option with treatment, subgroup and treatment*subgroup interaction as covariates.
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Kaplan Meier Plot of AE leading to discontinuation of Encorafenib
Safety Analysis Set



Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
Kaplan-Meier Plots for subgroups only created if p-value for interaction < 0.05.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
AE leading to discontinuation of Encorafenib excluding events related to underlying disease progression
Safety Analysis Set

	EC+FOLFOX (N=232)	Control 2 (N=68)
Number of subjects with events, n (%)	18 (7.8)	0 (0.0)
Number of censored subjects, n (%)	214 (92.2)	68 (100.0)
Kaplan-Meier estimates of Time to Event (months) [1]		
25%-ile (95% CI)	NE (30.8, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
Unstratified analysis		
Hazard Ratio (95% CI) [2]	NE	
p-value [3]		

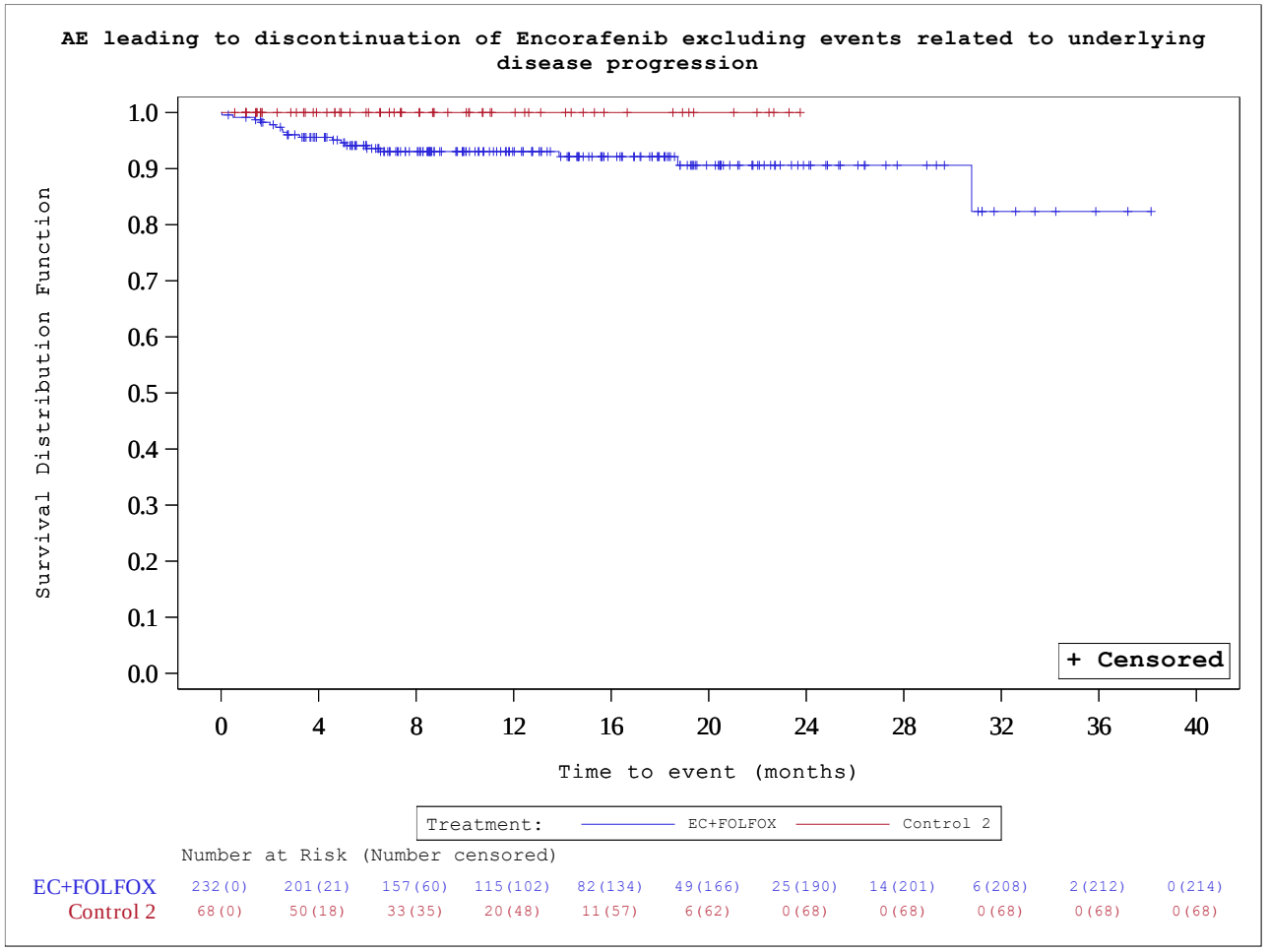
Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
AE leading to discontinuation of Encorafenib excluding events related to underlying disease progression - Subgroup analysis
Safety Analysis Set

Subgroup Level	EC+FOLFOX (N=232) n/ N (%)	EC+FOLFOX (N=232) Median (95% CI)[1]	Control 2 (N=68) n/ N (%)	Control 2 (N=68) Median (95% CI)[1]	Unstratified analysis Hazard Ratio (95% CI)[2]	Unstratified analysis p-Value[3]	Interaction p-Value[4]
Age (Years)							
< 65	9/ 148 (6.1)		0/ 42 (0.0)				
>= 65	9/ 84 (10.7)		0/ 26 (0.0)				
Sex							0.9998
Male	7/ 121 (5.8)	NE (NE , NE)	0/ 32 (0.0)	NE (NE , NE)	NE		
Female	11/ 111 (9.9)	NE (NE , NE)	0/ 36 (0.0)	NE (NE , NE)	NE		
Region							
Europe	8/ 108 (7.4)		0/ 38 (0.0)				
USA/Canada	1/ 15 (6.7)		0/ 7 (0.0)				
Rest of World	9/ 109 (8.3)		0/ 23 (0.0)				
ECOG-PS at Randomization							0.9998
0	8/ 130 (6.2)	NE (NE , NE)	0/ 44 (0.0)	NE (NE , NE)	NE		
1	10/ 102 (9.8)	NE (NE , NE)	0/ 24 (0.0)	NE (NE , NE)	NE		
Number of Organs Involved							0.9999
<= 2	8/ 116 (6.9)	NE (NE , NE)	0/ 33 (0.0)	NE (NE , NE)	NE		
>= 3	10/ 116 (8.6)	NE (NE , NE)	0/ 35 (0.0)	NE (NE , NE)	NE		
Presence of Liver Metastases							0.9997
Yes	14/ 146 (9.6)	NE (NE , NE)	0/ 42 (0.0)	NE (NE , NE)	NE		
No	4/ 86 (4.7)	NE (30.8, NE)	0/ 26 (0.0)	NE (NE , NE)	NE		
Side of Tumor							0.9999
Left	6/ 88 (6.8)	NE (NE , NE)	0/ 33 (0.0)	NE (NE , NE)	NE		
Right	12/ 144 (8.3)	NE (30.8, NE)	0/ 35 (0.0)	NE (NE , NE)	NE		

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.
[4] P-Value for interaction from Cox proportional hazards model using ties=exact option with treatment, subgroup and treatment*subgroup interaction as covariates.
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Kaplan Meier Plot of AE leading to discontinuation of Encorafenib excluding events related to underlying disease progression
Safety Analysis Set



Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
Kaplan-Meier Plots for subgroups only created if p-value for interaction < 0.05.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
AE leading to discontinuation of Cetuximab
Safety Analysis Set

	EC+FOLFOX (N=232)	Control 2 (N=68)
Number of subjects with events, n (%)	34 (14.7)	0 (0.0)
Number of censored subjects, n (%)	198 (85.3)	68 (100.0)
Kaplan-Meier estimates of Time to Event (months) [1]		
25%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
Unstratified analysis		
Hazard Ratio (95% CI) [2]	NE	
p-value [3]		

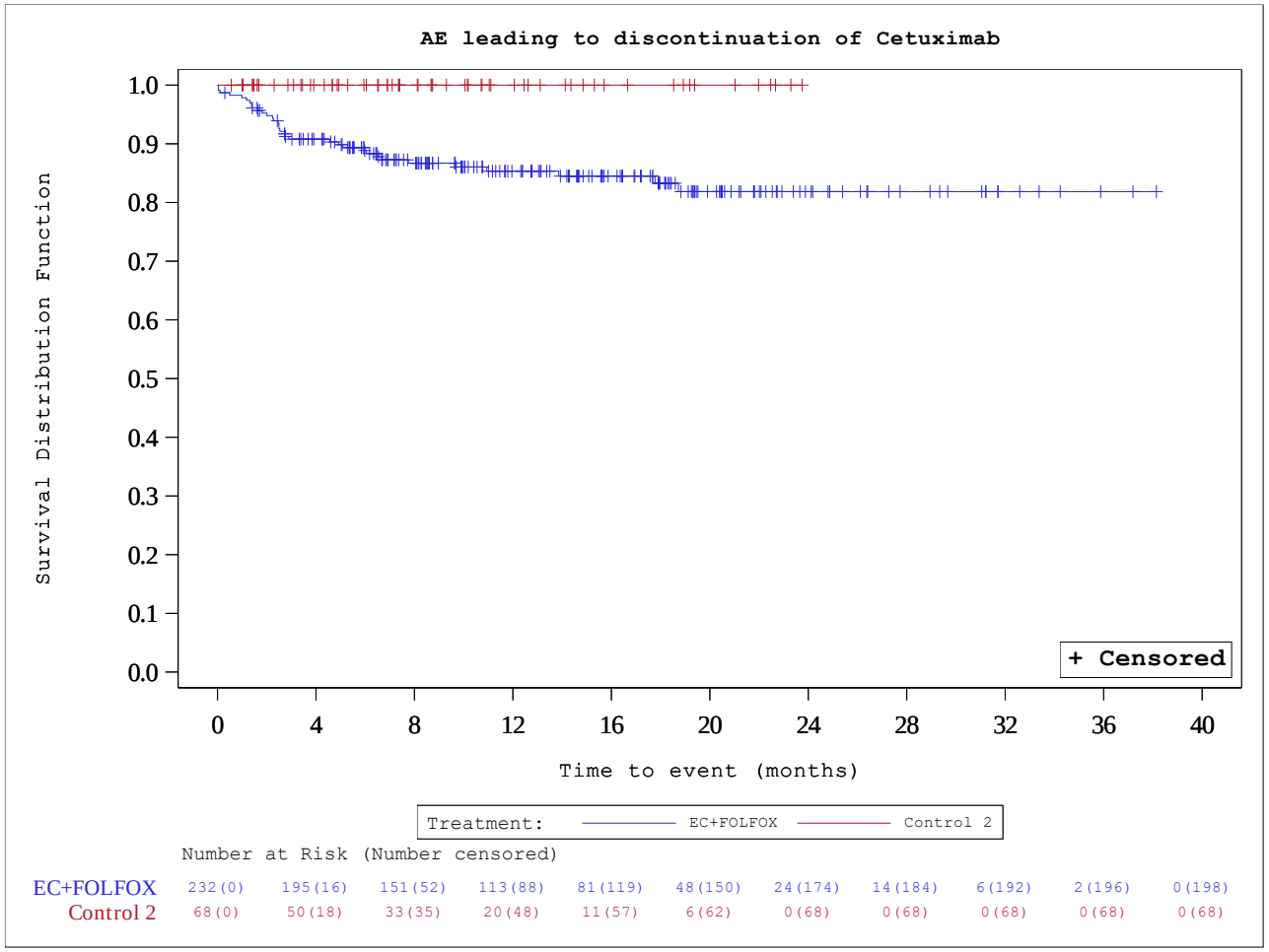
Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
AE leading to discontinuation of Cetuximab - Subgroup analysis
Safety Analysis Set

Subgroup	EC+FOLFOX (N=232)		Control 2 (N=68)		Unstratified analysis		Interaction
Level	n/ N (%)	Median (95% CI)[1]	n/ N (%)	Median (95% CI)[1]	Hazard Ratio (95% CI)[2]	p-Value[3]	p-Value[4]
Age (Years)							0.9999
< 65	19/ 148 (12.8)	NE (NE , NE)	0/ 42 (0.0)	NE (NE , NE)	NE		
>= 65	15/ 84 (17.9)	NE (NE , NE)	0/ 26 (0.0)	NE (NE , NE)	NE		
Sex							1.0000
Male	16/ 121 (13.2)	NE (NE , NE)	0/ 32 (0.0)	NE (NE , NE)	NE		
Female	18/ 111 (16.2)	NE (NE , NE)	0/ 36 (0.0)	NE (NE , NE)	NE		
Region							1.0000
Europe	12/ 108 (11.1)	NE (NE , NE)	0/ 38 (0.0)	NE (NE , NE)	NE		
USA/Canada	1/ 15 (6.7)	NE (NE , NE)	0/ 7 (0.0)	NE (NE , NE)	NE		
Rest of World	21/ 109 (19.3)	NE (NE , NE)	0/ 23 (0.0)	NE (NE , NE)	NE		
ECOG-PS at Randomization							0.9997
0	14/ 130 (10.8)	NE (NE , NE)	0/ 44 (0.0)	NE (NE , NE)	NE		
1	20/ 102 (19.6)	NE (NE , NE)	0/ 24 (0.0)	NE (NE , NE)	NE		
Number of Organs Involved							0.9996
<= 2	12/ 116 (10.3)	NE (NE , NE)	0/ 33 (0.0)	NE (NE , NE)	NE		
>= 3	22/ 116 (19.0)	NE (NE , NE)	0/ 35 (0.0)	NE (NE , NE)	NE		
Presence of Liver Metastases							0.9994
Yes	28/ 146 (19.2)	NE (NE , NE)	0/ 42 (0.0)	NE (NE , NE)	NE		
No	6/ 86 (7.0)	NE (NE , NE)	0/ 26 (0.0)	NE (NE , NE)	NE		
Side of Tumor							1.0000
Left	14/ 88 (15.9)	NE (NE , NE)	0/ 33 (0.0)	NE (NE , NE)	NE		
Right	20/ 144 (13.9)	NE (NE , NE)	0/ 35 (0.0)	NE (NE , NE)	NE		

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.
[4] P-Value for interaction from Cox proportional hazards model using ties=exact option with treatment, subgroup and treatment*subgroup interaction as covariates.
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Kaplan Meier Plot of AE leading to discontinuation of Cetuximab
Safety Analysis Set



Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
Kaplan-Meier Plots for subgroups only created if p-value for interaction < 0.05.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
AE leading to discontinuation of Cetuximab excluding events related to underlying disease progression
Safety Analysis Set

	EC+FOLFOX (N=232)	Control 2 (N=68)
Number of subjects with events, n (%)	21 (9.1)	0 (0.0)
Number of censored subjects, n (%)	211 (90.9)	68 (100.0)
Kaplan-Meier estimates of Time to Event (months) [1]		
25%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
Unstratified analysis		
Hazard Ratio (95% CI) [2]	NE	
p-value [3]		

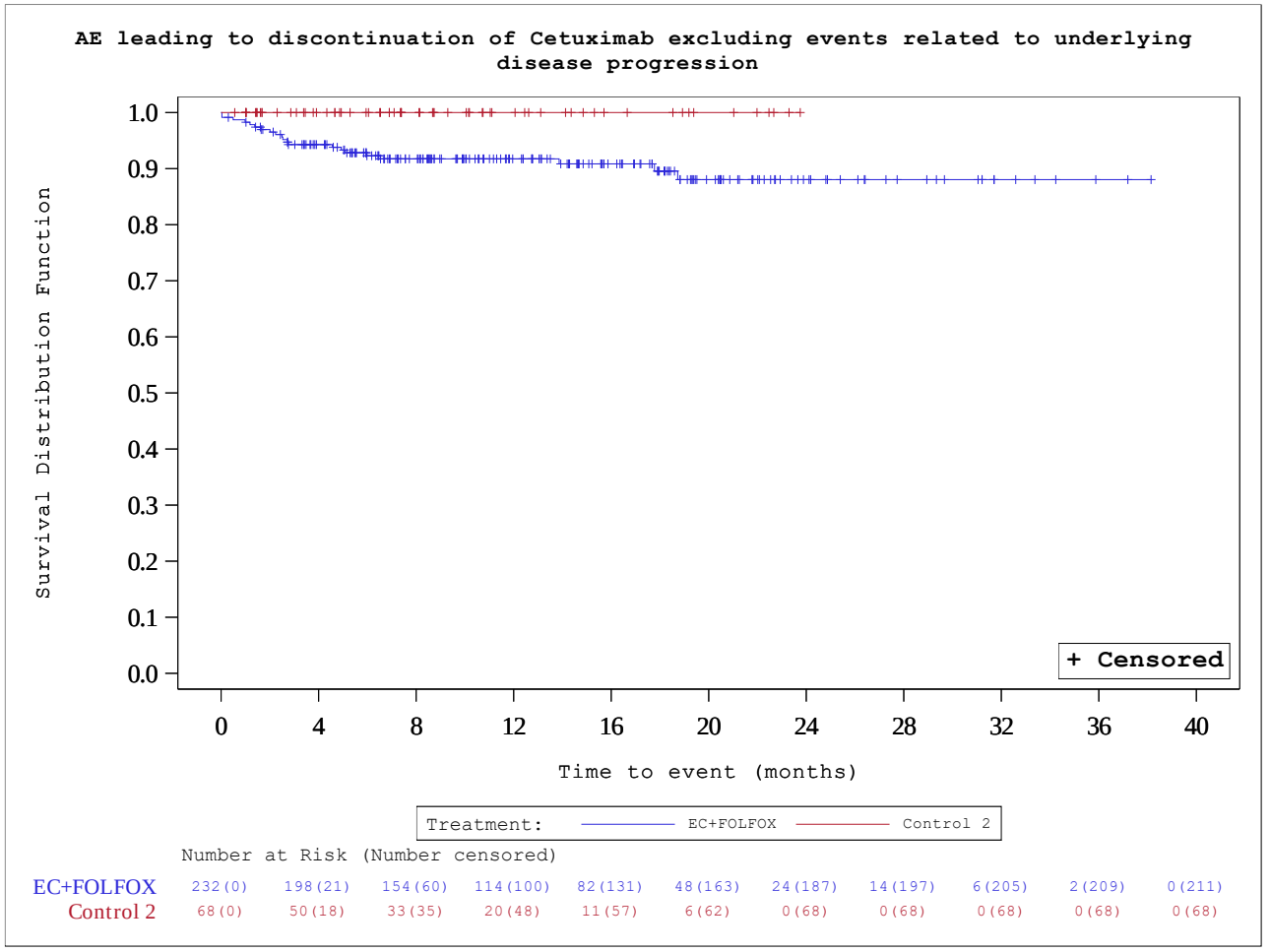
Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
AE leading to discontinuation of Cetuximab excluding events related to underlying disease progression - Subgroup analysis
Safety Analysis Set

Subgroup Level	EC+FOLFOX (N=232) n/ N (%)	EC+FOLFOX (N=232) Median (95% CI)[1]	Control 2 (N=68) n/ N (%)	Control 2 (N=68) Median (95% CI)[1]	Unstratified analysis Hazard Ratio (95% CI)[2]	Unstratified analysis p-Value[3]	Interaction p-Value[4]
Age (Years)							0.9998
< 65	11/ 148 (7.4)	NE (NE , NE)	0/ 42 (0.0)	NE (NE , NE)	NE		
>= 65	10/ 84 (11.9)	NE (NE , NE)	0/ 26 (0.0)	NE (NE , NE)	NE		
Sex							0.9998
Male	8/ 121 (6.6)	NE (NE , NE)	0/ 32 (0.0)	NE (NE , NE)	NE		
Female	13/ 111 (11.7)	NE (NE , NE)	0/ 36 (0.0)	NE (NE , NE)	NE		
Region							1.0000
Europe	8/ 108 (7.4)	NE (NE , NE)	0/ 38 (0.0)	NE (NE , NE)	NE		
USA/Canada	1/ 15 (6.7)	NE (NE , NE)	0/ 7 (0.0)	NE (NE , NE)	NE		
Rest of World	12/ 109 (11.0)	NE (NE , NE)	0/ 23 (0.0)	NE (NE , NE)	NE		
ECOG-PS at Randomization							0.9997
0	8/ 130 (6.2)	NE (NE , NE)	0/ 44 (0.0)	NE (NE , NE)	NE		
1	13/ 102 (12.7)	NE (NE , NE)	0/ 24 (0.0)	NE (NE , NE)	NE		
Number of Organs Involved							0.9998
<= 2	8/ 116 (6.9)	NE (NE , NE)	0/ 33 (0.0)	NE (NE , NE)	NE		
>= 3	13/ 116 (11.2)	NE (NE , NE)	0/ 35 (0.0)	NE (NE , NE)	NE		
Presence of Liver Metastases							0.9996
Yes	17/ 146 (11.6)	NE (NE , NE)	0/ 42 (0.0)	NE (NE , NE)	NE		
No	4/ 86 (4.7)	NE (NE , NE)	0/ 26 (0.0)	NE (NE , NE)	NE		
Side of Tumor							0.9998
Left	6/ 88 (6.8)	NE (NE , NE)	0/ 33 (0.0)	NE (NE , NE)	NE		
Right	15/ 144 (10.4)	NE (NE , NE)	0/ 35 (0.0)	NE (NE , NE)	NE		

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.
[4] P-Value for interaction from Cox proportional hazards model using ties=exact option with treatment, subgroup and treatment*subgroup interaction as covariates.
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Kaplan Meier Plot of AE leading to discontinuation of Cetuximab excluding events related to underlying disease progression
Safety Analysis Set



Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
Kaplan-Meier Plots for subgroups only created if p-value for interaction < 0.05.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
AE leading to discontinuation of other study intervention
Safety Analysis Set

	EC+FOLFOX (N=232)	Control 2 (N=68)
Number of subjects with events, n (%)	48 (20.7)	7 (10.3)
Number of censored subjects, n (%)	184 (79.3)	61 (89.7)
Kaplan-Meier estimates of Time to Event (months) [1]		
25%-ile (95% CI)	20.6 (10.9, NE)	NE (14.3, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
Unstratified analysis		
Hazard Ratio (95% CI) [2]	1.71 (0.77, 3.78)	
p-value [3]	0.1800	

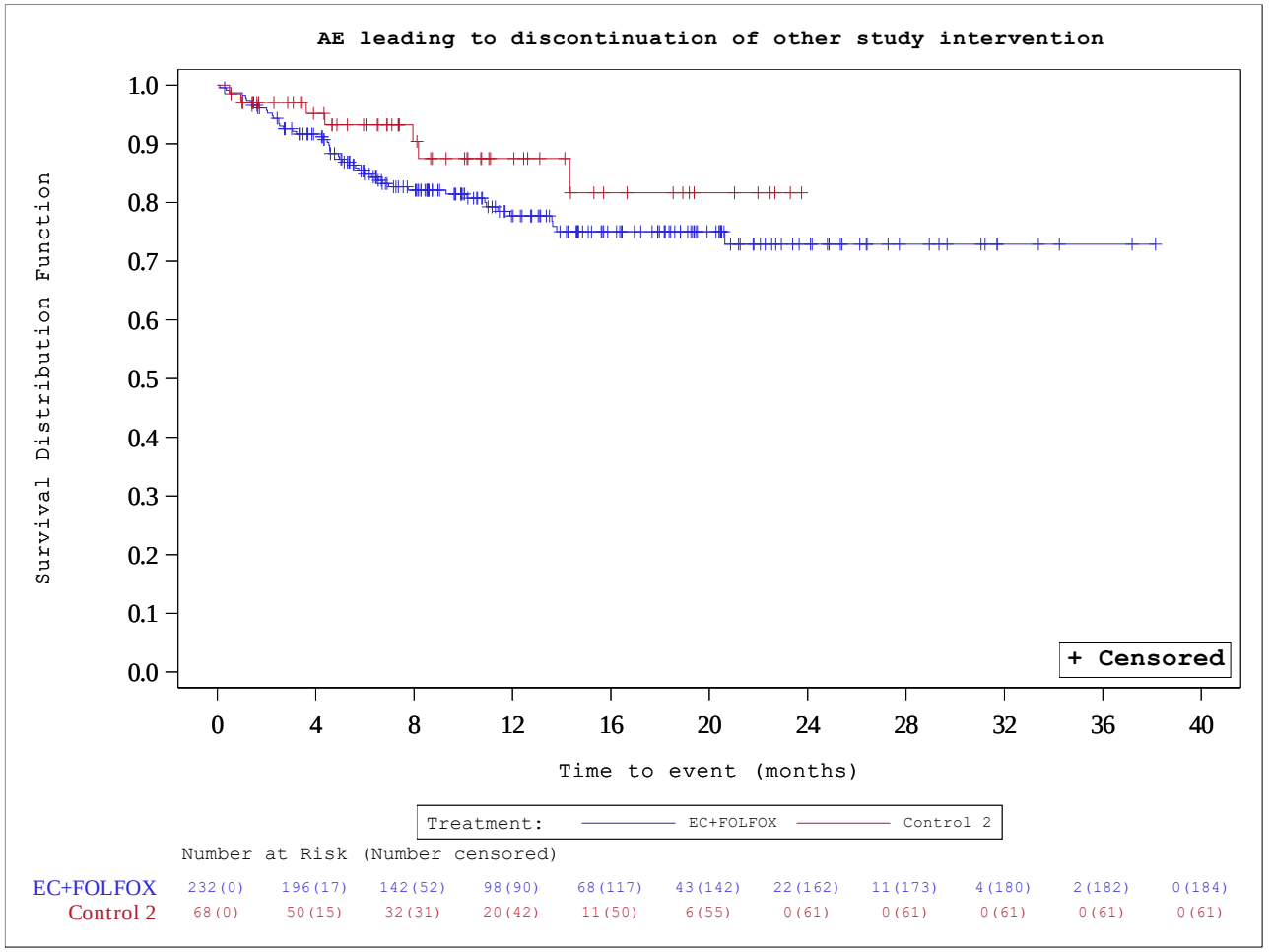
Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
AE leading to discontinuation of other study intervention - Subgroup analysis
Safety Analysis Set

Subgroup Level	EC+FOLFOX (N=232) n/ N (%)	EC+FOLFOX (N=232) Median (95% CI)[1]	Control 2 (N=68) n/ N (%)	Control 2 (N=68) Median (95% CI)[1]	Unstratified analysis Hazard Ratio (95% CI)[2]	Unstratified analysis p-Value[3]	Interaction p-Value[4]
Age (Years)							0.5061
< 65	28/ 148 (18.9)	NE (NE , NE)	3/ 42 (7.1)	NE (NE , NE)	2.30 (0.70, 7.55)	0.1594	
>= 65	20/ 84 (23.8)	NE (NE , NE)	4/ 26 (15.4)	NE (14.3, NE)	1.29 (0.44, 3.79)	0.6404	
Sex							0.4081
Male	24/ 121 (19.8)	NE (NE , NE)	4/ 32 (12.5)	NE (14.3, NE)	1.20 (0.42, 3.47)	0.7315	
Female	24/ 111 (21.6)	NE (NE , NE)	3/ 36 (8.3)	NE (NE , NE)	2.40 (0.72, 7.99)	0.1397	
Region							0.9655
Europe	19/ 108 (17.6)	NE (NE , NE)	4/ 38 (10.5)	NE (NE , NE)	1.23 (0.42, 3.62)	0.7112	
USA/Canada	3/ 15 (20.0)	NE (NE , NE)	0/ 7 (0.0)	NE (NE , NE)	NE		
Rest of World	26/ 109 (23.9)	NE (NE , NE)	3/ 23 (13.0)	NE (14.3, NE)	1.63 (0.49, 5.41)	0.4170	
ECOG-PS at Randomization							0.1395
0	28/ 130 (21.5)	NE (NE , NE)	3/ 44 (6.8)	NE (NE , NE)	2.84 (0.86, 9.35)	0.0722	
1	20/ 102 (19.6)	NE (NE , NE)	4/ 24 (16.7)	NE (NE , NE)	0.89 (0.30, 2.62)	0.8307	
Number of Organs Involved							0.1988
<= 2	29/ 116 (25.0)	NE (NE , NE)	3/ 33 (9.1)	NE (NE , NE)	2.80 (0.85, 9.20)	0.0760	
>= 3	19/ 116 (16.4)	NE (NE , NE)	4/ 35 (11.4)	NE (NE , NE)	1.03 (0.35, 3.06)	0.9537	
Presence of Liver Metastases							0.1525
Yes	29/ 146 (19.9)	NE (NE , NE)	6/ 42 (14.3)	NE (14.3, NE)	1.09 (0.45, 2.63)	0.8469	
No	19/ 86 (22.1)	NE (NE , NE)	1/ 26 (3.8)	NE (NE , NE)	5.52 (0.74, 41.25)	0.0610	
Side of Tumor							0.5732
Left	18/ 88 (20.5)	NE (NE , NE)	4/ 33 (12.1)	NE (14.3, NE)	1.32 (0.44, 3.90)	0.6187	
Right	30/ 144 (20.8)	NE (NE , NE)	3/ 35 (8.6)	NE (NE , NE)	2.15 (0.66, 7.04)	0.1958	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.
[4] P-Value for interaction from Cox proportional hazards model using ties=exact option with treatment, subgroup and treatment*subgroup interaction as covariates.
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Kaplan Meier Plot of AE leading to discontinuation of other study intervention
Safety Analysis Set



Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
Kaplan-Meier Plots for subgroups only created if p-value for interaction < 0.05.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
AE leading to discontinuation of other study intervention excluding events related to underlying disease progression
Safety Analysis Set

	EC+FOLFOX (N=232)	Control 2 (N=68)
Number of subjects with events, n (%)	30 (12.9)	3 (4.4)
Number of censored subjects, n (%)	202 (87.1)	65 (95.6)
Kaplan-Meier estimates of Time to Event (months) [1]		
25%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
Unstratified analysis		
Hazard Ratio (95% CI) [2]	2.40 (0.73, 7.89)	
p-value [3]	0.1350	

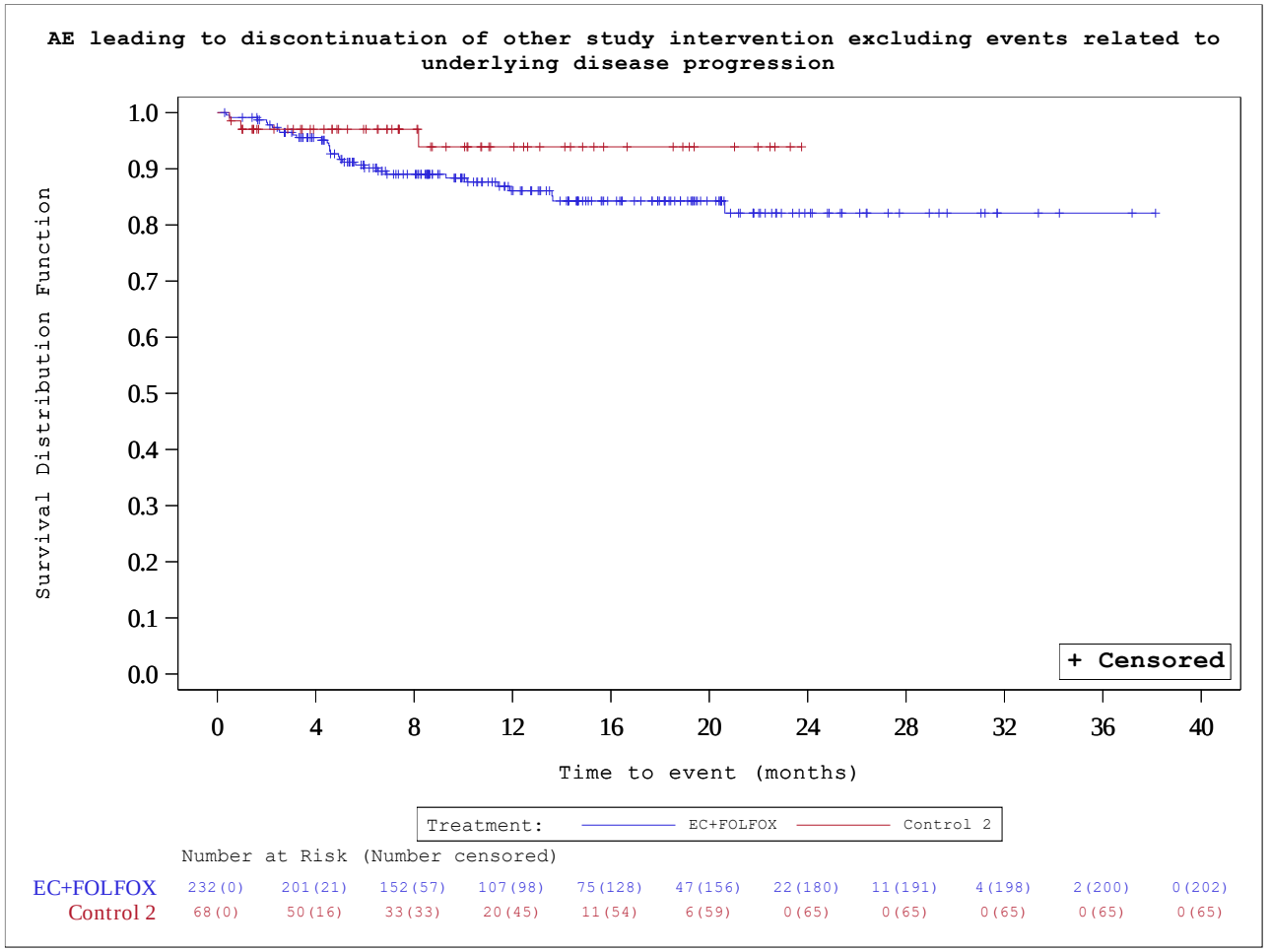
Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
AE leading to discontinuation of other study intervention excluding events related to underlying disease progression - Subgroup analysis
Safety Analysis Set

Subgroup Level	EC+FOLFOX (N=232) n/ N (%)	EC+FOLFOX (N=232) Median (95% CI)[1]	Control 2 (N=68) n/ N (%)	Control 2 (N=68) Median (95% CI)[1]	Unstratified analysis Hazard Ratio (95% CI)[2]	Unstratified analysis p-Value[3]	Interaction p-Value[4]
Age (Years)							0.8598
< 65	19/ 148 (12.8)	NE (NE , NE)	2/ 42 (4.8)	NE (NE , NE)	2.21 (0.52, 9.51)	0.2727	
>= 65	11/ 84 (13.1)	NE (NE , NE)	1/ 26 (3.8)	NE (NE , NE)	2.72 (0.35, 21.16)	0.3183	
Sex							0.5294
Male	17/ 121 (14.0)	NE (NE , NE)	2/ 32 (6.3)	NE (NE , NE)	1.63 (0.38, 7.07)	0.5097	
Female	13/ 111 (11.7)	NE (NE , NE)	1/ 36 (2.8)	NE (NE , NE)	3.81 (0.50, 29.12)	0.1662	
Region							0.9569
Europe	13/ 108 (12.0)	NE (NE , NE)	2/ 38 (5.3)	NE (NE , NE)	1.75 (0.39, 7.81)	0.4564	
USA/Canada	2/ 15 (13.3)	NE (NE , NE)	0/ 7 (0.0)	NE (NE , NE)	NE		
Rest of World	15/ 109 (13.8)	NE (NE , NE)	1/ 23 (4.3)	NE (NE , NE)	2.54 (0.33, 19.29)	0.3498	
ECOG-PS at Randomization							0.2463
0	17/ 130 (13.1)	NE (NE , NE)	1/ 44 (2.3)	NE (NE , NE)	4.80 (0.64, 36.13)	0.0918	
1	13/ 102 (12.7)	NE (NE , NE)	2/ 24 (8.3)	NE (NE , NE)	1.18 (0.26, 5.25)	0.8314	
Number of Organs Involved							0.9870
<= 2	20/ 116 (17.2)	NE (NE , NE)	0/ 33 (0.0)	NE (NE , NE)	NE		
>= 3	10/ 116 (8.6)	NE (NE , NE)	3/ 35 (8.6)	NE (NE , NE)	0.73 (0.20, 2.69)	0.6400	
Presence of Liver Metastases							0.9891
Yes	17/ 146 (11.6)	NE (NE , NE)	3/ 42 (7.1)	NE (NE , NE)	1.27 (0.37, 4.36)	0.6988	
No	13/ 86 (15.1)	NE (NE , NE)	0/ 26 (0.0)	NE (NE , NE)	NE		
Side of Tumor							0.6060
Left	12/ 88 (13.6)	NE (NE , NE)	1/ 33 (3.0)	NE (NE , NE)	3.42 (0.44, 26.40)	0.2097	
Right	18/ 144 (12.5)	NE (NE , NE)	2/ 35 (5.7)	NE (NE , NE)	1.85 (0.43, 7.97)	0.4027	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.
[4] P-Value for interaction from Cox proportional hazards model using ties=exact option with treatment, subgroup and treatment*subgroup interaction as covariates.
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Kaplan Meier Plot of AE leading to discontinuation of other study intervention excluding events related to underlying disease progression
Safety Analysis Set



Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
Kaplan-Meier Plots for subgroups only created if p-value for interaction < 0.05.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
AE leading to discontinuation of Encorafenib or Cetuximab
Safety Analysis Set

	EC+FOLFOX (N=232)	Control 2 (N=68)
Number of subjects with events, n (%)	36 (15.5)	0 (0.0)
Number of censored subjects, n (%)	196 (84.5)	68 (100.0)
Kaplan-Meier estimates of Time to Event (months) [1]		
25%-ile (95% CI)	30.8 (30.8, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
Unstratified analysis		
Hazard Ratio (95% CI) [2]	NE	
p-value [3]		

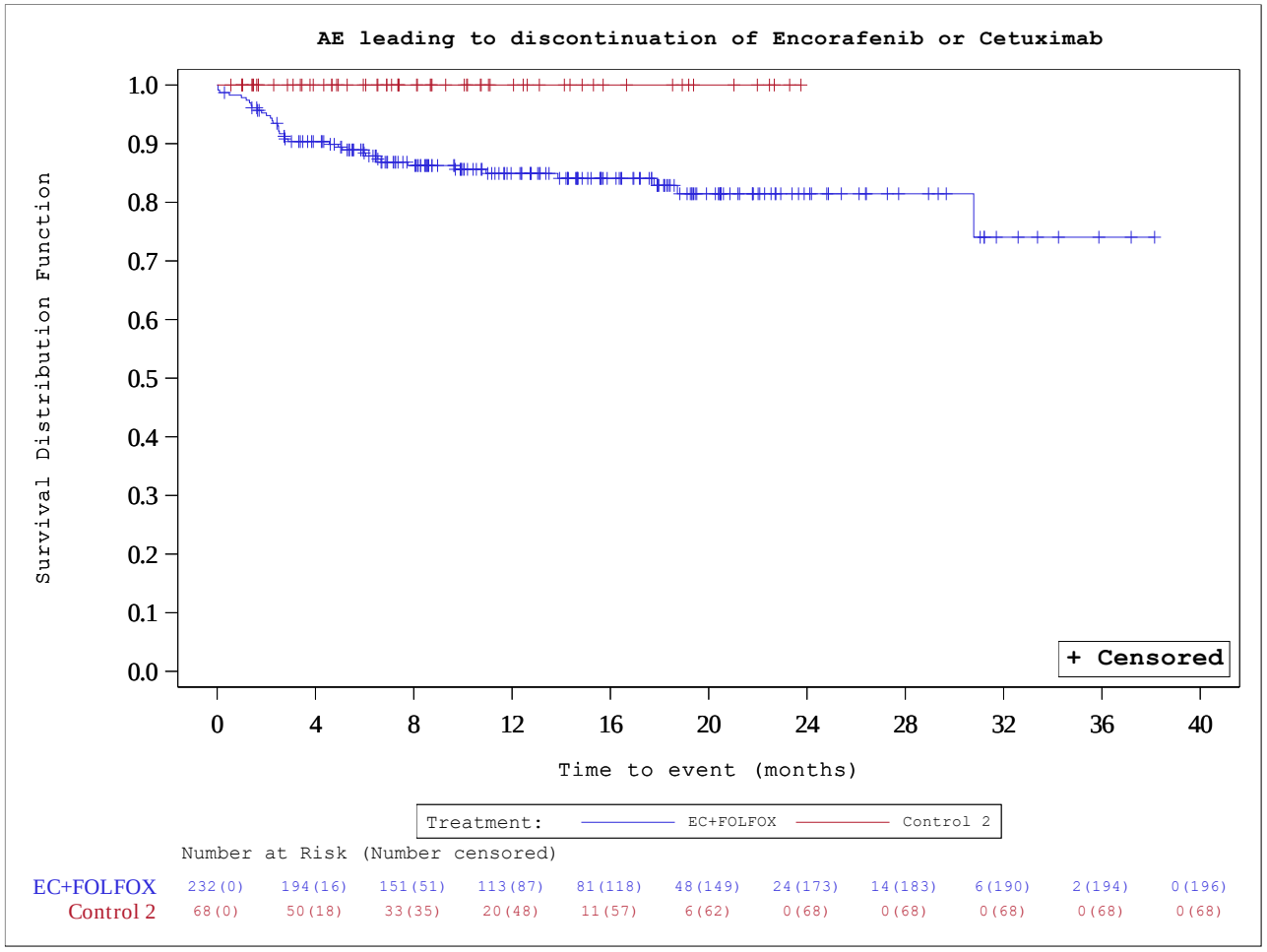
Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
AE leading to discontinuation of Encorafenib or Cetuximab - Subgroup analysis
Safety Analysis Set

Subgroup Level	EC+FOLFOX (N=232) n/ N (%)	EC+FOLFOX (N=232) Median (95% CI)[1]	Control 2 (N=68) n/ N (%)	Control 2 (N=68) Median (95% CI)[1]	Unstratified analysis Hazard Ratio (95% CI)[2]	Unstratified analysis p-Value[3]	Interaction p-Value[4]
Age (Years)							0.9998
< 65	19/ 148 (12.8)	NE (NE , NE)	0/ 42 (0.0)	NE (NE , NE)	NE		
>= 65	17/ 84 (20.2)	NE (30.8, NE)	0/ 26 (0.0)	NE (NE , NE)	NE		
Sex							1.0000
Male	18/ 121 (14.9)	NE (NE , NE)	0/ 32 (0.0)	NE (NE , NE)	NE		
Female	18/ 111 (16.2)	NE (NE , NE)	0/ 36 (0.0)	NE (NE , NE)	NE		
Region							1.0000
Europe	13/ 108 (12.0)	NE (30.8, NE)	0/ 38 (0.0)	NE (NE , NE)	NE		
USA/Canada	1/ 15 (6.7)	NE (NE , NE)	0/ 7 (0.0)	NE (NE , NE)	NE		
Rest of World	22/ 109 (20.2)	NE (NE , NE)	0/ 23 (0.0)	NE (NE , NE)	NE		
ECOG-PS at Randomization							0.9997
0	16/ 130 (12.3)	NE (NE , NE)	0/ 44 (0.0)	NE (NE , NE)	NE		
1	20/ 102 (19.6)	NE (NE , NE)	0/ 24 (0.0)	NE (NE , NE)	NE		
Number of Organs Involved							0.9996
<= 2	13/ 116 (11.2)	NE (NE , NE)	0/ 33 (0.0)	NE (NE , NE)	NE		
>= 3	23/ 116 (19.8)	NE (NE , NE)	0/ 35 (0.0)	NE (NE , NE)	NE		
Presence of Liver Metastases							0.9995
Yes	29/ 146 (19.9)	NE (NE , NE)	0/ 42 (0.0)	NE (NE , NE)	NE		
No	7/ 86 (8.1)	NE (30.8, NE)	0/ 26 (0.0)	NE (NE , NE)	NE		
Side of Tumor							1.0000
Left	14/ 88 (15.9)	NE (NE , NE)	0/ 33 (0.0)	NE (NE , NE)	NE		
Right	22/ 144 (15.3)	NE (30.8, NE)	0/ 35 (0.0)	NE (NE , NE)	NE		

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.
[4] P-Value for interaction from Cox proportional hazards model using ties=exact option with treatment, subgroup and treatment*subgroup interaction as covariates.
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Kaplan Meier Plot of AE leading to discontinuation of Encorafenib or Cetuximab
Safety Analysis Set



Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
Kaplan-Meier Plots for subgroups only created if p-value for interaction < 0.05.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
AE leading to discontinuation of Encorafenib or Cetuximab excluding events related to underlying disease progression
Safety Analysis Set

	EC+FOLFOX (N=232)	Control 2 (N=68)
Number of subjects with events, n (%)	22 (9.5)	0 (0.0)
Number of censored subjects, n (%)	210 (90.5)	68 (100.0)
Kaplan-Meier estimates of Time to Event (months) [1]		
25%-ile (95% CI)	NE (30.8, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
Unstratified analysis		
Hazard Ratio (95% CI) [2]	NE	
p-value [3]		

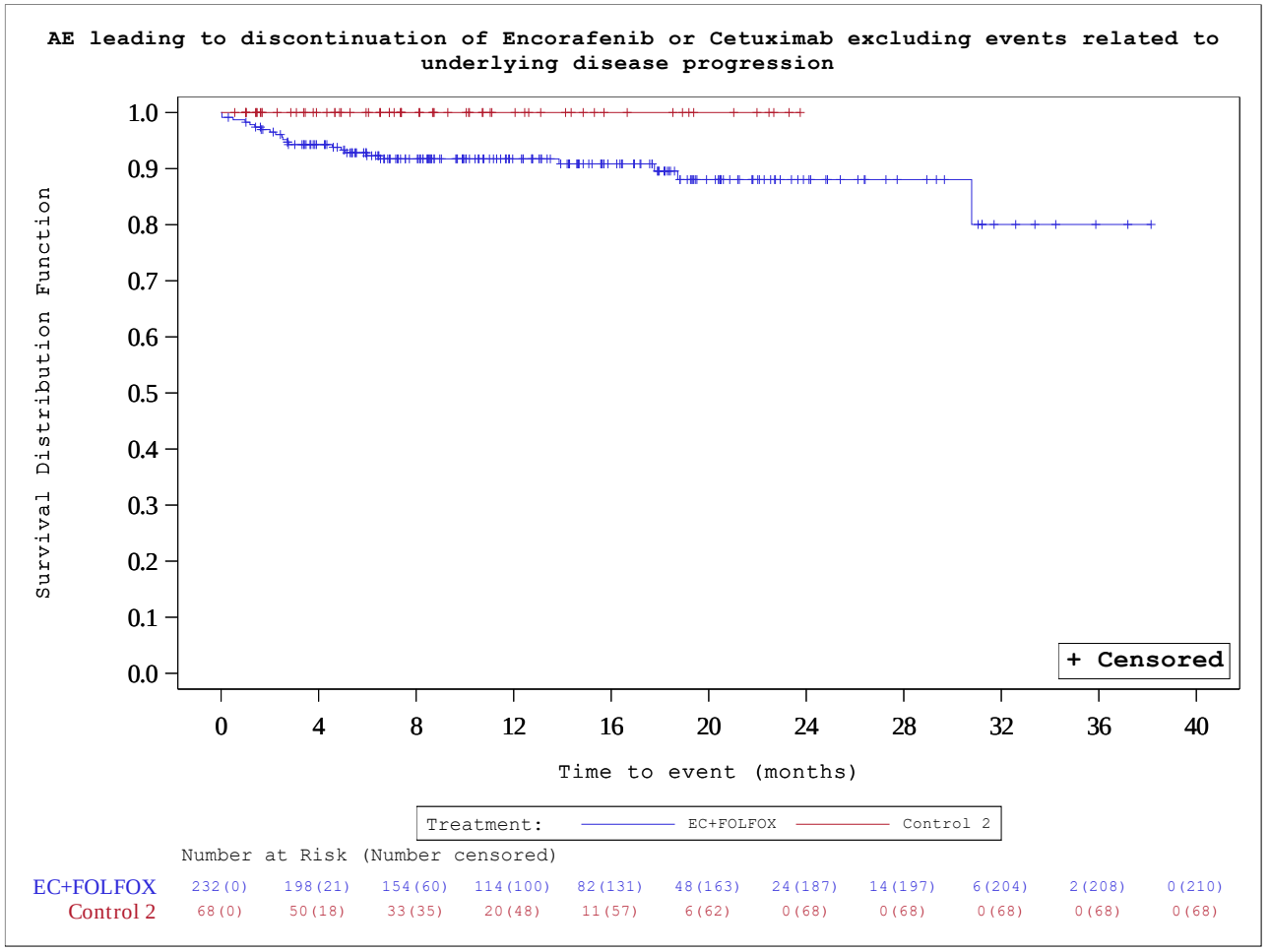
Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
AE leading to discontinuation of Encorafenib or Cetuximab excluding events related to underlying disease progression - Subgroup analysis
Safety Analysis Set

Subgroup Level	EC+FOLFOX (N=232) n/ N (%)	EC+FOLFOX (N=232) Median (95% CI)[1]	Control 2 (N=68) n/ N (%)	Control 2 (N=68) Median (95% CI)[1]	Unstratified analysis Hazard Ratio (95% CI)[2]	Unstratified analysis p-Value[3]	Interaction p-Value[4]
Age (Years)							0.9998
< 65	11/ 148 (7.4)	NE (NE , NE)	0/ 42 (0.0)	NE (NE , NE)	NE		
>= 65	11/ 84 (13.1)	NE (30.8, NE)	0/ 26 (0.0)	NE (NE , NE)	NE		
Sex							0.9998
Male	9/ 121 (7.4)	NE (NE , NE)	0/ 32 (0.0)	NE (NE , NE)	NE		
Female	13/ 111 (11.7)	NE (NE , NE)	0/ 36 (0.0)	NE (NE , NE)	NE		
Region							1.0000
Europe	9/ 108 (8.3)	NE (NE , NE)	0/ 38 (0.0)	NE (NE , NE)	NE		
USA/Canada	1/ 15 (6.7)	NE (NE , NE)	0/ 7 (0.0)	NE (NE , NE)	NE		
Rest of World	12/ 109 (11.0)	NE (NE , NE)	0/ 23 (0.0)	NE (NE , NE)	NE		
ECOG-PS at Randomization							0.9997
0	9/ 130 (6.9)	NE (NE , NE)	0/ 44 (0.0)	NE (NE , NE)	NE		
1	13/ 102 (12.7)	NE (NE , NE)	0/ 24 (0.0)	NE (NE , NE)	NE		
Number of Organs Involved							0.9998
<= 2	9/ 116 (7.8)	NE (NE , NE)	0/ 33 (0.0)	NE (NE , NE)	NE		
>= 3	13/ 116 (11.2)	NE (NE , NE)	0/ 35 (0.0)	NE (NE , NE)	NE		
Presence of Liver Metastases							0.9997
Yes	17/ 146 (11.6)	NE (NE , NE)	0/ 42 (0.0)	NE (NE , NE)	NE		
No	5/ 86 (5.8)	NE (30.8, NE)	0/ 26 (0.0)	NE (NE , NE)	NE		
Side of Tumor							0.9998
Left	6/ 88 (6.8)	NE (NE , NE)	0/ 33 (0.0)	NE (NE , NE)	NE		
Right	16/ 144 (11.1)	NE (30.8, NE)	0/ 35 (0.0)	NE (NE , NE)	NE		

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.
[4] P-Value for interaction from Cox proportional hazards model using ties=exact option with treatment, subgroup and treatment*subgroup interaction as covariates.
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Kaplan Meier Plot of AE leading to discontinuation of Encorafenib or Cetuximab excluding events related to underlying disease progression
Safety Analysis Set



Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
Kaplan-Meier Plots for subgroups only created if p-value for interaction < 0.05.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
AE leading to discontinuation of Encorafenib or Cetuximab or other study intervention
Safety Analysis Set

	EC+FOLFOX (N=232)	Control 2 (N=68)
Number of subjects with events, n (%)	62 (26.7)	7 (10.3)
Number of censored subjects, n (%)	170 (73.3)	61 (89.7)
Kaplan-Meier estimates of Time to Event (months) [1]		
25%-ile (95% CI)	10.9 (6.3, 20.6)	NE (14.3, NE)
Median (95% CI)	NE (30.8, NE)	NE (NE, NE)
75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
Unstratified analysis		
Hazard Ratio (95% CI) [2]	2.26 (1.03, 4.94)	
p-value [3]	0.0359	

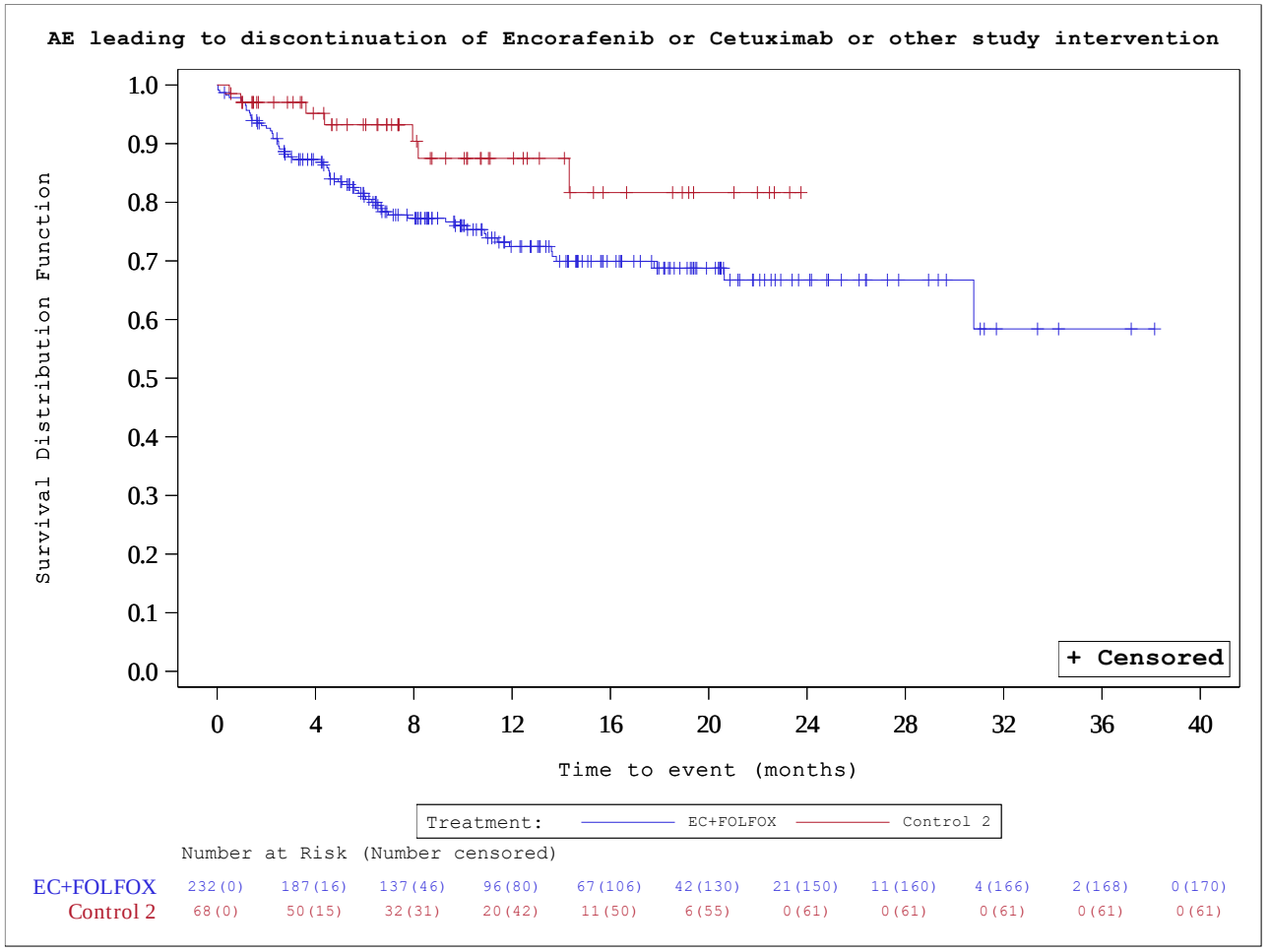
Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
AE leading to discontinuation of Encorafenib or Cetuximab or other study intervention - Subgroup analysis
Safety Analysis Set

Subgroup Level	EC+FOLFOX (N=232) n/ N (%)	EC+FOLFOX (N=232) Median (95% CI)[1]	Control 2 (N=68) n/ N (%)	Control 2 (N=68) Median (95% CI)[1]	Unstratified analysis Hazard Ratio (95% CI)[2]	Unstratified analysis p-Value[3]	Interaction p-Value[4]
Age (Years)							0.5130
< 65	36/ 148 (24.3)	NE (NE , NE)	3/ 42 (7.1)	NE (NE , NE)	3.02 (0.93, 9.81)	0.0528	
>= 65	26/ 84 (31.0)	NE (30.8, NE)	4/ 26 (15.4)	NE (14.3, NE)	1.73 (0.60, 4.99)	0.3031	
Sex							0.4704
Male	32/ 121 (26.4)	NE (30.8, NE)	4/ 32 (12.5)	NE (14.3, NE)	1.67 (0.59, 4.74)	0.3300	
Female	30/ 111 (27.0)	NE (NE , NE)	3/ 36 (8.3)	NE (NE , NE)	3.05 (0.93, 9.99)	0.0531	
Region							0.8985
Europe	23/ 108 (21.3)	NE (30.8, NE)	4/ 38 (10.5)	NE (NE , NE)	1.51 (0.52, 4.39)	0.4508	
USA/Canada	3/ 15 (20.0)	NE (NE , NE)	0/ 7 (0.0)	NE (NE , NE)	NE		
Rest of World	36/ 109 (33.0)	NE (NE , NE)	3/ 23 (13.0)	NE (14.3, NE)	2.37 (0.73, 7.71)	0.1386	
ECOG-PS at Randomization							0.2051
0	34/ 130 (26.2)	NE (30.8, NE)	3/ 44 (6.8)	NE (NE , NE)	3.45 (1.06, 11.24)	0.0290	
1	28/ 102 (27.5)	NE (NE , NE)	4/ 24 (16.7)	NE (NE , NE)	1.32 (0.46, 3.80)	0.6003	
Number of Organs Involved							0.4317
<= 2	32/ 116 (27.6)	NE (30.8, NE)	3/ 33 (9.1)	NE (NE , NE)	3.05 (0.93, 9.98)	0.0522	
>= 3	30/ 116 (25.9)	NE (NE , NE)	4/ 35 (11.4)	NE (NE , NE)	1.72 (0.60, 4.92)	0.3020	
Presence of Liver Metastases							0.2118
Yes	40/ 146 (27.4)	NE (NE , NE)	6/ 42 (14.3)	NE (14.3, NE)	1.58 (0.67, 3.74)	0.2895	
No	22/ 86 (25.6)	30.8 (30.8, NE)	1/ 26 (3.8)	NE (NE , NE)	6.23 (0.84, 46.35)	0.0407	
Side of Tumor							0.5322
Left	23/ 88 (26.1)	NE (NE , NE)	4/ 33 (12.1)	NE (14.3, NE)	1.74 (0.60, 5.03)	0.3034	
Right	39/ 144 (27.1)	30.8 (30.8, NE)	3/ 35 (8.6)	NE (NE , NE)	2.85 (0.88, 9.23)	0.0677	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.
[4] P-Value for interaction from Cox proportional hazards model using ties=exact option with treatment, subgroup and treatment*subgroup interaction as covariates.
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Kaplan Meier Plot of AE leading to discontinuation of Encorafenib or Cetuximab or other study intervention
Safety Analysis Set



Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
Kaplan-Meier Plots for subgroups only created if p-value for interaction < 0.05.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
AE leading to discontinuation of Encorafenib or Cetuximab or other study intervention excluding events related to underlying disease progression
Safety Analysis Set

	EC+FOLFOX (N=232)	Control 2 (N=68)
Number of subjects with events, n (%)	38 (16.4)	3 (4.4)
Number of censored subjects, n (%)	194 (83.6)	65 (95.6)
Kaplan-Meier estimates of Time to Event (months) [1]		
25%-ile (95% CI)	30.8 (17.8, NE)	NE (NE, NE)
Median (95% CI)	NE (30.8, NE)	NE (NE, NE)
75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
Unstratified analysis		
Hazard Ratio (95% CI) [2]	3.00 (0.92, 9.74)	
p-value [3]	0.0546	

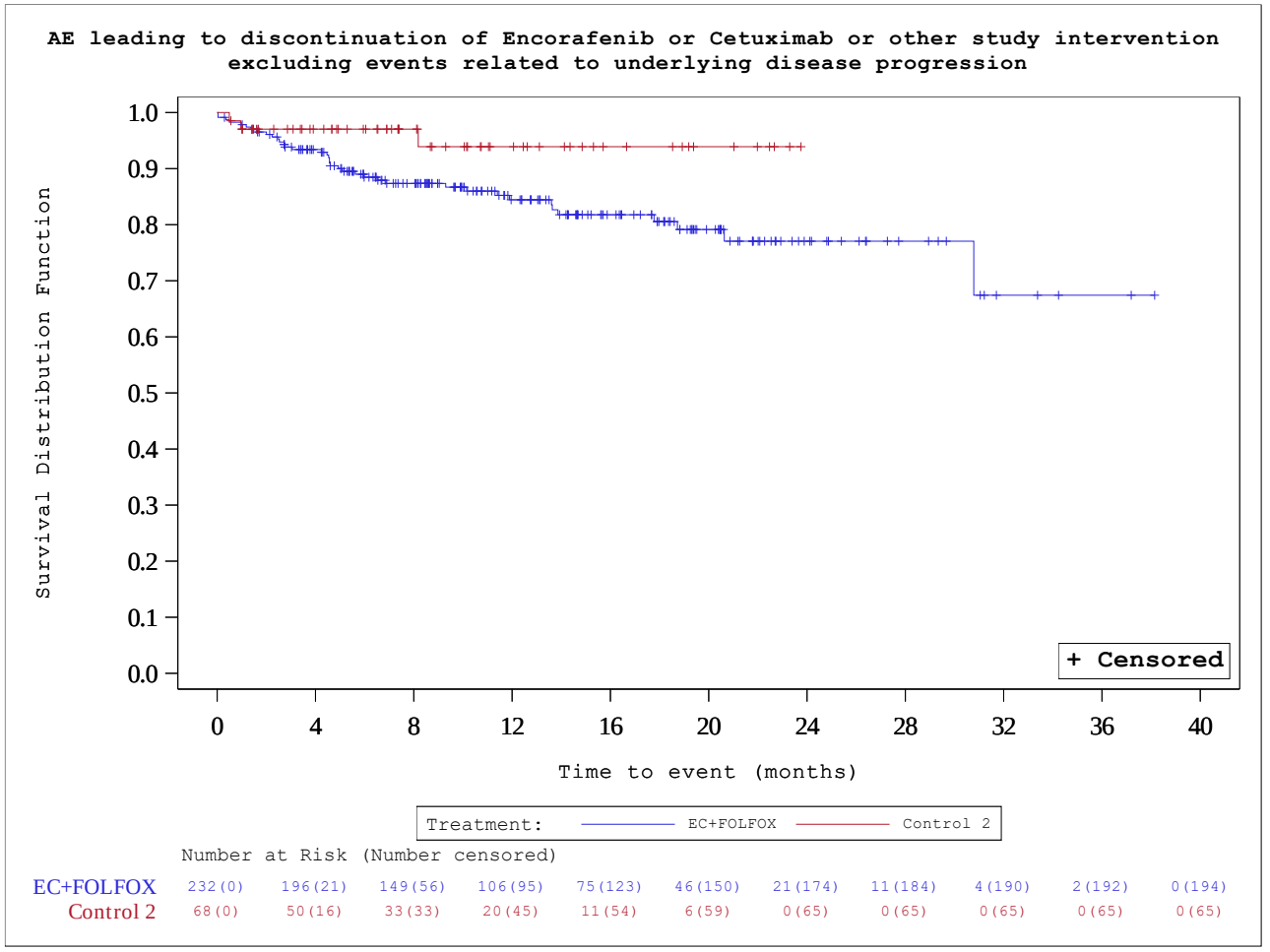
Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
AE leading to discontinuation of Encorafenib or Cetuximab or other study intervention excluding events related to underlying disease progression - Subgroup analysis
Safety Analysis Set

Subgroup Level	EC+FOLFOX (N=232) n/ N (%)	EC+FOLFOX (N=232) Median (95% CI)[1]	Control 2 (N=68) n/ N (%)	Control 2 (N=68) Median (95% CI)[1]	Unstratified analysis Hazard Ratio (95% CI)[2]	Unstratified analysis p-Value[3]	Interaction p-Value[4]
Age (Years)							0.6780
< 65	21/ 148 (14.2)	NE (NE , NE)	2/ 42 (4.8)	NE (NE , NE)	2.47 (0.58, 10.55)	0.2061	
>= 65	17/ 84 (20.2)	NE (30.8, NE)	1/ 26 (3.8)	NE (NE , NE)	3.94 (0.52, 29.87)	0.1520	
Sex							0.4588
Male	20/ 121 (16.5)	NE (30.8, NE)	2/ 32 (6.3)	NE (NE , NE)	1.93 (0.45, 8.29)	0.3700	
Female	18/ 111 (16.2)	NE (NE , NE)	1/ 36 (2.8)	NE (NE , NE)	5.04 (0.67, 37.84)	0.0803	
Region							0.9527
Europe	17/ 108 (15.7)	NE (30.8, NE)	2/ 38 (5.3)	NE (NE , NE)	2.17 (0.50, 9.51)	0.2923	
USA/Canada	2/ 15 (13.3)	NE (NE , NE)	0/ 7 (0.0)	NE (NE , NE)	NE		
Rest of World	19/ 109 (17.4)	NE (NE , NE)	1/ 23 (4.3)	NE (NE , NE)	3.27 (0.44, 24.47)	0.2222	
ECOG-PS at Randomization							0.2700
0	21/ 130 (16.2)	NE (30.8, NE)	1/ 44 (2.3)	NE (NE , NE)	5.68 (0.76, 42.32)	0.0556	
1	17/ 102 (16.7)	NE (NE , NE)	2/ 24 (8.3)	NE (NE , NE)	1.59 (0.36, 6.91)	0.5362	
Number of Organs Involved							0.9860
<= 2	22/ 116 (19.0)	NE (30.8, NE)	0/ 33 (0.0)	NE (NE , NE)	NE		
>= 3	16/ 116 (13.8)	NE (NE , NE)	3/ 35 (8.6)	NE (NE , NE)	1.13 (0.33, 3.94)	0.8425	
Presence of Liver Metastases							0.9882
Yes	22/ 146 (15.1)	NE (NE , NE)	3/ 42 (7.1)	NE (NE , NE)	1.63 (0.48, 5.45)	0.4266	
No	16/ 86 (18.6)	NE (30.8, NE)	0/ 26 (0.0)	NE (NE , NE)	NE		
Side of Tumor							0.7690
Left	13/ 88 (14.8)	NE (NE , NE)	1/ 33 (3.0)	NE (NE , NE)	3.83 (0.50, 29.39)	0.1644	
Right	25/ 144 (17.4)	NE (30.8, NE)	2/ 35 (5.7)	NE (NE , NE)	2.51 (0.59, 10.62)	0.1959	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.
[4] P-Value for interaction from Cox proportional hazards model using ties=exact option with treatment, subgroup and treatment*subgroup interaction as covariates.
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Kaplan Meier Plot of AE leading to discontinuation of Encorafenib or Cetuximab or other study intervention excluding events related to underlying disease progression
Safety Analysis Set



Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
Kaplan-Meier Plots for subgroups only created if p-value for interaction < 0.05.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
AE leading to death
Safety Analysis Set

	EC+FOLFOX (N=232)	Control 2 (N=68)
Number of subjects with events, n (%)	10 (4.3)	1 (1.5)
Number of censored subjects, n (%)	222 (95.7)	67 (98.5)
Kaplan-Meier estimates of Time to Event (months) [1]		
25%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
Unstratified analysis		
Hazard Ratio (95% CI) [2]	2.27 (0.29, 17.78)	
p-value [3]	0.4228	

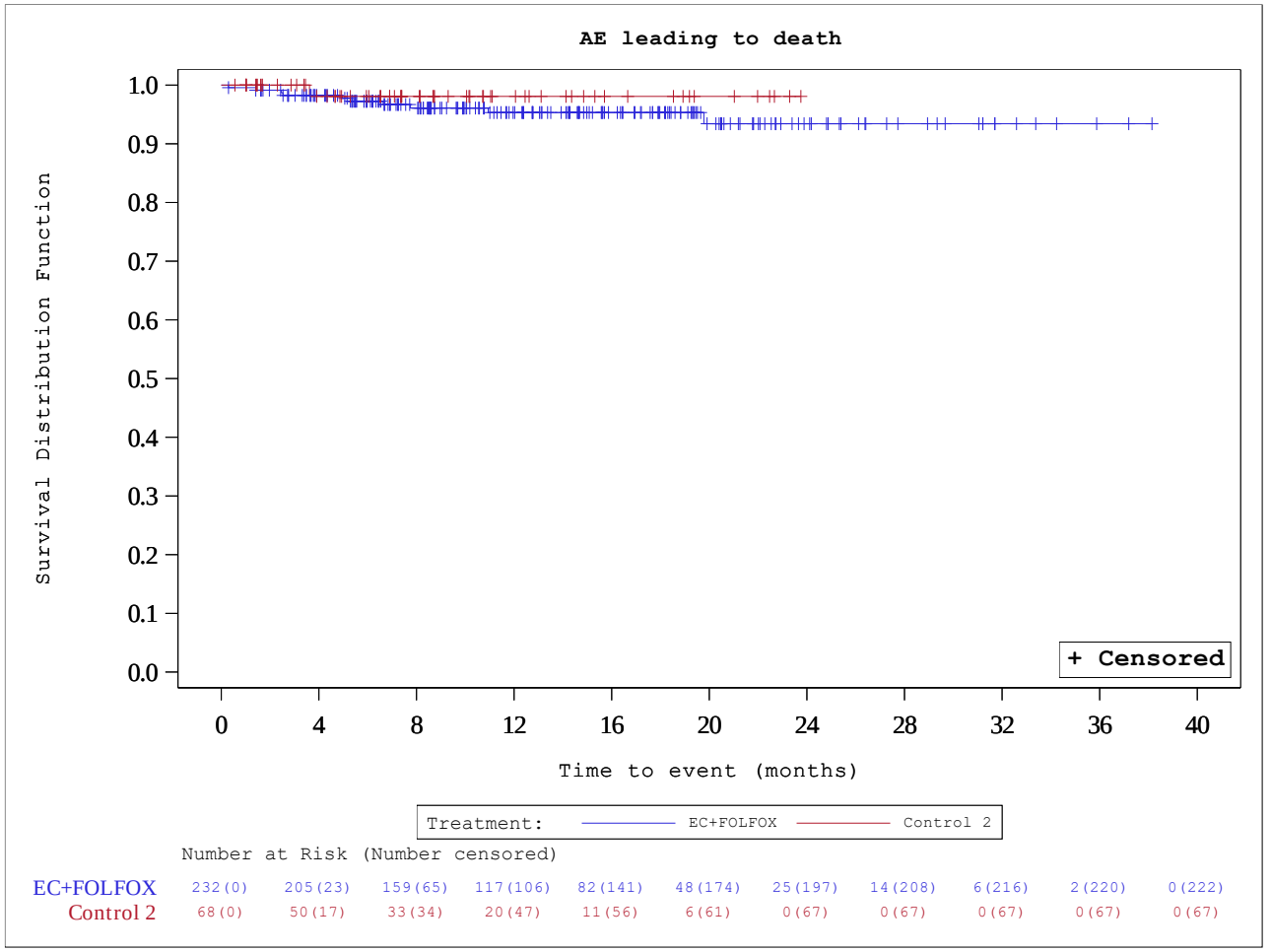
Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
AE leading to death - Subgroup analysis
Safety Analysis Set

Subgroup Level	EC+FOLFOX (N=232) n/ N (%)	EC+FOLFOX (N=232) Median (95% CI)[1]	Control 2 (N=68) n/ N (%)	Control 2 (N=68) Median (95% CI)[1]	Unstratified analysis Hazard Ratio (95% CI)[2]	Unstratified analysis p-Value[3]	Interaction p-Value[4]
Age (Years)							
< 65	5/ 148 (3.4)		0/ 42 (0.0)				
>= 65	5/ 84 (6.0)		1/ 26 (3.8)				
Sex							
Male	6/ 121 (5.0)		0/ 32 (0.0)				
Female	4/ 111 (3.6)		1/ 36 (2.8)				
Region							
Europe	5/ 108 (4.6)		0/ 38 (0.0)				
USA/Canada	1/ 15 (6.7)		0/ 7 (0.0)				
Rest of World	4/ 109 (3.7)		1/ 23 (4.3)				
ECOG-PS at Randomization							
0	6/ 130 (4.6)		0/ 44 (0.0)				
1	4/ 102 (3.9)		1/ 24 (4.2)				
Number of Organs Involved							
<= 2	2/ 116 (1.7)		0/ 33 (0.0)				
>= 3	8/ 116 (6.9)		1/ 35 (2.9)				
Presence of Liver Metastases							
Yes	7/ 146 (4.8)		1/ 42 (2.4)				
No	3/ 86 (3.5)		0/ 26 (0.0)				
Side of Tumor							
Left	5/ 88 (5.7)		0/ 33 (0.0)				
Right	5/ 144 (3.5)		1/ 35 (2.9)				

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.
[4] P-Value for interaction from Cox proportional hazards model using ties=exact option with treatment, subgroup and treatment*subgroup interaction as covariates.
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Kaplan Meier Plot of AE leading to death
Safety Analysis Set



Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
Kaplan-Meier Plots for subgroups only created if p-value for interaction < 0.05.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
AE leading to death excluding events related to underlying disease progression
Safety Analysis Set

	EC+FOLFOX (N=232)	Control 2 (N=68)
Number of subjects with events, n (%)	0 (0.0)	0 (0.0)
Number of censored subjects, n (%)	232 (100.0)	68 (100.0)
Kaplan-Meier estimates of Time to Event (months) [1]		
25%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
Unstratified analysis		
Hazard Ratio (95% CI) [2]	NE	
p-value [3]		

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
AE leading to death excluding events related to underlying disease progression - Subgroup analysis
Safety Analysis Set

Subgroup Level	EC+FOLFOX (N=232) n/ N (%)	EC+FOLFOX (N=232) Median (95% CI)[1]	Control 2 (N=68) n/ N (%)	Control 2 (N=68) Median (95% CI)[1]	Unstratified analysis Hazard Ratio (95% CI)[2]	Unstratified analysis p-Value[3]	Interaction p-Value[4]
Age (Years)							
< 65	0/ 148 (0.0)		0/ 42 (0.0)				
>= 65	0/ 84 (0.0)		0/ 26 (0.0)				
Sex							
Male	0/ 121 (0.0)		0/ 32 (0.0)				
Female	0/ 111 (0.0)		0/ 36 (0.0)				
Region							
Europe	0/ 108 (0.0)		0/ 38 (0.0)				
USA/Canada	0/ 15 (0.0)		0/ 7 (0.0)				
Rest of World	0/ 109 (0.0)		0/ 23 (0.0)				
ECOG-PS at Randomization							
0	0/ 130 (0.0)		0/ 44 (0.0)				
1	0/ 102 (0.0)		0/ 24 (0.0)				
Number of Organs Involved							
<= 2	0/ 116 (0.0)		0/ 33 (0.0)				
>= 3	0/ 116 (0.0)		0/ 35 (0.0)				
Presence of Liver Metastases							
Yes	0/ 146 (0.0)		0/ 42 (0.0)				
No	0/ 86 (0.0)		0/ 26 (0.0)				
Side of Tumor							
Left	0/ 88 (0.0)		0/ 33 (0.0)				
Right	0/ 144 (0.0)		0/ 35 (0.0)				

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.
[4] P-Value for interaction from Cox proportional hazards model using ties=exact option with treatment, subgroup and treatment*subgroup interaction as covariates.
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Kaplan Meier Plot of AE leading to death excluding events related to underlying disease progression
Safety Analysis Set

There are no events, hence no Surv plot is created.

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
Kaplan-Meier Plots for subgroups only created if p-value for interaction < 0.05.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Incidence of AE leading to discontinuation of Encorafenib by SOC, PT
Safety Analysis Set

System Organ Class (SOC) Preferred Term (PT)	EC+FOLFOX (N=232) n (%)	Control 2 (N=68) n (%)
Blood and lymphatic system disorders	1 (0.4)	0 (0.0)
Anaemia	1 (0.4)	0 (0.0)
Eye disorders	1 (0.4)	0 (0.0)
Orbital haematoma	1 (0.4)	0 (0.0)
Gastrointestinal disorders	8 (3.4)	0 (0.0)
Abdominal pain upper	1 (0.4)	0 (0.0)
Diarrhoea	1 (0.4)	0 (0.0)
Gastrointestinal perforation	1 (0.4)	0 (0.0)
Intestinal obstruction	2 (0.9)	0 (0.0)
Large intestine perforation	1 (0.4)	0 (0.0)
Nausea	1 (0.4)	0 (0.0)
Vomiting	1 (0.4)	0 (0.0)
General disorders and administration site conditions	5 (2.2)	0 (0.0)
Asthenia	2 (0.9)	0 (0.0)
Disease progression	3 (1.3)	0 (0.0)
Mucosal inflammation	1 (0.4)	0 (0.0)
Hepatobiliary disorders	1 (0.4)	0 (0.0)
Jaundice	1 (0.4)	0 (0.0)
Immune system disorders	2 (0.9)	0 (0.0)
Hypersensitivity	2 (0.9)	0 (0.0)
Infections and infestations	4 (1.7)	0 (0.0)
Abdominal sepsis	1 (0.4)	0 (0.0)
COVID-19	1 (0.4)	0 (0.0)
Peritonitis	1 (0.4)	0 (0.0)
Pneumonia	1 (0.4)	0 (0.0)
Sepsis	1 (0.4)	0 (0.0)
Septic shock	1 (0.4)	0 (0.0)
Injury, poisoning and procedural complications	1 (0.4)	0 (0.0)
Infusion related reaction	1 (0.4)	0 (0.0)
Investigations	6 (2.6)	0 (0.0)
Lipase increased	5 (2.2)	0 (0.0)
Weight decreased	1 (0.4)	0 (0.0)
Metabolism and nutrition disorders	2 (0.9)	0 (0.0)
Decreased appetite	1 (0.4)	0 (0.0)
Hyperlipasaemia	1 (0.4)	0 (0.0)
Musculoskeletal and connective tissue disorders	2 (0.9)	0 (0.0)
Arthralgia	1 (0.4)	0 (0.0)
Joint stiffness	1 (0.4)	0 (0.0)
Myalgia	1 (0.4)	0 (0.0)
Temporomandibular pain and dysfunction syndrome	1 (0.4)	0 (0.0)
Nervous system disorders	4 (1.7)	0 (0.0)
Cerebrovascular accident	1 (0.4)	0 (0.0)
Lacunar infarction	1 (0.4)	0 (0.0)
Peripheral sensory neuropathy	2 (0.9)	0 (0.0)
Respiratory, thoracic and mediastinal disorders	2 (0.9)	0 (0.0)
Interstitial lung disease	1 (0.4)	0 (0.0)
Pneumonitis	1 (0.4)	0 (0.0)

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Incidence of AE leading to discontinuation of Encorafenib by SOC, PT
Safety Analysis Set

System Organ Class (SOC) Preferred Term (PT)	EC+FOLFOX (N=232) n (%)	Control 2 (N=68) n (%)
Skin and subcutaneous tissue disorders	3 (1.3)	0 (0.0)
Pruritus	1 (0.4)	0 (0.0)
Rash	1 (0.4)	0 (0.0)
Skin disorder	1 (0.4)	0 (0.0)

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Incidence of AE leading to discontinuation of Cetuximab by SOC, PT
Safety Analysis Set

System Organ Class (SOC) Preferred Term (PT)	EC+FOLFOX (N=232) n (%)	Control 2 (N=68) n (%)
Blood and lymphatic system disorders	2 (0.9)	0 (0.0)
Anaemia	2 (0.9)	0 (0.0)
Neutropenia	1 (0.4)	0 (0.0)
Eye disorders	1 (0.4)	0 (0.0)
Orbital haematoma	1 (0.4)	0 (0.0)
Gastrointestinal disorders	7 (3.0)	0 (0.0)
Abdominal pain upper	1 (0.4)	0 (0.0)
Gastrointestinal perforation	1 (0.4)	0 (0.0)
Intestinal obstruction	2 (0.9)	0 (0.0)
Large intestine perforation	1 (0.4)	0 (0.0)
Nausea	1 (0.4)	0 (0.0)
Vomiting	1 (0.4)	0 (0.0)
General disorders and administration site conditions	5 (2.2)	0 (0.0)
Asthenia	2 (0.9)	0 (0.0)
Disease progression	3 (1.3)	0 (0.0)
Mucosal inflammation	1 (0.4)	0 (0.0)
Hepatobiliary disorders	1 (0.4)	0 (0.0)
Jaundice	1 (0.4)	0 (0.0)
Immune system disorders	2 (0.9)	0 (0.0)
Hypersensitivity	2 (0.9)	0 (0.0)
Infections and infestations	5 (2.2)	0 (0.0)
Abdominal sepsis	1 (0.4)	0 (0.0)
COVID-19	1 (0.4)	0 (0.0)
Paronychia	1 (0.4)	0 (0.0)
Peritonitis	1 (0.4)	0 (0.0)
Pneumonia	1 (0.4)	0 (0.0)
Sepsis	1 (0.4)	0 (0.0)
Septic shock	1 (0.4)	0 (0.0)
Injury, poisoning and procedural complications	3 (1.3)	0 (0.0)
Infusion related reaction	3 (1.3)	0 (0.0)
Investigations	6 (2.6)	0 (0.0)
Lipase increased	5 (2.2)	0 (0.0)
Weight decreased	1 (0.4)	0 (0.0)
Metabolism and nutrition disorders	2 (0.9)	0 (0.0)
Decreased appetite	1 (0.4)	0 (0.0)
Hyperlipasaemia	1 (0.4)	0 (0.0)
Musculoskeletal and connective tissue disorders	2 (0.9)	0 (0.0)
Arthralgia	1 (0.4)	0 (0.0)
Joint stiffness	1 (0.4)	0 (0.0)
Myalgia	1 (0.4)	0 (0.0)
Temporomandibular pain and dysfunction syndrome	1 (0.4)	0 (0.0)
Nervous system disorders	4 (1.7)	0 (0.0)
Cerebrovascular accident	1 (0.4)	0 (0.0)
Lacunar infarction	1 (0.4)	0 (0.0)
Peripheral sensory neuropathy	2 (0.9)	0 (0.0)
Respiratory, thoracic and mediastinal disorders	2 (0.9)	0 (0.0)
Interstitial lung disease	1 (0.4)	0 (0.0)
Pneumonitis	1 (0.4)	0 (0.0)

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Incidence of AE leading to discontinuation of Cetuximab by SOC, PT
Safety Analysis Set

System Organ Class (SOC) Preferred Term (PT)	EC+FOLFOX (N=232) n (%)	Control 2 (N=68) n (%)
Skin and subcutaneous tissue disorders	3 (1.3)	0 (0.0)
Pruritus	1 (0.4)	0 (0.0)
Rash	1 (0.4)	0 (0.0)
Rash maculo-papular	1 (0.4)	0 (0.0)
Skin disorder	1 (0.4)	0 (0.0)

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Incidence of AE leading to discontinuation of other study intervention by SOC, PT
Safety Analysis Set

System Organ Class (SOC) Preferred Term (PT)	EC+FOLFOX (N=232) n (%)	Control 2 (N=68) n (%)
Blood and lymphatic system disorders	5 (2.2)	0 (0.0)
Anaemia	5 (2.2)	0 (0.0)
Cardiac disorders	1 (0.4)	1 (1.5)
Acute coronary syndrome	1 (0.4)	0 (0.0)
Palpitations	0 (0.0)	1 (1.5)
Eye disorders	1 (0.4)	0 (0.0)
Orbital haematoma	1 (0.4)	0 (0.0)
Gastrointestinal disorders	7 (3.0)	3 (4.4)
Abdominal pain	1 (0.4)	1 (1.5)
Diarrhoea	1 (0.4)	0 (0.0)
Gastrointestinal perforation	1 (0.4)	0 (0.0)
Ileus	0 (0.0)	1 (1.5)
Intestinal obstruction	2 (0.9)	1 (1.5)
Large intestine perforation	1 (0.4)	0 (0.0)
Nausea	2 (0.9)	0 (0.0)
General disorders and administration site conditions	16 (6.9)	0 (0.0)
Asthenia	6 (2.6)	0 (0.0)
Chest pain	1 (0.4)	0 (0.0)
Disease progression	3 (1.3)	0 (0.0)
Fatigue	2 (0.9)	0 (0.0)
Malaise	1 (0.4)	0 (0.0)
Mucosal inflammation	1 (0.4)	0 (0.0)
Pyrexia	2 (0.9)	0 (0.0)
Infections and infestations	8 (3.4)	1 (1.5)
Abdominal infection	0 (0.0)	1 (1.5)
Abdominal sepsis	1 (0.4)	0 (0.0)
COVID-19	1 (0.4)	0 (0.0)
Cellulitis	1 (0.4)	0 (0.0)
Peritonitis	1 (0.4)	0 (0.0)
Pneumonia	1 (0.4)	0 (0.0)
Sepsis	2 (0.9)	0 (0.0)
Septic shock	1 (0.4)	0 (0.0)
Urinary tract infection	3 (1.3)	0 (0.0)
Injury, poisoning and procedural complications	1 (0.4)	1 (1.5)
Anastomotic complication	0 (0.0)	1 (1.5)
Infusion related reaction	1 (0.4)	0 (0.0)
Investigations	6 (2.6)	0 (0.0)
Lipase increased	1 (0.4)	0 (0.0)
Neutrophil count decreased	2 (0.9)	0 (0.0)
Platelet count decreased	3 (1.3)	0 (0.0)
Weight decreased	1 (0.4)	0 (0.0)
White blood cell count decreased	1 (0.4)	0 (0.0)
Metabolism and nutrition disorders	3 (1.3)	0 (0.0)
Decreased appetite	3 (1.3)	0 (0.0)
Musculoskeletal and connective tissue disorders	2 (0.9)	0 (0.0)
Arthralgia	1 (0.4)	0 (0.0)
Joint stiffness	1 (0.4)	0 (0.0)
Myalgia	1 (0.4)	0 (0.0)
Nervous system disorders	7 (3.0)	1 (1.5)
Cerebral haemorrhage	0 (0.0)	1 (1.5)

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.

System Organ Class (SOC) Preferred Term (PT)	EC+FOLFOX (N=232) n (%)	Control 2 (N=68) n (%)
Cerebrovascular accident	1 (0.4)	0 (0.0)
Lacunar infarction	1 (0.4)	0 (0.0)
Neuropathy peripheral	1 (0.4)	0 (0.0)
Paraesthesia	1 (0.4)	0 (0.0)
Peripheral sensory neuropathy	3 (1.3)	0 (0.0)
Respiratory, thoracic and mediastinal disorders	2 (0.9)	1 (1.5)
Interstitial lung disease	2 (0.9)	0 (0.0)
Pulmonary embolism	0 (0.0)	1 (1.5)
Respiratory failure	0 (0.0)	1 (1.5)
Skin and subcutaneous tissue disorders	2 (0.9)	0 (0.0)
Palmar-plantar erythrodysaesthesia syndrome	1 (0.4)	0 (0.0)
Skin disorder	1 (0.4)	0 (0.0)
Vascular disorders	1 (0.4)	0 (0.0)
Peripheral arterial occlusive disease	1 (0.4)	0 (0.0)

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Incidence of AE leading to discontinuation of Encorafenib or Cetuximab by SOC, PT
Safety Analysis Set

System Organ Class (SOC) Preferred Term (PT)	EC+FOLFOX (N=232) n (%)	Control 2 (N=68) n (%)
Blood and lymphatic system disorders	2 (0.9)	0 (0.0)
Anaemia	2 (0.9)	0 (0.0)
Neutropenia	1 (0.4)	0 (0.0)
Eye disorders	1 (0.4)	0 (0.0)
Orbital haematoma	1 (0.4)	0 (0.0)
Gastrointestinal disorders	8 (3.4)	0 (0.0)
Abdominal pain upper	1 (0.4)	0 (0.0)
Diarrhoea	1 (0.4)	0 (0.0)
Gastrointestinal perforation	1 (0.4)	0 (0.0)
Intestinal obstruction	2 (0.9)	0 (0.0)
Large intestine perforation	1 (0.4)	0 (0.0)
Nausea	1 (0.4)	0 (0.0)
Vomiting	1 (0.4)	0 (0.0)
General disorders and administration site conditions	5 (2.2)	0 (0.0)
Asthenia	2 (0.9)	0 (0.0)
Disease progression	3 (1.3)	0 (0.0)
Mucosal inflammation	1 (0.4)	0 (0.0)
Hepatobiliary disorders	1 (0.4)	0 (0.0)
Jaundice	1 (0.4)	0 (0.0)
Immune system disorders	3 (1.3)	0 (0.0)
Hypersensitivity	3 (1.3)	0 (0.0)
Infections and infestations	5 (2.2)	0 (0.0)
Abdominal sepsis	1 (0.4)	0 (0.0)
COVID-19	1 (0.4)	0 (0.0)
Paronychia	1 (0.4)	0 (0.0)
Peritonitis	1 (0.4)	0 (0.0)
Pneumonia	1 (0.4)	0 (0.0)
Sepsis	1 (0.4)	0 (0.0)
Septic shock	1 (0.4)	0 (0.0)
Injury, poisoning and procedural complications	3 (1.3)	0 (0.0)
Infusion related reaction	3 (1.3)	0 (0.0)
Investigations	6 (2.6)	0 (0.0)
Lipase increased	5 (2.2)	0 (0.0)
Weight decreased	1 (0.4)	0 (0.0)
Metabolism and nutrition disorders	2 (0.9)	0 (0.0)
Decreased appetite	1 (0.4)	0 (0.0)
Hyperlipasaemia	1 (0.4)	0 (0.0)
Musculoskeletal and connective tissue disorders	2 (0.9)	0 (0.0)
Arthralgia	1 (0.4)	0 (0.0)
Joint stiffness	1 (0.4)	0 (0.0)
Myalgia	1 (0.4)	0 (0.0)
Temporomandibular pain and dysfunction syndrome	1 (0.4)	0 (0.0)
Nervous system disorders	4 (1.7)	0 (0.0)
Cerebrovascular accident	1 (0.4)	0 (0.0)
Lacunar infarction	1 (0.4)	0 (0.0)
Peripheral sensory neuropathy	2 (0.9)	0 (0.0)
Respiratory, thoracic and mediastinal disorders	2 (0.9)	0 (0.0)
Interstitial lung disease	1 (0.4)	0 (0.0)

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.

System Organ Class (SOC) Preferred Term (PT)	EC+FOLFOX (N=232) n (%)	Control 2 (N=68) n (%)
Pneumonitis	1 (0.4)	0 (0.0)
Skin and subcutaneous tissue disorders	3 (1.3)	0 (0.0)
Pruritus	1 (0.4)	0 (0.0)
Rash	1 (0.4)	0 (0.0)
Rash maculo-papular	1 (0.4)	0 (0.0)
Skin disorder	1 (0.4)	0 (0.0)

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Frequent AE by SOC, PT (incidence >= 10% or >=10 patients and incidence >= 1%)
Safety Analysis Set

		EC+FOLFOX (N=232)	Control 2 (N=68)
SOC: Blood and lymphatic system disorders	Number of subjects with events, n (%)	145 (62.5)	30 (44.1)
	Number of censored subjects, n (%)	87 (37.5)	38 (55.9)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	1.0 (0.5, 1.8)	1.8 (1.0, 3.5)
	Median (95% CI)	4.4 (3.2, 6.3)	9.2 (3.5, NE)
	75%-ile (95% CI)	22.3 (15.6, NE)	NE (19.5, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	1.42 (0.96, 2.11)	
	p-value [3]	0.0776	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.

		EC+FOLFOX (N=232)	Control 2 (N=68)
SOC: Blood and lymphatic system disorders, PT: Anaemia	Number of subjects with events, n (%)	107 (46.1)	18 (26.5)
	Number of censored subjects, n (%)	125 (53.9)	50 (73.5)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	3.6 (2.7, 4.6)	6.3 (2.4, NE)
	Median (95% CI)	12.6 (7.6, 21.2)	NE (17.1, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	1.63 (0.99, 2.69)	
	p-value [3]	0.0519	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.

		EC+FOLFOX (N=232)	Control 2 (N=68)
SOC: Blood and lymphatic system disorders, PT: Neutropenia	Number of subjects with events, n (%)	56 (24.1)	18 (26.5)
	Number of censored subjects, n (%)	176 (75.9)	50 (73.5)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	26.7 (2.8, NE)	5.8 (2.3, NE)
	Median (95% CI)	NE (NE, NE)	NE (19.5, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	0.85 (0.50, 1.44)	
	p-value [3]	0.5283	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.

		EC+FOLFOX (N=232)	Control 2 (N=68)
SOC: Blood and lymphatic system disorders, PT: Thrombocytopenia	Number of subjects with events, n (%)	32 (13.8)	2 (2.9)
	Number of censored subjects, n (%)	200 (86.2)	66 (97.1)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Median (95% CI)	NE (NE, NE)	NE (NE, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	4.09 (0.98, 17.07)	
	p-value [3]	0.0362	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.

		EC+FOLFOX (N=232)	Control 2 (N=68)
SOC: Cardiac disorders	Number of subjects with events, n (%)	26 (11.2)	3 (4.4)
	Number of censored subjects, n (%)	206 (88.8)	65 (95.6)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Median (95% CI)	NE (NE, NE)	NE (NE, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	2.29 (0.69, 7.57)	
	p-value [3]	0.1634	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.

		EC+FOLFOX (N=232)	Control 2 (N=68)
SOC: Eye disorders	Number of subjects with events, n (%)	34 (14.7)	8 (11.8)
	Number of censored subjects, n (%)	198 (85.3)	60 (88.2)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	NE (20.5, NE)	NE (9.9, NE)
	Median (95% CI)	NE (NE, NE)	NE (NE, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	1.00 (0.46, 2.16)	
	p-value [3]	0.9912	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.

		EC+FOLFOX (N=232)	Control 2 (N=68)
SOC: Gastrointestinal disorders	Number of subjects with events, n (%)	202 (87.1)	62 (91.2)
	Number of censored subjects, n (%)	30 (12.9)	6 (8.8)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	0.1 (0.1, 0.1)	0.1 (0.0, 0.1)
	Median (95% CI)	0.5 (0.2, 0.5)	0.2 (0.1, 0.5)
	75%-ile (95% CI)	2.1 (1.2, 3.3)	1.2 (0.7, 3.3)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	0.79 (0.60, 1.06)	
	p-value [3]	0.1112	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.

		EC+FOLFOX (N=232)	Control 2 (N=68)
SOC: Gastrointestinal disorders, PT: Abdominal discomfort	Number of subjects with events, n (%)	10 (4.3)	1 (1.5)
	Number of censored subjects, n (%)	222 (95.7)	67 (98.5)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Median (95% CI)	NE (NE, NE)	NE (NE, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	2.11 (0.27, 16.75)	
	p-value [3]	0.4681	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.

		EC+FOLFOX (N=232)	Control 2 (N=68)
SOC: Gastrointestinal disorders, PT: Abdominal distension	Number of subjects with events, n (%)	14 (6.0)	3 (4.4)
	Number of censored subjects, n (%)	218 (94.0)	65 (95.6)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Median (95% CI)	NE (NE, NE)	NE (NE, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	1.16 (0.33, 4.04)	
	p-value [3]	0.8204	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Frequent AE by SOC, PT (incidence >= 10% or >=10 patients and incidence >= 1%)
Safety Analysis Set

		EC+FOLFOX (N=232)	Control 2 (N=68)
SOC: Gastrointestinal disorders, PT: Abdominal pain	Number of subjects with events, n (%)	47 (20.3)	15 (22.1)
	Number of censored subjects, n (%)	185 (79.7)	53 (77.9)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	25.2 (10.7, NE)	14.5 (4.1, NE)
	Median (95% CI)	NE (NE, NE)	NE (15.4, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	0.75 (0.42, 1.34)	
	p-value [3]	0.3275	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.

		EC+FOLFOX (N=232)	Control 2 (N=68)
SOC: Gastrointestinal disorders, PT: Abdominal pain upper	Number of subjects with events, n (%)	24 (10.3)	4 (5.9)
	Number of censored subjects, n (%)	208 (89.7)	64 (94.1)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Median (95% CI)	NE (NE, NE)	NE (NE, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	1.50 (0.52, 4.34)	
	p-value [3]	0.4508	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.

		EC+FOLFOX (N=232)	Control 2 (N=68)
SOC: Gastrointestinal disorders, PT: Constipation	Number of subjects with events, n (%)	63 (27.2)	20 (29.4)
	Number of censored subjects, n (%)	169 (72.8)	48 (70.6)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	8.4 (5.7, 17.4)	5.1 (0.7, NE)
	Median (95% CI)	NE (NE, NE)	NE (9.1, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	0.68 (0.41, 1.13)	
	p-value [3]	0.1383	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Frequent AE by SOC, PT (incidence >= 10% or >=10 patients and incidence >= 1%)
Safety Analysis Set

		EC+FOLFOX (N=232)	Control 2 (N=68)
SOC: Gastrointestinal disorders, PT: Diarrhoea	Number of subjects with events, n (%)	97 (41.8)	34 (50.0)
	Number of censored subjects, n (%)	135 (58.2)	34 (50.0)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	2.6 (1.4, 5.1)	1.3 (0.3, 3.3)
	Median (95% CI)	21.1 (11.0, NE)	6.7 (3.4, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (11.5, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	0.65 (0.44, 0.97)	
	p-value [3]	0.0320	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.

		EC+FOLFOX (N=232)	Control 2 (N=68)
SOC: Gastrointestinal disorders, PT: Gingival bleeding	Number of subjects with events, n (%)	10 (4.3)	0 (0.0)
	Number of censored subjects, n (%)	222 (95.7)	68 (100.0)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Median (95% CI)	NE (NE, NE)	NE (NE, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	NE	
	p-value [3]		

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.

		EC+FOLFOX (N=232)	Control 2 (N=68)
SOC: Gastrointestinal disorders, PT: Haemorrhoids	Number of subjects with events, n (%)	24 (10.3)	3 (4.4)
	Number of censored subjects, n (%)	208 (89.7)	65 (95.6)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	NE (30.9, NE)	NE (NE, NE)
	Median (95% CI)	NE (NE, NE)	NE (NE, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	1.96 (0.59, 6.55)	
	p-value [3]	0.2630	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.

		EC+FOLFOX (N=232)	Control 2 (N=68)
SOC: Gastrointestinal disorders, PT: Intestinal obstruction	Number of subjects with events, n (%)	13 (5.6)	6 (8.8)
	Number of censored subjects, n (%)	219 (94.4)	62 (91.2)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	NE (NE, NE)	NE (14.3, NE)
	Median (95% CI)	NE (NE, NE)	NE (NE, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	0.45 (0.17, 1.21)	
	p-value [3]	0.1054	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.

		EC+FOLFOX (N=232)	Control 2 (N=68)
SOC: Gastrointestinal disorders, PT: Nausea	Number of subjects with events, n (%)	125 (53.9)	40 (58.8)
	Number of censored subjects, n (%)	107 (46.1)	28 (41.2)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	0.1 (0.1, 0.5)	0.1 (0.1, 1.0)
	Median (95% CI)	5.3 (1.8, 17.5)	2.7 (1.4, 9.3)
	75%-ile (95% CI)	NE (NE, NE)	NE (7.1, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	0.81 (0.56, 1.15)	
	p-value [3]	0.2367	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.

		EC+FOLFOX (N=232)	Control 2 (N=68)
SOC: Gastrointestinal disorders, PT: Stomatitis	Number of subjects with events, n (%)	35 (15.1)	10 (14.7)
	Number of censored subjects, n (%)	197 (84.9)	58 (85.3)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	NE (20.1, NE)	17.0 (9.6, NE)
	Median (95% CI)	NE (NE, NE)	NE (17.0, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	0.88 (0.43, 1.77)	
	p-value [3]	0.7107	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.

		EC+FOLFOX (N=232)	Control 2 (N=68)
SOC: Gastrointestinal disorders, PT: Vomiting	Number of subjects with events, n (%)	84 (36.2)	22 (32.4)
	Number of censored subjects, n (%)	148 (63.8)	46 (67.6)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	1.8 (0.6, 4.4)	4.9 (1.6, 9.8)
	Median (95% CI)	NE (18.3, NE)	NE (9.2, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	1.11 (0.69, 1.78)	
	p-value [3]	0.6675	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Frequent AE by SOC, PT (incidence >= 10% or >=10 patients and incidence >= 1%)
Safety Analysis Set

		EC+FOLFOX (N=232)	Control 2 (N=68)
SOC: General disorders and administration site conditions	Number of subjects with events, n (%)	187 (80.6)	47 (69.1)
	Number of censored subjects, n (%)	45 (19.4)	21 (30.9)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	0.1 (0.1, 0.3)	0.1 (0.1, 0.5)
	Median (95% CI)	1.0 (0.5, 1.8)	1.7 (0.6, 2.7)
	75%-ile (95% CI)	5.4 (3.9, 11.6)	7.4 (2.7, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	1.11 (0.80, 1.53)	
	p-value [3]	0.5444	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.

		EC+FOLFOX (N=232)	Control 2 (N=68)
SOC: General disorders and administration site conditions, PT: Asthenia	Number of subjects with events, n (%)	68 (29.3)	8 (11.8)
	Number of censored subjects, n (%)	164 (70.7)	60 (88.2)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	5.1 (2.9, 20.6)	NE (NE, NE)
	Median (95% CI)	NE (NE, NE)	NE (NE, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	2.45 (1.18, 5.11)	
	p-value [3]	0.0131	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Frequent AE by SOC, PT (incidence >= 10% or >=10 patients and incidence >= 1%)
Safety Analysis Set

		EC+FOLFOX (N=232)	Control 2 (N=68)
SOC: General disorders and administration site conditions, PT: Chest pain	Number of subjects with events, n (%)	10 (4.3)	5 (7.4)
	Number of censored subjects, n (%)	222 (95.7)	63 (92.6)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Median (95% CI)	NE (NE, NE)	NE (NE, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	0.46 (0.16, 1.36)	
	p-value [3]	0.1500	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Frequent AE by SOC, PT (incidence >= 10% or >=10 patients and incidence >= 1%)
Safety Analysis Set

		EC+FOLFOX (N=232)	Control 2 (N=68)
SOC: General disorders and administration site conditions, PT: Fatigue	Number of subjects with events, n (%)	61 (26.3)	27 (39.7)
	Number of censored subjects, n (%)	171 (73.7)	41 (60.3)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	7.4 (2.2, NE)	1.5 (0.5, 4.6)
	Median (95% CI)	NE (NE, NE)	NE (4.6, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	0.56 (0.36, 0.89)	
	p-value [3]	0.0121	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.

		EC+FOLFOX (N=232)	Control 2 (N=68)
SOC: General disorders and administration site conditions, PT: Malaise	Number of subjects with events, n (%)	20 (8.6)	6 (8.8)
	Number of censored subjects, n (%)	212 (91.4)	62 (91.2)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Median (95% CI)	NE (NE, NE)	NE (NE, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	0.86 (0.34, 2.14)	
	p-value [3]	0.7474	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Frequent AE by SOC, PT (incidence >= 10% or >=10 patients and incidence >= 1%)
Safety Analysis Set

		EC+FOLFOX (N=232)	Control 2 (N=68)
SOC: General disorders and administration site conditions, PT: Mucosal inflammation	Number of subjects with events, n (%)	34 (14.7)	9 (13.2)
	Number of censored subjects, n (%)	198 (85.3)	59 (86.8)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Median (95% CI)	NE (NE, NE)	NE (NE, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	1.02 (0.49, 2.12)	
	p-value [3]	0.9693	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.

		EC+FOLFOX (N=232)	Control 2 (N=68)
SOC: General disorders and administration site conditions, PT: Oedema peripheral	Number of subjects with events, n (%)	16 (6.9)	4 (5.9)
	Number of censored subjects, n (%)	216 (93.1)	64 (94.1)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Median (95% CI)	NE (NE, NE)	NE (NE, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	0.91 (0.30, 2.73)	
	p-value [3]	0.8628	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Frequent AE by SOC, PT (incidence >= 10% or >=10 patients and incidence >= 1%)
Safety Analysis Set

		EC+FOLFOX (N=232)	Control 2 (N=68)
SOC: General disorders and administration site conditions, PT: Pain	Number of subjects with events, n (%)	19 (8.2)	4 (5.9)
	Number of censored subjects, n (%)	213 (91.8)	64 (94.1)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Median (95% CI)	NE (NE, NE)	NE (NE, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	1.11 (0.38, 3.28)	
	p-value [3]	0.8487	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.

		EC+FOLFOX (N=232)	Control 2 (N=68)
SOC: General disorders and administration site conditions, PT: Pyrexia	Number of subjects with events, n (%)	67 (28.9)	6 (8.8)
	Number of censored subjects, n (%)	165 (71.1)	62 (91.2)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	7.5 (4.1, 15.5)	NE (12.5, NE)
	Median (95% CI)	NE (26.7, NE)	NE (NE, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	3.10 (1.35, 7.16)	
	p-value [3]	0.0051	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.

		EC+FOLFOX (N=232)	Control 2 (N=68)
SOC: Hepatobiliary disorders	Number of subjects with events, n (%)	17 (7.3)	3 (4.4)
	Number of censored subjects, n (%)	215 (92.7)	65 (95.6)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Median (95% CI)	NE (NE, NE)	NE (NE, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	1.42 (0.41, 4.84)	
	p-value [3]	0.5759	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.

		EC+FOLFOX (N=232)	Control 2 (N=68)
SOC: Immune system disorders	Number of subjects with events, n (%)	25 (10.8)	1 (1.5)
	Number of censored subjects, n (%)	207 (89.2)	67 (98.5)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	29.9 (25.3, NE)	NE (NE, NE)
	Median (95% CI)	NE (29.9, NE)	NE (NE, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	5.81 (0.78, 43.09)	
	p-value [3]	0.0511	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.

		EC+FOLFOX (N=232)	Control 2 (N=68)
SOC: Immune system disorders, PT: Drug hypersensitivity	Number of subjects with events, n (%)	11 (4.7)	1 (1.5)
	Number of censored subjects, n (%)	221 (95.3)	67 (98.5)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	NE (29.9, NE)	NE (NE, NE)
	Median (95% CI)	NE (NE, NE)	NE (NE, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	2.26 (0.29, 17.86)	
	p-value [3]	0.4260	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.

		EC+FOLFOX (N=232)	Control 2 (N=68)
SOC: Infections and infestations	Number of subjects with events, n (%)	123 (53.0)	30 (44.1)
	Number of censored subjects, n (%)	109 (47.0)	38 (55.9)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	2.7 (2.1, 3.7)	2.9 (1.5, 5.0)
	Median (95% CI)	9.5 (7.4, 14.1)	7.7 (5.0, NE)
	75%-ile (95% CI)	NE (19.8, NE)	NE (10.8, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	0.94 (0.63, 1.40)	
	p-value [3]	0.7461	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.

		EC+FOLFOX (N=232)	Control 2 (N=68)
SOC: Infections and infestations, PT: COVID-19	Number of subjects with events, n (%)	34 (14.7)	3 (4.4)
	Number of censored subjects, n (%)	198 (85.3)	65 (95.6)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	26.2 (23.2, NE)	NE (NE, NE)
	Median (95% CI)	NE (NE, NE)	NE (NE, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	2.59 (0.79, 8.46)	
	p-value [3]	0.1015	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.

		EC+FOLFOX (N=232)	Control 2 (N=68)
SOC: Infections and infestations, PT: Nasopharyngitis	Number of subjects with events, n (%)	12 (5.2)	5 (7.4)
	Number of censored subjects, n (%)	220 (94.8)	63 (92.6)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Median (95% CI)	NE (NE, NE)	NE (NE, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	0.48 (0.17, 1.40)	
	p-value [3]	0.1723	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.

		EC+FOLFOX (N=232)	Control 2 (N=68)
SOC: Infections and infestations, PT: Paronychia	Number of subjects with events, n (%)	20 (8.6)	2 (2.9)
	Number of censored subjects, n (%)	212 (91.4)	66 (97.1)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	NE (22.7, NE)	NE (NE, NE)
	Median (95% CI)	NE (NE, NE)	NE (NE, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	2.15 (0.50, 9.25)	
	p-value [3]	0.2919	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.

		EC+FOLFOX (N=232)	Control 2 (N=68)
SOC: Infections and infestations, PT: Upper respiratory tract infection	Number of subjects with events, n (%)	16 (6.9)	2 (2.9)
	Number of censored subjects, n (%)	216 (93.1)	66 (97.1)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Median (95% CI)	NE (NE, NE)	NE (NE, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	1.70 (0.39, 7.43)	
	p-value [3]	0.4751	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.

		EC+FOLFOX (N=232)	Control 2 (N=68)
SOC: Infections and infestations, PT: Urinary tract infection	Number of subjects with events, n (%)	23 (9.9)	7 (10.3)
	Number of censored subjects, n (%)	209 (90.1)	61 (89.7)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	26.5 (25.4, NE)	21.7 (21.7, NE)
	Median (95% CI)	NE (30.0, NE)	NE (21.7, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	0.65 (0.27, 1.54)	
	p-value [3]	0.3188	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Frequent AE by SOC, PT (incidence >= 10% or >=10 patients and incidence >= 1%)
Safety Analysis Set

		EC+FOLFOX (N=232)	Control 2 (N=68)
SOC: Injury, poisoning and procedural complications	Number of subjects with events, n (%)	45 (19.4)	15 (22.1)
	Number of censored subjects, n (%)	187 (80.6)	53 (77.9)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	22.9 (12.0, NE)	12.0 (10.7, 17.1)
	Median (95% CI)	NE (NE, NE)	17.1 (13.8, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	0.64 (0.36, 1.16)	
	p-value [3]	0.1388	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.

		EC+FOLFOX (N=232)	Control 2 (N=68)
SOC: Injury, poisoning and procedural complications, PT: Fall	Number of subjects with events, n (%)	11 (4.7)	2 (2.9)
	Number of censored subjects, n (%)	221 (95.3)	66 (97.1)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	NE (29.8, NE)	NE (NE, NE)
	Median (95% CI)	NE (NE, NE)	NE (NE, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	1.21 (0.27, 5.55)	
	p-value [3]	0.8021	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Frequent AE by SOC, PT (incidence >= 10% or >=10 patients and incidence >= 1%)
Safety Analysis Set

		EC+FOLFOX (N=232)	Control 2 (N=68)
SOC: Injury, poisoning and procedural complications, PT: Infusion related reaction	Number of subjects with events, n (%)	16 (6.9)	1 (1.5)
	Number of censored subjects, n (%)	216 (93.1)	67 (98.5)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Median (95% CI)	NE (NE, NE)	NE (NE, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	4.15 (0.55, 31.29)	
	p-value [3]	0.1333	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Frequent AE by SOC, PT (incidence >= 10% or >=10 patients and incidence >= 1%)
Safety Analysis Set

		EC+FOLFOX (N=232)	Control 2 (N=68)
SOC: Investigations	Number of subjects with events, n (%)	164 (70.7)	36 (52.9)
	Number of censored subjects, n (%)	68 (29.3)	32 (47.1)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	0.5 (0.5, 0.5)	0.8 (0.5, 2.3)
	Median (95% CI)	1.4 (0.9, 2.4)	6.9 (2.3, 19.5)
	75%-ile (95% CI)	18.9 (6.2, NE)	NE (11.3, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	1.54 (1.07, 2.21)	
	p-value [3]	0.0184	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.

		EC+FOLFOX (N=232)	Control 2 (N=68)
SOC: Investigations, PT: Alanine aminotransferase increased	Number of subjects with events, n (%)	29 (12.5)	8 (11.8)
	Number of censored subjects, n (%)	203 (87.5)	60 (88.2)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	NE (NE, NE)	NE (10.2, NE)
	Median (95% CI)	NE (NE, NE)	NE (NE, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	1.00 (0.45, 2.18)	
	p-value [3]	0.9907	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.

		EC+FOLFOX (N=232)	Control 2 (N=68)
SOC: Investigations, PT: Aspartate aminotransferase increased	Number of subjects with events, n (%)	31 (13.4)	10 (14.7)
	Number of censored subjects, n (%)	201 (86.6)	58 (85.3)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	NE (NE, NE)	NE (7.0, NE)
	Median (95% CI)	NE (NE, NE)	NE (NE, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	0.84 (0.41, 1.72)	
	p-value [3]	0.6415	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.

		EC+FOLFOX (N=232)	Control 2 (N=68)
SOC: Investigations, PT: Blood alkaline phosphatase increased	Number of subjects with events, n (%)	16 (6.9)	2 (2.9)
	Number of censored subjects, n (%)	216 (93.1)	66 (97.1)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	NE (NE, NE)	NE (16.4, NE)
	Median (95% CI)	NE (NE, NE)	NE (NE, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	1.96 (0.45, 8.55)	
	p-value [3]	0.3608	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.

		EC+FOLFOX (N=232)	Control 2 (N=68)
SOC: Investigations, PT: Electrocardiogram QT prolonged	Number of subjects with events, n (%)	11 (4.7)	0 (0.0)
	Number of censored subjects, n (%)	221 (95.3)	68 (100.0)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Median (95% CI)	NE (NE, NE)	NE (NE, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	NE	
	p-value [3]		

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.

		EC+FOLFOX (N=232)	Control 2 (N=68)
SOC: Investigations, PT: Lipase increased	Number of subjects with events, n (%)	52 (22.4)	4 (5.9)
	Number of censored subjects, n (%)	180 (77.6)	64 (94.1)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	NE (3.4, NE)	NE (NE, NE)
	Median (95% CI)	NE (NE, NE)	NE (NE, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	3.86 (1.40, 10.68)	
	p-value [3]	0.0050	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.

		EC+FOLFOX (N=232)	Control 2 (N=68)
SOC: Investigations, PT: Lymphocyte count decreased	Number of subjects with events, n (%)	11 (4.7)	2 (2.9)
	Number of censored subjects, n (%)	221 (95.3)	66 (97.1)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Median (95% CI)	NE (NE, NE)	NE (NE, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	1.51 (0.33, 6.81)	
	p-value [3]	0.5901	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.

		EC+FOLFOX (N=232)	Control 2 (N=68)
SOC: Investigations, PT: Neutrophil count decreased	Number of subjects with events, n (%)	79 (34.1)	20 (29.4)
	Number of censored subjects, n (%)	153 (65.9)	48 (70.6)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	1.8 (0.6, 4.8)	2.8 (0.5, NE)
	Median (95% CI)	NE (NE, NE)	NE (19.5, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (19.5, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	1.09 (0.67, 1.79)	
	p-value [3]	0.7245	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Frequent AE by SOC, PT (incidence >= 10% or >=10 patients and incidence >= 1%)
Safety Analysis Set

		EC+FOLFOX (N=232)	Control 2 (N=68)
SOC: Investigations, PT: Platelet count decreased	Number of subjects with events, n (%)	53 (22.8)	4 (5.9)
	Number of censored subjects, n (%)	179 (77.2)	64 (94.1)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	25.5 (4.0, NE)	NE (NE, NE)
	Median (95% CI)	NE (NE, NE)	NE (NE, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	3.65 (1.32, 10.10)	
	p-value [3]	0.0075	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.

		EC+FOLFOX (N=232)	Control 2 (N=68)
SOC: Investigations, PT: Weight decreased	Number of subjects with events, n (%)	44 (19.0)	9 (13.2)
	Number of censored subjects, n (%)	188 (81.0)	59 (86.8)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	NE (9.4, NE)	NE (10.6, NE)
	Median (95% CI)	NE (NE, NE)	NE (NE, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	1.34 (0.66, 2.75)	
	p-value [3]	0.4170	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.

		EC+FOLFOX (N=232)	Control 2 (N=68)
SOC: Investigations, PT: White blood cell count decreased	Number of subjects with events, n (%)	43 (18.5)	14 (20.6)
	Number of censored subjects, n (%)	189 (81.5)	54 (79.4)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	NE (NE, NE)	19.5 (3.3, NE)
	Median (95% CI)	NE (NE, NE)	NE (19.5, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	0.86 (0.47, 1.56)	
	p-value [3]	0.6099	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.

		EC+FOLFOX (N=232)	Control 2 (N=68)
SOC: Metabolism and nutrition disorders	Number of subjects with events, n (%)	144 (62.1)	37 (54.4)
	Number of censored subjects, n (%)	88 (37.9)	31 (45.6)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	0.5 (0.4, 0.7)	1.4 (0.6, 4.4)
	Median (95% CI)	3.4 (2.1, 4.8)	7.4 (4.8, 12.1)
	75%-ile (95% CI)	24.3 (22.3, NE)	13.6 (9.2, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	1.17 (0.81, 1.68)	
	p-value [3]	0.4112	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.

		EC+FOLFOX (N=232)	Control 2 (N=68)
SOC: Metabolism and nutrition disorders, PT: Decreased appetite	Number of subjects with events, n (%)	87 (37.5)	23 (33.8)
	Number of censored subjects, n (%)	145 (62.5)	45 (66.2)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	1.1 (0.5, 3.7)	3.8 (1.0, 7.8)
	Median (95% CI)	24.3 (22.3, NE)	NE (7.4, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	1.04 (0.65, 1.65)	
	p-value [3]	0.8762	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Frequent AE by SOC, PT (incidence >= 10% or >=10 patients and incidence >= 1%)
Safety Analysis Set

		EC+FOLFOX (N=232)	Control 2 (N=68)
SOC: Metabolism and nutrition disorders, PT: Hyperglycaemia	Number of subjects with events, n (%)	20 (8.6)	3 (4.4)
	Number of censored subjects, n (%)	212 (91.4)	65 (95.6)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Median (95% CI)	NE (NE, NE)	NE (NE, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	1.67 (0.49, 5.63)	
	p-value [3]	0.4037	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.

		EC+FOLFOX (N=232)	Control 2 (N=68)
SOC: Metabolism and nutrition disorders, PT: Hypoalbuminaemia	Number of subjects with events, n (%)	30 (12.9)	2 (2.9)
	Number of censored subjects, n (%)	202 (87.1)	66 (97.1)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Median (95% CI)	NE (NE, NE)	NE (NE, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	4.12 (0.98, 17.23)	
	p-value [3]	0.0355	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.

		EC+FOLFOX (N=232)	Control 2 (N=68)
SOC: Metabolism and nutrition disorders, PT: Hypocalcaemia	Number of subjects with events, n (%)	11 (4.7)	1 (1.5)
	Number of censored subjects, n (%)	221 (95.3)	67 (98.5)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Median (95% CI)	NE (NE, NE)	NE (NE, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	3.01 (0.39, 23.29)	
	p-value [3]	0.2677	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.

		EC+FOLFOX (N=232)	Control 2 (N=68)
SOC: Metabolism and nutrition disorders, PT: Hypokalaemia	Number of subjects with events, n (%)	41 (17.7)	11 (16.2)
	Number of censored subjects, n (%)	191 (82.3)	57 (83.8)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	NE (16.8, NE)	NE (7.3, NE)
	Median (95% CI)	NE (NE, NE)	NE (NE, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	0.94 (0.48, 1.84)	
	p-value [3]	0.8600	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.

		EC+FOLFOX (N=232)	Control 2 (N=68)
SOC: Metabolism and nutrition disorders, PT: Hypomagnesaemia	Number of subjects with events, n (%)	38 (16.4)	0 (0.0)
	Number of censored subjects, n (%)	194 (83.6)	68 (100.0)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	NE (20.7, NE)	NE (NE, NE)
	Median (95% CI)	NE (NE, NE)	NE (NE, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	NE	
	p-value [3]		

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.

		EC+FOLFOX (N=232)	Control 2 (N=68)
SOC: Metabolism and nutrition disorders, PT: Hyponatraemia	Number of subjects with events, n (%)	11 (4.7)	5 (7.4)
	Number of censored subjects, n (%)	221 (95.3)	63 (92.6)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Median (95% CI)	NE (NE, NE)	NE (NE, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	0.58 (0.20, 1.66)	
	p-value [3]	0.3027	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.

		EC+FOLFOX (N=232)	Control 2 (N=68)
SOC: Metabolism and nutrition disorders, PT: Hypophosphataemia	Number of subjects with events, n (%)	14 (6.0)	3 (4.4)
	Number of censored subjects, n (%)	218 (94.0)	65 (95.6)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Median (95% CI)	NE (NE, NE)	NE (NE, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	1.24 (0.35, 4.30)	
	p-value [3]	0.7403	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.

		EC+FOLFOX (N=232)	Control 2 (N=68)
SOC: Musculoskeletal and connective tissue disorders	Number of subjects with events, n (%)	133 (57.3)	19 (27.9)
	Number of censored subjects, n (%)	99 (42.7)	49 (72.1)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	2.6 (1.8, 3.3)	5.1 (1.5, NE)
	Median (95% CI)	8.6 (6.6, 11.3)	NE (NE, NE)
	75%-ile (95% CI)	NE (16.5, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	2.02 (1.25, 3.27)	
	p-value [3]	0.0034	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.

		EC+FOLFOX (N=232)	Control 2 (N=68)
SOC: Musculoskeletal and connective tissue disorders, PT: Arthralgia	Number of subjects with events, n (%)	73 (31.5)	3 (4.4)
	Number of censored subjects, n (%)	159 (68.5)	65 (95.6)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	8.5 (6.4, 11.3)	NE (NE, NE)
	Median (95% CI)	NE (18.9, NE)	NE (NE, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	6.50 (2.05, 20.63)	
	p-value [3]	0.0002	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Frequent AE by SOC, PT (incidence >= 10% or >=10 patients and incidence >= 1%)
Safety Analysis Set

		EC+FOLFOX (N=232)	Control 2 (N=68)
SOC: Musculoskeletal and connective tissue disorders, PT: Back pain	Number of subjects with events, n (%)	24 (10.3)	11 (16.2)
	Number of censored subjects, n (%)	208 (89.7)	57 (83.8)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	NE (27.2, NE)	NE (5.1, NE)
	Median (95% CI)	NE (NE, NE)	NE (NE, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	0.48 (0.23, 0.98)	
	p-value [3]	0.0397	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.

		EC+FOLFOX (N=232)	Control 2 (N=68)
SOC: Musculoskeletal and connective tissue disorders, PT: Myalgia	Number of subjects with events, n (%)	38 (16.4)	2 (2.9)
	Number of censored subjects, n (%)	194 (83.6)	66 (97.1)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	NE (13.1, NE)	NE (NE, NE)
	Median (95% CI)	NE (NE, NE)	NE (NE, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	4.77 (1.15, 19.78)	
	p-value [3]	0.0176	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.

		EC+FOLFOX (N=232)	Control 2 (N=68)
SOC: Musculoskeletal and connective tissue disorders, PT: Pain in extremity	Number of subjects with events, n (%)	21 (9.1)	2 (2.9)
	Number of censored subjects, n (%)	211 (90.9)	66 (97.1)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Median (95% CI)	NE (NE, NE)	NE (NE, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	2.64 (0.62, 11.30)	
	p-value [3]	0.1724	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.

		EC+FOLFOX (N=232)	Control 2 (N=68)
SOC: Neoplasms benign, malignant and unspecified (incl cysts and polyps)	Number of subjects with events, n (%)	43 (18.5)	3 (4.4)
	Number of censored subjects, n (%)	189 (81.5)	65 (95.6)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	NE (12.9, NE)	NE (NE, NE)
	Median (95% CI)	NE (NE, NE)	NE (NE, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	3.91 (1.21, 12.62)	
	p-value [3]	0.0137	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.

		EC+FOLFOX (N=232)	Control 2 (N=68)
SOC: Neoplasms benign, malignant and unspecified (incl cysts and polyps), PT: Melanocytic naevus	Number of subjects with events, n (%)	13 (5.6)	0 (0.0)
	Number of censored subjects, n (%)	219 (94.4)	68 (100.0)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Median (95% CI)	NE (NE, NE)	NE (NE, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	NE	
	p-value [3]		

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Frequent AE by SOC, PT (incidence >= 10% or >=10 patients and incidence >= 1%)
Safety Analysis Set

		EC+FOLFOX (N=232)	Control 2 (N=68)
SOC: Nervous system disorders	Number of subjects with events, n (%)	191 (82.3)	28 (41.2)
	Number of censored subjects, n (%)	41 (17.7)	40 (58.8)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	0.4 (0.2, 0.5)	1.4 (0.8, 6.0)
	Median (95% CI)	1.4 (1.1, 1.8)	14.0 (6.0, NE)
	75%-ile (95% CI)	4.6 (3.4, 5.5)	NE (14.5, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	3.06 (2.05, 4.58)	
	p-value [3]	<.0001	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.

		EC+FOLFOX (N=232)	Control 2 (N=68)
SOC: Nervous system disorders, PT: Dizziness	Number of subjects with events, n (%)	23 (9.9)	4 (5.9)
	Number of censored subjects, n (%)	209 (90.1)	64 (94.1)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	29.2 (29.2, NE)	NE (NE, NE)
	Median (95% CI)	NE (NE, NE)	NE (NE, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	1.41 (0.48, 4.12)	
	p-value [3]	0.5253	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.

		EC+FOLFOX (N=232)	Control 2 (N=68)
SOC: Nervous system disorders, PT: Dysgeusia	Number of subjects with events, n (%)	35 (15.1)	3 (4.4)
	Number of censored subjects, n (%)	197 (84.9)	65 (95.6)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Median (95% CI)	NE (NE, NE)	NE (NE, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	3.23 (0.99, 10.50)	
	p-value [3]	0.0392	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.

		EC+FOLFOX (N=232)	Control 2 (N=68)
SOC: Nervous system disorders, PT: Headache	Number of subjects with events, n (%)	35 (15.1)	10 (14.7)
	Number of censored subjects, n (%)	197 (84.9)	58 (85.3)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	NE (NE, NE)	NE (8.4, NE)
	Median (95% CI)	NE (NE, NE)	NE (NE, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	0.93 (0.46, 1.88)	
	p-value [3]	0.8237	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.

		EC+FOLFOX (N=232)	Control 2 (N=68)
SOC: Nervous system disorders, PT: Neuropathy peripheral	Number of subjects with events, n (%)	64 (27.6)	1 (1.5)
	Number of censored subjects, n (%)	168 (72.4)	67 (98.5)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	5.7 (4.7, NE)	NE (NE, NE)
	Median (95% CI)	NE (NE, NE)	NE (NE, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	19.12 (2.65, 137.76)	
	p-value [3]	<.0001	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.

		EC+FOLFOX (N=232)	Control 2 (N=68)
SOC: Nervous system disorders, PT: Neurotoxicity	Number of subjects with events, n (%)	26 (11.2)	1 (1.5)
	Number of censored subjects, n (%)	206 (88.8)	67 (98.5)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Median (95% CI)	NE (NE, NE)	NE (NE, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	7.63 (1.04, 56.22)	
	p-value [3]	0.0184	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.

		EC+FOLFOX (N=232)	Control 2 (N=68)
SOC: Nervous system disorders, PT: Paraesthesia	Number of subjects with events, n (%)	34 (14.7)	0 (0.0)
	Number of censored subjects, n (%)	198 (85.3)	68 (100.0)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	NE (23.0, NE)	NE (NE, NE)
	Median (95% CI)	NE (NE, NE)	NE (NE, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	NE	
	p-value [3]		

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.

		EC+FOLFOX (N=232)	Control 2 (N=68)
SOC: Nervous system disorders, PT: Peripheral sensory neuropathy	Number of subjects with events, n (%)	62 (26.7)	3 (4.4)
	Number of censored subjects, n (%)	170 (73.3)	65 (95.6)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	5.1 (3.2, NE)	NE (NE, NE)
	Median (95% CI)	NE (NE, NE)	NE (NE, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	6.28 (1.97, 20.02)	
	p-value [3]	0.0004	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Frequent AE by SOC, PT (incidence >= 10% or >=10 patients and incidence >= 1%)
Safety Analysis Set

		EC+FOLFOX (N=232)	Control 2 (N=68)
SOC: Psychiatric disorders	Number of subjects with events, n (%)	43 (18.5)	14 (20.6)
	Number of censored subjects, n (%)	189 (81.5)	54 (79.4)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	NE (15.4, NE)	11.3 (5.6, NE)
	Median (95% CI)	NE (NE, NE)	NE (20.5, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (20.5, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	0.72 (0.39, 1.33)	
	p-value [3]	0.2933	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.

		EC+FOLFOX (N=232)	Control 2 (N=68)
SOC: Psychiatric disorders, PT: Insomnia	Number of subjects with events, n (%)	29 (12.5)	10 (14.7)
	Number of censored subjects, n (%)	203 (87.5)	58 (85.3)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	NE (NE, NE)	20.5 (6.4, NE)
	Median (95% CI)	NE (NE, NE)	NE (20.5, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	0.69 (0.34, 1.43)	
	p-value [3]	0.3156	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.

		EC+FOLFOX (N=232)	Control 2 (N=68)
SOC: Renal and urinary disorders	Number of subjects with events, n (%)	43 (18.5)	10 (14.7)
	Number of censored subjects, n (%)	189 (81.5)	58 (85.3)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	21.6 (16.3, NE)	NE (9.7, NE)
	Median (95% CI)	NE (NE, NE)	NE (NE, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	1.09 (0.55, 2.17)	
	p-value [3]	0.8052	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.

		EC+FOLFOX (N=232)	Control 2 (N=68)
SOC: Renal and urinary disorders, PT: Haematuria	Number of subjects with events, n (%)	10 (4.3)	3 (4.4)
	Number of censored subjects, n (%)	222 (95.7)	65 (95.6)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Median (95% CI)	NE (NE, NE)	NE (NE, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	0.79 (0.22, 2.89)	
	p-value [3]	0.7246	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.

		EC+FOLFOX (N=232)	Control 2 (N=68)
SOC: Reproductive system and breast disorders	Number of subjects with events, n (%)	21 (9.1)	2 (2.9)
	Number of censored subjects, n (%)	211 (90.9)	66 (97.1)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Median (95% CI)	NE (NE, NE)	NE (NE, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	2.50 (0.58, 10.67)	
	p-value [3]	0.2006	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.

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Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Frequent AE by SOC, PT (incidence >= 10% or >=10 patients and incidence >= 1%)
Safety Analysis Set

		EC+FOLFOX (N=232)	Control 2 (N=68)
SOC: Respiratory, thoracic and mediastinal disorders	Number of subjects with events, n (%)	112 (48.3)	25 (36.8)
	Number of censored subjects, n (%)	120 (51.7)	43 (63.2)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	2.3 (1.5, 3.2)	3.0 (1.2, 7.4)
	Median (95% CI)	12.6 (7.3, NE)	NE (7.4, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	1.18 (0.76, 1.82)	
	p-value [3]	0.4573	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.

		EC+FOLFOX (N=232)	Control 2 (N=68)
SOC: Respiratory, thoracic and mediastinal disorders, PT: Cough	Number of subjects with events, n (%)	24 (10.3)	6 (8.8)
	Number of censored subjects, n (%)	208 (89.7)	62 (91.2)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	34.9 (34.9, NE)	NE (9.5, NE)
	Median (95% CI)	NE (34.9, NE)	NE (NE, NE)
	75%-ile (95% CI)	NE (34.9, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	0.94 (0.38, 2.32)	
	p-value [3]	0.8982	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.

		EC+FOLFOX (N=232)	Control 2 (N=68)
SOC: Respiratory, thoracic and mediastinal disorders, PT: Dyspnoea	Number of subjects with events, n (%)	23 (9.9)	5 (7.4)
	Number of censored subjects, n (%)	209 (90.1)	63 (92.6)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Median (95% CI)	NE (NE, NE)	NE (NE, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	1.15 (0.43, 3.03)	
	p-value [3]	0.7814	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.

		EC+FOLFOX (N=232)	Control 2 (N=68)
SOC: Respiratory, thoracic and mediastinal disorders, PT: Epistaxis	Number of subjects with events, n (%)	41 (17.7)	8 (11.8)
	Number of censored subjects, n (%)	191 (82.3)	60 (88.2)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	NE (14.0, NE)	NE (8.5, NE)
	Median (95% CI)	NE (NE, NE)	NE (NE, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	1.27 (0.59, 2.71)	
	p-value [3]	0.5368	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.

		EC+FOLFOX (N=232)	Control 2 (N=68)
SOC: Respiratory, thoracic and mediastinal disorders, PT: Pulmonary embolism	Number of subjects with events, n (%)	9 (3.9)	7 (10.3)
	Number of censored subjects, n (%)	223 (96.1)	61 (89.7)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	NE (NE, NE)	19.8 (19.8, NE)
	Median (95% CI)	NE (NE, NE)	NE (19.8, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	0.30 (0.11, 0.82)	
	p-value [3]	0.0130	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.

		EC+FOLFOX (N=232)	Control 2 (N=68)
SOC: Respiratory, thoracic and mediastinal disorders, PT: Rhinorrhoea	Number of subjects with events, n (%)	11 (4.7)	3 (4.4)
	Number of censored subjects, n (%)	221 (95.3)	65 (95.6)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	35.0 (35.0, NE)	NE (NE, NE)
	Median (95% CI)	NE (35.0, NE)	NE (NE, NE)
	75%-ile (95% CI)	NE (35.0, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	0.78 (0.21, 2.83)	
	p-value [3]	0.7025	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Frequent AE by SOC, PT (incidence >= 10% or >=10 patients and incidence >= 1%)
Safety Analysis Set

		EC+FOLFOX (N=232)	Control 2 (N=68)
SOC: Skin and subcutaneous tissue disorders	Number of subjects with events, n (%)	188 (81.0)	28 (41.2)
	Number of censored subjects, n (%)	44 (19.0)	40 (58.8)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	0.5 (0.4, 0.5)	1.1 (0.7, 6.1)
	Median (95% CI)	1.0 (0.9, 1.6)	18.1 (6.1, NE)
	75%-ile (95% CI)	4.2 (3.0, 8.1)	NE (18.1, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	2.85 (1.91, 4.24)	
	p-value [3]	<.0001	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.

		EC+FOLFOX (N=232)	Control 2 (N=68)
SOC: Skin and subcutaneous tissue disorders, PT: Alopecia	Number of subjects with events, n (%)	53 (22.8)	15 (22.1)
	Number of censored subjects, n (%)	179 (77.2)	53 (77.9)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	12.8 (4.6, NE)	NE (1.0, NE)
	Median (95% CI)	NE (NE, NE)	NE (NE, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	0.90 (0.51, 1.59)	
	p-value [3]	0.7133	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.

		EC+FOLFOX (N=232)	Control 2 (N=68)
SOC: Skin and subcutaneous tissue disorders, PT: Dermatitis acneiform	Number of subjects with events, n (%)	43 (18.5)	0 (0.0)
	Number of censored subjects, n (%)	189 (81.5)	68 (100.0)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	NE (15.5, NE)	NE (NE, NE)
	Median (95% CI)	NE (NE, NE)	NE (NE, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	NE	
	p-value [3]		

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.

		EC+FOLFOX (N=232)	Control 2 (N=68)
SOC: Skin and subcutaneous tissue disorders, PT: Dry skin	Number of subjects with events, n (%)	38 (16.4)	5 (7.4)
	Number of censored subjects, n (%)	194 (83.6)	63 (92.6)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	23.7 (18.6, NE)	NE (18.1, NE)
	Median (95% CI)	NE (NE, NE)	NE (NE, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	1.93 (0.76, 4.91)	
	p-value [3]	0.1618	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.

		EC+FOLFOX (N=232)	Control 2 (N=68)
SOC: Skin and subcutaneous tissue disorders, PT: Nail disorder	Number of subjects with events, n (%)	10 (4.3)	0 (0.0)
	Number of censored subjects, n (%)	222 (95.7)	68 (100.0)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Median (95% CI)	NE (NE, NE)	NE (NE, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	NE	
	p-value [3]		

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.

Pierre Fabre Pharma GmbH: Final
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Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Frequent AE by SOC, PT (incidence >= 10% or >=10 patients and incidence >= 1%)
Safety Analysis Set

		EC+FOLFOX (N=232)	Control 2 (N=68)
SOC: Skin and subcutaneous tissue disorders, PT: Palmar-plantar erythrodysaesthesia syndrome	Number of subjects with events, n (%)	37 (15.9)	5 (7.4)
	Number of censored subjects, n (%)	195 (84.1)	63 (92.6)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	NE (14.8, NE)	NE (NE, NE)
	Median (95% CI)	NE (NE, NE)	NE (NE, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	1.82 (0.71, 4.63)	
	p-value [3]	0.2032	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.

		EC+FOLFOX (N=232)	Control 2 (N=68)
SOC: Skin and subcutaneous tissue disorders, PT: Pigmentation disorder	Number of subjects with events, n (%)	17 (7.3)	0 (0.0)
	Number of censored subjects, n (%)	215 (92.7)	68 (100.0)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Median (95% CI)	NE (NE, NE)	NE (NE, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	NE	
	p-value [3]		

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.

		EC+FOLFOX (N=232)	Control 2 (N=68)
SOC: Skin and subcutaneous tissue disorders, PT: Pruritus	Number of subjects with events, n (%)	32 (13.8)	1 (1.5)
	Number of censored subjects, n (%)	200 (86.2)	67 (98.5)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	28.1 (21.9, NE)	NE (NE, NE)
	Median (95% CI)	NE (NE, NE)	NE (NE, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	7.97 (1.09, 58.42)	
	p-value [3]	0.0151	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.

		EC+FOLFOX (N=232)	Control 2 (N=68)
SOC: Skin and subcutaneous tissue disorders, PT: Rash	Number of subjects with events, n (%)	70 (30.2)	1 (1.5)
	Number of censored subjects, n (%)	162 (69.8)	67 (98.5)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	7.6 (3.3, 14.0)	NE (NE, NE)
	Median (95% CI)	NE (24.0, NE)	NE (NE, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	19.79 (2.75, 142.49)	
	p-value [3]	<.0001	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.

		EC+FOLFOX (N=232)	Control 2 (N=68)
SOC: Skin and subcutaneous tissue disorders, PT: Skin hyperpigmentation	Number of subjects with events, n (%)	43 (18.5)	3 (4.4)
	Number of censored subjects, n (%)	189 (81.5)	65 (95.6)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	NE (15.2, NE)	NE (NE, NE)
	Median (95% CI)	NE (NE, NE)	NE (NE, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	4.09 (1.27, 13.21)	
	p-value [3]	0.0105	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.

		EC+FOLFOX (N=232)	Control 2 (N=68)
SOC: Skin and subcutaneous tissue disorders, PT: Skin lesion	Number of subjects with events, n (%)	13 (5.6)	0 (0.0)
	Number of censored subjects, n (%)	219 (94.4)	68 (100.0)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Median (95% CI)	NE (NE, NE)	NE (NE, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	NE	
	p-value [3]		

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.

		EC+FOLFOX (N=232)	Control 2 (N=68)
SOC: Vascular disorders	Number of subjects with events, n (%)	36 (15.5)	19 (27.9)
	Number of censored subjects, n (%)	196 (84.5)	49 (72.1)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	NE (20.6, NE)	4.9 (2.7, NE)
	Median (95% CI)	NE (NE, NE)	NE (10.6, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	0.43 (0.24, 0.75)	
	p-value [3]	0.0022	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.

		EC+FOLFOX (N=232)	Control 2 (N=68)
SOC: Vascular disorders, PT: Hypertension	Number of subjects with events, n (%)	9 (3.9)	10 (14.7)
	Number of censored subjects, n (%)	223 (96.1)	58 (85.3)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	NE (NE, NE)	NE (8.7, NE)
	Median (95% CI)	NE (NE, NE)	NE (NE, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	0.20 (0.08, 0.49)	
	p-value [3]	0.0001	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.

		EC+FOLFOX (N=232)	Control 2 (N=68)
SOC: Vascular disorders, PT: Hypotension	Number of subjects with events, n (%)	11 (4.7)	2 (2.9)
	Number of censored subjects, n (%)	221 (95.3)	66 (97.1)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Median (95% CI)	NE (NE, NE)	NE (NE, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	1.42 (0.31, 6.43)	
	p-value [3]	0.6444	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Frequent AE by SOC, PT (incidence >= 10% or >=10 patients and incidence >= 1%) - Subgroup analysis
Safety Analysis Set

SOC/PT	Subgroup Level	EC+FOLFOX (N=232) n/ N (%)	EC+FOLFOX (N=232) Median (95% CI)[1]	Control 2 (N=68) n/ N (%)	Control 2 (N=68) Median (95% CI)[1]	Unstratified analysis Hazard Ratio (95% CI)[2]	Unstratified analysis p-Value[3]	Interaction p-Value[4]
SOC: Blood and lymphatic system disorders, PT: Thrombocytopenia	Age (Years)							0.9645
	< 65	18/ 148 (12.2)	NE (NE , NE)	1/ 42 (2.4)	NE (NE , NE)	4.26 (0.57, 31.98)	0.1241	
	>= 65	14/ 84 (16.7)	NE (NE , NE)	1/ 26 (3.8)	NE (NE , NE)	4.20 (0.55, 31.97)	0.1313	
	Sex							0.9771
	Male	19/ 121 (15.7)	NE (NE , NE)	1/ 32 (3.1)	NE (NE , NE)	4.17 (0.56, 31.13)	0.1307	
	Female	13/ 111 (11.7)	NE (NE , NE)	1/ 36 (2.8)	NE (NE , NE)	3.66 (0.48, 28.03)	0.1813	
	Region							0.9999
	Europe	18/ 108 (16.7)	NE (NE , NE)	2/ 38 (5.3)	NE (NE , NE)	2.65 (0.61, 11.44)	0.1740	
	USA/Canada	2/ 15 (13.3)	NE (NE , NE)	0/ 7 (0.0)	NE (NE , NE)	NE		
	Rest of World	12/ 109 (11.0)	NE (NE , NE)	0/ 23 (0.0)	NE (NE , NE)	NE		
	ECOG-PS at Randomization							0.9861
	0	15/ 130 (11.5)	NE (NE , NE)	2/ 44 (4.5)	NE (NE , NE)	2.26 (0.52, 9.88)	0.2669	
	1	17/ 102 (16.7)	NE (NE , NE)	0/ 24 (0.0)	NE (NE , NE)	NE		
	Number of Organs Involved							0.9425
	<= 2	15/ 116 (12.9)	NE (NE , NE)	1/ 33 (3.0)	NE (NE , NE)	4.17 (0.55, 31.59)	0.1332	
	>= 3	17/ 116 (14.7)	NE (NE , NE)	1/ 35 (2.9)	NE (NE , NE)	3.77 (0.50, 28.41)	0.1664	
	Presence of Liver Metastases							0.9899
	Yes	23/ 146 (15.8)	NE (NE , NE)	2/ 42 (4.8)	NE (NE , NE)	2.74 (0.64, 11.62)	0.1545	
	No	9/ 86 (10.5)	NE (NE , NE)	0/ 26 (0.0)	NE (NE , NE)	NE		
	Side of Tumor							0.9889
	Left	12/ 88 (13.6)	NE (NE , NE)	0/ 33 (0.0)	NE (NE , NE)	NE		
	Right	20/ 144 (13.9)	NE (NE , NE)	2/ 35 (5.7)	NE (NE , NE)	2.14 (0.50, 9.17)	0.2932	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
Subgroup analysis was done for SOCs / PTs with significant overall treatment effect (significant log-rank).
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.
[4] P-Value for interaction from Cox proportional hazards model using ties=exact option with treatment, subgroup and treatment*subgroup interaction as covariates.
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Frequent AE by SOC, PT (incidence >= 10% or >=10 patients and incidence >= 1%) - Subgroup analysis
Safety Analysis Set

SOC/PT	Subgroup Level	EC+FOLFOX (N=232) n/ N (%)	EC+FOLFOX (N=232) Median (95% CI)[1]	Control 2 (N=68) n/ N (%)	Control 2 (N=68) Median (95% CI)[1]	Unstratified analysis Hazard Ratio (95% CI)[2]	Unstratified analysis p-Value[3]	Interaction p-Value[4]
SOC: Gastrointestinal disorders, PT: Diarrhoea	Age (Years)							0.7680
	< 65	56/ 148 (37.8)	NE (14.8, NE)	18/ 42 (42.9)	11.5 (3.0, NE)	0.68 (0.40, 1.17)	0.1600	
	>= 65	41/ 84 (48.8)	11.0 (5.6, NE)	16/ 26 (61.5)	5.5 (1.2, NE)	0.63 (0.35, 1.13)	0.1164	
	Sex							0.7723
	Male	51/ 121 (42.1)	17.1 (9.2, NE)	16/ 32 (50.0)	3.6 (2.7, NE)	0.57 (0.32, 1.01)	0.0512	
	Female	46/ 111 (41.4)	NE (9.9, NE)	18/ 36 (50.0)	7.9 (3.0, NE)	0.70 (0.41, 1.21)	0.2030	
	Region							0.3423
	Europe	54/ 108 (50.0)	9.9 (6.3, 21.1)	24/ 38 (63.2)	3.6 (2.1, 7.9)	0.53 (0.33, 0.87)	0.0111	
	USA/Canada	10/ 15 (66.7)	2.3 (0.4, NE)	4/ 7 (57.1)	9.2 (0.1, NE)	1.12 (0.35, 3.61)	0.8441	
	Rest of World	33/ 109 (30.3)	NE (NE , NE)	6/ 23 (26.1)	NE (NE , NE)	1.01 (0.42, 2.42)	0.9741	
	ECOG-PS at Randomization							0.5417
	0	51/ 130 (39.2)	NE (14.8, NE)	22/ 44 (50.0)	6.6 (2.9, NE)	0.57 (0.35, 0.95)	0.0287	
	1	46/ 102 (45.1)	10.8 (5.8, NE)	12/ 24 (50.0)	7.9 (3.0, NE)	0.76 (0.40, 1.44)	0.4012	
	Number of Organs Involved							0.6863
	<= 2	46/ 116 (39.7)	NE (11.7, NE)	17/ 33 (51.5)	7.9 (3.3, NE)	0.60 (0.34, 1.05)	0.0698	
	>= 3	51/ 116 (44.0)	21.1 (7.7, NE)	17/ 35 (48.6)	6.6 (2.7, NE)	0.71 (0.41, 1.24)	0.2253	
	Presence of Liver Metastases							0.8613
	Yes	60/ 146 (41.1)	NE (9.0, NE)	21/ 42 (50.0)	6.6 (3.6, 11.5)	0.67 (0.40, 1.10)	0.1091	
	No	37/ 86 (43.0)	21.1 (9.9, NE)	13/ 26 (50.0)	7.9 (1.2, NE)	0.62 (0.33, 1.17)	0.1345	
	Side of Tumor							0.3548
	Left	34/ 88 (38.6)	NE (9.7, NE)	13/ 33 (39.4)	NE (5.5, NE)	0.81 (0.42, 1.53)	0.5076	
	Right	63/ 144 (43.8)	17.1 (8.9, NE)	21/ 35 (60.0)	3.6 (1.3, 11.5)	0.54 (0.33, 0.89)	0.0148	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
Subgroup analysis was done for SOCs / PTs with significant overall treatment effect (significant log-rank).
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.
[4] P-Value for interaction from Cox proportional hazards model using ties=exact option with treatment, subgroup and treatment*subgroup interaction as covariates.
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Frequent AE by SOC, PT (incidence >= 10% or >=10 patients and incidence >= 1%) - Subgroup analysis
Safety Analysis Set

SOC/PT	Subgroup Level	EC+FOLFOX (N=232) n/ N (%)	EC+FOLFOX (N=232) Median (95% CI)[1]	Control 2 (N=68) n/ N (%)	Control 2 (N=68) Median (95% CI)[1]	Unstratified analysis Hazard Ratio (95% CI)[2]	Unstratified analysis p-Value[3]	Interaction p-Value[4]
SOC: General disorders and administration site conditions, PT: Asthenia	Age (Years)							0.3134
	< 65	39/ 148 (26.4)	NE (NE , NE)	3/ 42 (7.1)	NE (NE , NE)	3.73 (1.15, 12.07)	0.0184	
	>= 65	29/ 84 (34.5)	NE (15.1, NE)	5/ 26 (19.2)	NE (NE , NE)	1.67 (0.64, 4.32)	0.2898	
	Sex							0.0501
	Male	31/ 121 (25.6)	NE (NE , NE)	6/ 32 (18.8)	NE (NE , NE)	1.18 (0.49, 2.83)	0.7184	
	Female	37/ 111 (33.3)	NE (20.6, NE)	2/ 36 (5.6)	NE (NE , NE)	6.30 (1.52, 26.15)	0.0035	
	Region							0.9998
	Europe	48/ 108 (44.4)	15.1 (6.4, NE)	8/ 38 (21.1)	NE (NE , NE)	2.17 (1.03, 4.60)	0.0381	
	USA/Canada	1/ 15 (6.7)	NE (NE , NE)	0/ 7 (0.0)	NE (NE , NE)	NE		
	Rest of World	19/ 109 (17.4)	NE (NE , NE)	0/ 23 (0.0)	NE (NE , NE)	NE		
	ECOG-PS at Randomization							0.4036
	0	37/ 130 (28.5)	NE (NE , NE)	4/ 44 (9.1)	NE (NE , NE)	3.18 (1.14, 8.94)	0.0199	
	1	31/ 102 (30.4)	NE (NE , NE)	4/ 24 (16.7)	NE (NE , NE)	1.64 (0.58, 4.65)	0.3517	
	Number of Organs Involved							0.9826
	<= 2	34/ 116 (29.3)	NE (NE , NE)	4/ 33 (12.1)	NE (NE , NE)	2.46 (0.87, 6.94)	0.0780	
	>= 3	34/ 116 (29.3)	NE (21.4, NE)	4/ 35 (11.4)	NE (NE , NE)	2.53 (0.90, 7.14)	0.0691	
	Presence of Liver Metastases							0.1166
	Yes	41/ 146 (28.1)	NE (21.4, NE)	7/ 42 (16.7)	NE (NE , NE)	1.55 (0.70, 3.47)	0.2795	
	No	27/ 86 (31.4)	NE (NE , NE)	1/ 26 (3.8)	NE (NE , NE)	8.94 (1.21, 65.78)	0.0091	
	Side of Tumor							0.0694
	Left	26/ 88 (29.5)	NE (NE , NE)	1/ 33 (3.0)	NE (NE , NE)	10.41 (1.41, 76.70)	0.0042	
	Right	42/ 144 (29.2)	NE (21.4, NE)	7/ 35 (20.0)	NE (NE , NE)	1.38 (0.62, 3.08)	0.4236	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
Subgroup analysis was done for SOCs / PTs with significant overall treatment effect (significant log-rank).
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.
[4] P-Value for interaction from Cox proportional hazards model using ties=exact option with treatment, subgroup and treatment*subgroup interaction as covariates.
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Frequent AE by SOC, PT (incidence >= 10% or >=10 patients and incidence >= 1%) - Subgroup analysis
Safety Analysis Set

SOC/PT	Subgroup Level	EC+FOLFOX (N=232) n/ N (%)	EC+FOLFOX (N=232) Median (95% CI)[1]	Control 2 (N=68) n/ N (%)	Control 2 (N=68) Median (95% CI)[1]	Unstratified analysis Hazard Ratio (95% CI)[2]	Unstratified analysis p-Value[3]	Interaction p-Value[4]
SOC: General disorders and administration site conditions, PT: Fatigue	Age (Years)							0.1311
	< 65	38/ 148 (25.7)	NE (NE , NE)	20/ 42 (47.6)	6.0 (2.7, NE)	0.44 (0.26, 0.76)	0.0024	
	>= 65	23/ 84 (27.4)	NE (NE , NE)	7/ 26 (26.9)	NE (NE , NE)	0.93 (0.40, 2.17)	0.8676	
	Sex							0.8836
	Male	29/ 121 (24.0)	NE (NE , NE)	12/ 32 (37.5)	NE (4.6, NE)	0.55 (0.28, 1.08)	0.0722	
	Female	32/ 111 (28.8)	NE (NE , NE)	15/ 36 (41.7)	NE (3.3, NE)	0.59 (0.32, 1.10)	0.0951	
	Region							0.4175
	Europe	32/ 108 (29.6)	NE (NE , NE)	18/ 38 (47.4)	6.0 (2.4, NE)	0.48 (0.27, 0.86)	0.0119	
	USA/Canada	8/ 15 (53.3)	3.3 (0.4, NE)	5/ 7 (71.4)	3.1 (0.6, NE)	0.73 (0.24, 2.25)	0.5718	
	Rest of World	21/ 109 (19.3)	NE (NE , NE)	4/ 23 (17.4)	NE (NE , NE)	1.04 (0.36, 3.05)	0.9403	
	ECOG-PS at Randomization							0.3708
	0	36/ 130 (27.7)	NE (NE , NE)	20/ 44 (45.5)	7.4 (3.1, NE)	0.49 (0.28, 0.85)	0.0092	
	1	25/ 102 (24.5)	NE (NE , NE)	7/ 24 (29.2)	NE (6.0, NE)	0.80 (0.34, 1.85)	0.5891	
	Number of Organs Involved							0.5885
	<= 2	30/ 116 (25.9)	NE (NE , NE)	12/ 33 (36.4)	NE (4.8, NE)	0.65 (0.33, 1.27)	0.2039	
	>= 3	31/ 116 (26.7)	NE (NE , NE)	15/ 35 (42.9)	4.6 (3.1, NE)	0.48 (0.26, 0.90)	0.0188	
	Presence of Liver Metastases							0.0883
	Yes	43/ 146 (29.5)	NE (NE , NE)	15/ 42 (35.7)	NE (4.4, NE)	0.75 (0.42, 1.36)	0.3350	
	No	18/ 86 (20.9)	NE (NE , NE)	12/ 26 (46.2)	7.4 (0.8, NE)	0.34 (0.16, 0.71)	0.0027	
	Side of Tumor							0.2480
	Left	19/ 88 (21.6)	NE (NE , NE)	14/ 33 (42.4)	7.4 (2.4, NE)	0.39 (0.19, 0.79)	0.0063	
	Right	42/ 144 (29.2)	NE (NE , NE)	13/ 35 (37.1)	NE (4.4, NE)	0.72 (0.39, 1.35)	0.2976	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
Subgroup analysis was done for SOCs / PTs with significant overall treatment effect (significant log-rank).
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.
[4] P-Value for interaction from Cox proportional hazards model using ties=exact option with treatment, subgroup and treatment*subgroup interaction as covariates.
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Frequent AE by SOC, PT (incidence >= 10% or >=10 patients and incidence >= 1%) - Subgroup analysis
Safety Analysis Set

SOC/PT	Subgroup Level	EC+FOLFOX (N=232) n/ N (%)	EC+FOLFOX (N=232) Median (95% CI)[1]	Control 2 (N=68) n/ N (%)	Control 2 (N=68) Median (95% CI)[1]	Unstratified analysis Hazard Ratio (95% CI)[2]	Unstratified analysis p-Value[3]	Interaction p-Value[4]
SOC: General disorders and administration site conditions, PT: Pyrexia	Age (Years)							0.9312
	< 65	45/ 148 (30.4)	NE (26.7, NE)	4/ 42 (9.5)	NE (NE , NE)	3.01 (1.08, 8.39)	0.0263	
	>= 65	22/ 84 (26.2)	NE (NE , NE)	2/ 26 (7.7)	NE (NE , NE)	3.38 (0.79, 14.41)	0.0796	
	Sex							0.2341
	Male	34/ 121 (28.1)	NE (26.7, NE)	1/ 32 (3.1)	NE (NE , NE)	7.98 (1.09, 58.28)	0.0149	
	Female	33/ 111 (29.7)	NE (NE , NE)	5/ 36 (13.9)	NE (NE , NE)	2.18 (0.85, 5.60)	0.0963	
	Region							0.8814
	Europe	29/ 108 (26.9)	NE (NE , NE)	3/ 38 (7.9)	NE (NE , NE)	3.19 (0.97, 10.48)	0.0437	
	USA/Canada	3/ 15 (20.0)	NE (NE , NE)	1/ 7 (14.3)	NE (NE , NE)	1.48 (0.15, 14.22)	0.7333	
	Rest of World	35/ 109 (32.1)	26.7 (18.7, NE)	2/ 23 (8.7)	NE (12.5, NE)	3.37 (0.81, 14.04)	0.0764	
	ECOG-PS at Randomization							0.2427
	0	41/ 130 (31.5)	26.7 (26.7, NE)	3/ 44 (6.8)	NE (NE , NE)	4.61 (1.42, 14.90)	0.0050	
	1	26/ 102 (25.5)	NE (NE , NE)	3/ 24 (12.5)	NE (NE , NE)	1.81 (0.55, 6.02)	0.3243	
	Number of Organs Involved							0.8205
	<= 2	38/ 116 (32.8)	NE (18.7, NE)	4/ 33 (12.1)	NE (NE , NE)	2.96 (1.06, 8.30)	0.0301	
	>= 3	29/ 116 (25.0)	26.7 (26.7, NE)	2/ 35 (5.7)	NE (NE , NE)	3.60 (0.86, 15.16)	0.0616	
	Presence of Liver Metastases							0.6352
	Yes	31/ 146 (21.2)	NE (NE , NE)	3/ 42 (7.1)	NE (NE , NE)	2.67 (0.81, 8.73)	0.0918	
	No	36/ 86 (41.9)	26.7 (13.0, NE)	3/ 26 (11.5)	NE (12.9, NE)	3.84 (1.18, 12.51)	0.0160	
	Side of Tumor							0.3293
	Left	25/ 88 (28.4)	NE (26.7, NE)	4/ 33 (12.1)	NE (12.9, NE)	2.09 (0.72, 6.02)	0.1655	
	Right	42/ 144 (29.2)	NE (NE , NE)	2/ 35 (5.7)	NE (NE , NE)	5.15 (1.25, 21.27)	0.0115	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
Subgroup analysis was done for SOCs / PTs with significant overall treatment effect (significant log-rank).
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.
[4] P-Value for interaction from Cox proportional hazards model using ties=exact option with treatment, subgroup and treatment*subgroup interaction as covariates.
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Frequent AE by SOC, PT (incidence >= 10% or >=10 patients and incidence >= 1%) - Subgroup analysis
Safety Analysis Set

SOC/PT	Subgroup Level	EC+FOLFOX (N=232) n/ N (%)	EC+FOLFOX (N=232) Median (95% CI)[1]	Control 2 (N=68) n/ N (%)	Control 2 (N=68) Median (95% CI)[1]	Unstratified analysis Hazard Ratio (95% CI)[2]	Unstratified analysis p-Value[3]	Interaction p-Value[4]
SOC: Investigations	Age (Years)							0.6911
	< 65	108/ 148 (73.0)	1.4 (0.9, 2.4)	24/ 42 (57.1)	3.3 (1.7, 19.5)	1.46 (0.94, 2.27)	0.0906	
	>= 65	56/ 84 (66.7)	1.9 (0.9, 4.6)	12/ 26 (46.2)	10.2 (1.9, NE)	1.70 (0.91, 3.18)	0.0927	
	Sex							0.9167
	Male	85/ 121 (70.2)	1.9 (1.0, 3.0)	17/ 32 (53.1)	6.9 (1.9, NE)	1.51 (0.90, 2.55)	0.1209	
	Female	79/ 111 (71.2)	1.2 (0.6, 2.5)	19/ 36 (52.8)	3.7 (1.7, NE)	1.57 (0.95, 2.59)	0.0756	
	Region							0.0916
	Europe	63/ 108 (58.3)	4.6 (3.0, 16.4)	13/ 38 (34.2)	NE (3.7, NE)	1.87 (1.03, 3.41)	0.0364	
	USA/Canada	15/ 15 (100.0)	0.5 (0.5, 0.9)	4/ 7 (57.1)	1.8 (0.4, NE)	2.86 (0.93, 8.83)	0.0616	
	Rest of World	86/ 109 (78.9)	0.9 (0.5, 1.3)	19/ 23 (82.6)	0.6 (0.5, 3.0)	0.97 (0.59, 1.60)	0.9229	
	ECOG-PS at Randomization							0.0620
	0	97/ 130 (74.6)	1.6 (0.9, 2.8)	21/ 44 (47.7)	10.2 (3.0, NE)	2.00 (1.25, 3.21)	0.0034	
	1	67/ 102 (65.7)	1.4 (0.8, 3.0)	15/ 24 (62.5)	1.7 (0.5, NE)	1.01 (0.58, 1.77)	0.9595	
	Number of Organs Involved							0.3750
	<= 2	86/ 116 (74.1)	1.6 (0.9, 3.4)	17/ 33 (51.5)	10.2 (2.8, NE)	1.81 (1.07, 3.04)	0.0239	
	>= 3	78/ 116 (67.2)	1.4 (0.9, 2.7)	19/ 35 (54.3)	3.3 (1.1, NE)	1.32 (0.80, 2.19)	0.2761	
	Presence of Liver Metastases							0.5394
	Yes	100/ 146 (68.5)	1.4 (0.9, 2.8)	23/ 42 (54.8)	3.7 (1.8, NE)	1.42 (0.90, 2.24)	0.1275	
	No	64/ 86 (74.4)	1.5 (0.8, 3.0)	13/ 26 (50.0)	11.3 (2.8, NE)	1.78 (0.98, 3.24)	0.0557	
	Side of Tumor							0.0849
	Left	60/ 88 (68.2)	1.9 (1.0, 3.3)	20/ 33 (60.6)	2.3 (1.0, 19.5)	1.10 (0.66, 1.83)	0.7220	
	Right	104/ 144 (72.2)	1.1 (0.9, 2.5)	16/ 35 (45.7)	10.2 (3.3, NE)	2.08 (1.22, 3.52)	0.0055	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
Subgroup analysis was done for SOCs / PTs with significant overall treatment effect (significant log-rank).
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.
[4] P-Value for interaction from Cox proportional hazards model using ties=exact option with treatment, subgroup and treatment*subgroup interaction as covariates.
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Frequent AE by SOC, PT (incidence >= 10% or >=10 patients and incidence >= 1%) - Subgroup analysis
Safety Analysis Set

SOC/PT	Subgroup Level	EC+FOLFOX (N=232) n/ N (%)	EC+FOLFOX (N=232) Median (95% CI)[1]	Control 2 (N=68) n/ N (%)	Control 2 (N=68) Median (95% CI)[1]	Unstratified analysis Hazard Ratio (95% CI)[2]	Unstratified analysis p-Value[3]	Interaction p-Value[4]
SOC: Investigations, PT: Lipase increased	Age (Years)							0.8468
	< 65	37/ 148 (25.0)	NE (NE , NE)	3/ 42 (7.1)	NE (NE , NE)	3.61 (1.11, 11.70)	0.0223	
	>= 65	15/ 84 (17.9)	NE (NE , NE)	1/ 26 (3.8)	NE (NE , NE)	4.53 (0.60, 34.29)	0.1085	
	Sex							0.3992
	Male	31/ 121 (25.6)	NE (NE , NE)	3/ 32 (9.4)	NE (NE , NE)	2.59 (0.79, 8.47)	0.1030	
	Female	21/ 111 (18.9)	NE (NE , NE)	1/ 36 (2.8)	NE (NE , NE)	7.23 (0.97, 53.71)	0.0236	
	Region							0.9997
	Europe	18/ 108 (16.7)	NE (NE , NE)	2/ 38 (5.3)	NE (NE , NE)	2.98 (0.69, 12.87)	0.1239	
	USA/Canada	7/ 15 (46.7)	NE (1.9, NE)	0/ 7 (0.0)	NE (NE , NE)	NE		
	Rest of World	27/ 109 (24.8)	NE (NE , NE)	2/ 23 (8.7)	NE (11.3, NE)	3.06 (0.73, 12.86)	0.1086	
	ECOG-PS at Randomization							0.7152
	0	30/ 130 (23.1)	NE (NE , NE)	3/ 44 (6.8)	NE (NE , NE)	3.38 (1.03, 11.08)	0.0326	
	1	22/ 102 (21.6)	NE (NE , NE)	1/ 24 (4.2)	NE (NE , NE)	5.29 (0.71, 39.29)	0.0679	
	Number of Organs Involved							0.2464
	<= 2	28/ 116 (24.1)	NE (NE , NE)	1/ 33 (3.0)	NE (NE , NE)	8.79 (1.20, 64.61)	0.0098	
	>= 3	24/ 116 (20.7)	NE (NE , NE)	3/ 35 (8.6)	NE (NE , NE)	2.27 (0.68, 7.55)	0.1694	
	Presence of Liver Metastases							0.8614
	Yes	30/ 146 (20.5)	NE (NE , NE)	2/ 42 (4.8)	NE (NE , NE)	4.26 (1.02, 17.83)	0.0306	
	No	22/ 86 (25.6)	NE (NE , NE)	2/ 26 (7.7)	NE (NE , NE)	3.49 (0.82, 14.83)	0.0717	
	Side of Tumor							0.3463
	Left	21/ 88 (23.9)	NE (NE , NE)	1/ 33 (3.0)	NE (NE , NE)	8.01 (1.08, 59.52)	0.0155	
	Right	31/ 144 (21.5)	NE (NE , NE)	3/ 35 (8.6)	NE (NE , NE)	2.57 (0.79, 8.41)	0.1053	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
Subgroup analysis was done for SOCs / PTs with significant overall treatment effect (significant log-rank).
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.
[4] P-Value for interaction from Cox proportional hazards model using ties=exact option with treatment, subgroup and treatment*subgroup interaction as covariates.
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Frequent AE by SOC, PT (incidence >= 10% or >=10 patients and incidence >= 1%) - Subgroup analysis
Safety Analysis Set

SOC/PT	Subgroup Level	EC+FOLFOX (N=232) n/ N (%)	EC+FOLFOX (N=232) Median (95% CI)[1]	Control 2 (N=68) n/ N (%)	Control 2 (N=68) Median (95% CI)[1]	Unstratified analysis Hazard Ratio (95% CI)[2]	Unstratified analysis p-Value[3]	Interaction p-Value[4]
SOC: Investigations, PT: Platelet count decreased	Age (Years)							0.5361
	< 65	33/ 148 (22.3)	NE (NE , NE)	3/ 42 (7.1)	NE (NE , NE)	2.93 (0.90, 9.55)	0.0615	
	>= 65	20/ 84 (23.8)	NE (25.5, NE)	1/ 26 (3.8)	NE (NE , NE)	5.81 (0.78, 43.39)	0.0519	
	Sex							0.8344
	Male	28/ 121 (23.1)	NE (25.5, NE)	2/ 32 (6.3)	NE (NE , NE)	3.20 (0.76, 13.44)	0.0939	
	Female	25/ 111 (22.5)	NE (NE , NE)	2/ 36 (5.6)	NE (NE , NE)	4.09 (0.97, 17.27)	0.0377	
	Region							0.8997
	Europe	14/ 108 (13.0)	NE (NE , NE)	1/ 38 (2.6)	NE (NE , NE)	4.15 (0.54, 31.72)	0.1364	
	USA/Canada	2/ 15 (13.3)	NE (NE , NE)	0/ 7 (0.0)	NE (NE , NE)	NE		
	Rest of World	37/ 109 (33.9)	NE (NE , NE)	3/ 23 (13.0)	NE (NE , NE)	2.56 (0.79, 8.30)	0.1046	
	ECOG-PS at Randomization							0.1097
	0	30/ 130 (23.1)	NE (NE , NE)	1/ 44 (2.3)	NE (NE , NE)	10.39 (1.42, 76.21)	0.0042	
	1	23/ 102 (22.5)	NE (25.5, NE)	3/ 24 (12.5)	NE (NE , NE)	1.47 (0.44, 4.90)	0.5327	
	Number of Organs Involved							0.9011
	<= 2	27/ 116 (23.3)	NE (NE , NE)	2/ 33 (6.1)	NE (NE , NE)	3.81 (0.90, 16.05)	0.0499	
	>= 3	26/ 116 (22.4)	NE (NE , NE)	2/ 35 (5.7)	NE (NE , NE)	3.38 (0.80, 14.23)	0.0781	
	Presence of Liver Metastases							0.1498
	Yes	34/ 146 (23.3)	NE (NE , NE)	1/ 42 (2.4)	NE (NE , NE)	9.55 (1.31, 69.80)	0.0064	
	No	19/ 86 (22.1)	NE (NE , NE)	3/ 26 (11.5)	NE (NE , NE)	1.66 (0.49, 5.64)	0.4112	
	Side of Tumor							0.3251
	Left	21/ 88 (23.9)	NE (NE , NE)	3/ 33 (9.1)	NE (NE , NE)	2.39 (0.71, 8.03)	0.1446	
	Right	32/ 144 (22.2)	NE (NE , NE)	1/ 35 (2.9)	NE (NE , NE)	7.50 (1.02, 54.91)	0.0194	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
Subgroup analysis was done for SOCs / PTs with significant overall treatment effect (significant log-rank).
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.
[4] P-Value for interaction from Cox proportional hazards model using ties=exact option with treatment, subgroup and treatment*subgroup interaction as covariates.
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Frequent AE by SOC, PT (incidence >= 10% or >=10 patients and incidence >= 1%) - Subgroup analysis
Safety Analysis Set

SOC/PT	Subgroup Level	EC+FOLFOX (N=232) n/ N (%)	EC+FOLFOX (N=232) Median (95% CI)[1]	Control 2 (N=68) n/ N (%)	Control 2 (N=68) Median (95% CI)[1]	Unstratified analysis Hazard Ratio (95% CI)[2]	Unstratified analysis p-Value[3]	Interaction p-Value[4]
SOC: Metabolism and nutrition disorders, PT: Hypoalbuminaemia	Age (Years)							0.9798
	< 65	16/ 148 (10.8)	NE (NE , NE)	1/ 42 (2.4)	NE (NE , NE)	4.22 (0.56, 31.85)	0.1285	
	>= 65	14/ 84 (16.7)	NE (NE , NE)	1/ 26 (3.8)	NE (NE , NE)	4.17 (0.55, 31.75)	0.1329	
	Sex							0.9893
	Male	15/ 121 (12.4)	NE (NE , NE)	0/ 32 (0.0)	NE (NE , NE)	NE		
	Female	15/ 111 (13.5)	NE (NE , NE)	2/ 36 (5.6)	NE (NE , NE)	2.36 (0.54, 10.31)	0.2405	
	Region							0.9999
	Europe	4/ 108 (3.7)	NE (NE , NE)	0/ 38 (0.0)	NE (NE , NE)	NE		
	USA/Canada	5/ 15 (33.3)	NE (5.1, NE)	0/ 7 (0.0)	NE (NE , NE)	NE		
	Rest of World	21/ 109 (19.3)	NE (NE , NE)	2/ 23 (8.7)	NE (NE , NE)	2.10 (0.49, 8.95)	0.3057	
	ECOG-PS at Randomization							0.9878
	0	11/ 130 (8.5)	NE (NE , NE)	0/ 44 (0.0)	NE (NE , NE)	NE		
	1	19/ 102 (18.6)	NE (NE , NE)	2/ 24 (8.3)	NE (12.1, NE)	1.93 (0.45, 8.32)	0.3677	
	Number of Organs Involved							0.9226
	<= 2	15/ 116 (12.9)	NE (NE , NE)	1/ 33 (3.0)	NE (NE , NE)	4.41 (0.58, 33.36)	0.1162	
	>= 3	15/ 116 (12.9)	NE (NE , NE)	1/ 35 (2.9)	NE (NE , NE)	3.86 (0.51, 29.28)	0.1590	
	Presence of Liver Metastases							0.4721
	Yes	23/ 146 (15.8)	NE (NE , NE)	1/ 42 (2.4)	NE (NE , NE)	6.05 (0.82, 44.84)	0.0444	
	No	7/ 86 (8.1)	NE (NE , NE)	1/ 26 (3.8)	NE (NE , NE)	1.93 (0.24, 15.67)	0.5332	
	Side of Tumor							0.9891
	Left	12/ 88 (13.6)	NE (NE , NE)	1/ 33 (3.0)	NE (NE , NE)	4.04 (0.52, 31.08)	0.1470	
	Right	18/ 144 (12.5)	NE (NE , NE)	1/ 35 (2.9)	NE (NE , NE)	4.19 (0.56, 31.40)	0.1293	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
Subgroup analysis was done for SOCs / PTs with significant overall treatment effect (significant log-rank).
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.
[4] P-Value for interaction from Cox proportional hazards model using ties=exact option with treatment, subgroup and treatment*subgroup interaction as covariates.
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Frequent AE by SOC, PT (incidence >= 10% or >=10 patients and incidence >= 1%) - Subgroup analysis
Safety Analysis Set

SOC/PT	Subgroup Level	EC+FOLFOX (N=232) n/ N (%)	EC+FOLFOX (N=232) Median (95% CI)[1]	Control 2 (N=68) n/ N (%)	Control 2 (N=68) Median (95% CI)[1]	Unstratified analysis Hazard Ratio (95% CI)[2]	Unstratified analysis p-Value[3]	Interaction p-Value[4]
SOC: Musculoskeletal and connective tissue disorders	Age (Years)							0.4152
	< 65	92/ 148 (62.2)	7.0 (5.7, 10.0)	15/ 42 (35.7)	NE (7.0, NE)	1.80 (1.04, 3.10)	0.0330	
	>= 65	41/ 84 (48.8)	12.4 (6.9, 15.6)	4/ 26 (15.4)	NE (NE , NE)	2.77 (0.99, 7.75)	0.0423	
	Sex							0.8609
	Male	64/ 121 (52.9)	10.0 (6.4, 16.5)	8/ 32 (25.0)	NE (7.8, NE)	1.99 (0.95, 4.15)	0.0621	
	Female	69/ 111 (62.2)	7.2 (5.7, 11.1)	11/ 36 (30.6)	NE (7.6, NE)	2.12 (1.12, 4.00)	0.0183	
	Region							0.2983
	Europe	63/ 108 (58.3)	10.8 (6.9, 11.5)	12/ 38 (31.6)	NE (7.0, NE)	1.42 (0.76, 2.64)	0.2648	
	USA/Canada	9/ 15 (60.0)	3.9 (2.8, NE)	1/ 7 (14.3)	NE (NE , NE)	4.51 (0.57, 35.85)	0.1188	
	Rest of World	61/ 109 (56.0)	7.4 (5.8, 13.4)	6/ 23 (26.1)	NE (7.6, NE)	2.44 (1.06, 5.65)	0.0309	
	ECOG-PS at Randomization							0.5122
	0	69/ 130 (53.1)	10.9 (7.6, 16.5)	13/ 44 (29.5)	NE (NE , NE)	1.74 (0.96, 3.16)	0.0617	
	1	64/ 102 (62.7)	6.4 (4.5, 11.1)	6/ 24 (25.0)	NE (7.6, NE)	2.40 (1.04, 5.55)	0.0348	
	Number of Organs Involved							0.1763
	<= 2	64/ 116 (55.2)	11.1 (7.2, 16.5)	12/ 33 (36.4)	NE (7.0, NE)	1.48 (0.80, 2.74)	0.2097	
	>= 3	69/ 116 (59.5)	6.7 (4.9, 9.4)	7/ 35 (20.0)	NE (7.8, NE)	2.94 (1.35, 6.41)	0.0043	
	Presence of Liver Metastases							0.1803
	Yes	79/ 146 (54.1)	8.6 (6.7, 12.4)	8/ 42 (19.0)	NE (NE , NE)	2.81 (1.36, 5.82)	0.0035	
	No	54/ 86 (62.8)	7.4 (5.8, 11.5)	11/ 26 (42.3)	NE (3.3, NE)	1.45 (0.75, 2.77)	0.2631	
	Side of Tumor							0.0746
	Left	49/ 88 (55.7)	9.6 (6.9, 13.4)	12/ 33 (36.4)	NE (5.1, NE)	1.29 (0.69, 2.43)	0.4274	
	Right	84/ 144 (58.3)	7.6 (5.4, 11.3)	7/ 35 (20.0)	NE (NE , NE)	3.20 (1.48, 6.91)	0.0018	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
Subgroup analysis was done for SOCs / PTs with significant overall treatment effect (significant log-rank).
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.
[4] P-Value for interaction from Cox proportional hazards model using ties=exact option with treatment, subgroup and treatment*subgroup interaction as covariates.
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Frequent AE by SOC, PT (incidence >= 10% or >=10 patients and incidence >= 1%) - Subgroup analysis
Safety Analysis Set

SOC/PT	Subgroup Level	EC+FOLFOX (N=232) n/ N (%)	EC+FOLFOX (N=232) Median (95% CI)[1]	Control 2 (N=68) n/ N (%)	Control 2 (N=68) Median (95% CI)[1]	Unstratified analysis Hazard Ratio (95% CI)[2]	Unstratified analysis p-Value[3]	Interaction p-Value[4]
SOC: Musculoskeletal and connective tissue disorders, PT: Arthralgia	Age (Years)							0.9861
	< 65	49/ 148 (33.1)	NE (18.9, NE)	3/ 42 (7.1)	NE (NE , NE)	4.46 (1.39, 14.32)	0.0059	
	>= 65	24/ 84 (28.6)	NE (13.4, NE)	0/ 26 (0.0)	NE (NE , NE)	NE		
	Sex							0.9813
	Male	35/ 121 (28.9)	NE (17.4, NE)	3/ 32 (9.4)	NE (NE , NE)	2.58 (0.79, 8.40)	0.1025	
	Female	38/ 111 (34.2)	20.7 (13.3, NE)	0/ 36 (0.0)	NE (NE , NE)	NE		
	Region							0.9998
	Europe	39/ 108 (36.1)	18.9 (12.5, NE)	3/ 38 (7.9)	NE (NE , NE)	3.58 (1.10, 11.60)	0.0233	
	USA/Canada	4/ 15 (26.7)	NE (5.0, NE)	0/ 7 (0.0)	NE (NE , NE)	NE		
	Rest of World	30/ 109 (27.5)	NE (20.3, NE)	0/ 23 (0.0)	NE (NE , NE)	NE		
	ECOG-PS at Randomization							0.9808
	0	38/ 130 (29.2)	NE (18.9, NE)	3/ 44 (6.8)	NE (NE , NE)	3.95 (1.22, 12.79)	0.0135	
	1	35/ 102 (34.3)	NE (11.3, NE)	0/ 24 (0.0)	NE (NE , NE)	NE		
	Number of Organs Involved							0.4228
	<= 2	37/ 116 (31.9)	NE (17.4, NE)	1/ 33 (3.0)	NE (NE , NE)	10.92 (1.50, 79.63)	0.0030	
	>= 3	36/ 116 (31.0)	NE (13.4, NE)	2/ 35 (5.7)	NE (NE , NE)	4.21 (1.01, 17.56)	0.0316	
	Presence of Liver Metastases							0.6744
	Yes	43/ 146 (29.5)	NE (16.5, NE)	2/ 42 (4.8)	NE (NE , NE)	5.46 (1.32, 22.54)	0.0084	
	No	30/ 86 (34.9)	20.3 (17.3, NE)	1/ 26 (3.8)	NE (NE , NE)	8.95 (1.22, 65.66)	0.0089	
	Side of Tumor							0.4071
	Left	26/ 88 (29.5)	NE (17.3, NE)	2/ 33 (6.1)	NE (NE , NE)	4.10 (0.97, 17.33)	0.0369	
	Right	47/ 144 (32.6)	20.7 (14.0, NE)	1/ 35 (2.9)	NE (NE , NE)	11.17 (1.54, 81.00)	0.0026	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
Subgroup analysis was done for SOCs / PTs with significant overall treatment effect (significant log-rank).
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.
[4] P-Value for interaction from Cox proportional hazards model using ties=exact option with treatment, subgroup and treatment*subgroup interaction as covariates.
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

SOC/PT	Subgroup Level	EC+FOLFOX (N=232) n/ N (%)	EC+FOLFOX (N=232) Median (95% CI)[1]	Control 2 (N=68) n/ N (%)	Control 2 (N=68) Median (95% CI)[1]	Unstratified analysis Hazard Ratio (95% CI)[2]	Unstratified analysis p-Value[3]	Interaction p-Value[4]
SOC: Musculoskeletal and connective tissue disorders, PT: Back pain	Age (Years)							0.1598
	< 65	12/ 148 (8.1)	NE (NE , NE)	8/ 42 (19.0)	NE (NE , NE)	0.30 (0.12, 0.75)	0.0060	
	>= 65	12/ 84 (14.3)	NE (NE , NE)	3/ 26 (11.5)	NE (NE , NE)	1.00 (0.28, 3.55)	0.9991	
	Sex							0.4675
	Male	11/ 121 (9.1)	NE (NE , NE)	3/ 32 (9.4)	NE (13.8, NE)	0.63 (0.17, 2.31)	0.4847	
	Female	13/ 111 (11.7)	NE (NE , NE)	8/ 36 (22.2)	NE (NE , NE)	0.43 (0.18, 1.04)	0.0526	
	Region							0.6883
	Europe	9/ 108 (8.3)	NE (27.2, NE)	5/ 38 (13.2)	NE (13.8, NE)	0.41 (0.13, 1.26)	0.1074	
	USA/Canada	3/ 15 (20.0)	NE (NE , NE)	1/ 7 (14.3)	NE (NE , NE)	1.18 (0.12, 11.34)	0.8889	
	Rest of World	12/ 109 (11.0)	NE (NE , NE)	5/ 23 (21.7)	NE (NE , NE)	0.40 (0.14, 1.14)	0.0760	
	ECOG-PS at Randomization							0.5071
	0	10/ 130 (7.7)	NE (NE , NE)	7/ 44 (15.9)	NE (NE , NE)	0.36 (0.13, 0.98)	0.0368	
	1	14/ 102 (13.7)	NE (NE , NE)	4/ 24 (16.7)	NE (NE , NE)	0.53 (0.17, 1.64)	0.2668	
	Number of Organs Involved							0.3753
	<= 2	11/ 116 (9.5)	NE (NE , NE)	7/ 33 (21.2)	NE (NE , NE)	0.35 (0.13, 0.92)	0.0253	
	>= 3	13/ 116 (11.2)	NE (NE , NE)	4/ 35 (11.4)	NE (NE , NE)	0.69 (0.22, 2.12)	0.5104	
	Presence of Liver Metastases							0.1528
	Yes	15/ 146 (10.3)	NE (27.2, NE)	4/ 42 (9.5)	NE (NE , NE)	0.75 (0.25, 2.30)	0.6208	
	No	9/ 86 (10.5)	NE (NE , NE)	7/ 26 (26.9)	NE (13.8, NE)	0.31 (0.12, 0.84)	0.0152	
	Side of Tumor							0.2926
	Left	11/ 88 (12.5)	NE (NE , NE)	8/ 33 (24.2)	NE (13.8, NE)	0.37 (0.15, 0.94)	0.0304	
	Right	13/ 144 (9.0)	NE (NE , NE)	3/ 35 (8.6)	NE (NE , NE)	0.84 (0.24, 2.95)	0.7838	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
Subgroup analysis was done for SOCs / PTs with significant overall treatment effect (significant log-rank).
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.
[4] P-Value for interaction from Cox proportional hazards model using ties=exact option with treatment, subgroup and treatment*subgroup interaction as covariates.
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Frequent AE by SOC, PT (incidence >= 10% or >=10 patients and incidence >= 1%) - Subgroup analysis
Safety Analysis Set

SOC/PT	Subgroup Level	EC+FOLFOX (N=232) n/ N (%)	EC+FOLFOX (N=232) Median (95% CI)[1]	Control 2 (N=68) n/ N (%)	Control 2 (N=68) Median (95% CI)[1]	Unstratified analysis Hazard Ratio (95% CI)[2]	Unstratified analysis p-Value[3]	Interaction p-Value[4]
SOC: Musculoskeletal and connective tissue disorders, PT: Myalgia	Age (Years)							0.9903
	< 65	29/ 148 (19.6)	NE (NE , NE)	2/ 42 (4.8)	NE (NE , NE)	3.51 (0.84, 14.75)	0.0670	
	>= 65	9/ 84 (10.7)	NE (NE , NE)	0/ 26 (0.0)	NE (NE , NE)	NE		
	Sex							0.7394
	Male	18/ 121 (14.9)	NE (NE , NE)	1/ 32 (3.1)	NE (NE , NE)	3.86 (0.51, 29.01)	0.1566	
	Female	20/ 111 (18.0)	NE (NE , NE)	1/ 36 (2.8)	NE (NE , NE)	5.86 (0.79, 43.77)	0.0504	
	Region							0.3974
	Europe	20/ 108 (18.5)	NE (NE , NE)	1/ 38 (2.6)	NE (NE , NE)	4.91 (0.66, 36.75)	0.0860	
	USA/Canada	1/ 15 (6.7)	NE (NE , NE)	1/ 7 (14.3)	NE (14.4, NE)	0.57 (0.03, 9.43)	0.6878	
	Rest of World	17/ 109 (15.6)	NE (NE , NE)	0/ 23 (0.0)	NE (NE , NE)	NE		
	ECOG-PS at Randomization							0.9857
	0	18/ 130 (13.8)	NE (NE , NE)	2/ 44 (4.5)	NE (NE , NE)	2.57 (0.60, 11.13)	0.1893	
	1	20/ 102 (19.6)	NE (NE , NE)	0/ 24 (0.0)	NE (NE , NE)	NE		
	Number of Organs Involved							0.9889
	<= 2	16/ 116 (13.8)	NE (NE , NE)	2/ 33 (6.1)	NE (NE , NE)	2.19 (0.50, 9.51)	0.2848	
	>= 3	22/ 116 (19.0)	NE (23.7, NE)	0/ 35 (0.0)	NE (NE , NE)	NE		
	Presence of Liver Metastases							0.9867
	Yes	26/ 146 (17.8)	NE (NE , NE)	0/ 42 (0.0)	NE (NE , NE)	NE		
	No	12/ 86 (14.0)	NE (NE , NE)	2/ 26 (7.7)	NE (NE , NE)	1.43 (0.32, 6.42)	0.6416	
	Side of Tumor							0.9876
	Left	16/ 88 (18.2)	NE (NE , NE)	2/ 33 (6.1)	NE (NE , NE)	2.49 (0.57, 10.87)	0.2098	
	Right	22/ 144 (15.3)	NE (NE , NE)	0/ 35 (0.0)	NE (NE , NE)	NE		

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
Subgroup analysis was done for SOCs / PTs with significant overall treatment effect (significant log-rank).
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.
[4] P-Value for interaction from Cox proportional hazards model using ties=exact option with treatment, subgroup and treatment*subgroup interaction as covariates.
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Frequent AE by SOC, PT (incidence >= 10% or >=10 patients and incidence >= 1%) - Subgroup analysis
Safety Analysis Set

SOC/PT	Subgroup Level	EC+FOLFOX (N=232) n/ N (%)	EC+FOLFOX (N=232) Median (95% CI)[1]	Control 2 (N=68) n/ N (%)	Control 2 (N=68) Median (95% CI)[1]	Unstratified analysis Hazard Ratio (95% CI)[2]	Unstratified analysis p-Value[3]	Interaction p-Value[4]
SOC: Neoplasms benign, malignant and unspecified (incl cysts and polyps)	Age (Years)							0.6427
	< 65	24/ 148 (16.2)	NE (NE , NE)	2/ 42 (4.8)	NE (NE , NE)	3.13 (0.74, 13.25)	0.1018	
	>= 65	19/ 84 (22.6)	NE (NE , NE)	1/ 26 (3.8)	NE (NE , NE)	5.48 (0.73, 41.02)	0.0624	
	Sex							0.4715
	Male	23/ 121 (19.0)	NE (NE , NE)	2/ 32 (6.3)	NE (NE , NE)	2.52 (0.59, 10.70)	0.1948	
	Female	20/ 111 (18.0)	NE (NE , NE)	1/ 36 (2.8)	NE (NE , NE)	6.47 (0.87, 48.21)	0.0360	
	Region							0.9990
	Europe	22/ 108 (20.4)	NE (NE , NE)	2/ 38 (5.3)	NE (NE , NE)	3.32 (0.78, 14.16)	0.0854	
	USA/Canada	3/ 15 (20.0)	NE (NE , NE)	0/ 7 (0.0)	NE (NE , NE)	NE		
	Rest of World	18/ 109 (16.5)	NE (NE , NE)	1/ 23 (4.3)	NE (NE , NE)	3.62 (0.48, 27.12)	0.1808	
	ECOG-PS at Randomization							0.8701
	0	26/ 130 (20.0)	NE (NE , NE)	2/ 44 (4.5)	NE (NE , NE)	4.16 (0.99, 17.54)	0.0348	
	1	17/ 102 (16.7)	NE (NE , NE)	1/ 24 (4.2)	NE (NE , NE)	3.69 (0.49, 27.78)	0.1735	
	Number of Organs Involved							0.6913
	<= 2	22/ 116 (19.0)	NE (NE , NE)	2/ 33 (6.1)	NE (NE , NE)	3.18 (0.75, 13.53)	0.0977	
	>= 3	21/ 116 (18.1)	NE (NE , NE)	1/ 35 (2.9)	NE (NE , NE)	5.13 (0.69, 38.25)	0.0753	
	Presence of Liver Metastases							0.3009
	Yes	29/ 146 (19.9)	NE (NE , NE)	1/ 42 (2.4)	NE (NE , NE)	7.40 (1.01, 54.38)	0.0207	
	No	14/ 86 (16.3)	NE (NE , NE)	2/ 26 (7.7)	NE (NE , NE)	2.14 (0.49, 9.44)	0.3015	
	Side of Tumor							0.9856
	Left	13/ 88 (14.8)	NE (NE , NE)	3/ 33 (9.1)	NE (NE , NE)	1.40 (0.40, 4.92)	0.6014	
	Right	30/ 144 (20.8)	NE (NE , NE)	0/ 35 (0.0)	NE (NE , NE)	NE		

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
Subgroup analysis was done for SOCs / PTs with significant overall treatment effect (significant log-rank).
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.
[4] P-Value for interaction from Cox proportional hazards model using ties=exact option with treatment, subgroup and treatment*subgroup interaction as covariates.
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Frequent AE by SOC, PT (incidence >= 10% or >=10 patients and incidence >= 1%) - Subgroup analysis
Safety Analysis Set

SOC/PT	Subgroup Level	EC+FOLFOX (N=232) n/ N (%)	EC+FOLFOX (N=232) Median (95% CI)[1]	Control 2 (N=68) n/ N (%)	Control 2 (N=68) Median (95% CI)[1]	Unstratified analysis Hazard Ratio (95% CI)[2]	Unstratified analysis p-Value[3]	Interaction p-Value[4]
SOC: Nervous system disorders	Age (Years)							0.7819
	< 65	127/ 148 (85.8)	1.3 (0.9, 1.8)	18/ 42 (42.9)	14.0 (2.7, NE)	2.78 (1.69, 4.58)	<.0001	
	>= 65	64/ 84 (76.2)	1.8 (1.1, 2.8)	10/ 26 (38.5)	11.5 (5.6, NE)	3.46 (1.76, 6.80)	0.0001	
	Sex							0.5423
	Male	99/ 121 (81.8)	1.4 (1.0, 2.0)	11/ 32 (34.4)	14.5 (5.1, NE)	3.72 (1.97, 7.01)	<.0001	
	Female	92/ 111 (82.9)	1.4 (0.9, 2.0)	17/ 36 (47.2)	8.4 (2.7, NE)	2.72 (1.61, 4.60)	<.0001	
	Region							0.2185
	Europe	95/ 108 (88.0)	1.2 (0.7, 1.7)	13/ 38 (34.2)	NE (8.4, NE)	4.60 (2.55, 8.32)	<.0001	
	USA/Canada	13/ 15 (86.7)	0.5 (0.2, 1.8)	5/ 7 (71.4)	6.5 (0.8, 14.0)	2.45 (0.79, 7.63)	0.1042	
	Rest of World	83/ 109 (76.1)	2.0 (1.4, 3.3)	10/ 23 (43.5)	14.5 (2.7, NE)	2.44 (1.26, 4.74)	0.0056	
	ECOG-PS at Randomization							0.3373
	0	110/ 130 (84.6)	1.4 (0.9, 1.9)	22/ 44 (50.0)	11.5 (5.1, NE)	2.73 (1.71, 4.35)	<.0001	
	1	81/ 102 (79.4)	1.6 (1.0, 2.1)	6/ 24 (25.0)	NE (NE , NE)	4.36 (1.90, 10.01)	0.0001	
	Number of Organs Involved							0.4502
	<= 2	99/ 116 (85.3)	1.5 (1.0, 2.0)	18/ 33 (54.5)	8.4 (2.7, NE)	2.76 (1.65, 4.60)	<.0001	
	>= 3	92/ 116 (79.3)	1.3 (0.9, 1.8)	10/ 35 (28.6)	NE (6.0, NE)	3.63 (1.89, 6.99)	<.0001	
	Presence of Liver Metastases							0.1497
	Yes	117/ 146 (80.1)	1.4 (1.0, 1.9)	18/ 42 (42.9)	11.5 (5.1, NE)	2.37 (1.44, 3.90)	0.0004	
	No	74/ 86 (86.0)	1.3 (0.9, 2.3)	10/ 26 (38.5)	14.5 (6.0, NE)	5.02 (2.46, 10.27)	<.0001	
	Side of Tumor							0.2755
	Left	71/ 88 (80.7)	1.8 (1.1, 3.0)	10/ 33 (30.3)	NE (NE , NE)	3.67 (1.88, 7.15)	<.0001	
	Right	120/ 144 (83.3)	1.3 (0.9, 1.8)	18/ 35 (51.4)	6.5 (5.1, 14.0)	2.54 (1.54, 4.19)	0.0001	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
Subgroup analysis was done for SOCs / PTs with significant overall treatment effect (significant log-rank).
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.
[4] P-Value for interaction from Cox proportional hazards model using ties=exact option with treatment, subgroup and treatment*subgroup interaction as covariates.
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Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Frequent AE by SOC, PT (incidence >= 10% or >=10 patients and incidence >= 1%) - Subgroup analysis
Safety Analysis Set

SOC/PT	Subgroup Level	EC+FOLFOX (N=232) n/ N (%)	EC+FOLFOX (N=232) Median (95% CI)[1]	Control 2 (N=68) n/ N (%)	Control 2 (N=68) Median (95% CI)[1]	Unstratified analysis Hazard Ratio (95% CI)[2]	Unstratified analysis p-Value[3]	Interaction p-Value[4]
SOC: Nervous system disorders, PT: Dysgeusia	Age (Years)							0.5996
	< 65	19/ 148 (12.8)	NE (NE , NE)	2/ 42 (4.8)	NE (NE , NE)	2.54 (0.59, 10.92)	0.1932	
	>= 65	16/ 84 (19.0)	NE (NE , NE)	1/ 26 (3.8)	NE (NE , NE)	4.69 (0.62, 35.42)	0.0983	
	Sex							0.6505
	Male	19/ 121 (15.7)	NE (NE , NE)	1/ 32 (3.1)	NE (NE , NE)	4.48 (0.60, 33.51)	0.1090	
	Female	16/ 111 (14.4)	NE (NE , NE)	2/ 36 (5.6)	NE (NE , NE)	2.51 (0.58, 10.91)	0.2052	
	Region							0.1845
	Europe	18/ 108 (16.7)	NE (NE , NE)	1/ 38 (2.6)	NE (NE , NE)	5.90 (0.79, 44.25)	0.0496	
	USA/Canada	2/ 15 (13.3)	NE (NE , NE)	2/ 7 (28.6)	NE (8.3, NE)	0.49 (0.07, 3.57)	0.4724	
	Rest of World	15/ 109 (13.8)	NE (NE , NE)	0/ 23 (0.0)	NE (NE , NE)	NE		
	ECOG-PS at Randomization							0.9180
	0	21/ 130 (16.2)	NE (NE , NE)	2/ 44 (4.5)	NE (NE , NE)	3.35 (0.79, 14.31)	0.0825	
	1	14/ 102 (13.7)	NE (NE , NE)	1/ 24 (4.2)	NE (NE , NE)	3.21 (0.42, 24.38)	0.2343	
	Number of Organs Involved							0.4665
	<= 2	15/ 116 (12.9)	NE (NE , NE)	2/ 33 (6.1)	NE (NE , NE)	2.11 (0.48, 9.25)	0.3094	
	>= 3	20/ 116 (17.2)	NE (NE , NE)	1/ 35 (2.9)	NE (NE , NE)	5.56 (0.75, 41.47)	0.0590	
	Presence of Liver Metastases							0.8493
	Yes	22/ 146 (15.1)	NE (NE , NE)	2/ 42 (4.8)	NE (NE , NE)	3.08 (0.72, 13.09)	0.1082	
	No	13/ 86 (15.1)	NE (NE , NE)	1/ 26 (3.8)	NE (NE , NE)	3.67 (0.48, 28.14)	0.1795	
	Side of Tumor							0.2240
	Left	8/ 88 (9.1)	NE (NE , NE)	2/ 33 (6.1)	NE (NE , NE)	1.35 (0.29, 6.35)	0.7053	
	Right	27/ 144 (18.8)	NE (NE , NE)	1/ 35 (2.9)	NE (NE , NE)	6.43 (0.87, 47.34)	0.0353	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
Subgroup analysis was done for SOCs / PTs with significant overall treatment effect (significant log-rank).
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.
[4] P-Value for interaction from Cox proportional hazards model using ties=exact option with treatment, subgroup and treatment*subgroup interaction as covariates.
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Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Frequent AE by SOC, PT (incidence >= 10% or >=10 patients and incidence >= 1%) - Subgroup analysis
Safety Analysis Set

SOC/PT	Subgroup Level	EC+FOLFOX (N=232) n/ N (%)	EC+FOLFOX (N=232) Median (95% CI)[1]	Control 2 (N=68) n/ N (%)	Control 2 (N=68) Median (95% CI)[1]	Unstratified analysis Hazard Ratio (95% CI)[2]	Unstratified analysis p-Value[3]	Interaction p-Value[4]
SOC: Nervous system disorders, PT: Neuropathy peripheral	Age (Years)							0.9875
	< 65	44/ 148 (29.7)	NE (NE , NE)	1/ 42 (2.4)	NE (NE , NE)	12.99 (1.79, 94.30)	0.0010	
	>= 65	20/ 84 (23.8)	NE (NE , NE)	0/ 26 (0.0)	NE (NE , NE)	NE		
	Sex							0.9863
	Male	32/ 121 (26.4)	NE (NE , NE)	0/ 32 (0.0)	NE (NE , NE)	NE		
	Female	32/ 111 (28.8)	NE (NE , NE)	1/ 36 (2.8)	NE (NE , NE)	10.94 (1.49, 80.08)	0.0031	
	Region							0.9999
	Europe	37/ 108 (34.3)	NE (NE , NE)	0/ 38 (0.0)	NE (NE , NE)	NE		
	USA/Canada	5/ 15 (33.3)	NE (4.8, NE)	1/ 7 (14.3)	NE (NE , NE)	2.52 (0.29, 21.63)	0.3815	
	Rest of World	22/ 109 (20.2)	NE (NE , NE)	0/ 23 (0.0)	NE (NE , NE)	NE		
	ECOG-PS at Randomization							0.9884
	0	38/ 130 (29.2)	NE (NE , NE)	1/ 44 (2.3)	NE (NE , NE)	13.61 (1.87, 99.14)	0.0007	
	1	26/ 102 (25.5)	NE (NE , NE)	0/ 24 (0.0)	NE (NE , NE)	NE		
	Number of Organs Involved							0.9843
	<= 2	32/ 116 (27.6)	NE (NE , NE)	0/ 33 (0.0)	NE (NE , NE)	NE		
	>= 3	32/ 116 (27.6)	NE (NE , NE)	1/ 35 (2.9)	NE (NE , NE)	8.74 (1.19, 63.98)	0.0099	
	Presence of Liver Metastases							0.9867
	Yes	42/ 146 (28.8)	NE (NE , NE)	1/ 42 (2.4)	NE (NE , NE)	11.63 (1.60, 84.55)	0.0021	
	No	22/ 86 (25.6)	NE (NE , NE)	0/ 26 (0.0)	NE (NE , NE)	NE		
	Side of Tumor							0.9855
	Left	23/ 88 (26.1)	NE (NE , NE)	0/ 33 (0.0)	NE (NE , NE)	NE		
	Right	41/ 144 (28.5)	NE (NE , NE)	1/ 35 (2.9)	NE (NE , NE)	10.08 (1.39, 73.31)	0.0047	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
Subgroup analysis was done for SOCs / PTs with significant overall treatment effect (significant log-rank).
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.
[4] P-Value for interaction from Cox proportional hazards model using ties=exact option with treatment, subgroup and treatment*subgroup interaction as covariates.
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Frequent AE by SOC, PT (incidence >= 10% or >=10 patients and incidence >= 1%) - Subgroup analysis
Safety Analysis Set

SOC/PT	Subgroup Level	EC+FOLFOX (N=232) n/ N (%)	EC+FOLFOX (N=232) Median (95% CI)[1]	Control 2 (N=68) n/ N (%)	Control 2 (N=68) Median (95% CI)[1]	Unstratified analysis Hazard Ratio (95% CI)[2]	Unstratified analysis p-Value[3]	Interaction p-Value[4]
SOC: Nervous system disorders, PT: Neurotoxicity	Age (Years)							0.9910
	< 65	13/ 148 (8.8)	NE (NE , NE)	1/ 42 (2.4)	NE (NE , NE)	3.60 (0.47, 27.52)	0.1869	
	>= 65	13/ 84 (15.5)	NE (NE , NE)	0/ 26 (0.0)	NE (NE , NE)	NE		
	Sex							0.9892
	Male	13/ 121 (10.7)	NE (NE , NE)	1/ 32 (3.1)	NE (NE , NE)	3.45 (0.45, 26.38)	0.2040	
	Female	13/ 111 (11.7)	NE (NE , NE)	0/ 36 (0.0)	NE (NE , NE)	NE		
	Region							1.0000
	Europe	23/ 108 (21.3)	NE (NE , NE)	1/ 38 (2.6)	NE (NE , NE)	8.39 (1.13, 62.12)	0.0124	
	USA/Canada	0/ 15 (0.0)	NE (NE , NE)	0/ 7 (0.0)	NE (NE , NE)	NE		
	Rest of World	3/ 109 (2.8)	NE (NE , NE)	0/ 23 (0.0)	NE (NE , NE)	NE		
	ECOG-PS at Randomization							0.9881
	0	14/ 130 (10.8)	NE (NE , NE)	0/ 44 (0.0)	NE (NE , NE)	NE		
	1	12/ 102 (11.8)	NE (NE , NE)	1/ 24 (4.2)	NE (NE , NE)	2.79 (0.36, 21.48)	0.3034	
	Number of Organs Involved							0.9898
	<= 2	13/ 116 (11.2)	NE (NE , NE)	1/ 33 (3.0)	NE (NE , NE)	3.79 (0.50, 28.99)	0.1671	
	>= 3	13/ 116 (11.2)	NE (NE , NE)	0/ 35 (0.0)	NE (NE , NE)	NE		
	Presence of Liver Metastases							0.9887
	Yes	15/ 146 (10.3)	NE (NE , NE)	0/ 42 (0.0)	NE (NE , NE)	NE		
	No	11/ 86 (12.8)	NE (NE , NE)	1/ 26 (3.8)	NE (NE , NE)	3.31 (0.43, 25.64)	0.2244	
	Side of Tumor							0.9898
	Left	11/ 88 (12.5)	NE (NE , NE)	0/ 33 (0.0)	NE (NE , NE)	NE		
	Right	15/ 144 (10.4)	NE (NE , NE)	1/ 35 (2.9)	NE (NE , NE)	3.63 (0.48, 27.45)	0.1821	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
Subgroup analysis was done for SOCs / PTs with significant overall treatment effect (significant log-rank).
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.
[4] P-Value for interaction from Cox proportional hazards model using ties=exact option with treatment, subgroup and treatment*subgroup interaction as covariates.
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Frequent AE by SOC, PT (incidence >= 10% or >=10 patients and incidence >= 1%) - Subgroup analysis
Safety Analysis Set

SOC/PT	Subgroup Level	EC+FOLFOX (N=232) n/ N (%)	EC+FOLFOX (N=232) Median (95% CI)[1]	Control 2 (N=68) n/ N (%)	Control 2 (N=68) Median (95% CI)[1]	Unstratified analysis Hazard Ratio (95% CI)[2]	Unstratified analysis p-Value[3]	Interaction p-Value[4]
SOC: Nervous system disorders, PT: Peripheral sensory neuropathy	Age (Years)							0.9179
	< 65	44/ 148 (29.7)	NE (NE , NE)	2/ 42 (4.8)	NE (NE , NE)	6.50 (1.58, 26.80)	0.0028	
	>= 65	18/ 84 (21.4)	NE (NE , NE)	1/ 26 (3.8)	NE (NE , NE)	5.75 (0.77, 43.11)	0.0537	
	Sex							0.9845
	Male	37/ 121 (30.6)	NE (NE , NE)	0/ 32 (0.0)	NE (NE , NE)	NE		
	Female	25/ 111 (22.5)	NE (NE , NE)	3/ 36 (8.3)	NE (NE , NE)	2.82 (0.85, 9.35)	0.0758	
	Region							0.8199
	Europe	20/ 108 (18.5)	NE (NE , NE)	1/ 38 (2.6)	NE (NE , NE)	6.81 (0.91, 50.74)	0.0298	
	USA/Canada	6/ 15 (40.0)	NE (2.6, NE)	1/ 7 (14.3)	NE (13.0, NE)	4.06 (0.46, 35.58)	0.1762	
	Rest of World	36/ 109 (33.0)	NE (NE , NE)	1/ 23 (4.3)	NE (NE , NE)	8.46 (1.16, 61.71)	0.0114	
	ECOG-PS at Randomization							0.9887
	0	34/ 130 (26.2)	NE (NE , NE)	2/ 44 (4.5)	NE (NE , NE)	6.15 (1.48, 25.61)	0.0043	
	1	28/ 102 (27.5)	NE (NE , NE)	1/ 24 (4.2)	NE (NE , NE)	6.28 (0.85, 46.18)	0.0384	
	Number of Organs Involved							0.9844
	<= 2	32/ 116 (27.6)	NE (NE , NE)	3/ 33 (9.1)	NE (NE , NE)	3.40 (1.04, 11.12)	0.0311	
	>= 3	30/ 116 (25.9)	NE (NE , NE)	0/ 35 (0.0)	NE (NE , NE)	NE		
	Presence of Liver Metastases							0.9820
	Yes	38/ 146 (26.0)	NE (NE , NE)	0/ 42 (0.0)	NE (NE , NE)	NE		
	No	24/ 86 (27.9)	NE (NE , NE)	3/ 26 (11.5)	NE (NE , NE)	2.63 (0.79, 8.75)	0.1005	
	Side of Tumor							0.4645
	Left	22/ 88 (25.0)	NE (NE , NE)	2/ 33 (6.1)	NE (NE , NE)	4.06 (0.95, 17.27)	0.0399	
	Right	40/ 144 (27.8)	NE (NE , NE)	1/ 35 (2.9)	NE (NE , NE)	10.34 (1.42, 75.22)	0.0041	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
Subgroup analysis was done for SOCs / PTs with significant overall treatment effect (significant log-rank).
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.
[4] P-Value for interaction from Cox proportional hazards model using ties=exact option with treatment, subgroup and treatment*subgroup interaction as covariates.
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Frequent AE by SOC, PT (incidence >= 10% or >=10 patients and incidence >= 1%) - Subgroup analysis
Safety Analysis Set

SOC/PT	Subgroup Level	EC+FOLFOX (N=232) n/ N (%)	EC+FOLFOX (N=232) Median (95% CI)[1]	Control 2 (N=68) n/ N (%)	Control 2 (N=68) Median (95% CI)[1]	Unstratified analysis Hazard Ratio (95% CI)[2]	Unstratified analysis p-Value[3]	Interaction p-Value[4]
SOC: Respiratory, thoracic and mediastinal disorders, PT: Pulmonary embolism	Age (Years)							0.4822
	< 65	5/ 148 (3.4)	NE (NE , NE)	5/ 42 (11.9)	NE (19.8, NE)	0.22 (0.06, 0.77)	0.0091	
	>= 65	4/ 84 (4.8)	NE (NE , NE)	2/ 26 (7.7)	NE (NE , NE)	0.56 (0.10, 3.06)	0.4969	
	Sex							
	Male	5/ 121 (4.1)		4/ 32 (12.5)				
	Female	4/ 111 (3.6)		3/ 36 (8.3)				
	Region							
	Europe	5/ 108 (4.6)		2/ 38 (5.3)				
	USA/Canada	2/ 15 (13.3)		3/ 7 (42.9)				
	Rest of World	2/ 109 (1.8)		2/ 23 (8.7)				
	ECOG-PS at Randomization							
	0	4/ 130 (3.1)		4/ 44 (9.1)				
	1	5/ 102 (4.9)		3/ 24 (12.5)				
	Number of Organs Involved							
	<= 2	6/ 116 (5.2)		2/ 33 (6.1)				
	>= 3	3/ 116 (2.6)		5/ 35 (14.3)				
	Presence of Liver Metastases							0.7522
	Yes	6/ 146 (4.1)	NE (NE , NE)	5/ 42 (11.9)	19.8 (19.8, NE)	0.26 (0.08, 0.87)	0.0190	
	No	3/ 86 (3.5)	NE (NE , NE)	2/ 26 (7.7)	NE (NE , NE)	0.41 (0.07, 2.48)	0.3172	
	Side of Tumor							0.5515
	Left	1/ 88 (1.1)	NE (NE , NE)	2/ 33 (6.1)	NE (NE , NE)	0.14 (0.01, 1.52)	0.0581	
	Right	8/ 144 (5.6)	NE (NE , NE)	5/ 35 (14.3)	NE (19.8, NE)	0.33 (0.11, 1.01)	0.0414	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
Subgroup analysis was done for SOCs / PTs with significant overall treatment effect (significant log-rank).
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.
[4] P-Value for interaction from Cox proportional hazards model using ties=exact option with treatment, subgroup and treatment*subgroup interaction as covariates.
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Frequent AE by SOC, PT (incidence >= 10% or >=10 patients and incidence >= 1%) - Subgroup analysis
Safety Analysis Set

SOC/PT	Subgroup Level	EC+FOLFOX (N=232) n/ N (%)	EC+FOLFOX (N=232) Median (95% CI)[1]	Control 2 (N=68) n/ N (%)	Control 2 (N=68) Median (95% CI)[1]	Unstratified analysis Hazard Ratio (95% CI)[2]	Unstratified analysis p-Value[3]	Interaction p-Value[4]
SOC: Skin and subcutaneous tissue disorders	Age (Years)							0.9183
	< 65	118/ 148 (79.7)	1.0 (0.7, 1.9)	17/ 42 (40.5)	18.1 (6.1, NE)	2.86 (1.72, 4.75)	<.0001	
	>= 65	70/ 84 (83.3)	1.2 (0.9, 1.8)	11/ 26 (42.3)	6.8 (2.8, NE)	2.90 (1.53, 5.49)	0.0006	
	Sex							0.6194
	Male	94/ 121 (77.7)	1.0 (0.8, 1.8)	12/ 32 (37.5)	11.0 (6.2, NE)	3.17 (1.73, 5.78)	<.0001	
	Female	94/ 111 (84.7)	1.0 (0.8, 1.9)	16/ 36 (44.4)	NE (1.1, NE)	2.60 (1.53, 4.43)	0.0002	
	Region							0.1909
	Europe	91/ 108 (84.3)	1.3 (0.9, 2.0)	11/ 38 (28.9)	18.1 (6.8, NE)	4.31 (2.30, 8.07)	<.0001	
	USA/Canada	13/ 15 (86.7)	0.8 (0.4, 2.8)	5/ 7 (71.4)	1.5 (1.0, 11.0)	2.19 (0.71, 6.75)	0.1621	
	Rest of World	84/ 109 (77.1)	1.0 (0.6, 1.8)	12/ 23 (52.2)	3.5 (0.6, NE)	1.94 (1.06, 3.55)	0.0281	
	ECOG-PS at Randomization							0.5330
	0	105/ 130 (80.8)	1.0 (0.9, 1.8)	20/ 44 (45.5)	11.0 (3.5, NE)	2.58 (1.60, 4.17)	<.0001	
	1	83/ 102 (81.4)	1.2 (0.8, 1.9)	8/ 24 (33.3)	NE (1.4, NE)	3.35 (1.62, 6.94)	0.0005	
	Number of Organs Involved							0.1313
	<= 2	97/ 116 (83.6)	0.8 (0.5, 1.0)	13/ 33 (39.4)	NE (6.2, NE)	3.66 (2.05, 6.55)	<.0001	
	>= 3	91/ 116 (78.4)	1.6 (1.0, 2.4)	15/ 35 (42.9)	18.1 (1.5, 18.1)	2.06 (1.19, 3.56)	0.0081	
	Presence of Liver Metastases							0.5244
	Yes	121/ 146 (82.9)	1.0 (0.8, 1.6)	17/ 42 (40.5)	11.0 (6.2, 18.1)	3.13 (1.88, 5.21)	<.0001	
	No	67/ 86 (77.9)	1.1 (0.9, 1.9)	11/ 26 (42.3)	NE (1.0, NE)	2.30 (1.22, 4.36)	0.0082	
	Side of Tumor							0.1425
	Left	64/ 88 (72.7)	1.9 (1.0, 3.0)	14/ 33 (42.4)	NE (1.0, NE)	2.02 (1.13, 3.60)	0.0149	
	Right	124/ 144 (86.1)	0.9 (0.7, 1.2)	14/ 35 (40.0)	18.1 (6.2, NE)	3.72 (2.13, 6.48)	<.0001	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
Subgroup analysis was done for SOCs / PTs with significant overall treatment effect (significant log-rank).
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.
[4] P-Value for interaction from Cox proportional hazards model using ties=exact option with treatment, subgroup and treatment*subgroup interaction as covariates.
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

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Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Frequent AE by SOC, PT (incidence >= 10% or >=10 patients and incidence >= 1%) - Subgroup analysis
Safety Analysis Set

SOC/PT	Subgroup Level	EC+FOLFOX (N=232) n/ N (%)	EC+FOLFOX (N=232) Median (95% CI)[1]	Control 2 (N=68) n/ N (%)	Control 2 (N=68) Median (95% CI)[1]	Unstratified analysis Hazard Ratio (95% CI)[2]	Unstratified analysis p-Value[3]	Interaction p-Value[4]
SOC: Skin and subcutaneous tissue disorders, PT: Pruritus	Age (Years)							0.9915
	< 65	22/ 148 (14.9)	NE (NE , NE)	1/ 42 (2.4)	NE (NE , NE)	5.65 (0.76, 41.97)	0.0555	
	>= 65	10/ 84 (11.9)	NE (28.1, NE)	0/ 26 (0.0)	NE (NE , NE)	NE		
	Sex							0.9903
	Male	16/ 121 (13.2)	NE (28.1, NE)	0/ 32 (0.0)	NE (NE , NE)	NE		
	Female	16/ 111 (14.4)	NE (NE , NE)	1/ 36 (2.8)	NE (NE , NE)	4.86 (0.64, 36.65)	0.0898	
	Region							0.9999
	Europe	16/ 108 (14.8)	NE (28.1, NE)	0/ 38 (0.0)	NE (NE , NE)	NE		
	USA/Canada	1/ 15 (6.7)	NE (NE , NE)	0/ 7 (0.0)	NE (NE , NE)	NE		
	Rest of World	15/ 109 (13.8)	NE (NE , NE)	1/ 23 (4.3)	NE (NE , NE)	2.82 (0.37, 21.39)	0.2928	
	ECOG-PS at Randomization							0.9874
	0	17/ 130 (13.1)	NE (NE , NE)	0/ 44 (0.0)	NE (NE , NE)	NE		
	1	15/ 102 (14.7)	NE (NE , NE)	1/ 24 (4.2)	NE (NE , NE)	2.75 (0.36, 20.92)	0.3093	
	Number of Organs Involved							0.9885
	<= 2	19/ 116 (16.4)	NE (NE , NE)	0/ 33 (0.0)	NE (NE , NE)	NE		
	>= 3	13/ 116 (11.2)	NE (21.9, NE)	1/ 35 (2.9)	NE (NE , NE)	3.00 (0.39, 23.11)	0.2673	
	Presence of Liver Metastases							0.9901
	Yes	18/ 146 (12.3)	NE (NE , NE)	1/ 42 (2.4)	NE (NE , NE)	4.17 (0.56, 31.37)	0.1311	
	No	14/ 86 (16.3)	NE (28.1, NE)	0/ 26 (0.0)	NE (NE , NE)	NE		
	Side of Tumor							0.9888
	Left	9/ 88 (10.2)	NE (NE , NE)	1/ 33 (3.0)	NE (NE , NE)	2.45 (0.31, 19.63)	0.3820	
	Right	23/ 144 (16.0)	NE (28.1, NE)	0/ 35 (0.0)	NE (NE , NE)	NE		

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
Subgroup analysis was done for SOCs / PTs with significant overall treatment effect (significant log-rank).
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.
[4] P-Value for interaction from Cox proportional hazards model using ties=exact option with treatment, subgroup and treatment*subgroup interaction as covariates.
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Frequent AE by SOC, PT (incidence >= 10% or >=10 patients and incidence >= 1%) - Subgroup analysis
Safety Analysis Set

SOC/PT	Subgroup Level	EC+FOLFOX (N=232) n/ N (%)	EC+FOLFOX (N=232) Median (95% CI)[1]	Control 2 (N=68) n/ N (%)	Control 2 (N=68) Median (95% CI)[1]	Unstratified analysis Hazard Ratio (95% CI)[2]	Unstratified analysis p-Value[3]	Interaction p-Value[4]
SOC: Skin and subcutaneous tissue disorders, PT: Rash	Age (Years)							0.9828
	< 65	44/ 148 (29.7)	NE (24.0, NE)	0/ 42 (0.0)	NE (NE , NE)	NE		
	>= 65	26/ 84 (31.0)	NE (30.0, NE)	1/ 26 (3.8)	NE (NE , NE)	7.64 (1.04, 56.44)	0.0185	
	Sex							0.9862
	Male	33/ 121 (27.3)	NE (24.0, NE)	0/ 32 (0.0)	NE (NE , NE)	NE		
	Female	37/ 111 (33.3)	30.0 (30.0, NE)	1/ 36 (2.8)	NE (NE , NE)	12.47 (1.71, 90.96)	0.0014	
	Region							0.9997
	Europe	38/ 108 (35.2)	NE (18.4, NE)	0/ 38 (0.0)	NE (NE , NE)	NE		
	USA/Canada	5/ 15 (33.3)	19.8 (19.8, NE)	0/ 7 (0.0)	NE (NE , NE)	NE		
	Rest of World	27/ 109 (24.8)	NE (30.0, NE)	1/ 23 (4.3)	NE (NE , NE)	5.02 (0.68, 37.05)	0.0783	
	ECOG-PS at Randomization							0.9885
	0	43/ 130 (33.1)	NE (24.0, NE)	1/ 44 (2.3)	NE (NE , NE)	14.69 (2.02, 106.74)	0.0004	
	1	27/ 102 (26.5)	30.0 (19.8, NE)	0/ 24 (0.0)	NE (NE , NE)	NE		
	Number of Organs Involved							0.9857
	<= 2	33/ 116 (28.4)	NE (NE , NE)	1/ 33 (3.0)	NE (NE , NE)	9.67 (1.32, 70.79)	0.0060	
	>= 3	37/ 116 (31.9)	30.0 (18.4, NE)	0/ 35 (0.0)	NE (NE , NE)	NE		
	Presence of Liver Metastases							0.9838
	Yes	40/ 146 (27.4)	30.0 (24.0, NE)	0/ 42 (0.0)	NE (NE , NE)	NE		
	No	30/ 86 (34.9)	NE (14.9, NE)	1/ 26 (3.8)	NE (NE , NE)	9.71 (1.32, 71.19)	0.0060	
	Side of Tumor							0.9857
	Left	25/ 88 (28.4)	NE (19.8, NE)	0/ 33 (0.0)	NE (NE , NE)	NE		
	Right	45/ 144 (31.3)	NE (24.0, NE)	1/ 35 (2.9)	NE (NE , NE)	11.31 (1.56, 82.09)	0.0024	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
Subgroup analysis was done for SOCs / PTs with significant overall treatment effect (significant log-rank).
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.
[4] P-Value for interaction from Cox proportional hazards model using ties=exact option with treatment, subgroup and treatment*subgroup interaction as covariates.
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Frequent AE by SOC, PT (incidence >= 10% or >=10 patients and incidence >= 1%) - Subgroup analysis
Safety Analysis Set

SOC/PT	Subgroup Level	EC+FOLFOX (N=232) n/ N (%)	EC+FOLFOX (N=232) Median (95% CI)[1]	Control 2 (N=68) n/ N (%)	Control 2 (N=68) Median (95% CI)[1]	Unstratified analysis Hazard Ratio (95% CI)[2]	Unstratified analysis p-Value[3]	Interaction p-Value[4]
SOC: Skin and subcutaneous tissue disorders, PT: Skin hyperpigmentation	Age (Years)							0.2452
	< 65	30/ 148 (20.3)	NE (NE , NE)	1/ 42 (2.4)	NE (NE , NE)	8.40 (1.15, 61.50)	0.0120	
	>= 65	13/ 84 (15.5)	NE (NE , NE)	2/ 26 (7.7)	NE (NE , NE)	1.87 (0.42, 8.32)	0.4043	
	Sex							0.5750
	Male	24/ 121 (19.8)	NE (NE , NE)	1/ 32 (3.1)	NE (NE , NE)	6.25 (0.85, 46.20)	0.0395	
	Female	19/ 111 (17.1)	NE (NE , NE)	2/ 36 (5.6)	NE (NE , NE)	2.92 (0.68, 12.56)	0.1312	
	Region							0.8140
	Europe	13/ 108 (12.0)	NE (NE , NE)	1/ 38 (2.6)	NE (NE , NE)	3.57 (0.46, 27.44)	0.1916	
	USA/Canada	4/ 15 (26.7)	NE (NE , NE)	1/ 7 (14.3)	NE (NE , NE)	1.87 (0.21, 16.78)	0.5680	
	Rest of World	26/ 109 (23.9)	NE (NE , NE)	1/ 23 (4.3)	NE (NE , NE)	5.82 (0.79, 42.92)	0.0496	
	ECOG-PS at Randomization							0.9636
	0	25/ 130 (19.2)	NE (NE , NE)	2/ 44 (4.5)	NE (NE , NE)	4.27 (1.01, 18.01)	0.0314	
	1	18/ 102 (17.6)	NE (NE , NE)	1/ 24 (4.2)	NE (NE , NE)	3.82 (0.51, 28.73)	0.1609	
	Number of Organs Involved							0.5148
	<= 2	22/ 116 (19.0)	NE (NE , NE)	1/ 33 (3.0)	NE (NE , NE)	6.52 (0.88, 48.35)	0.0345	
	>= 3	21/ 116 (18.1)	NE (NE , NE)	2/ 35 (5.7)	NE (NE , NE)	2.96 (0.69, 12.62)	0.1246	
	Presence of Liver Metastases							0.9876
	Yes	26/ 146 (17.8)	NE (NE , NE)	3/ 42 (7.1)	NE (NE , NE)	2.26 (0.68, 7.49)	0.1706	
	No	17/ 86 (19.8)	NE (NE , NE)	0/ 26 (0.0)	NE (NE , NE)	NE		
	Side of Tumor							0.6692
	Left	16/ 88 (18.2)	NE (NE , NE)	1/ 33 (3.0)	NE (NE , NE)	5.83 (0.77, 43.96)	0.0521	
	Right	27/ 144 (18.8)	NE (NE , NE)	2/ 35 (5.7)	NE (NE , NE)	3.23 (0.77, 13.59)	0.0906	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
Subgroup analysis was done for SOCs / PTs with significant overall treatment effect (significant log-rank).
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.
[4] P-Value for interaction from Cox proportional hazards model using ties=exact option with treatment, subgroup and treatment*subgroup interaction as covariates.
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Frequent AE by SOC, PT (incidence >= 10% or >=10 patients and incidence >= 1%) - Subgroup analysis
Safety Analysis Set

SOC/PT	Subgroup Level	EC+FOLFOX (N=232) n/ N (%)	EC+FOLFOX (N=232) Median (95% CI)[1]	Control 2 (N=68) n/ N (%)	Control 2 (N=68) Median (95% CI)[1]	Unstratified analysis Hazard Ratio (95% CI)[2]	Unstratified analysis p-Value[3]	Interaction p-Value[4]
SOC: Vascular disorders	Age (Years)							0.8106
	< 65	19/ 148 (12.8)	NE (NE , NE)	9/ 42 (21.4)	NE (NE , NE)	0.46 (0.21, 1.03)	0.0524	
	>= 65	17/ 84 (20.2)	NE (NE , NE)	10/ 26 (38.5)	10.6 (4.9, NE)	0.43 (0.19, 0.94)	0.0301	
	Sex							0.1252
	Male	15/ 121 (12.4)	NE (NE , NE)	10/ 32 (31.3)	NE (6.7, NE)	0.25 (0.11, 0.58)	0.0004	
	Female	21/ 111 (18.9)	NE (NE , NE)	9/ 36 (25.0)	NE (10.6, NE)	0.64 (0.29, 1.41)	0.2659	
	Region							0.4107
	Europe	17/ 108 (15.7)	NE (NE , NE)	13/ 38 (34.2)	NE (7.4, NE)	0.33 (0.16, 0.69)	0.0019	
	USA/Canada	4/ 15 (26.7)	NE (NE , NE)	3/ 7 (42.9)	10.6 (3.4, NE)	0.62 (0.14, 2.81)	0.5387	
	Rest of World	15/ 109 (13.8)	NE (NE , NE)	3/ 23 (13.0)	NE (NE , NE)	0.84 (0.24, 2.93)	0.7860	
	ECOG-PS at Randomization							0.1737
	0	17/ 130 (13.1)	NE (NE , NE)	14/ 44 (31.8)	NE (8.7, NE)	0.30 (0.15, 0.62)	0.0006	
	1	19/ 102 (18.6)	NE (NE , NE)	5/ 24 (20.8)	NE (NE , NE)	0.72 (0.27, 1.94)	0.5128	
	Number of Organs Involved							0.2062
	<= 2	18/ 116 (15.5)	NE (NE , NE)	13/ 33 (39.4)	NE (7.4, NE)	0.31 (0.15, 0.64)	0.0008	
	>= 3	18/ 116 (15.5)	NE (NE , NE)	6/ 35 (17.1)	NE (NE , NE)	0.70 (0.28, 1.78)	0.4488	
	Presence of Liver Metastases							0.2659
	Yes	21/ 146 (14.4)	NE (NE , NE)	13/ 42 (31.0)	NE (7.4, NE)	0.31 (0.15, 0.63)	0.0006	
	No	15/ 86 (17.4)	NE (NE , NE)	6/ 26 (23.1)	NE (10.6, NE)	0.65 (0.25, 1.68)	0.3712	
	Side of Tumor							0.1750
	Left	13/ 88 (14.8)	NE (NE , NE)	5/ 33 (15.2)	NE (NE , NE)	0.78 (0.28, 2.22)	0.6452	
	Right	23/ 144 (16.0)	NE (NE , NE)	14/ 35 (40.0)	10.6 (6.7, NE)	0.31 (0.16, 0.60)	0.0003	

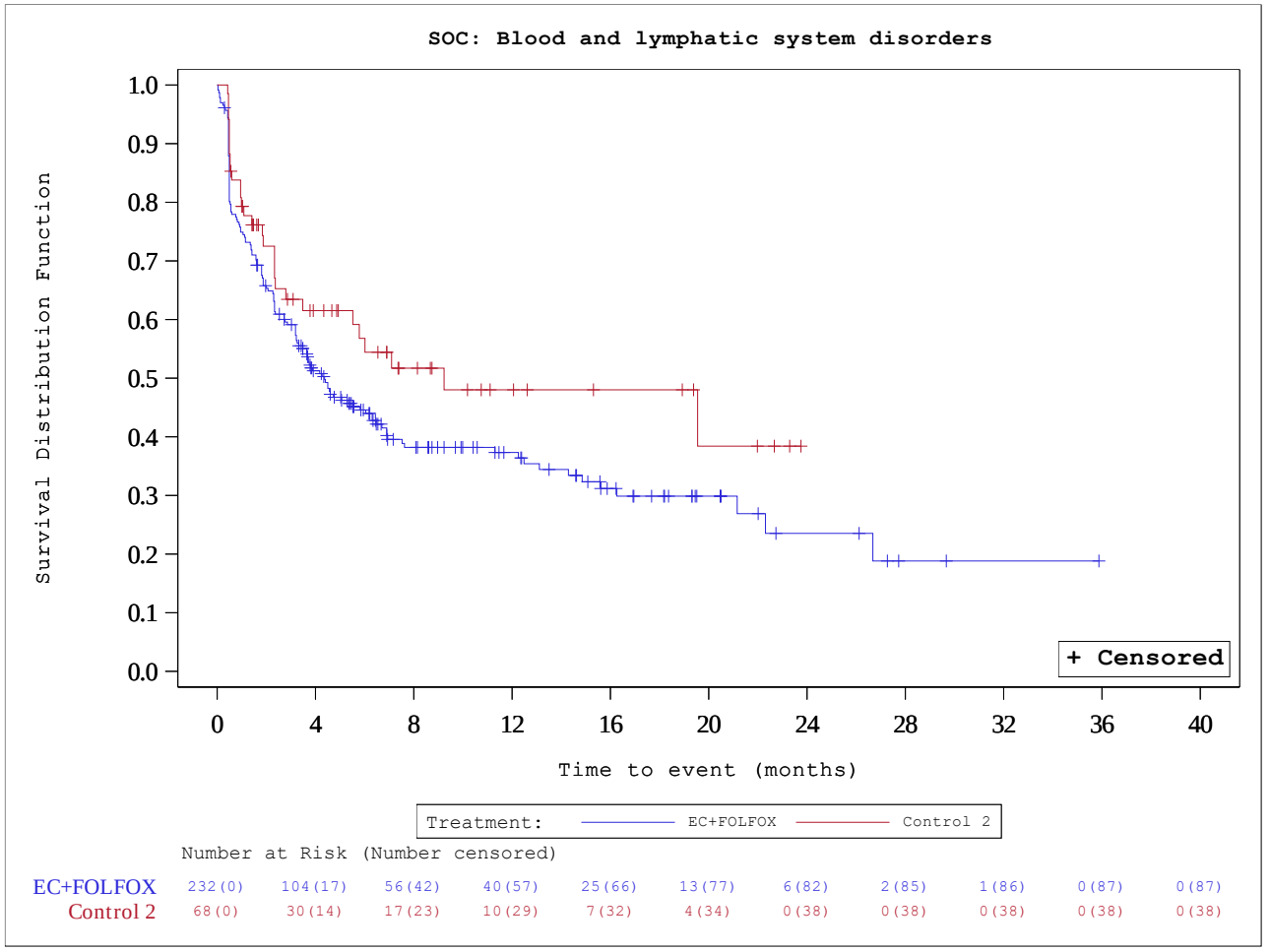
Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
Subgroup analysis was done for SOCs / PTs with significant overall treatment effect (significant log-rank).
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.
[4] P-Value for interaction from Cox proportional hazards model using ties=exact option with treatment, subgroup and treatment*subgroup interaction as covariates.
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Frequent AE by SOC, PT (incidence >= 10% or >=10 patients and incidence >= 1%) - Subgroup analysis
Safety Analysis Set

SOC/PT	Subgroup Level	EC+FOLFOX (N=232) n/ N (%)	EC+FOLFOX (N=232) Median (95% CI)[1]	Control 2 (N=68) n/ N (%)	Control 2 (N=68) Median (95% CI)[1]	Unstratified analysis Hazard Ratio (95% CI)[2]	Unstratified analysis p-Value[3]	Interaction p-Value[4]
SOC: Vascular disorders, PT: Hypertension	Age (Years)							0.2020
	< 65	4/ 148 (2.7)	NE (NE , NE)	7/ 42 (16.7)	NE (NE , NE)	0.12 (0.03, 0.41)	<.0001	
	>= 65	5/ 84 (6.0)	NE (NE , NE)	3/ 26 (11.5)	NE (NE , NE)	0.38 (0.09, 1.64)	0.1783	
	Sex							0.2591
	Male	2/ 121 (1.7)	NE (NE , NE)	4/ 32 (12.5)	NE (NE , NE)	0.09 (0.02, 0.52)	0.0007	
	Female	7/ 111 (6.3)	NE (NE , NE)	6/ 36 (16.7)	NE (NE , NE)	0.29 (0.10, 0.87)	0.0192	
	Region							0.9563
	Europe	5/ 108 (4.6)	NE (NE , NE)	8/ 38 (21.1)	NE (NE , NE)	0.16 (0.05, 0.49)	0.0003	
	USA/Canada	1/ 15 (6.7)	NE (NE , NE)	2/ 7 (28.6)	NE (10.6, NE)	0.27 (0.02, 3.05)	0.2579	
	Rest of World	3/ 109 (2.8)	NE (NE , NE)	0/ 23 (0.0)	NE (NE , NE)	NE		
	ECOG-PS at Randomization							0.8141
	0	6/ 130 (4.6)	NE (NE , NE)	7/ 44 (15.9)	NE (NE , NE)	0.21 (0.07, 0.64)	0.0024	
	1	3/ 102 (2.9)	NE (NE , NE)	3/ 24 (12.5)	NE (NE , NE)	0.19 (0.04, 0.96)	0.0247	
	Number of Organs Involved							0.6726
	<= 2	5/ 116 (4.3)	NE (NE , NE)	5/ 33 (15.2)	NE (NE , NE)	0.24 (0.07, 0.83)	0.0149	
	>= 3	4/ 116 (3.4)	NE (NE , NE)	5/ 35 (14.3)	NE (NE , NE)	0.16 (0.04, 0.62)	0.0024	
	Presence of Liver Metastases							0.7359
	Yes	5/ 146 (3.4)	NE (NE , NE)	6/ 42 (14.3)	NE (NE , NE)	0.16 (0.05, 0.53)	0.0006	
	No	4/ 86 (4.7)	NE (NE , NE)	4/ 26 (15.4)	NE (NE , NE)	0.24 (0.06, 0.97)	0.0297	
	Side of Tumor							0.4748
	Left	1/ 88 (1.1)	NE (NE , NE)	3/ 33 (9.1)	NE (NE , NE)	0.12 (0.01, 1.11)	0.0241	
	Right	8/ 144 (5.6)	NE (NE , NE)	7/ 35 (20.0)	NE (10.6, NE)	0.21 (0.08, 0.59)	0.0010	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
Subgroup analysis was done for SOCs / PTs with significant overall treatment effect (significant log-rank).
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.
[4] P-Value for interaction from Cox proportional hazards model using ties=exact option with treatment, subgroup and treatment*subgroup interaction as covariates.
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Kaplan Meier Plot of frequent Frequent AE by SOC, PT (incidence >= 10% or >=10 patients and incidence >= 1%)
Safety Analysis Set



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Kaplan-Meier Plots for subgroups only created if p-value for interaction < 0.05.

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Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
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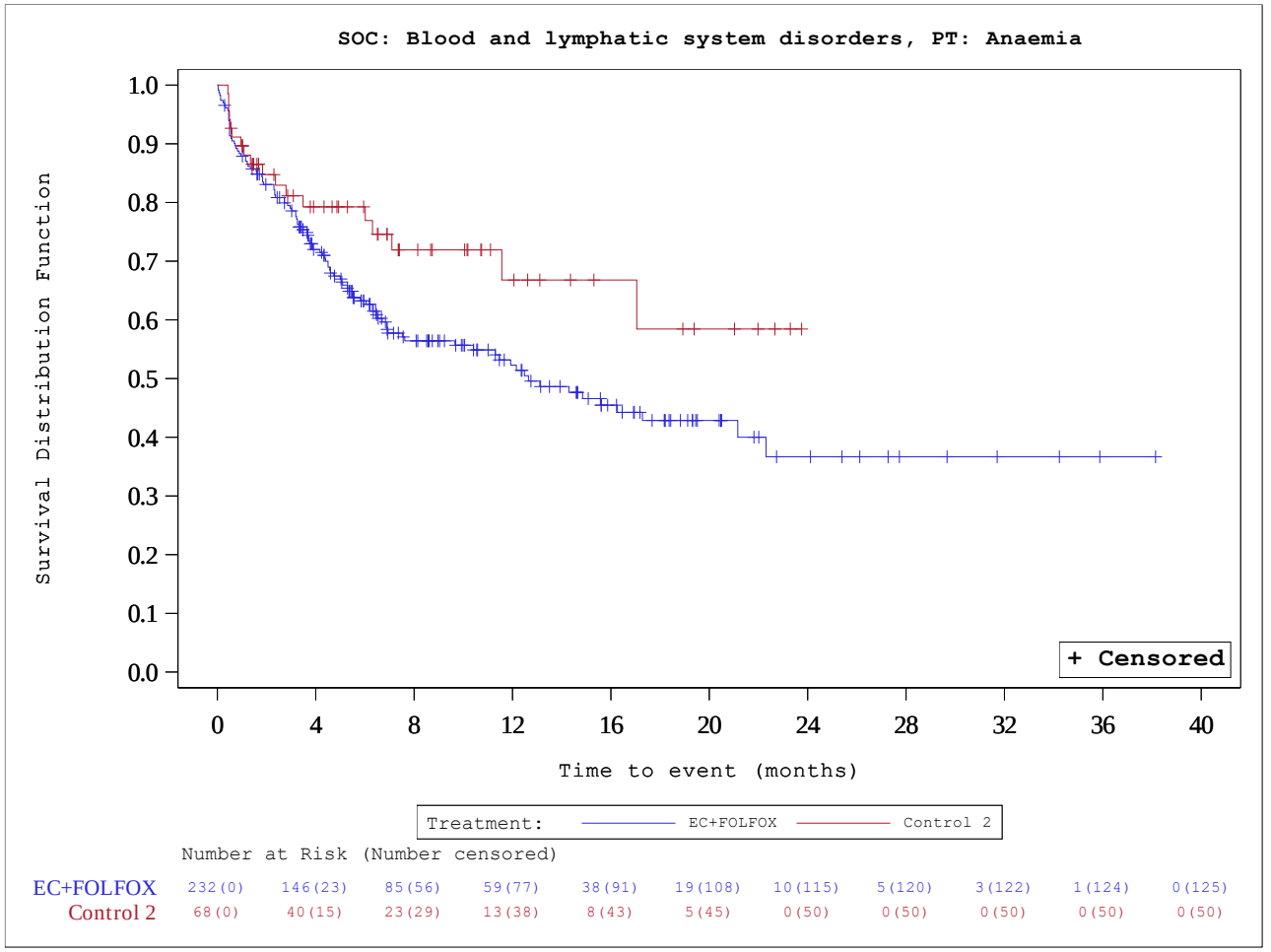

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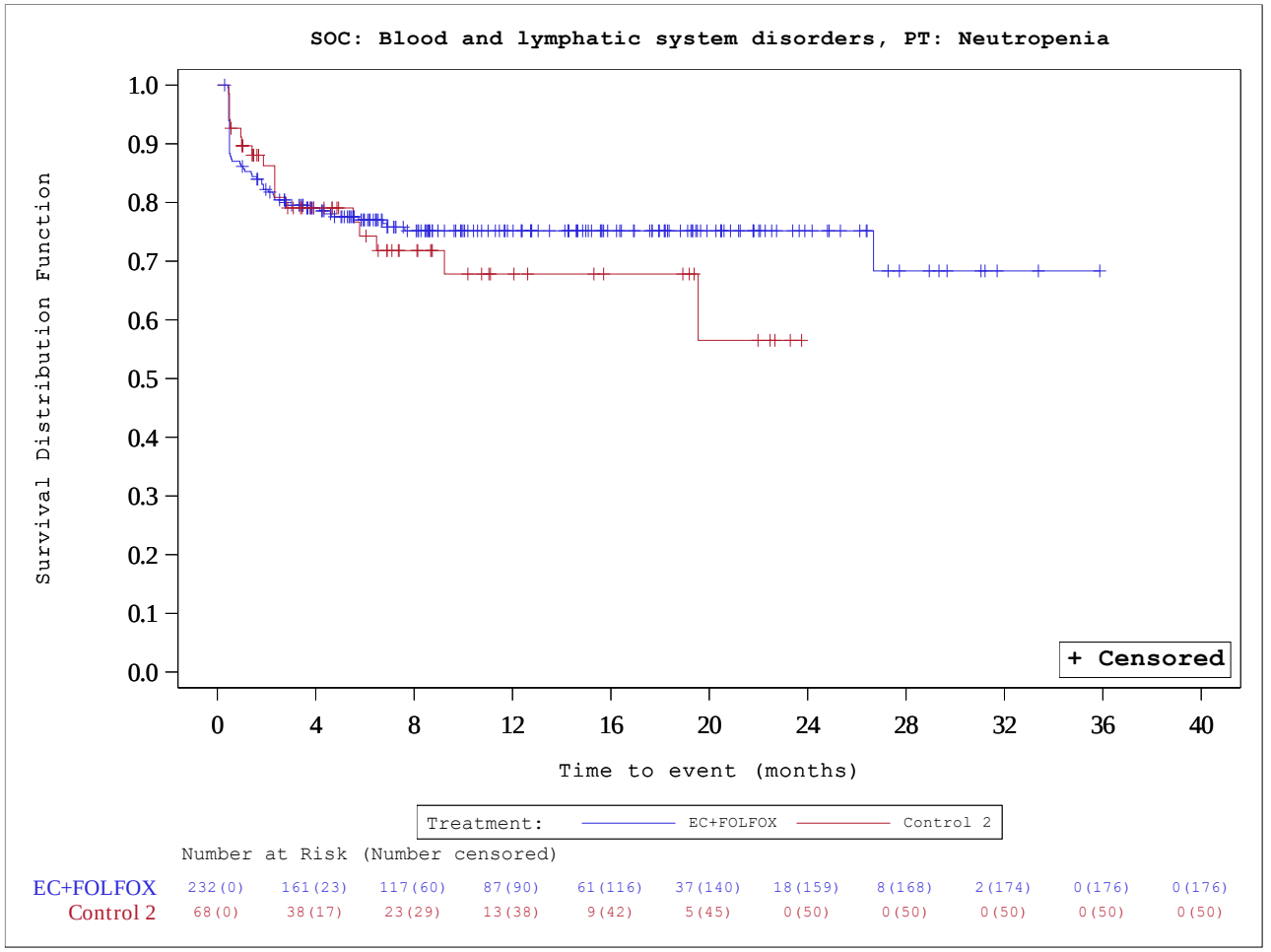

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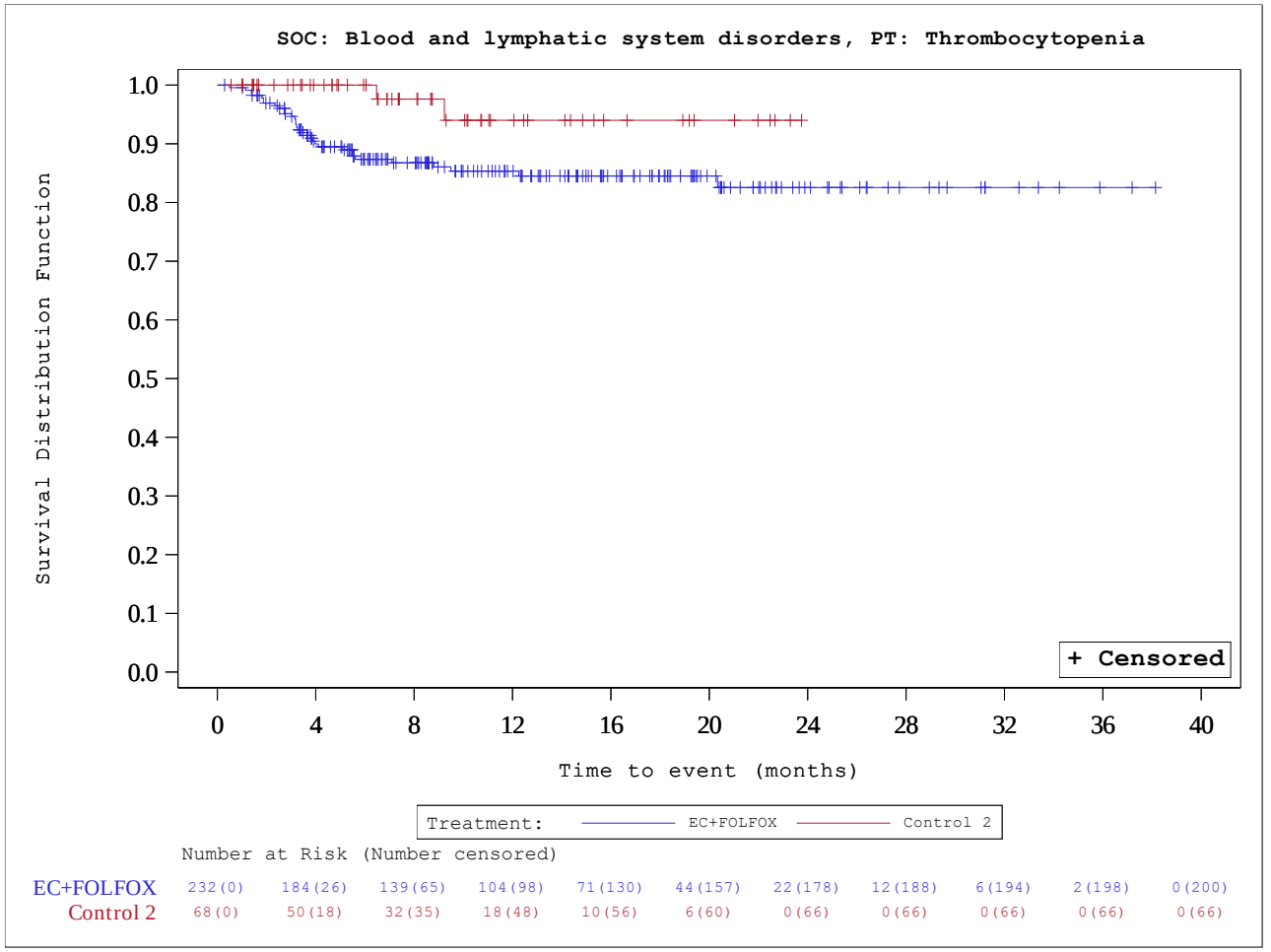

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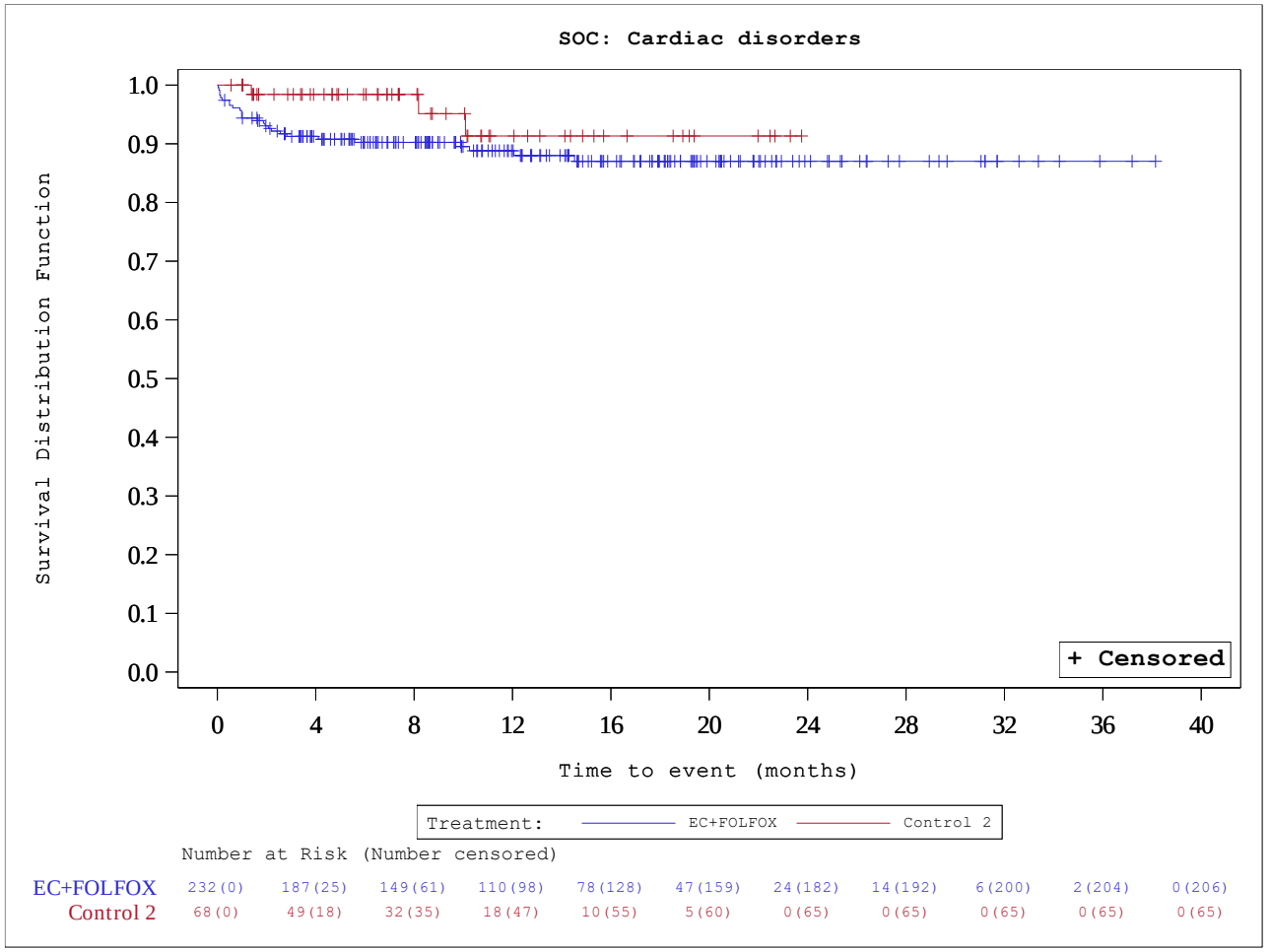

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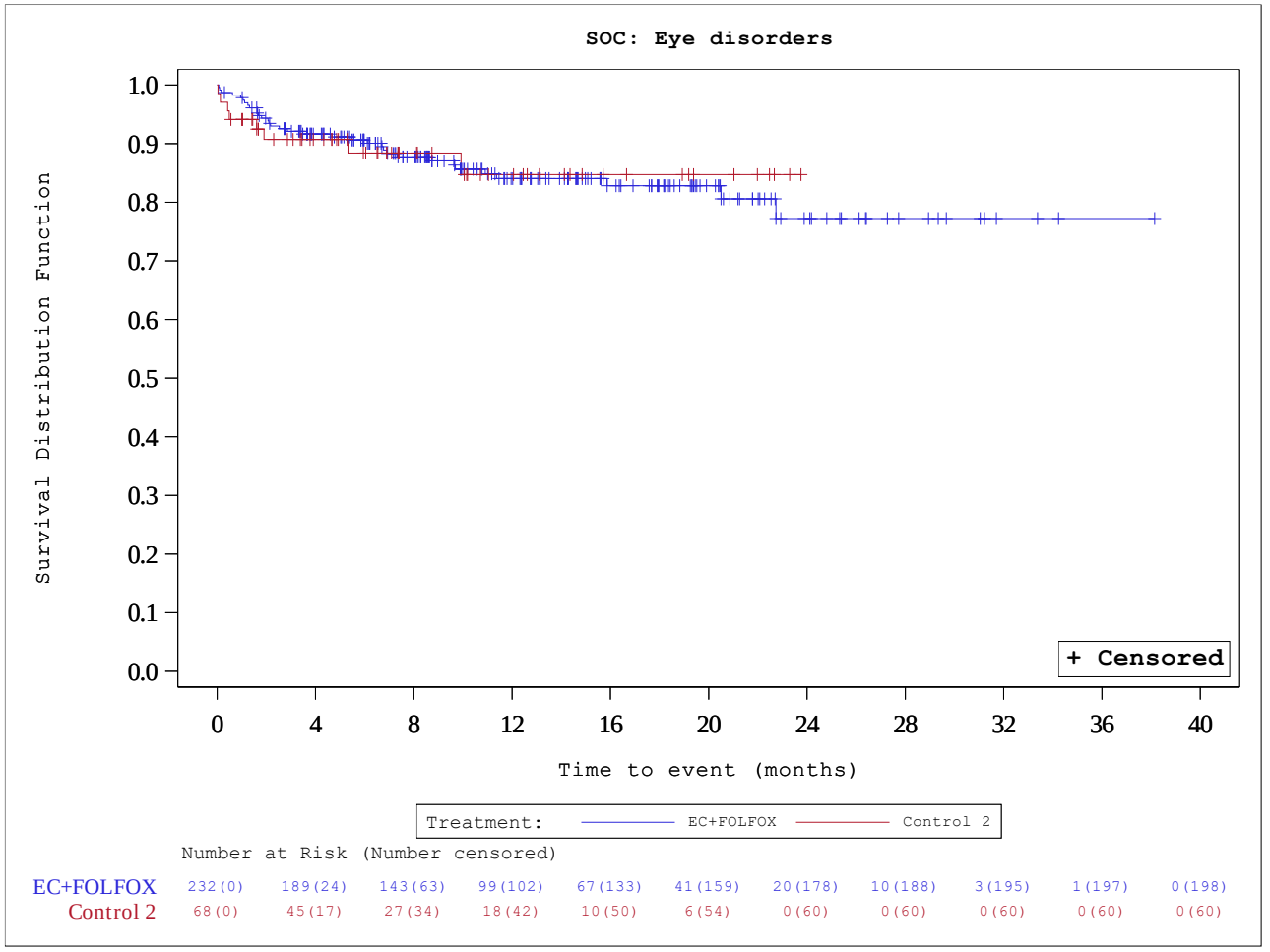

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Kaplan-Meier Plots for subgroups only created if p-value for interaction < 0.05.

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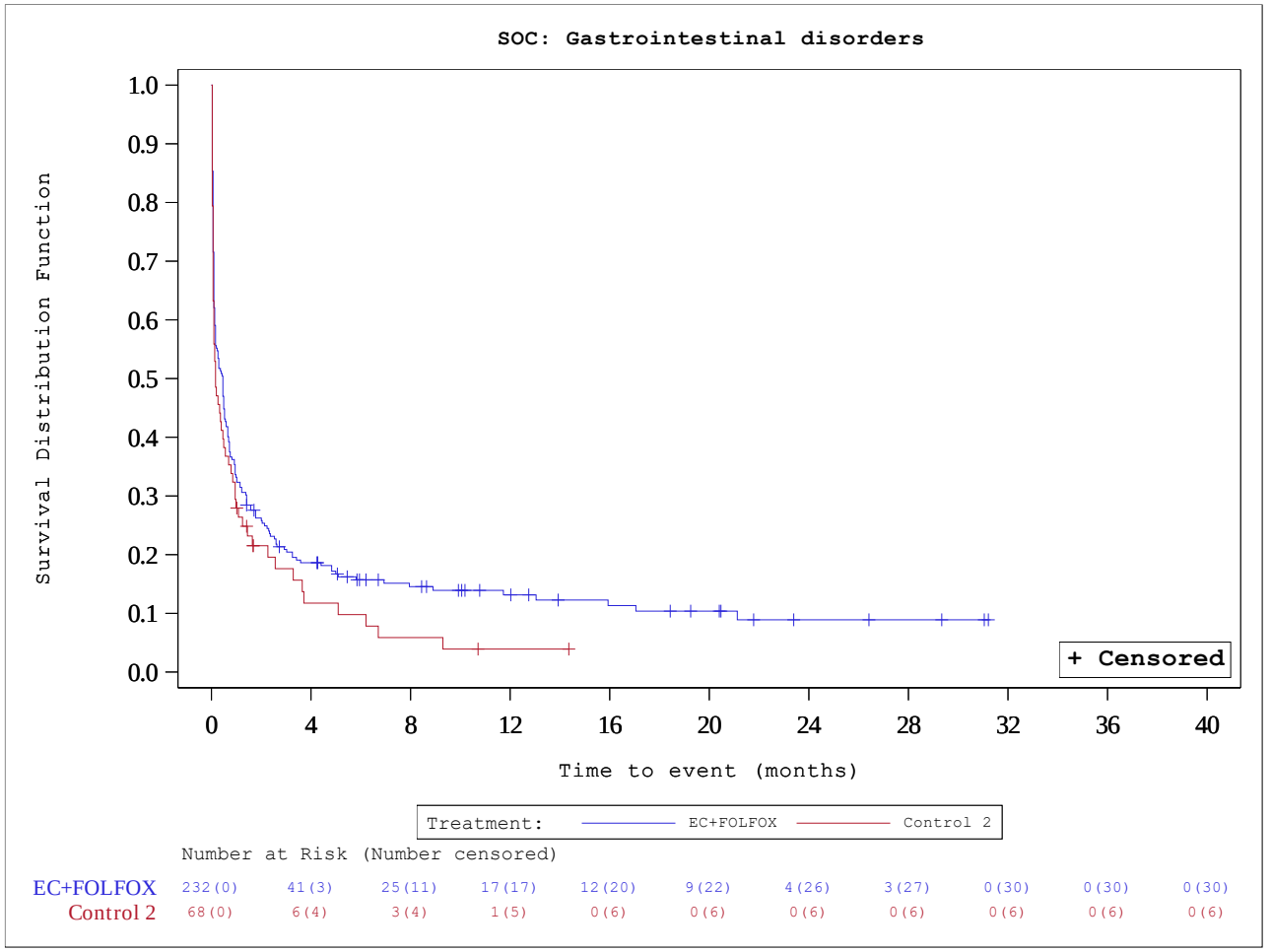
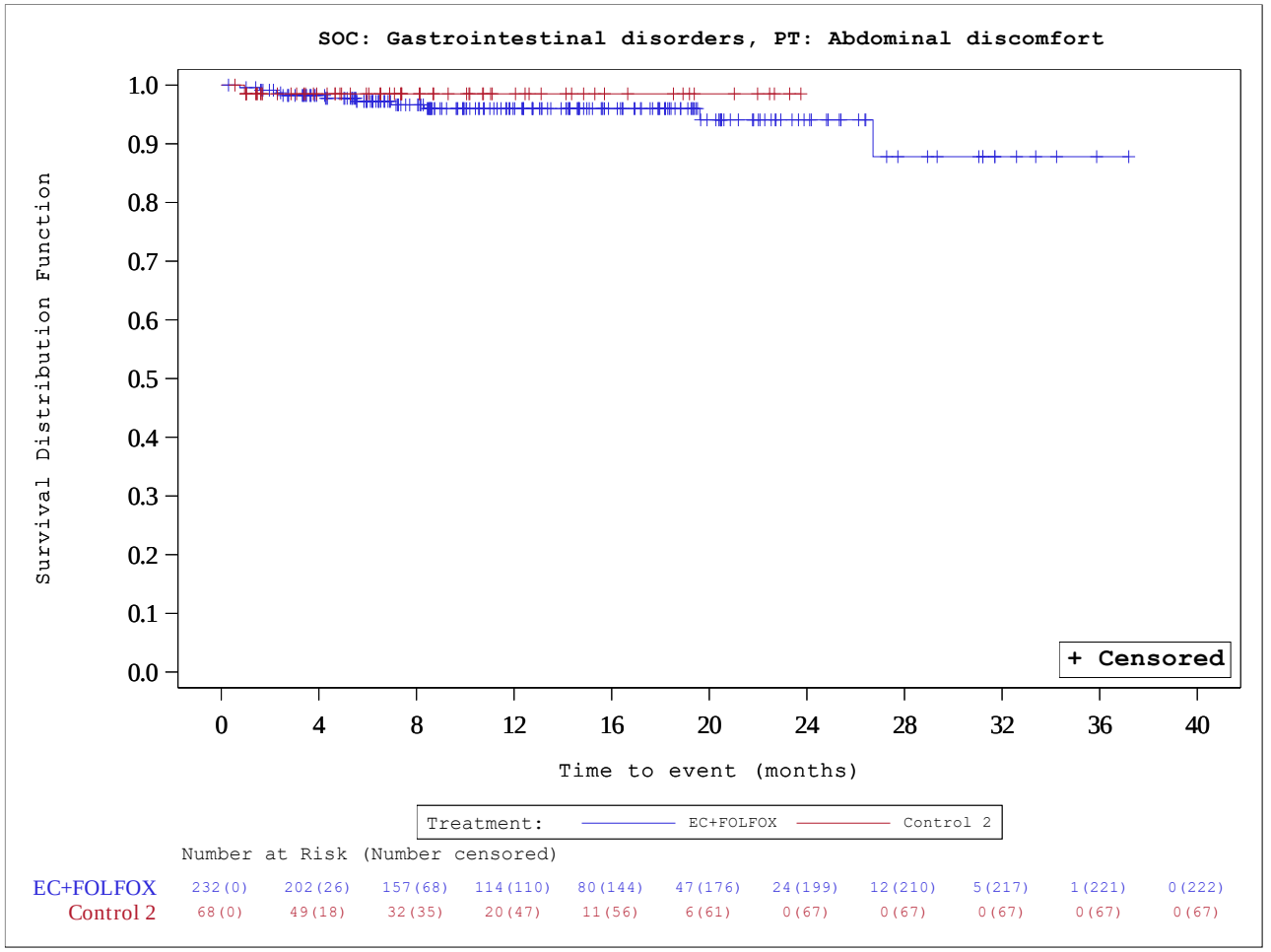


Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
Subgroup analysis was done for SOCs / PTs with significant overall treatment effect (significant log-rank).
Kaplan-Meier Plots for subgroups only created if p-value for interaction < 0.05.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Kaplan Meier Plot of frequent Frequent AE by SOC, PT (incidence >= 10% or >=10 patients and incidence >= 1%)
Safety Analysis Set



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Kaplan-Meier Plots for subgroups only created if p-value for interaction < 0.05.

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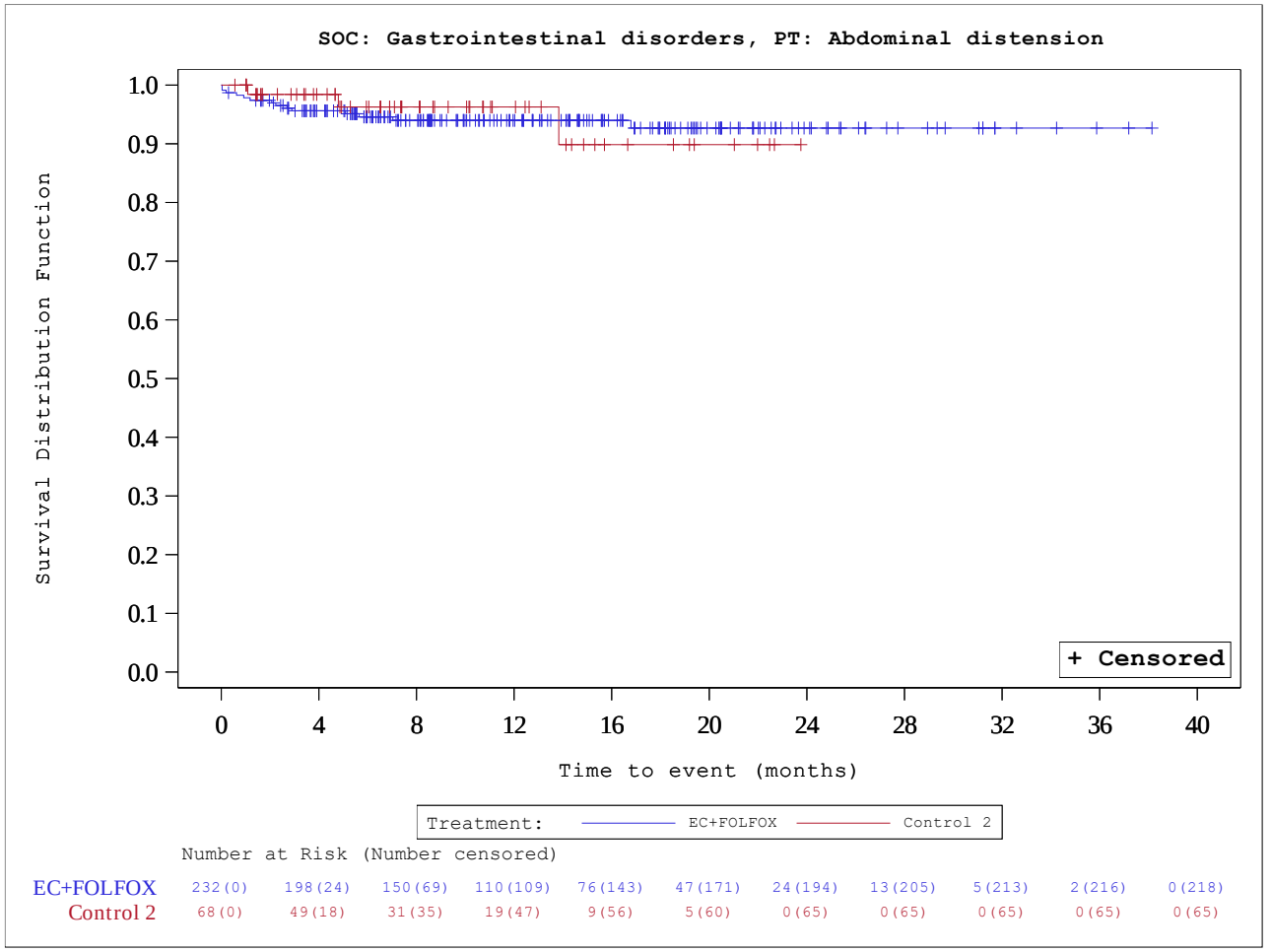

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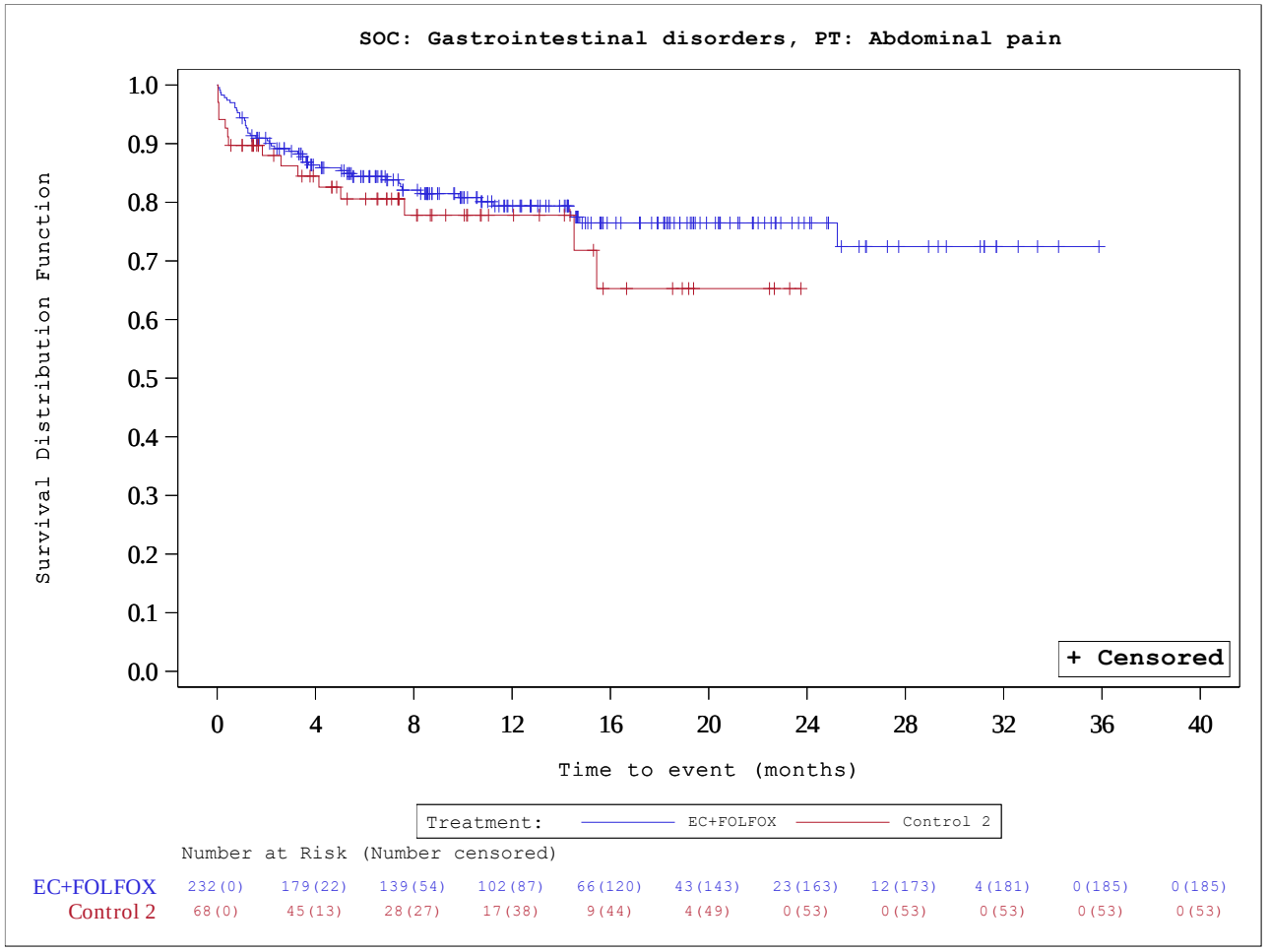

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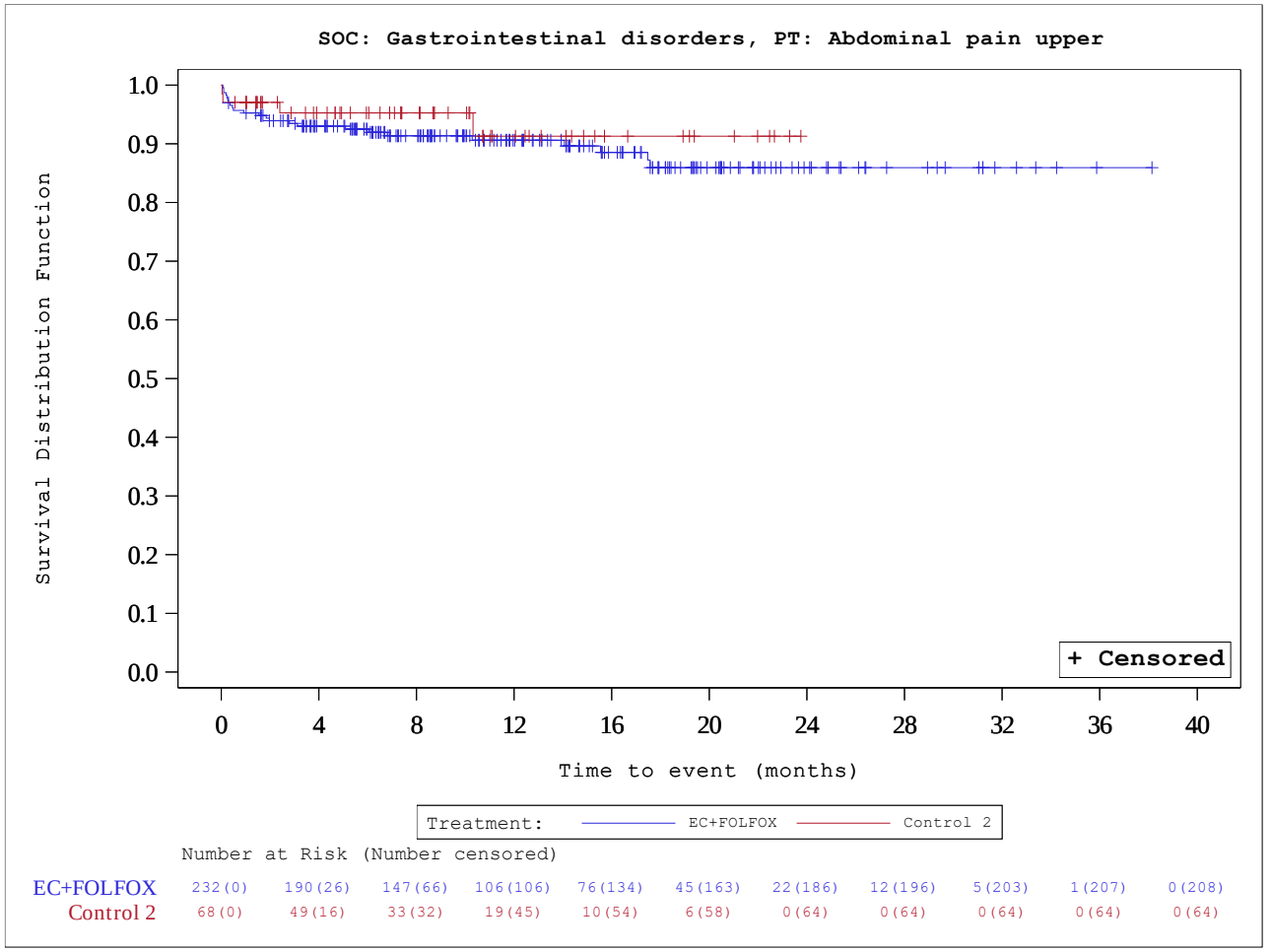

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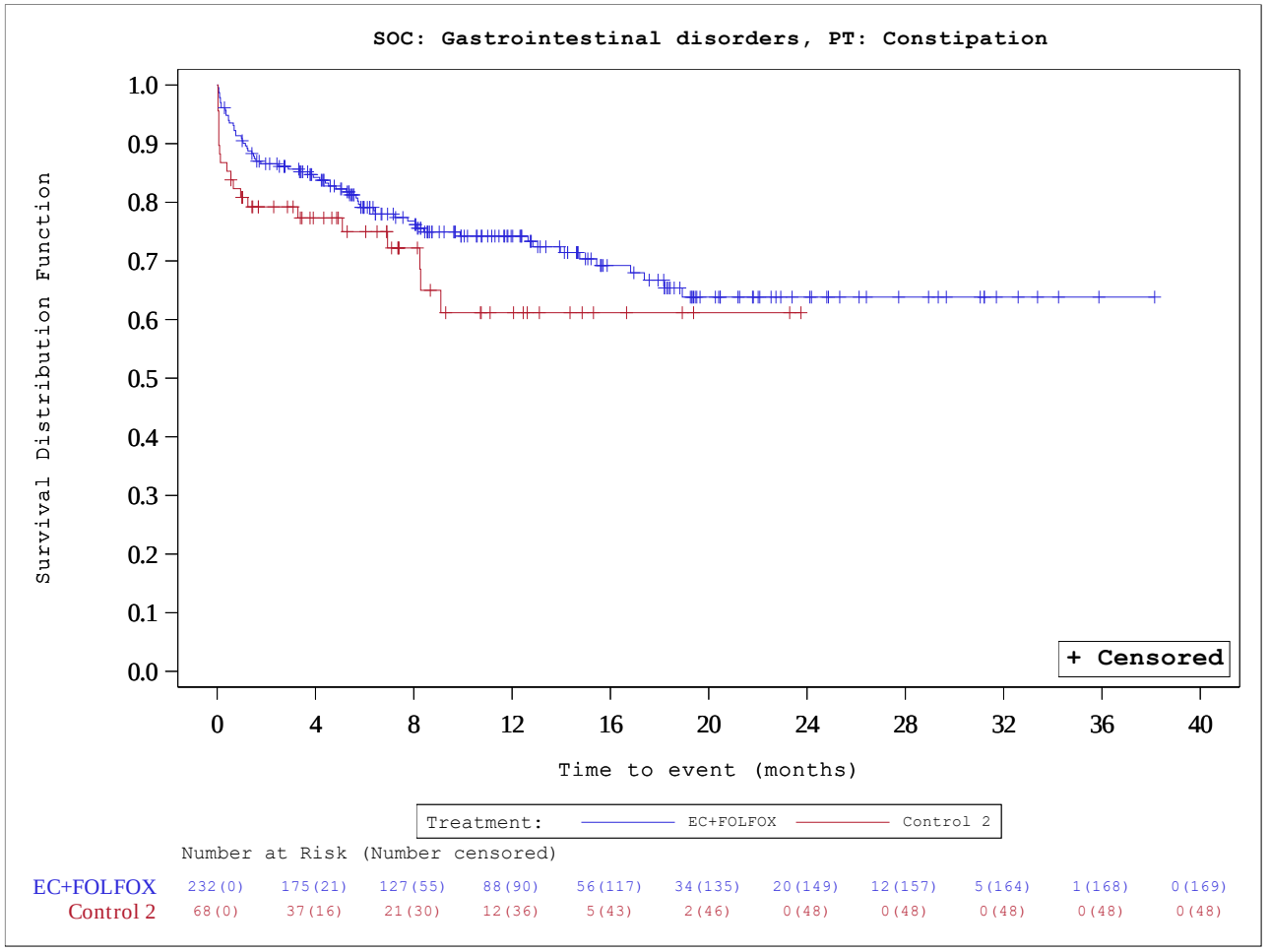

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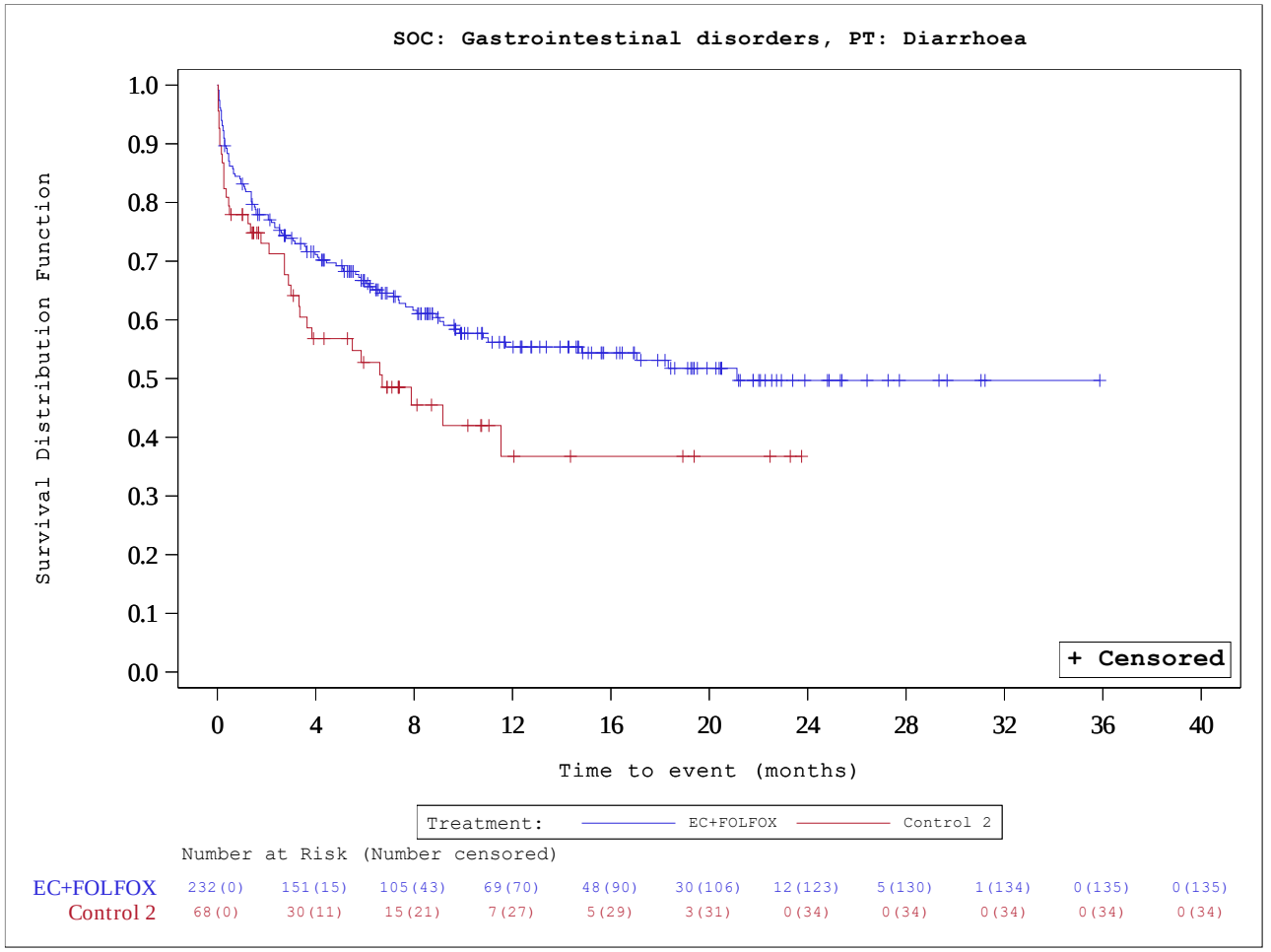

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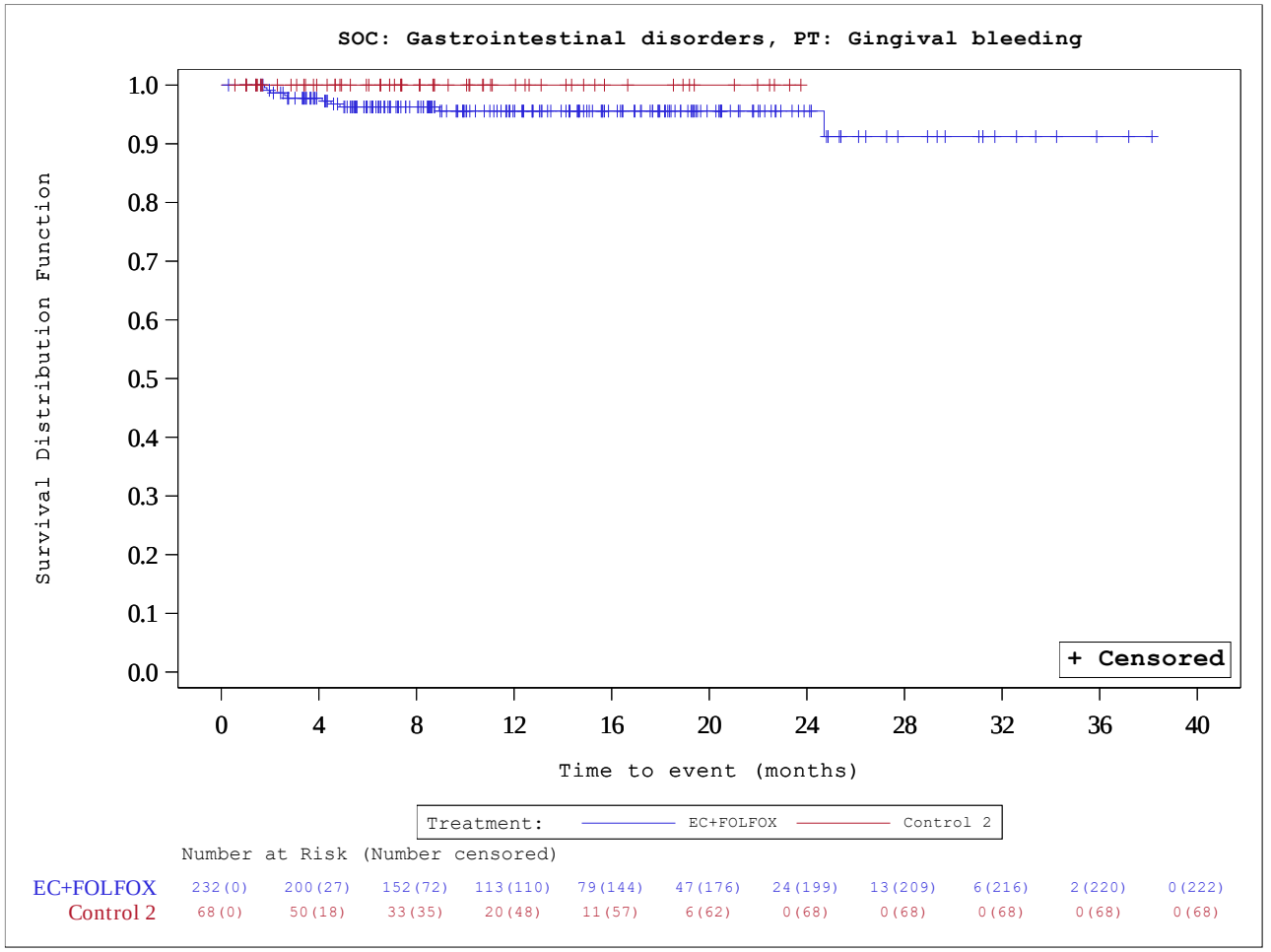

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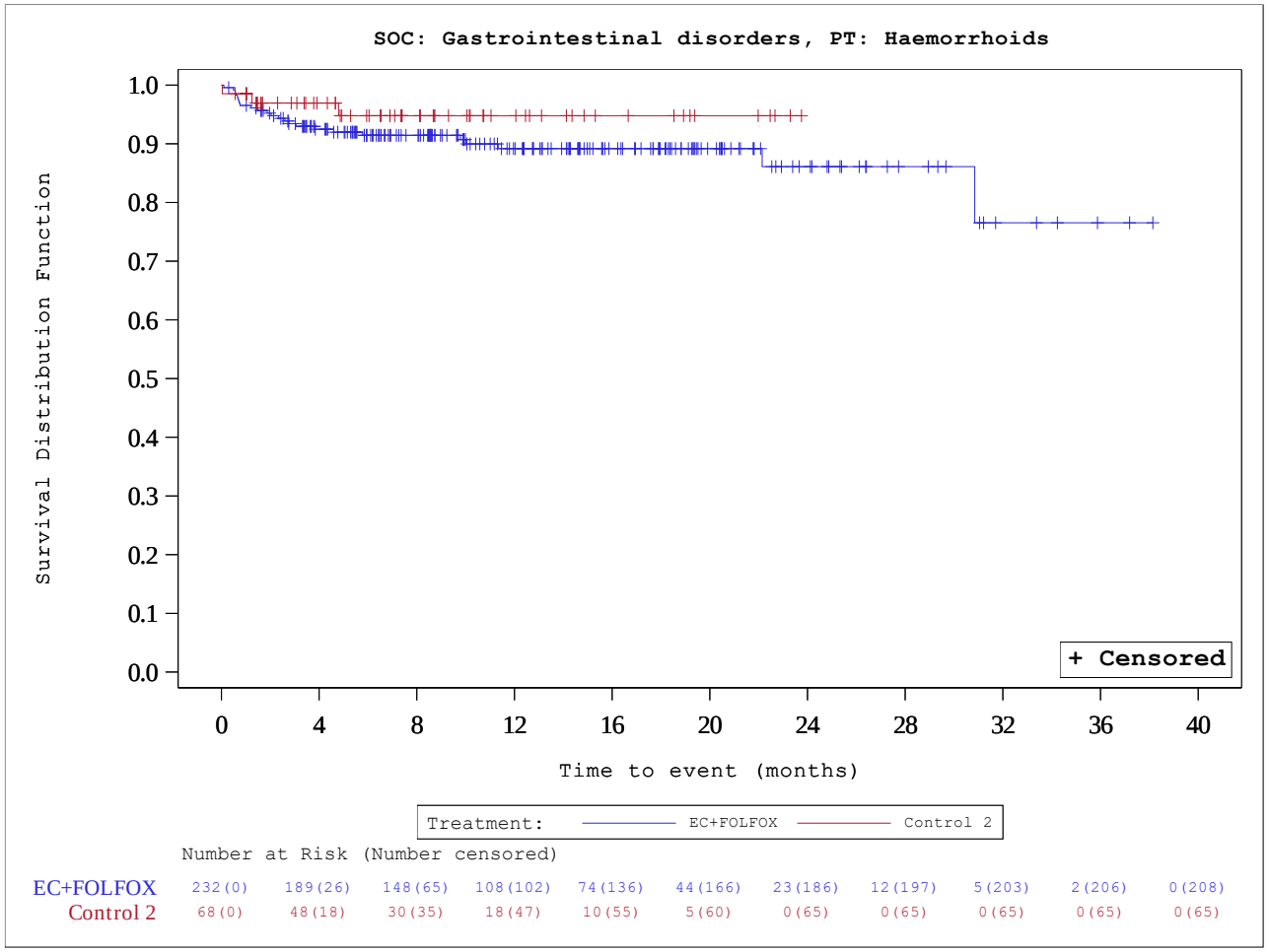

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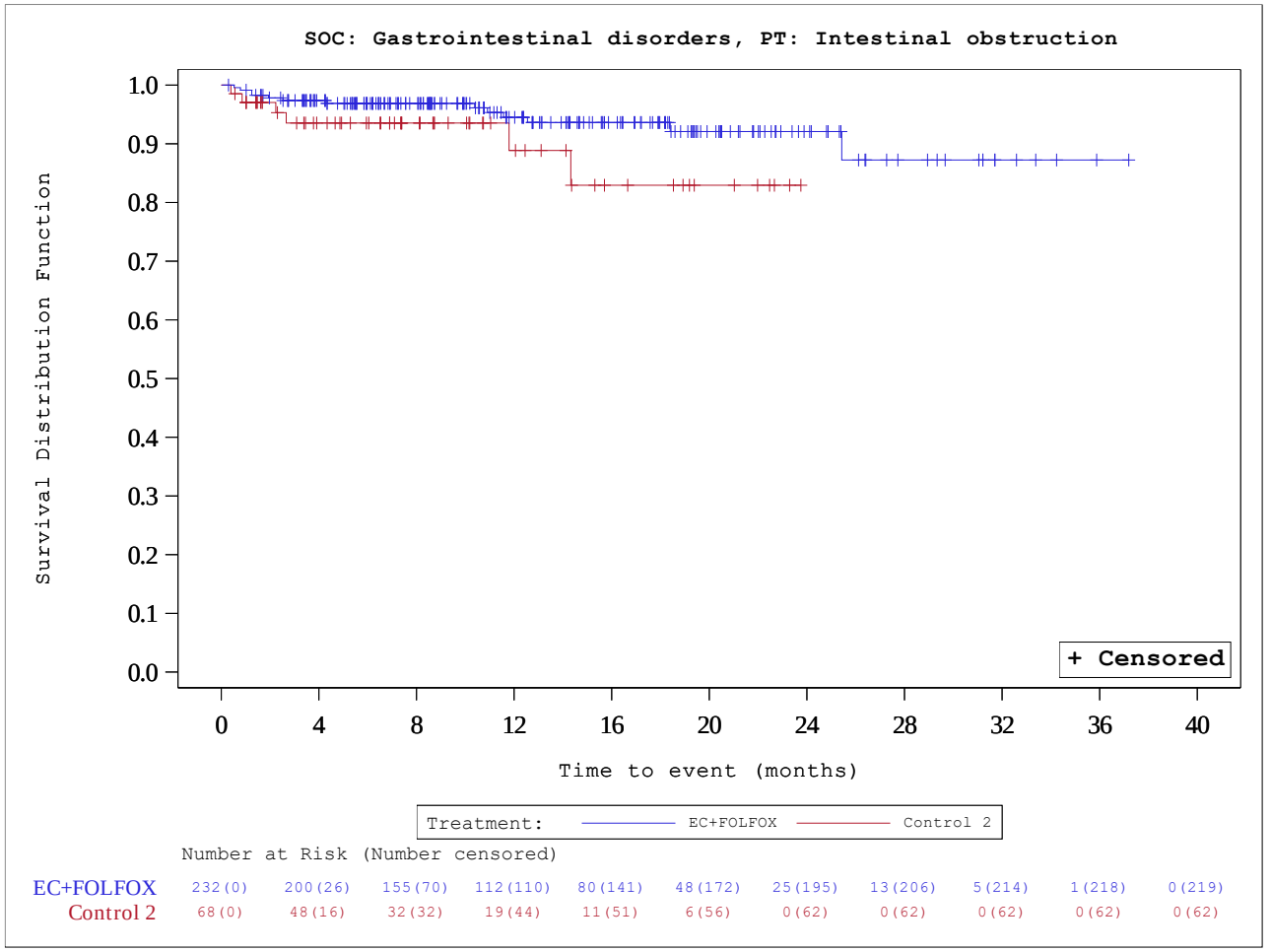

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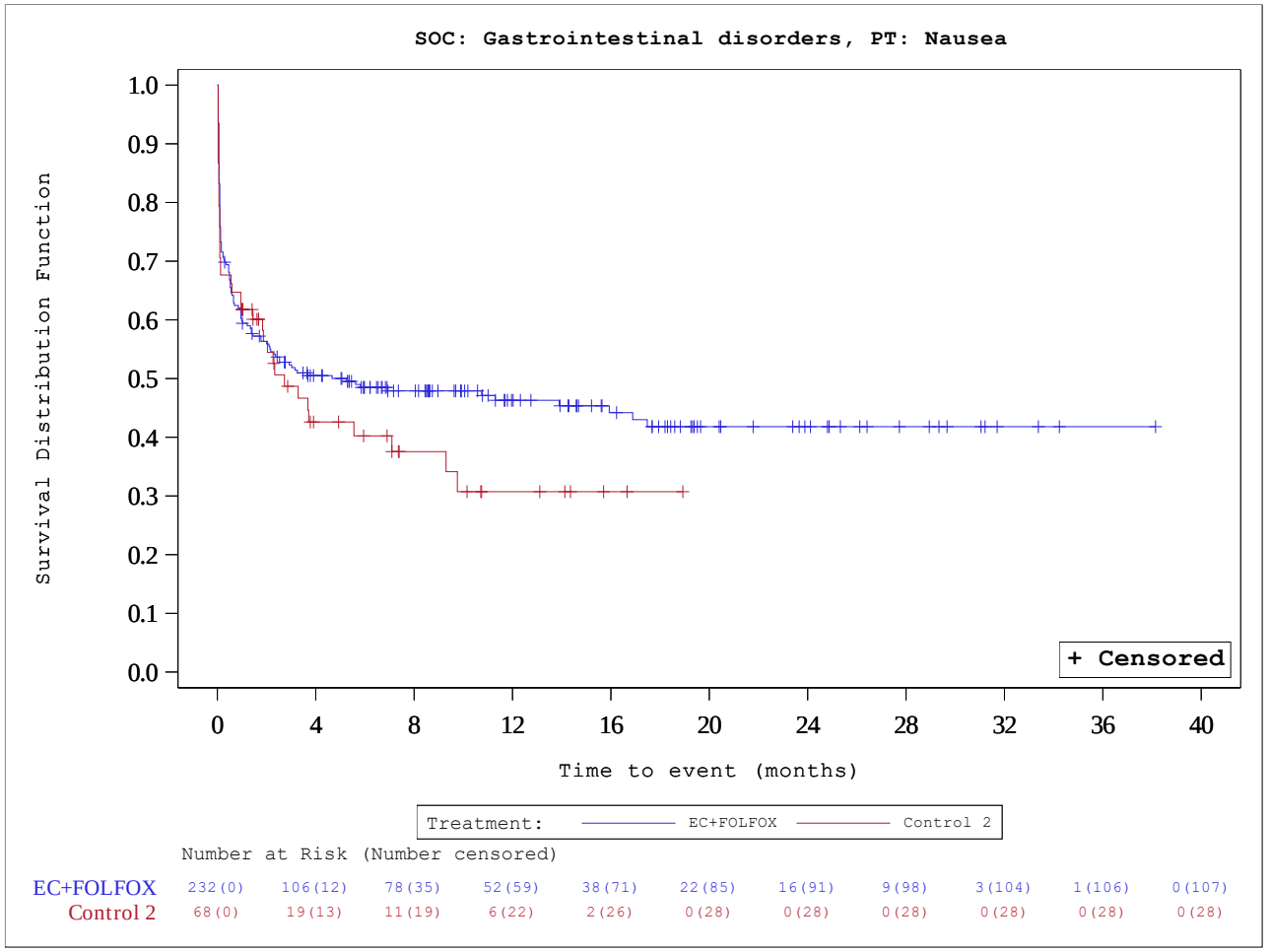

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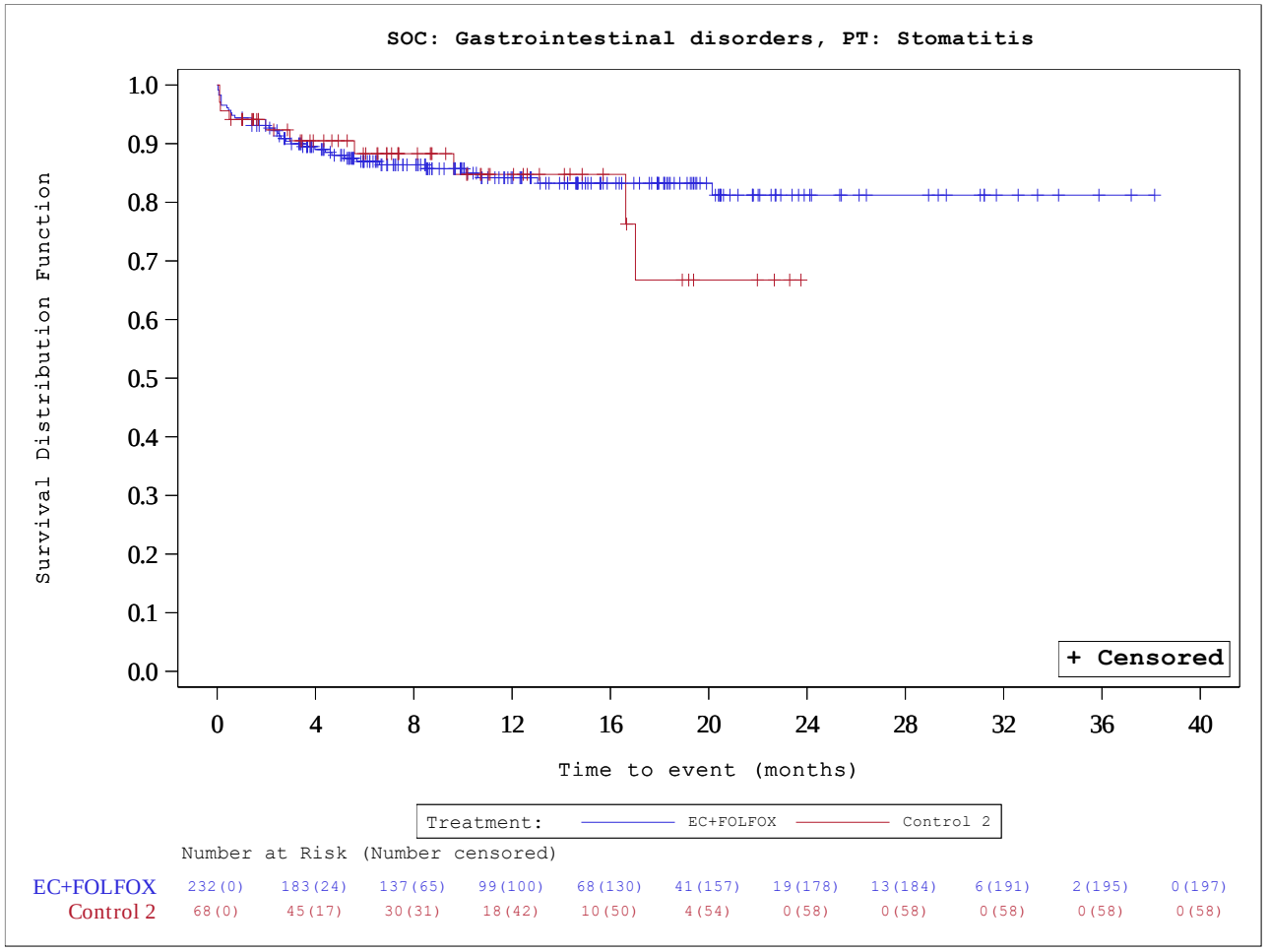

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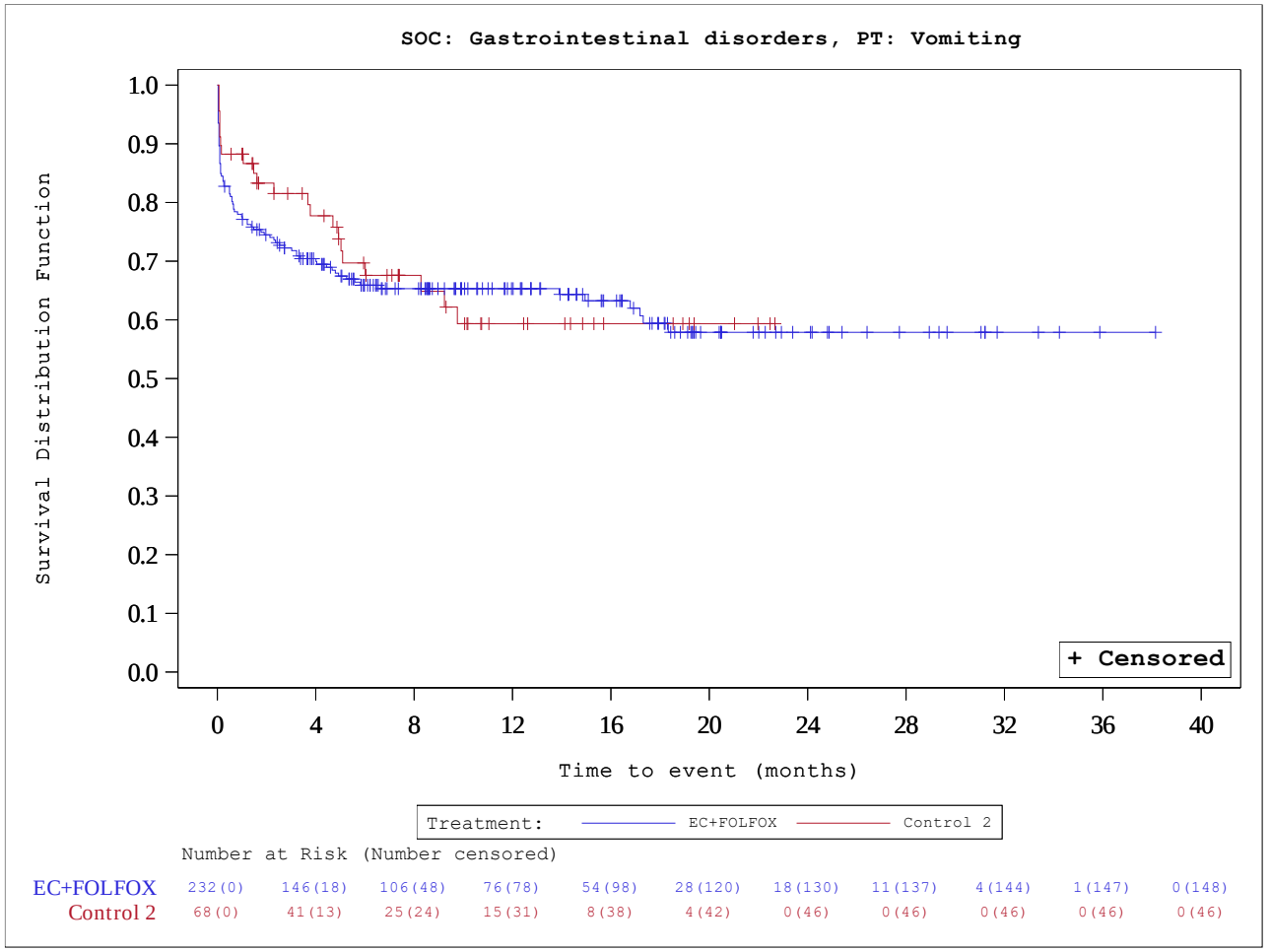

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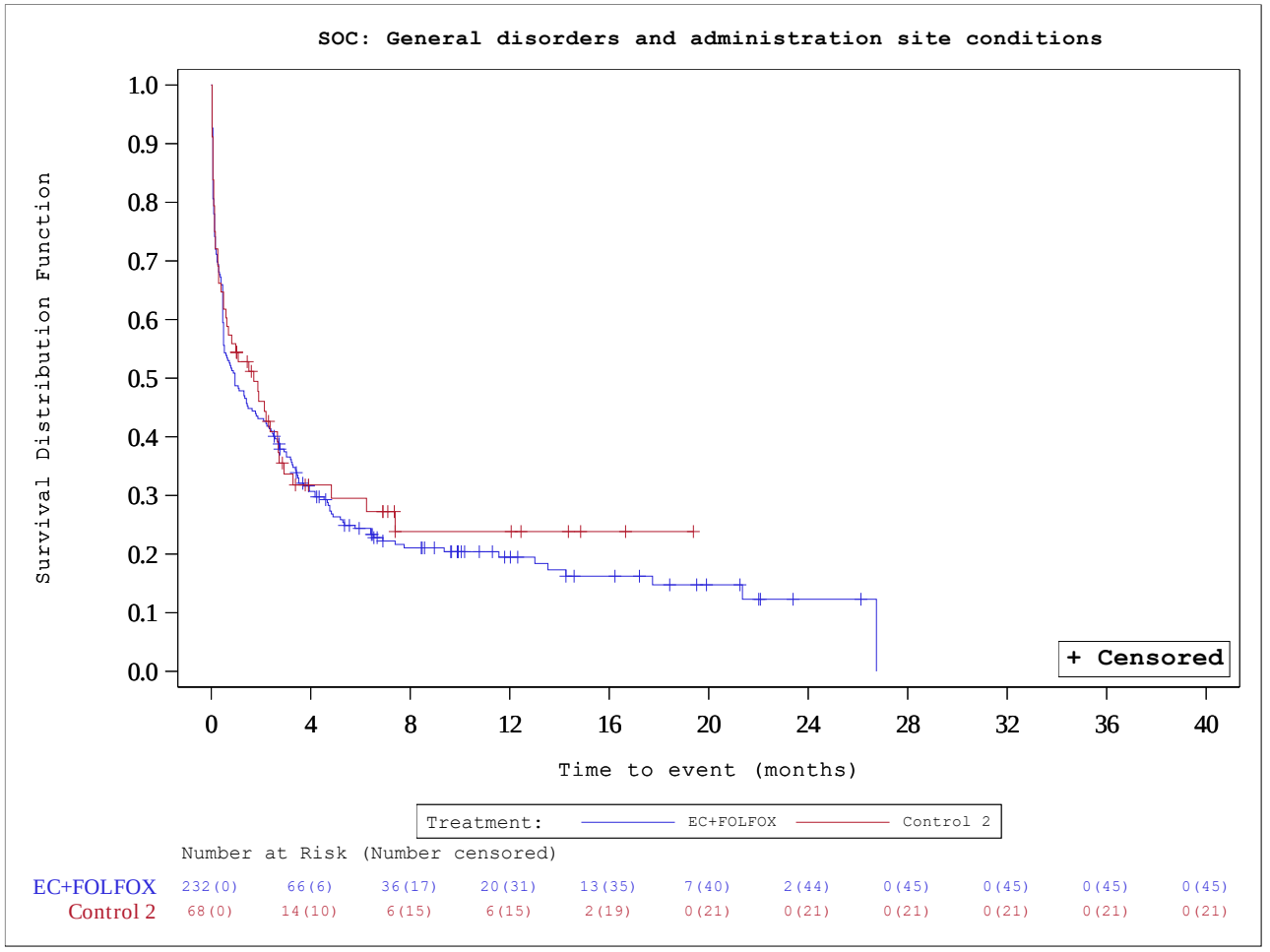

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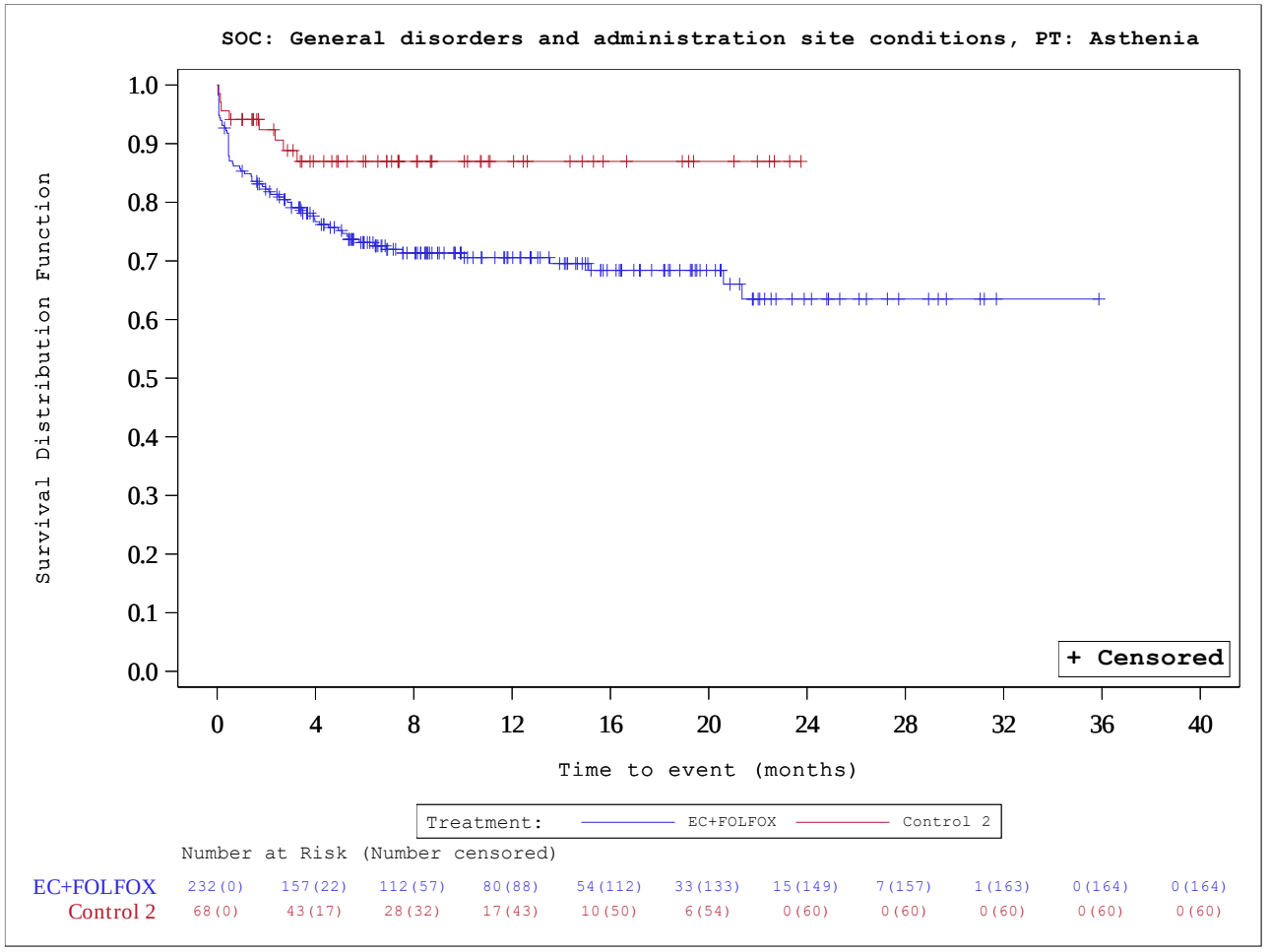

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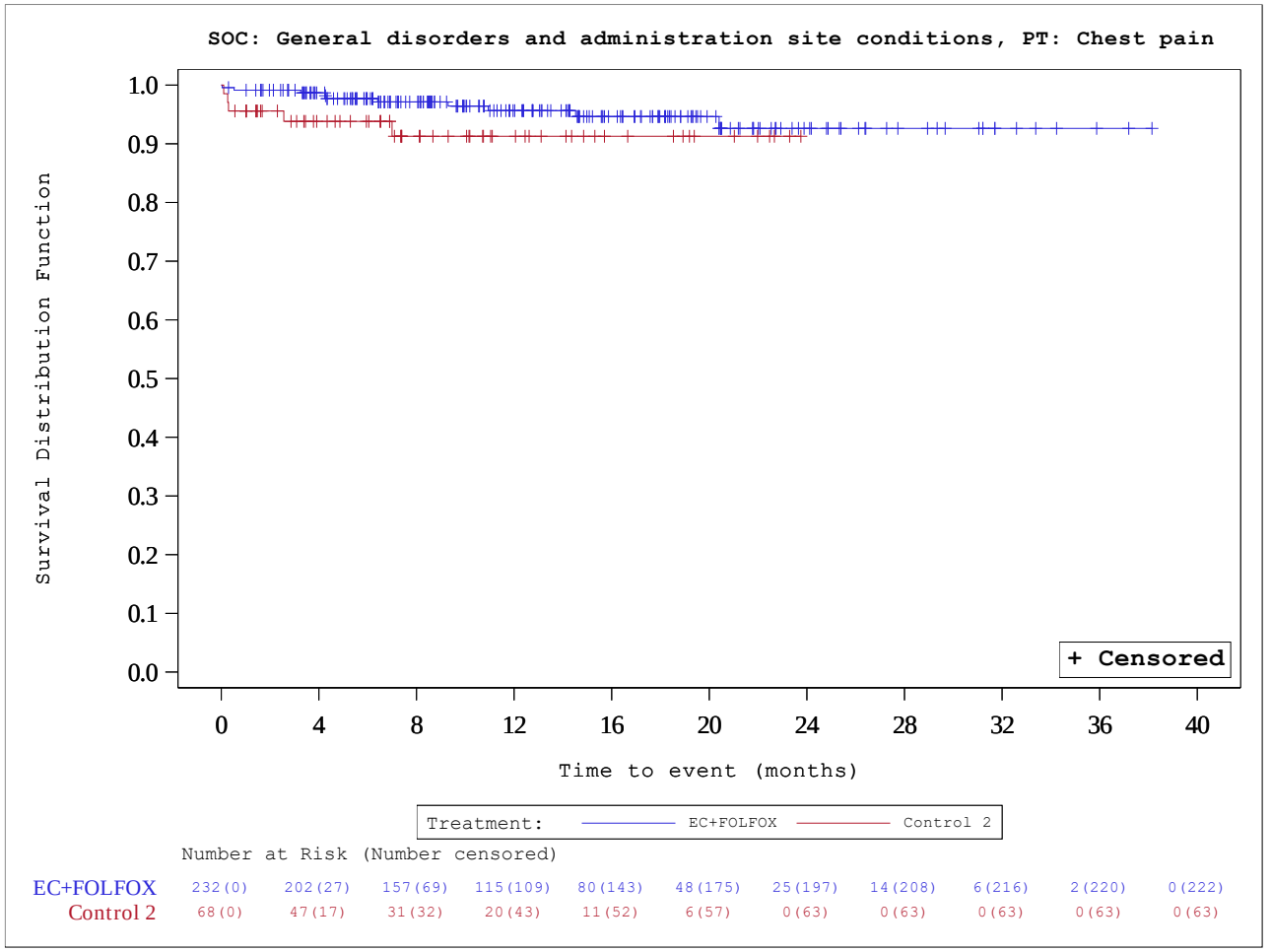

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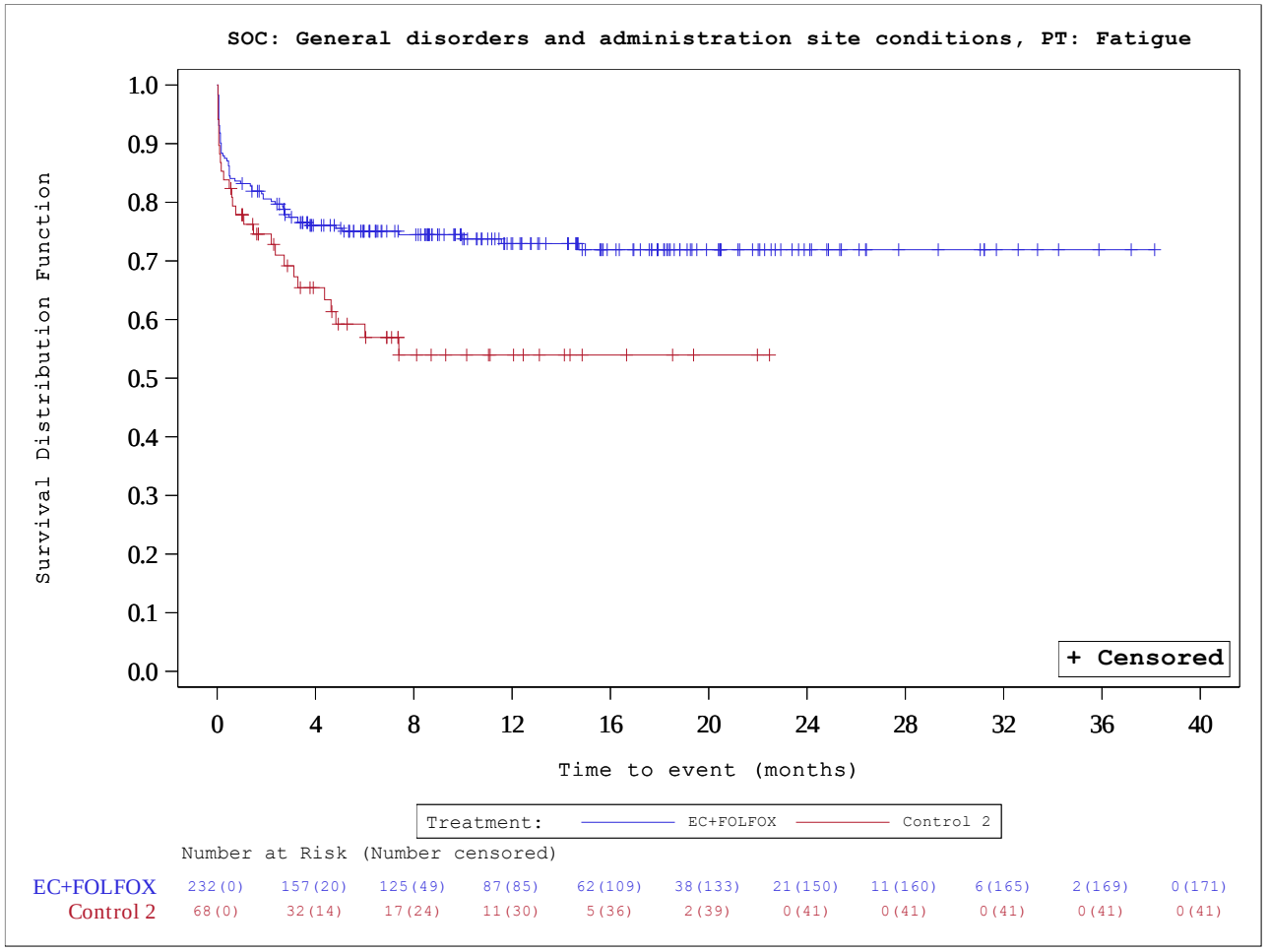

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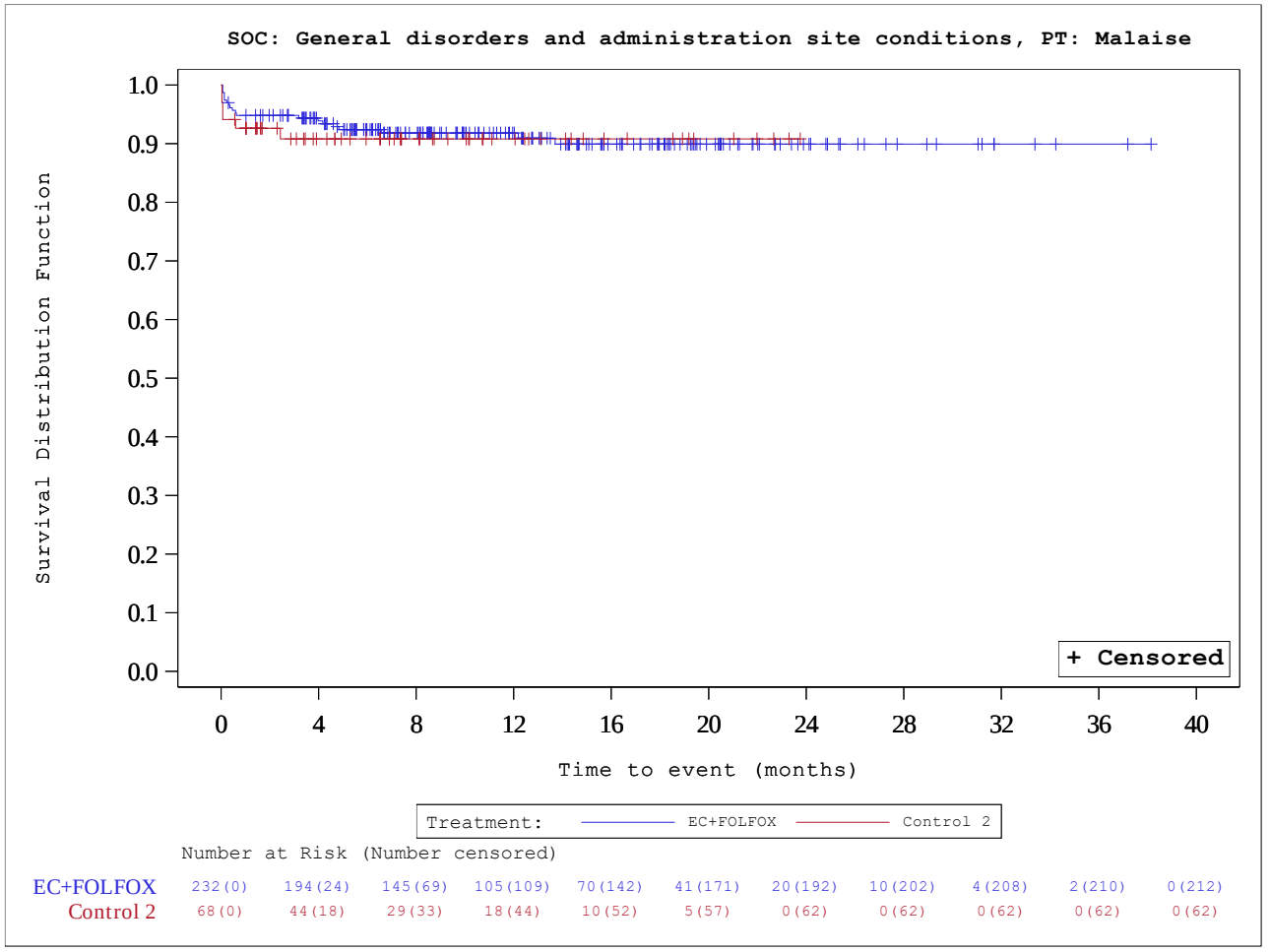

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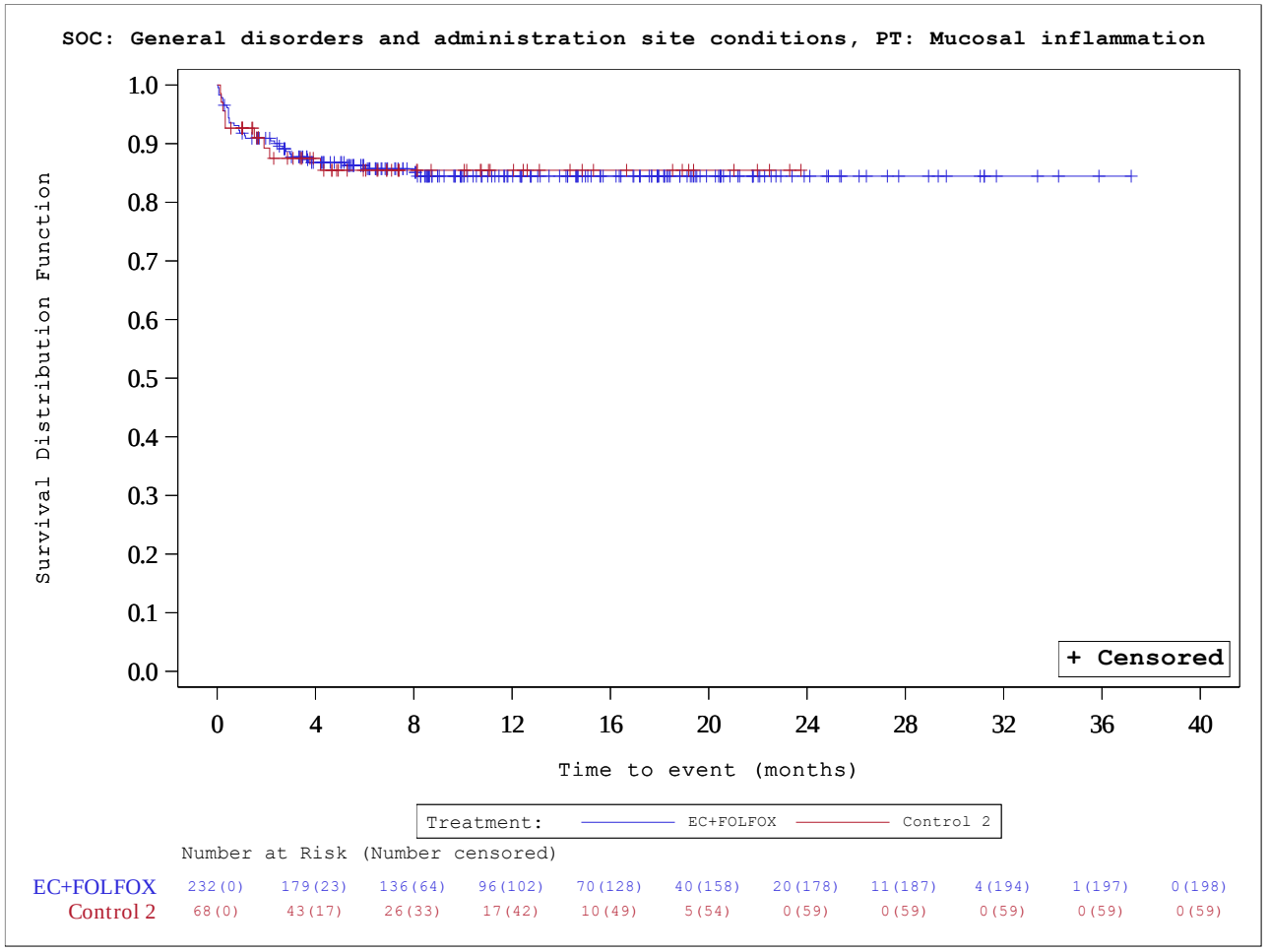

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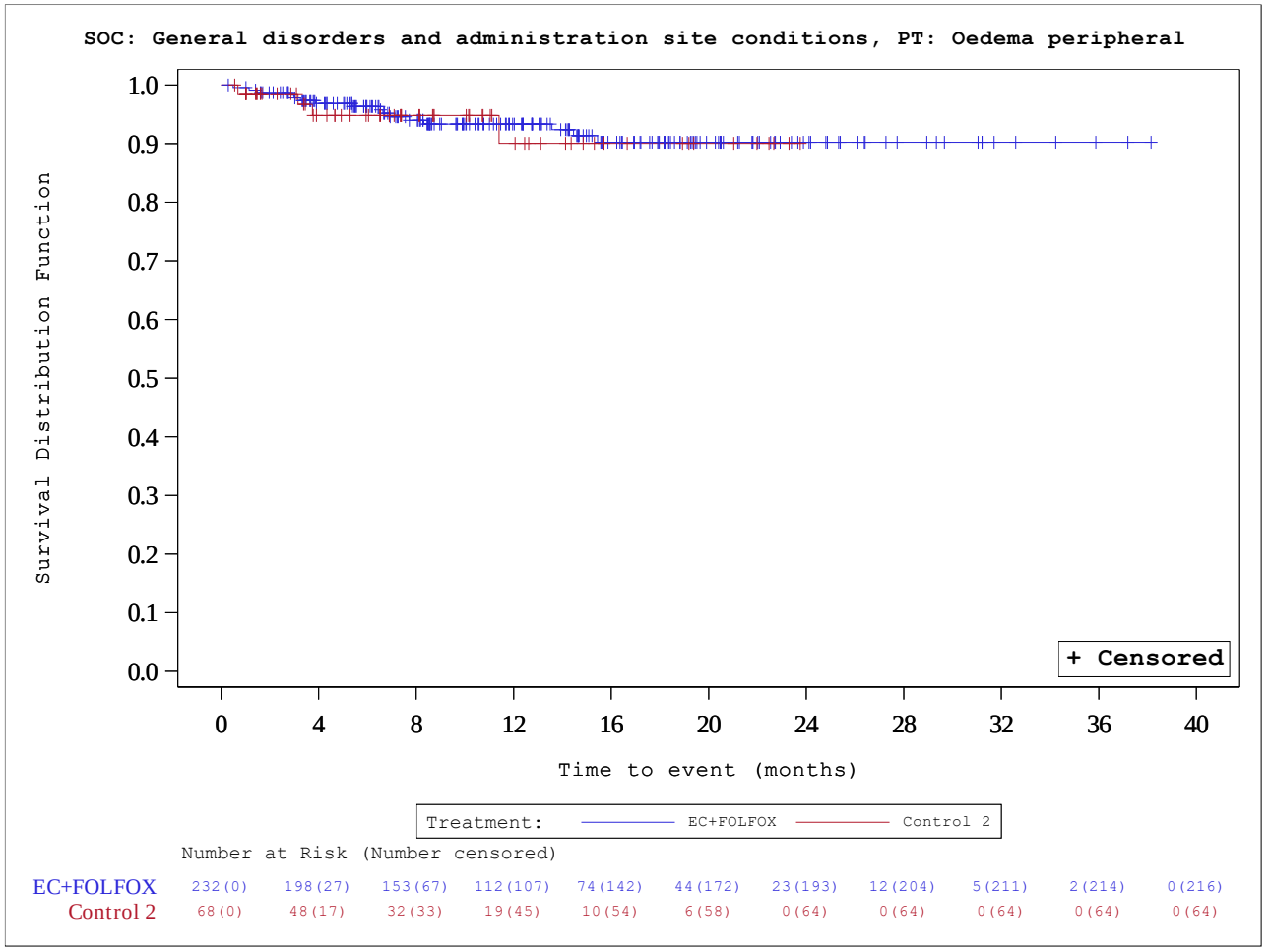

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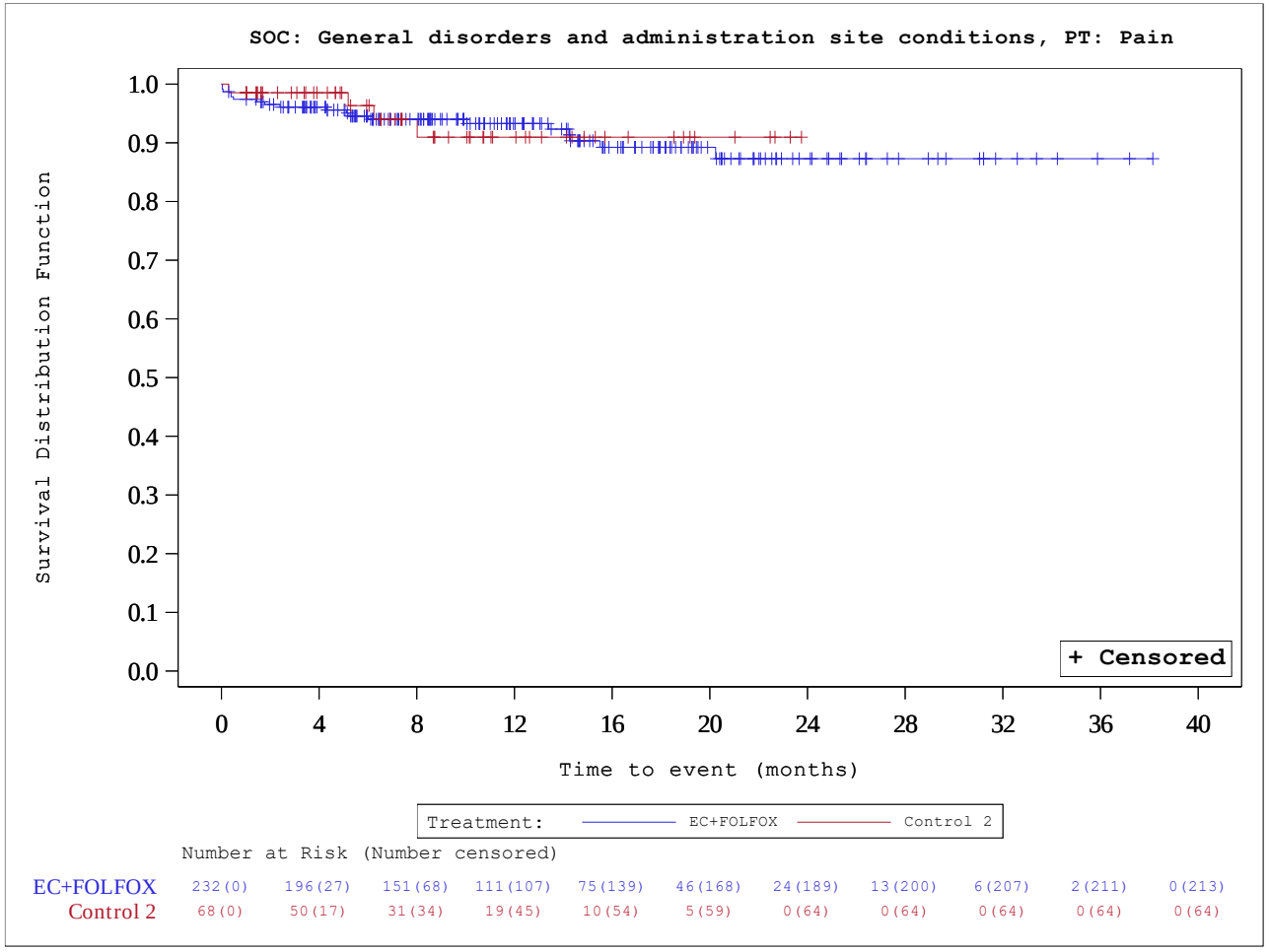

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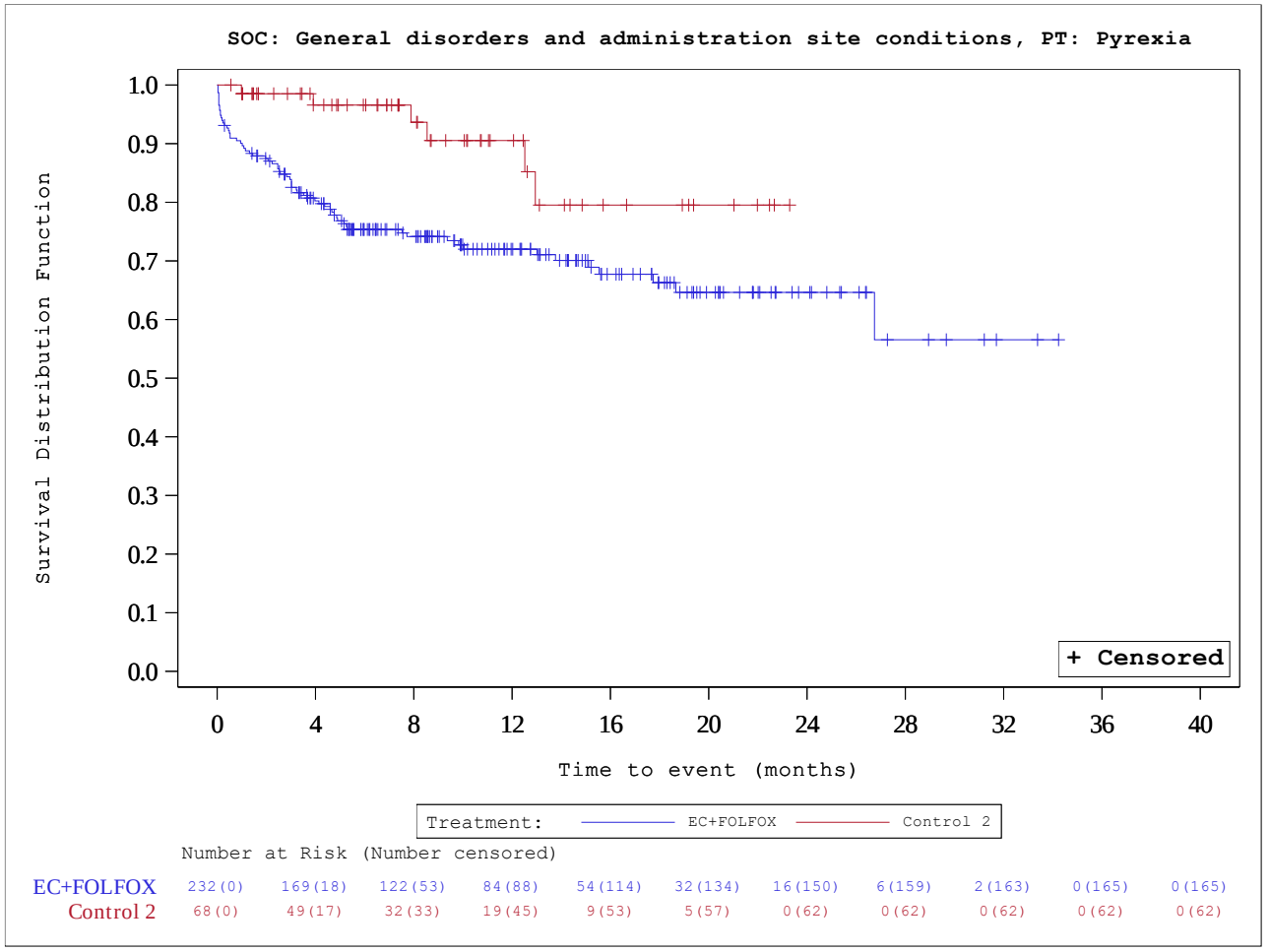

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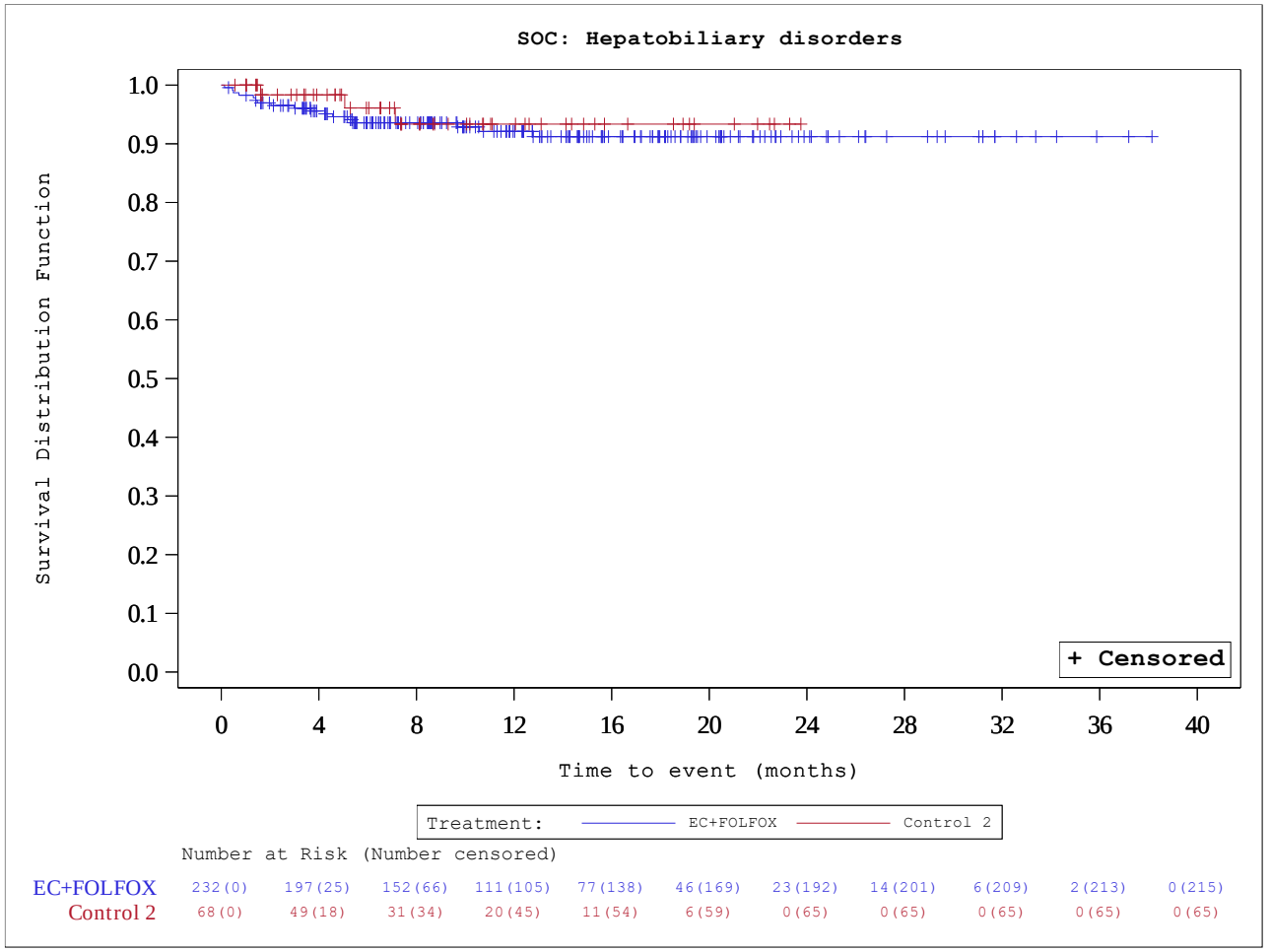

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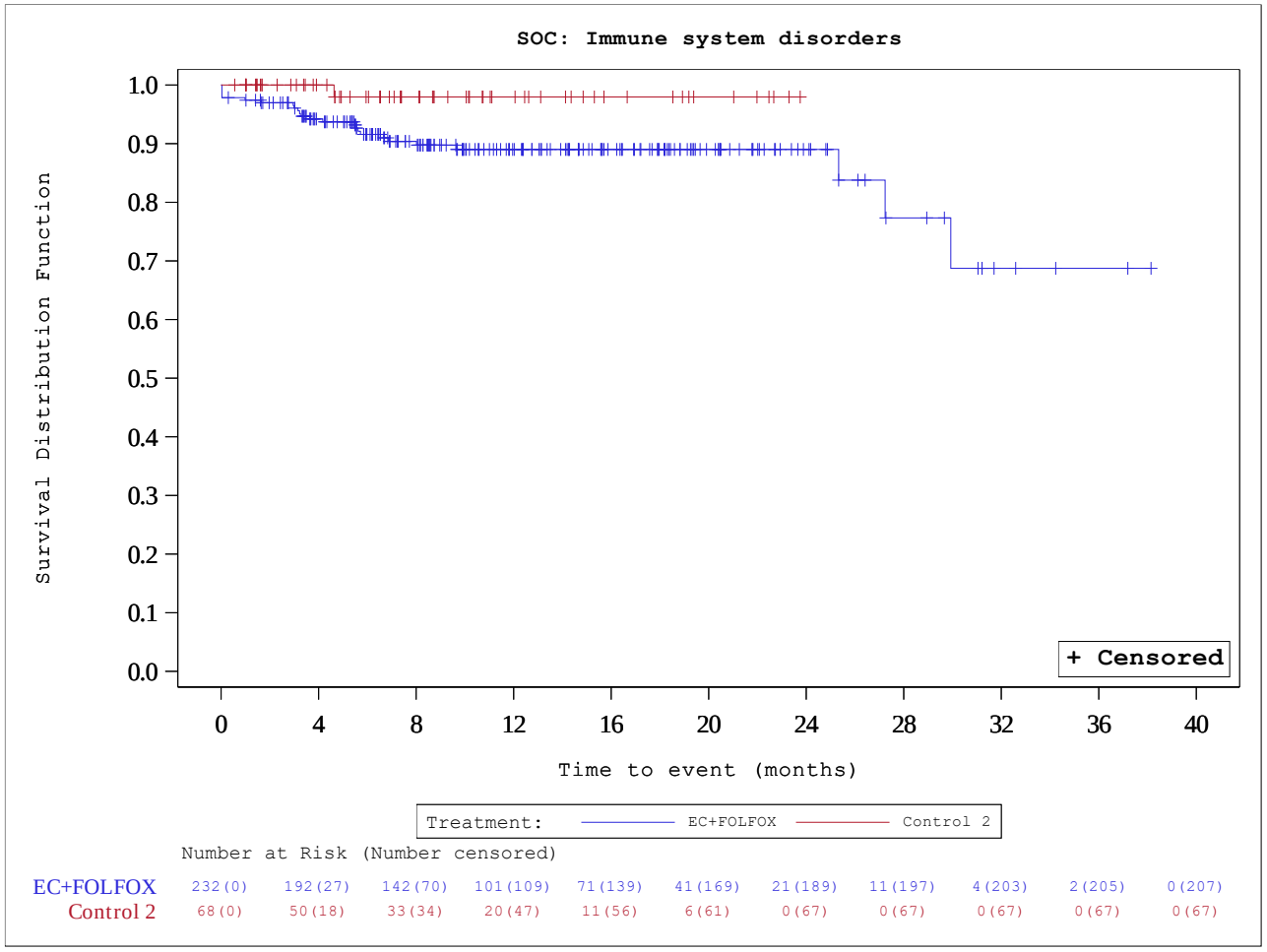

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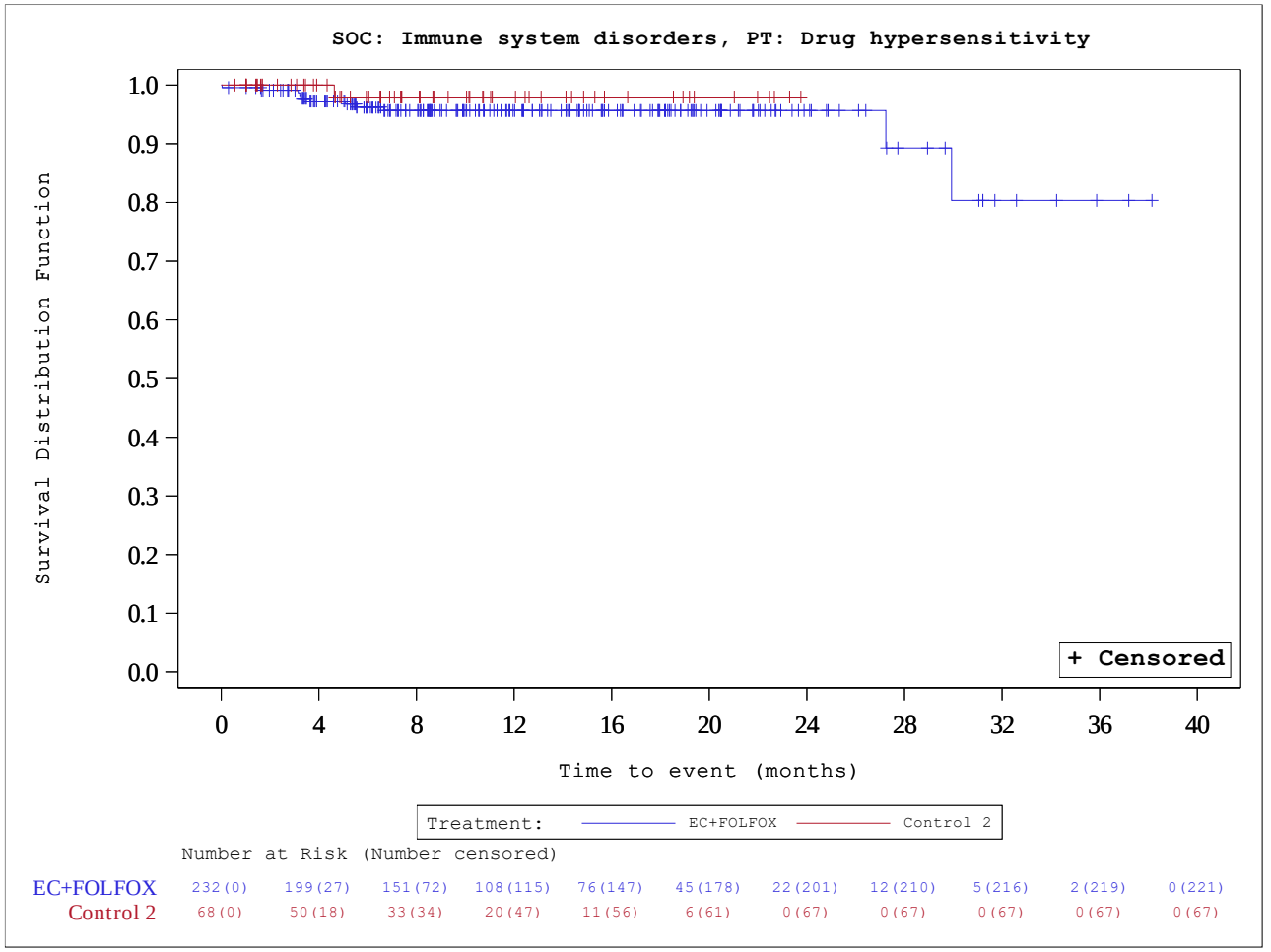

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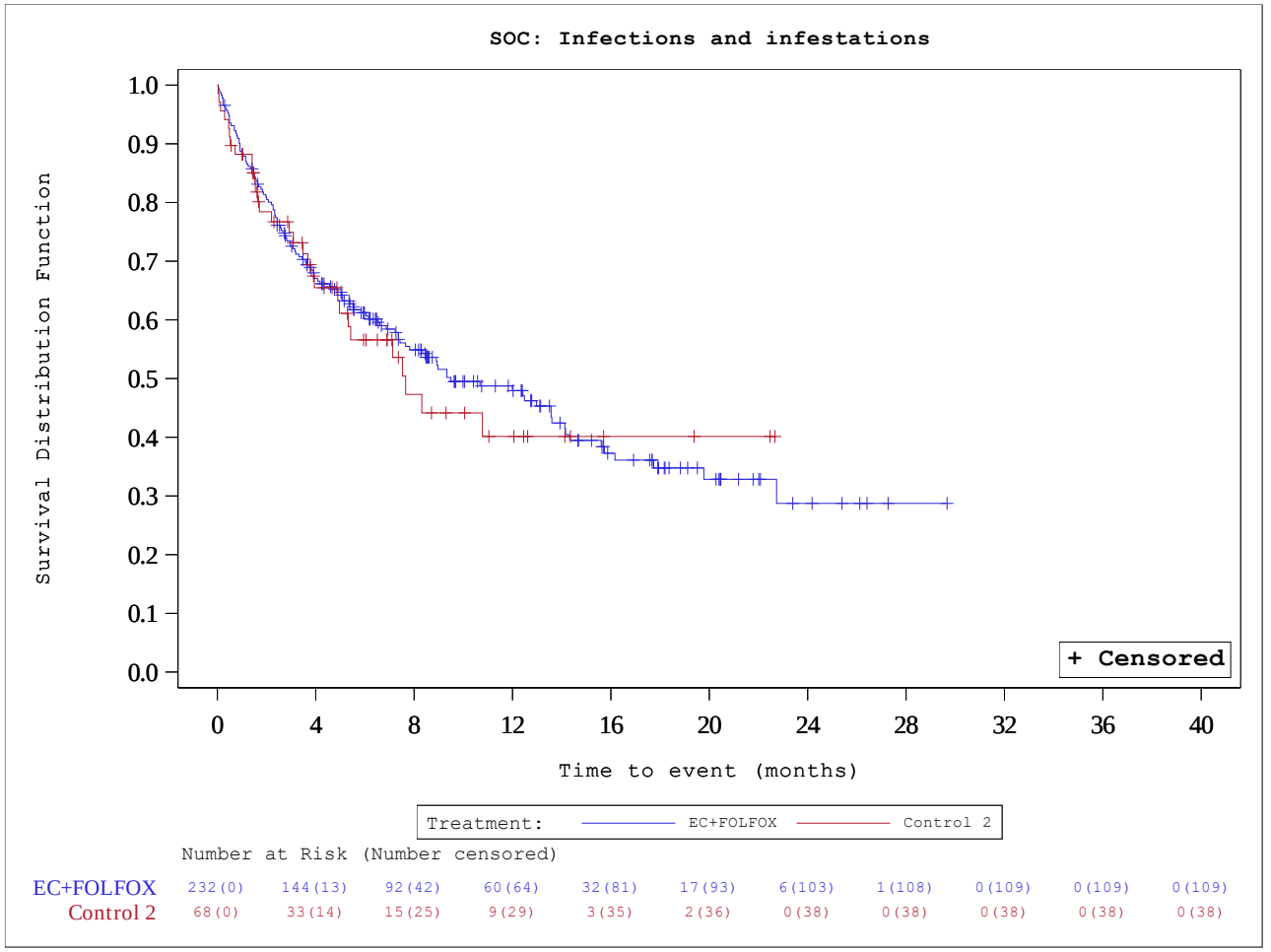

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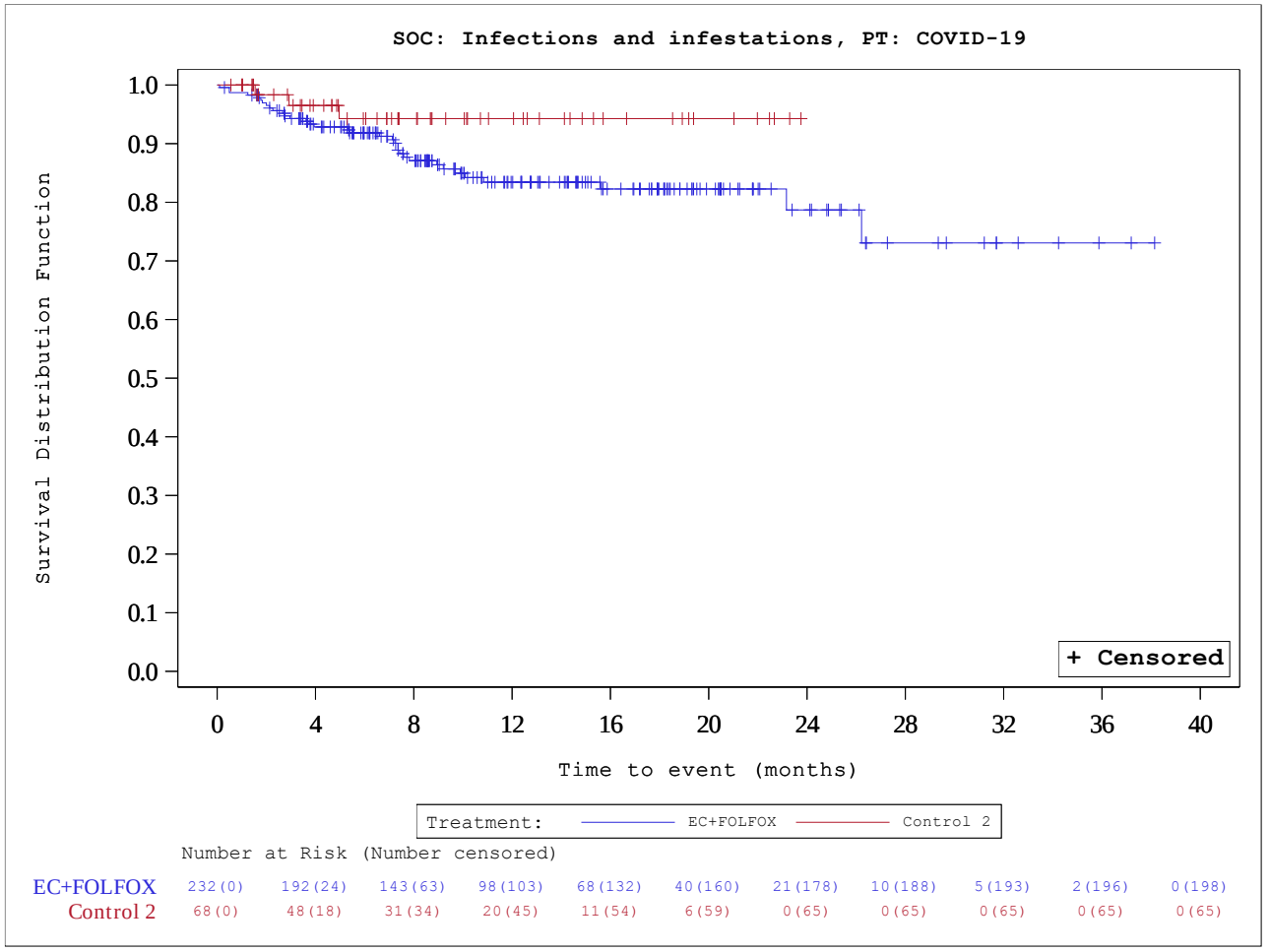

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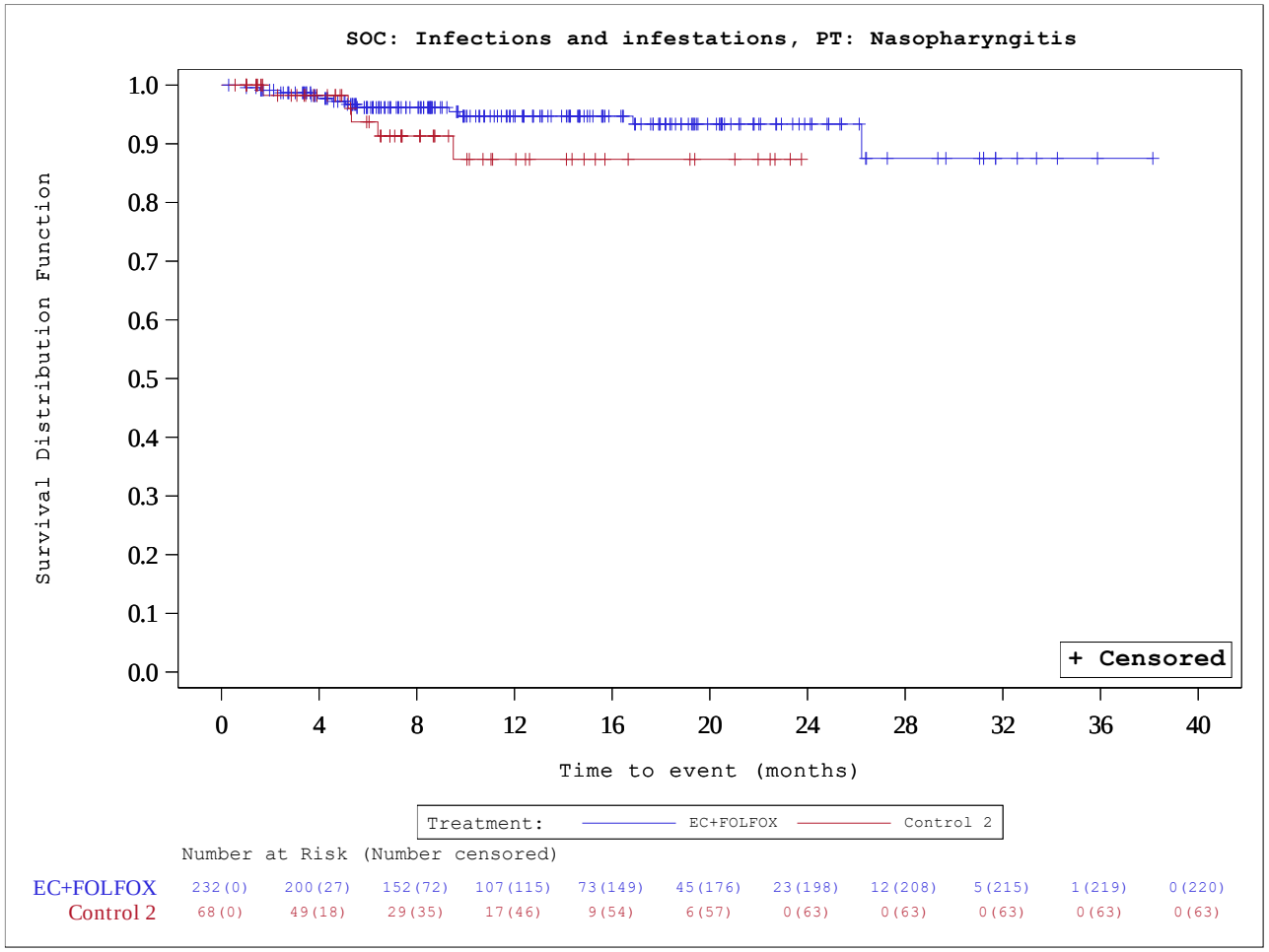

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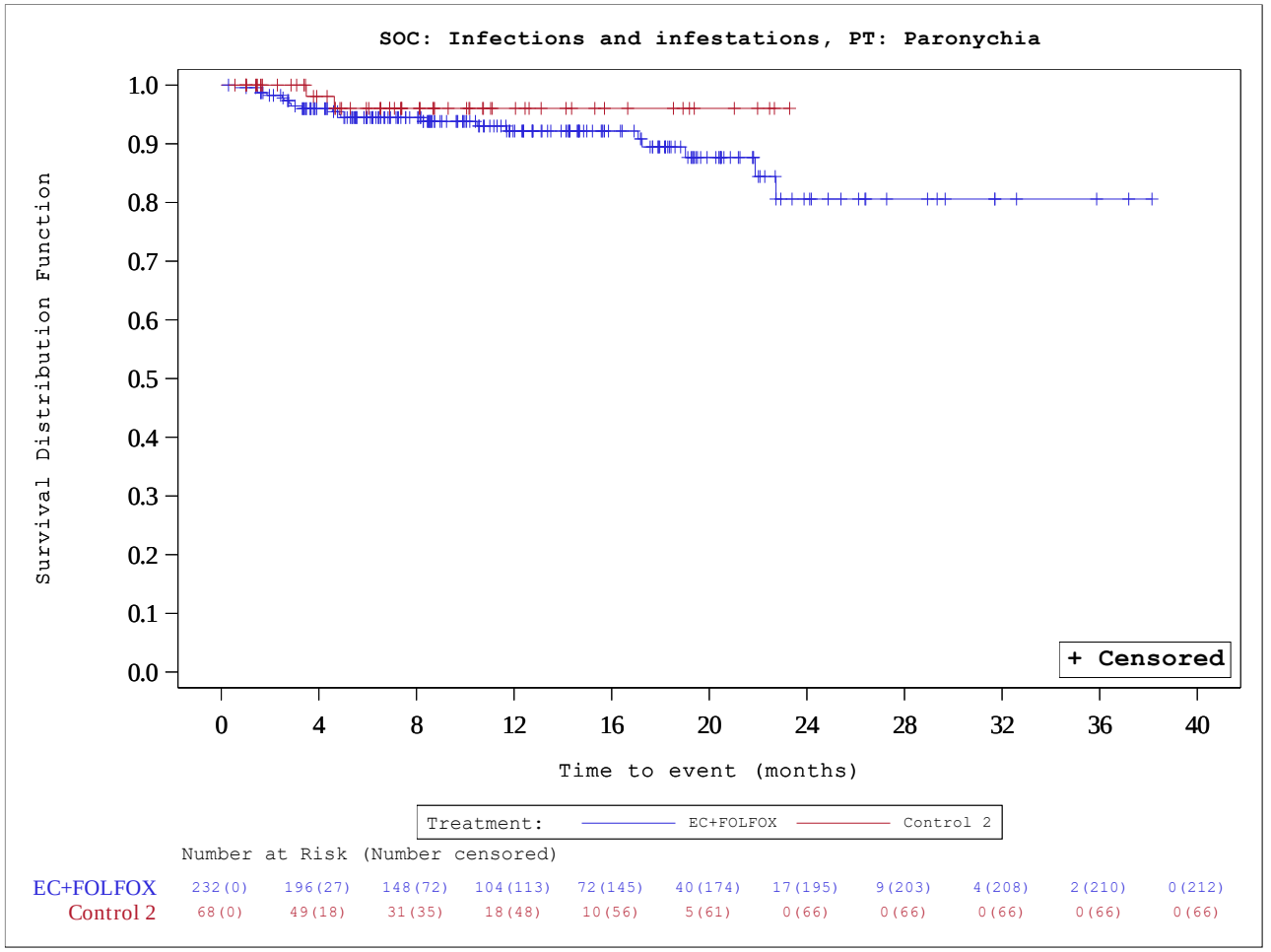

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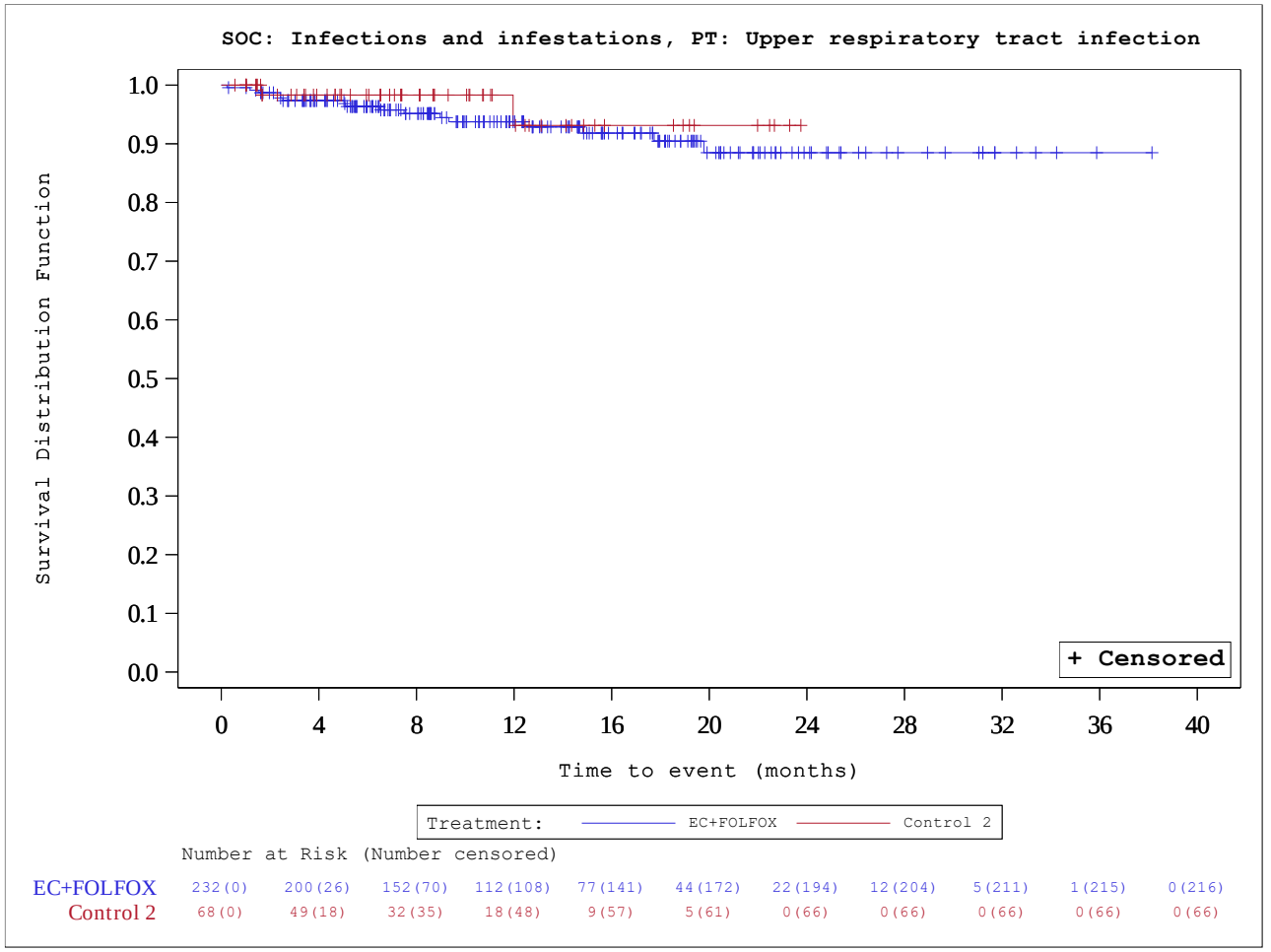

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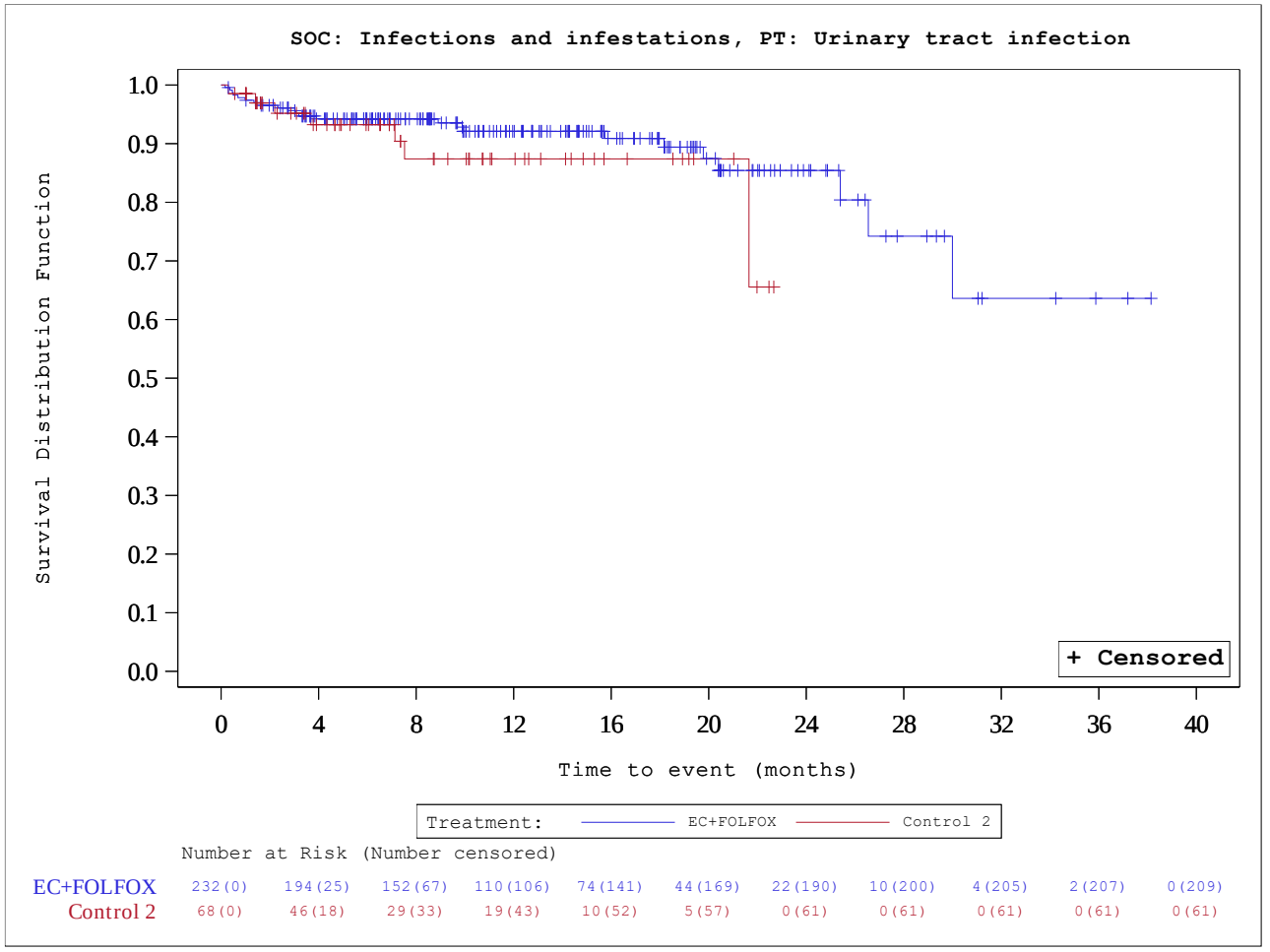

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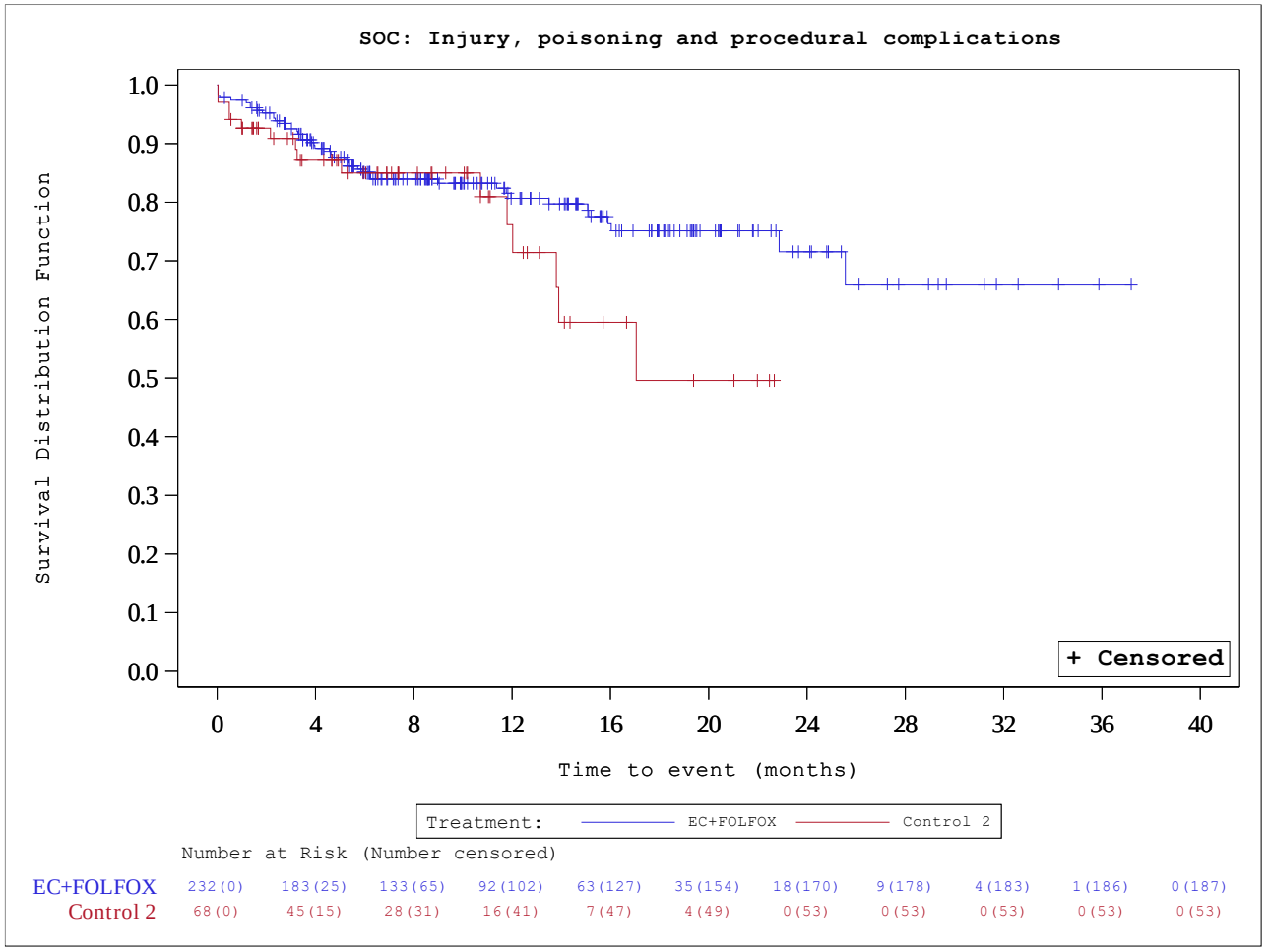

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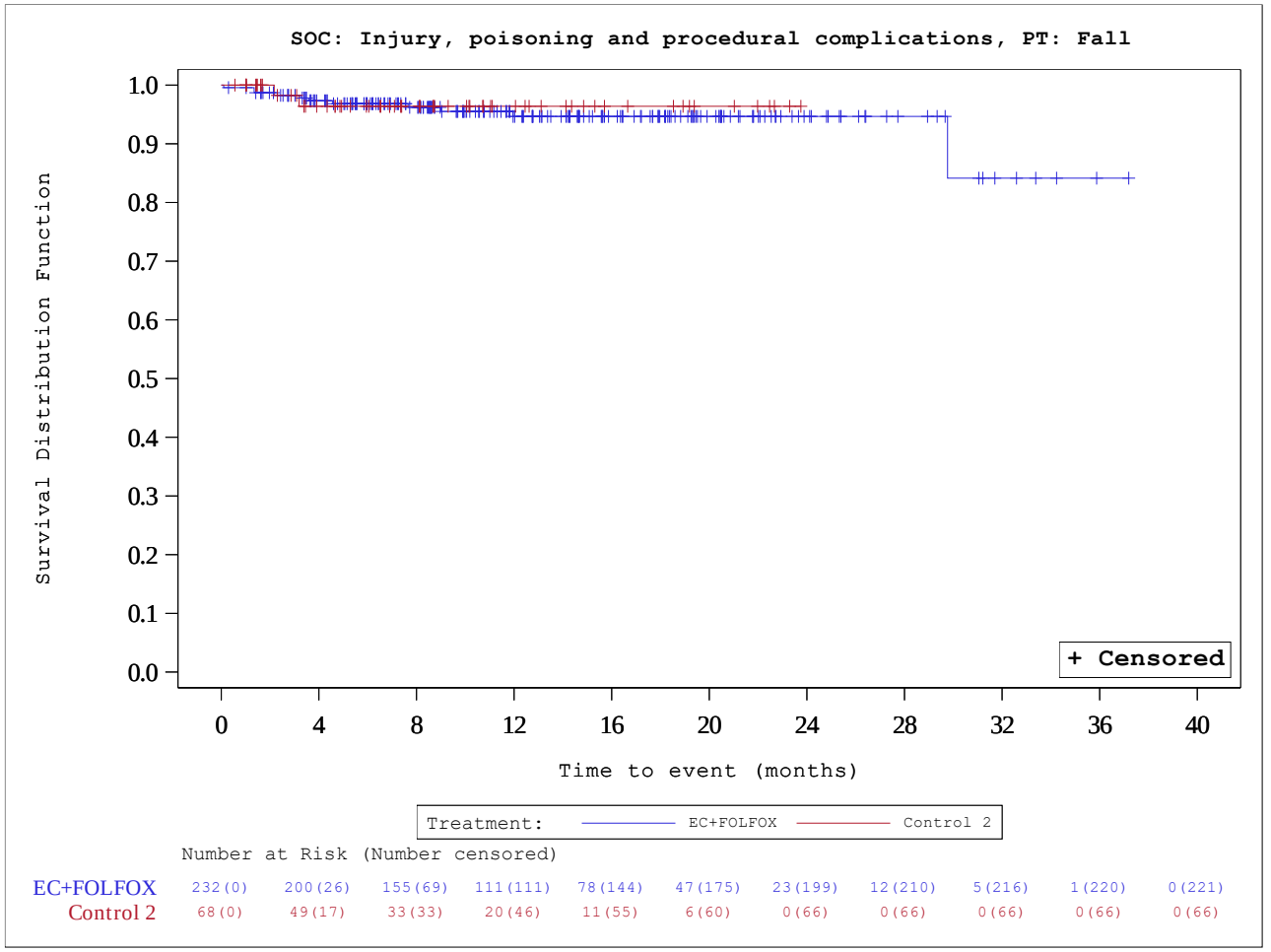

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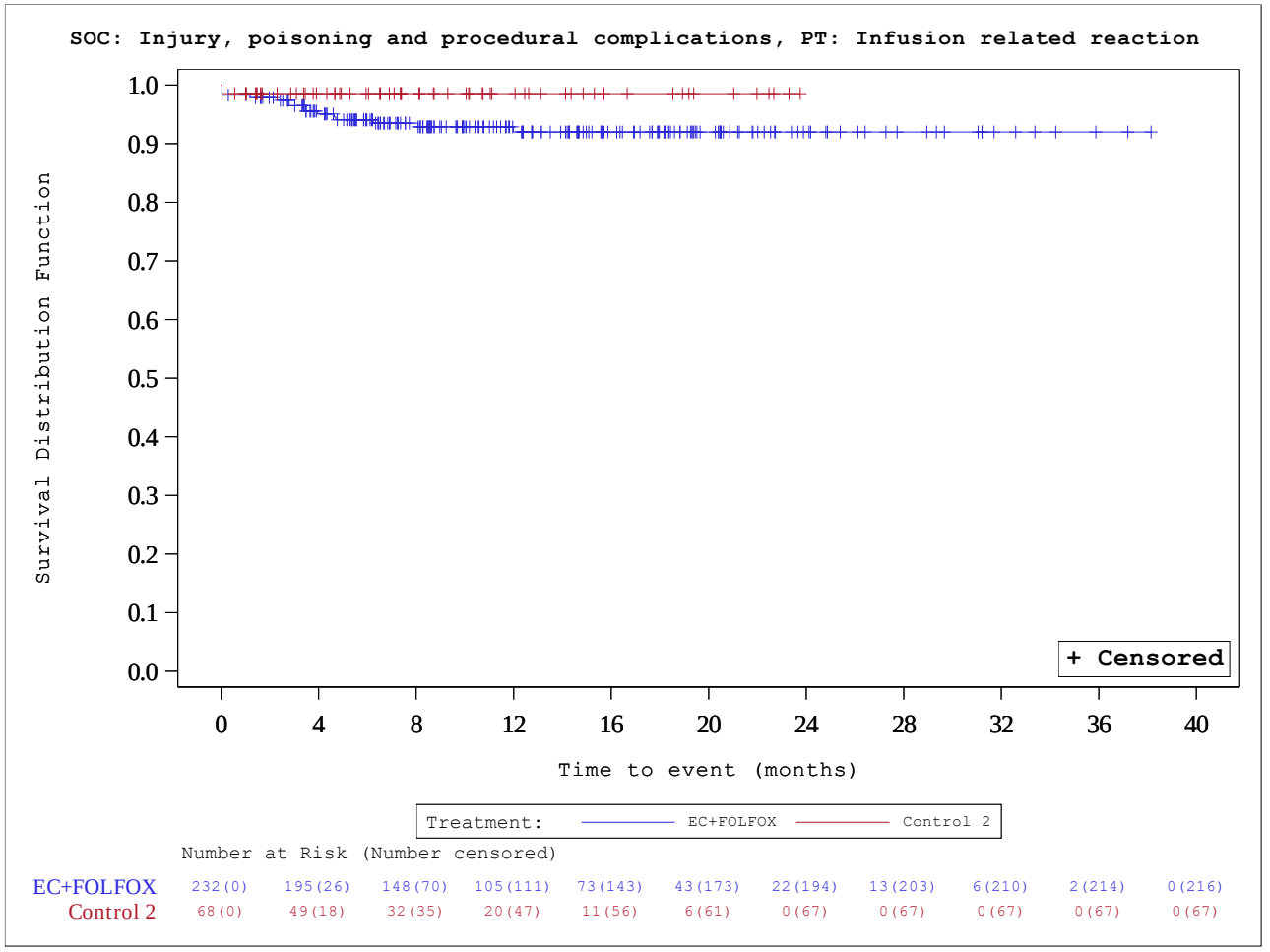

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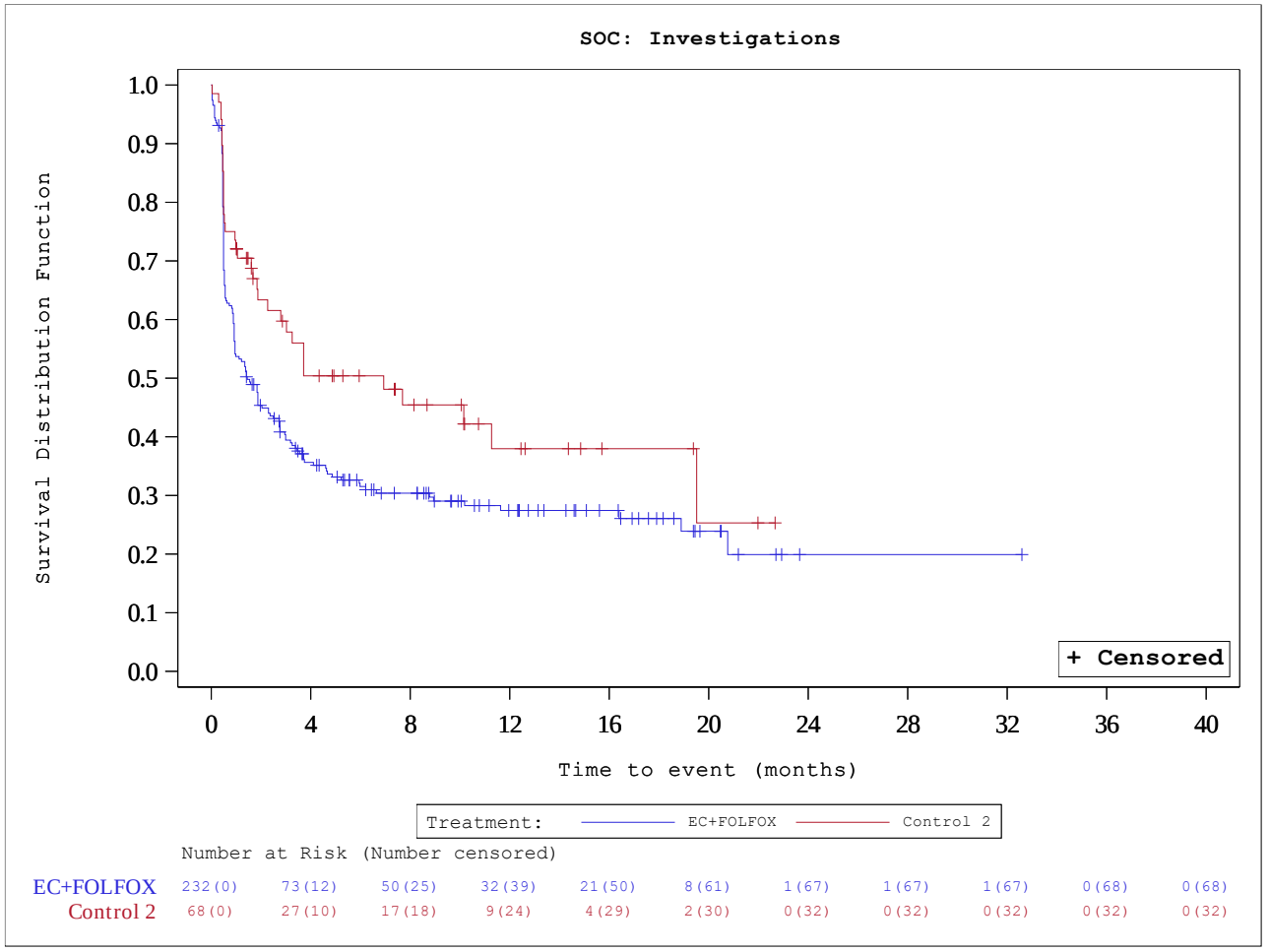

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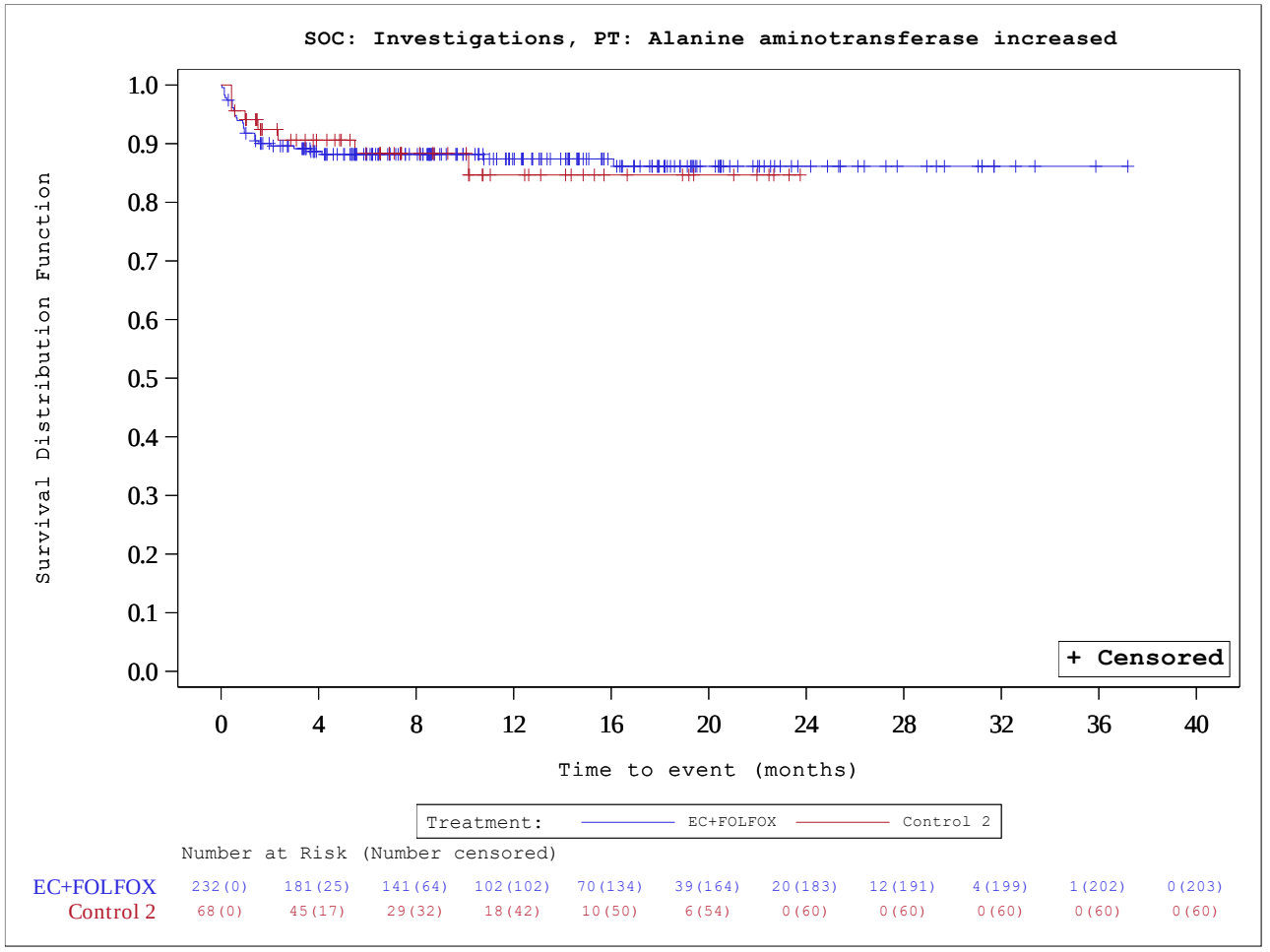

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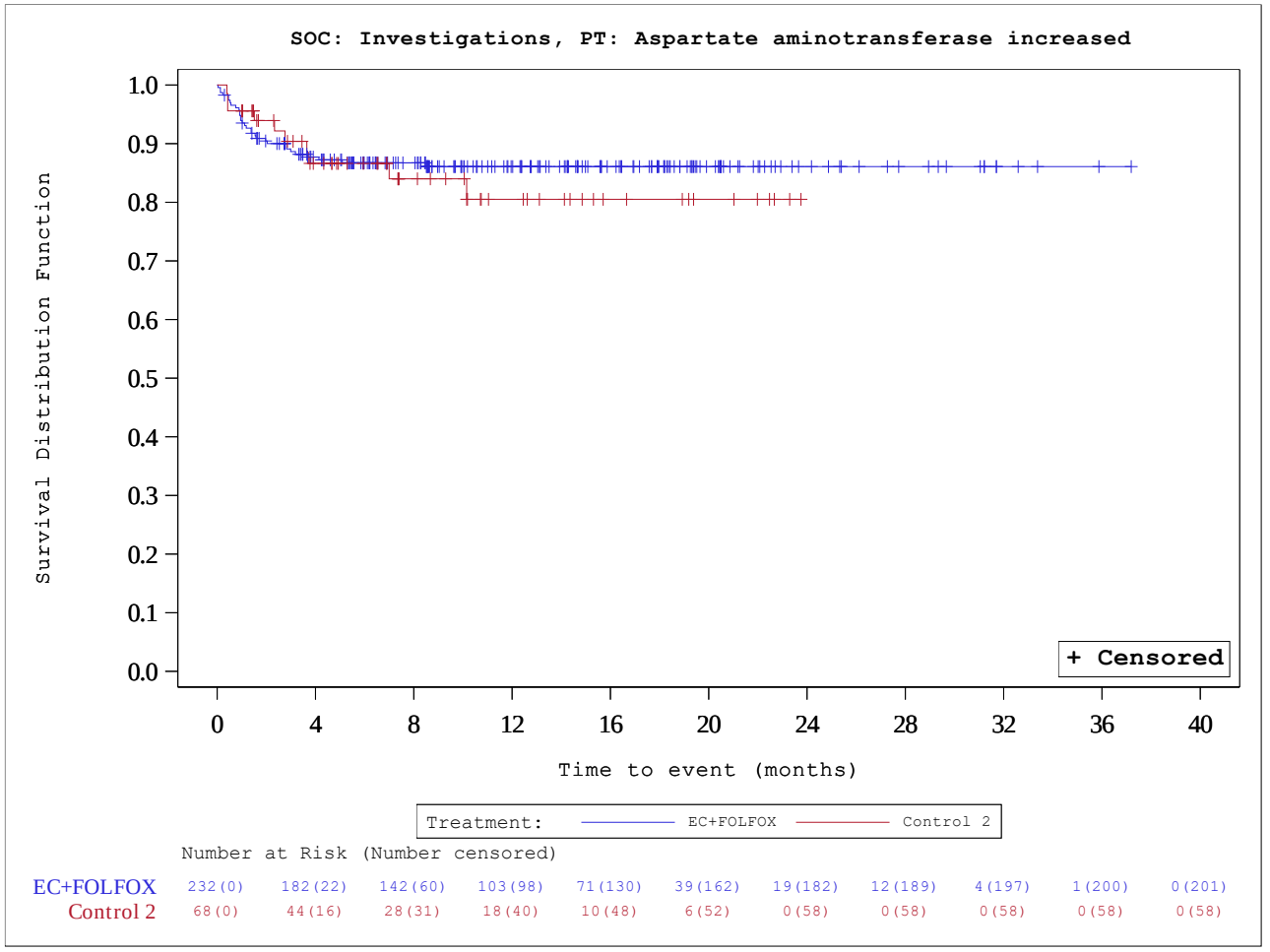

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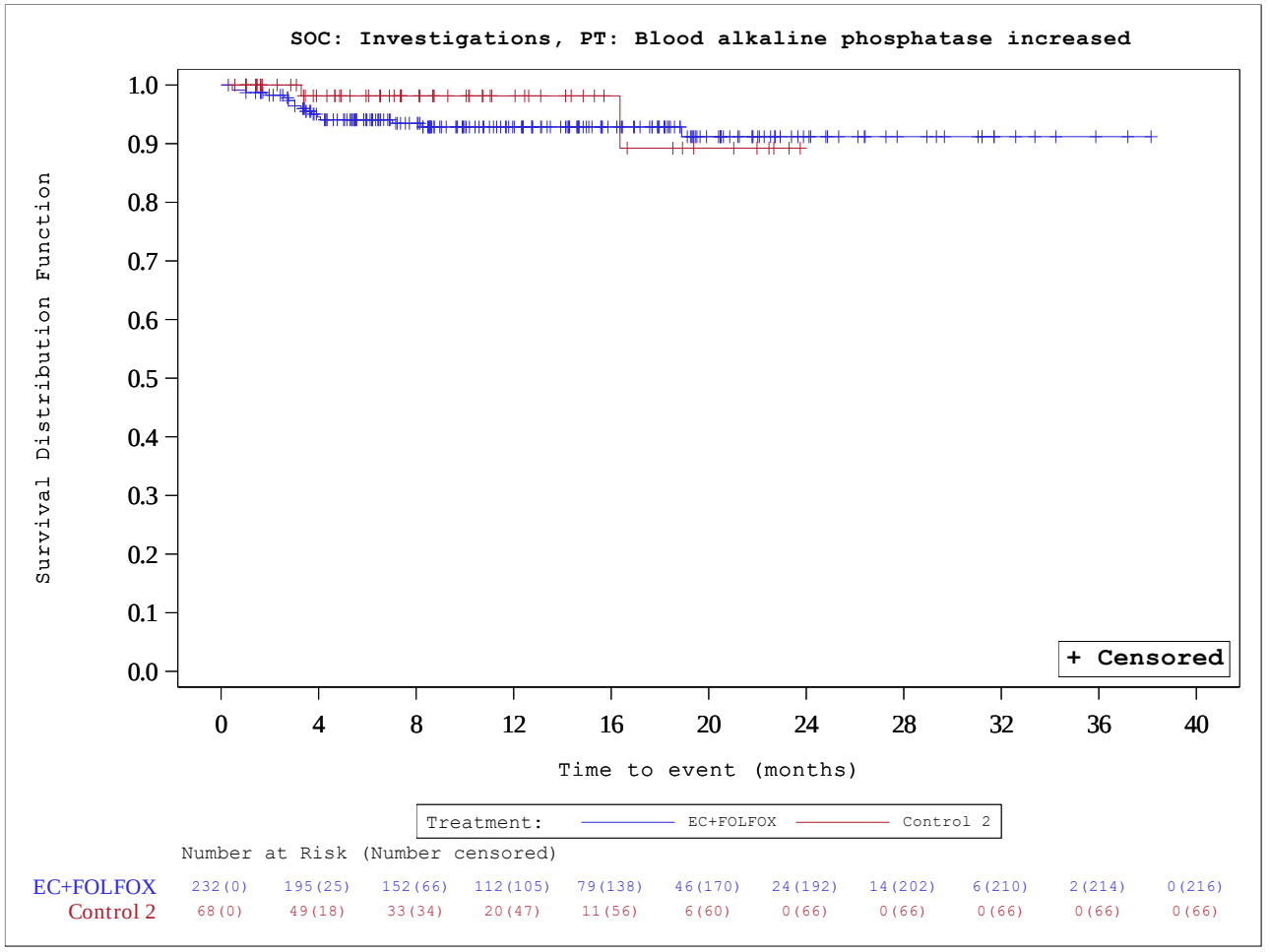

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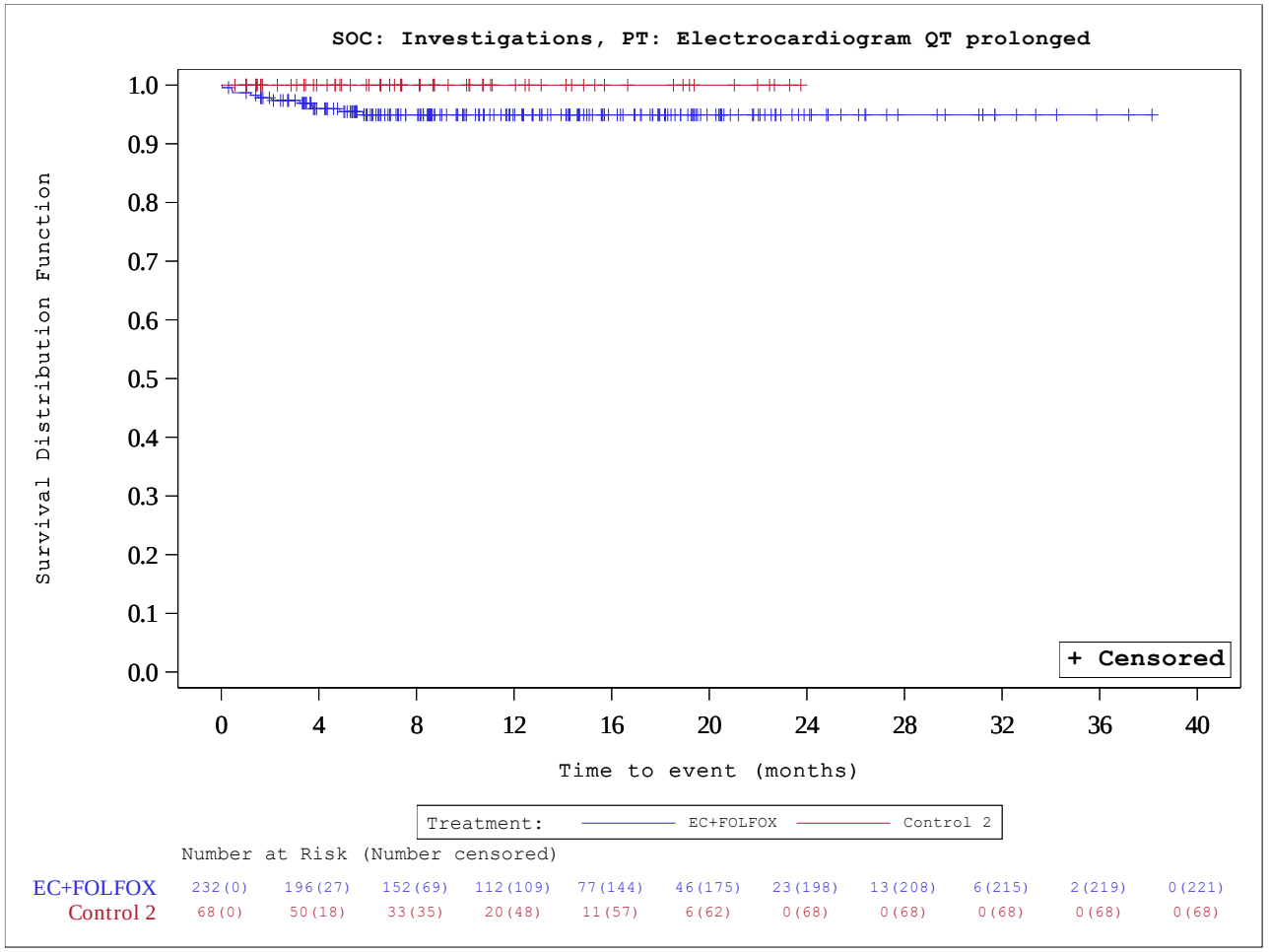

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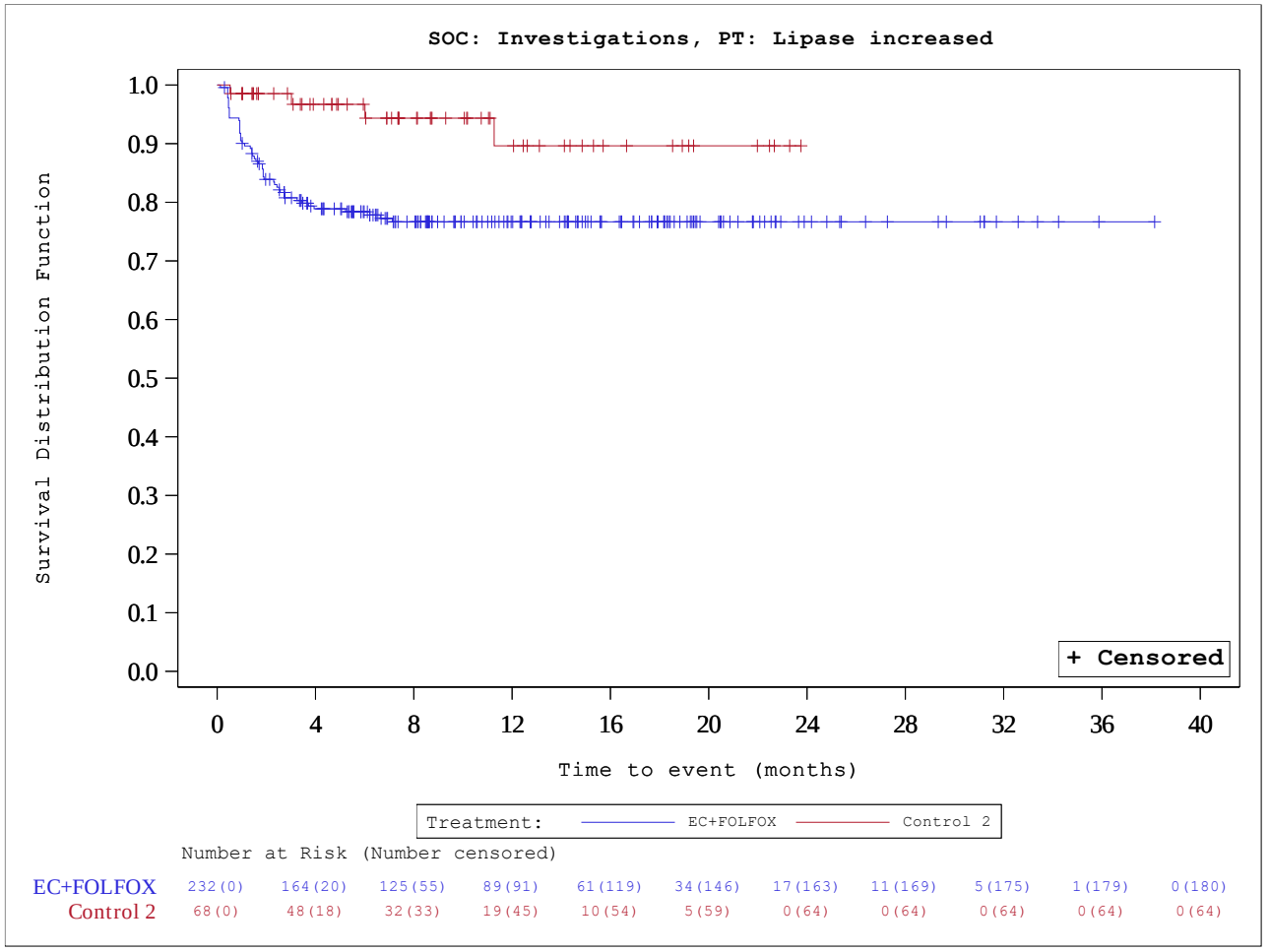

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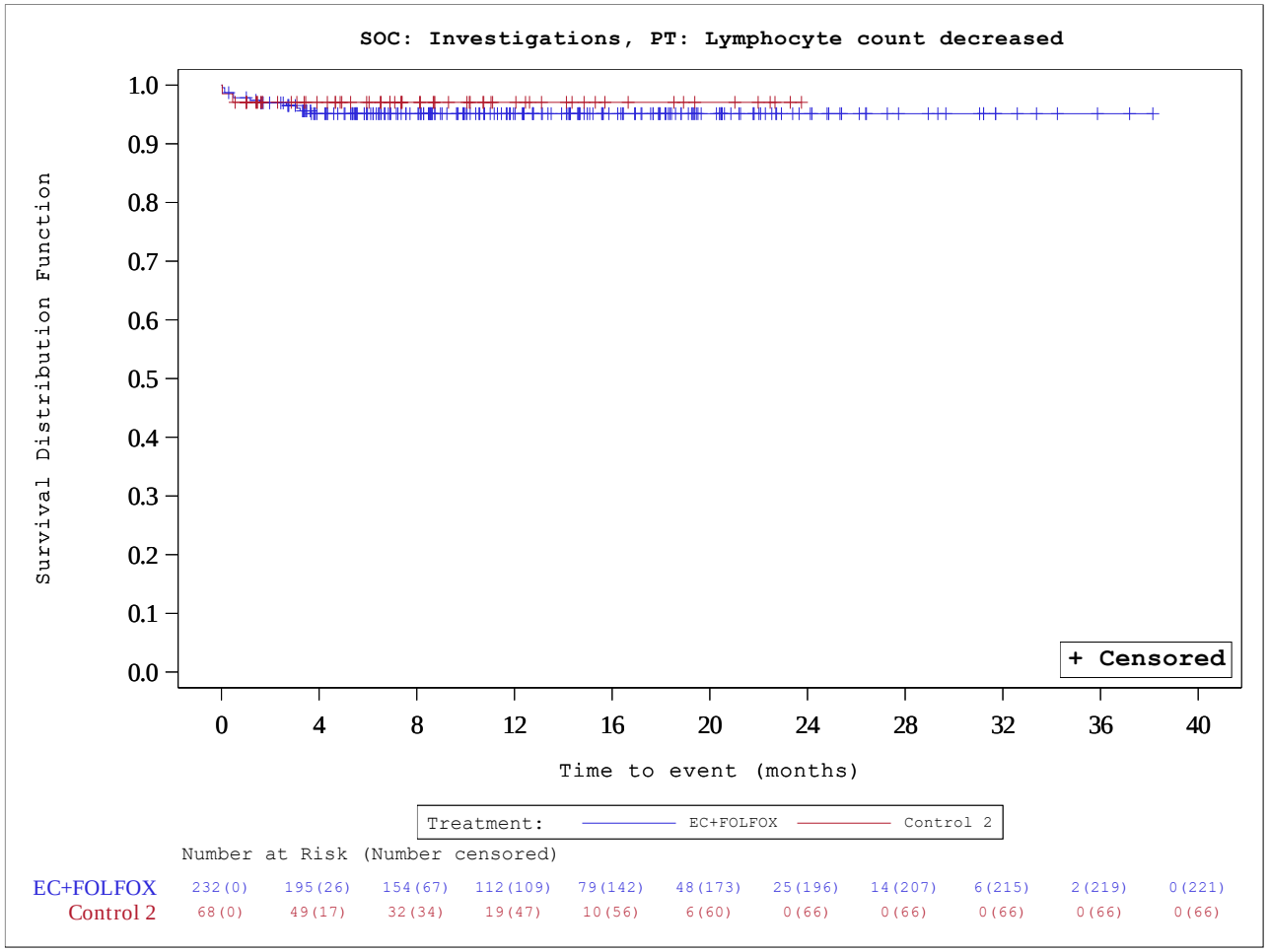

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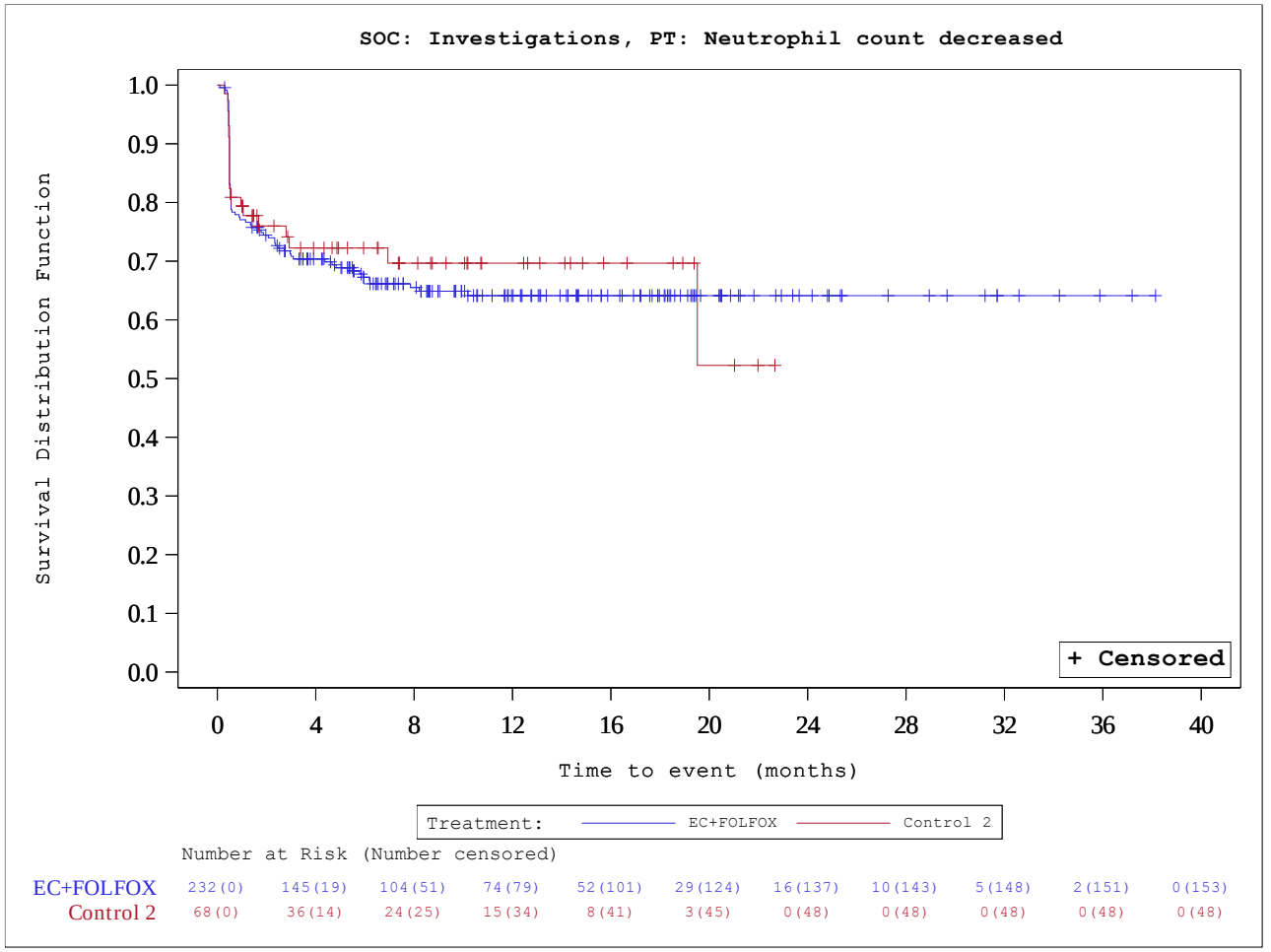

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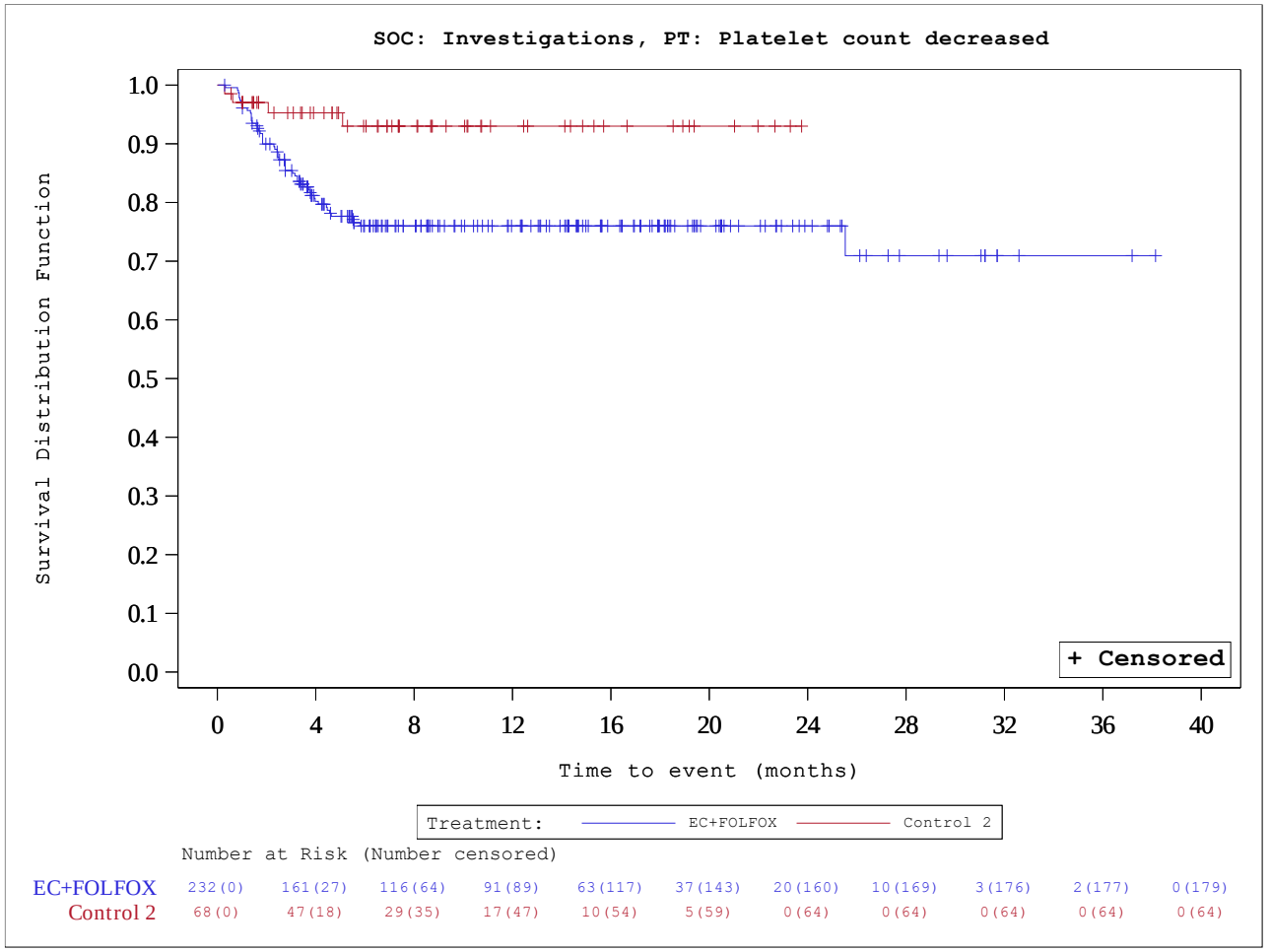

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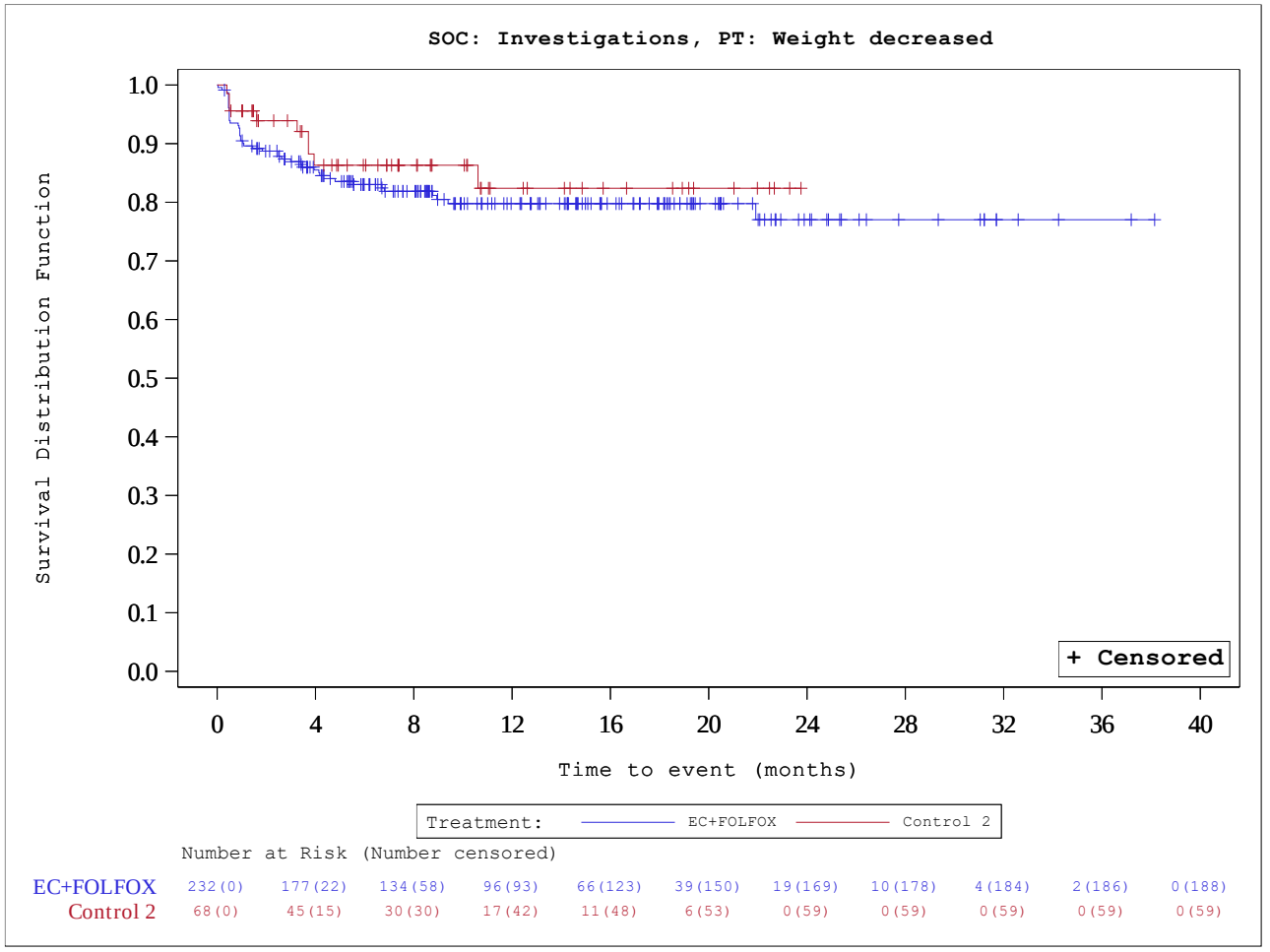

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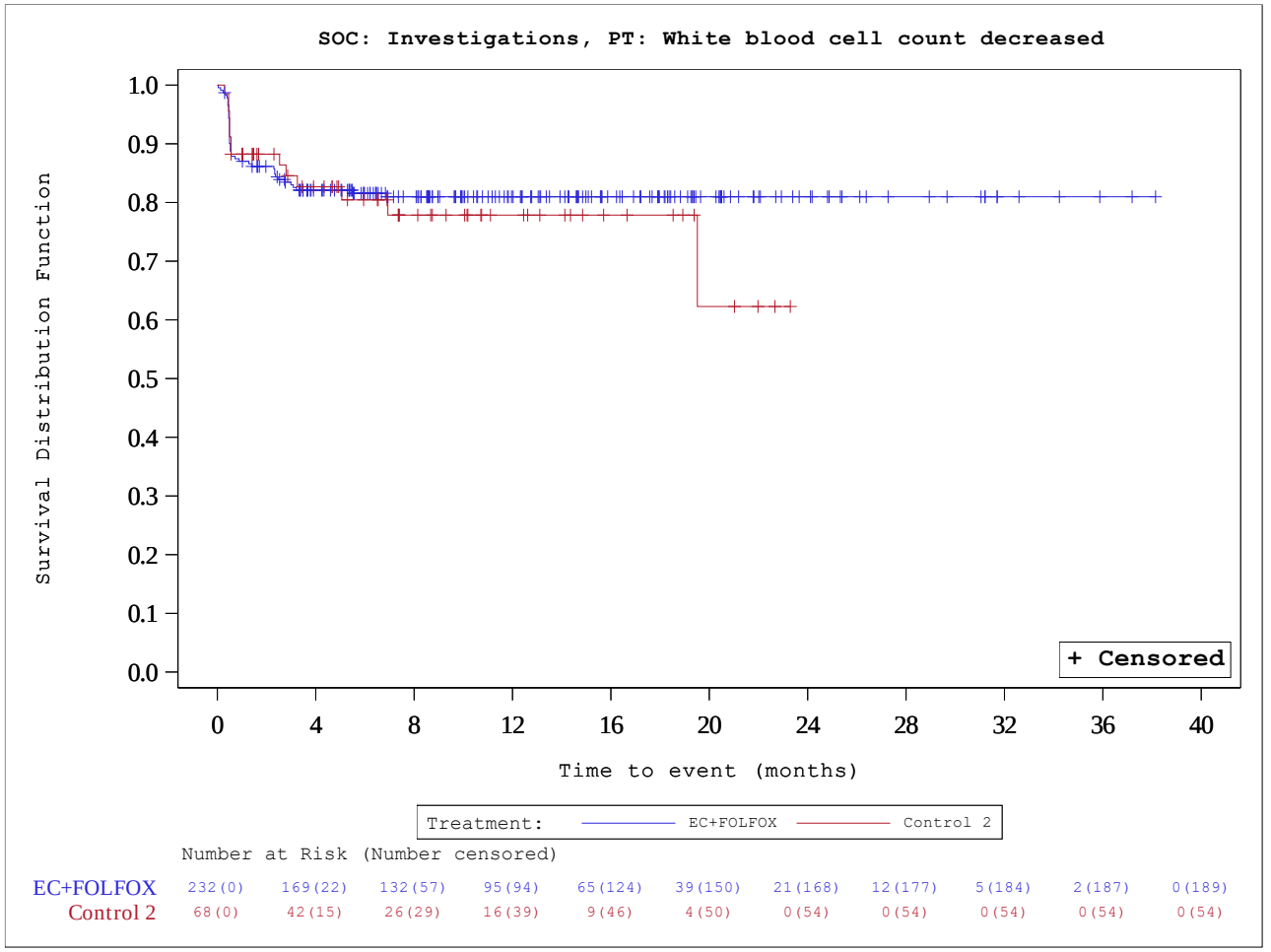

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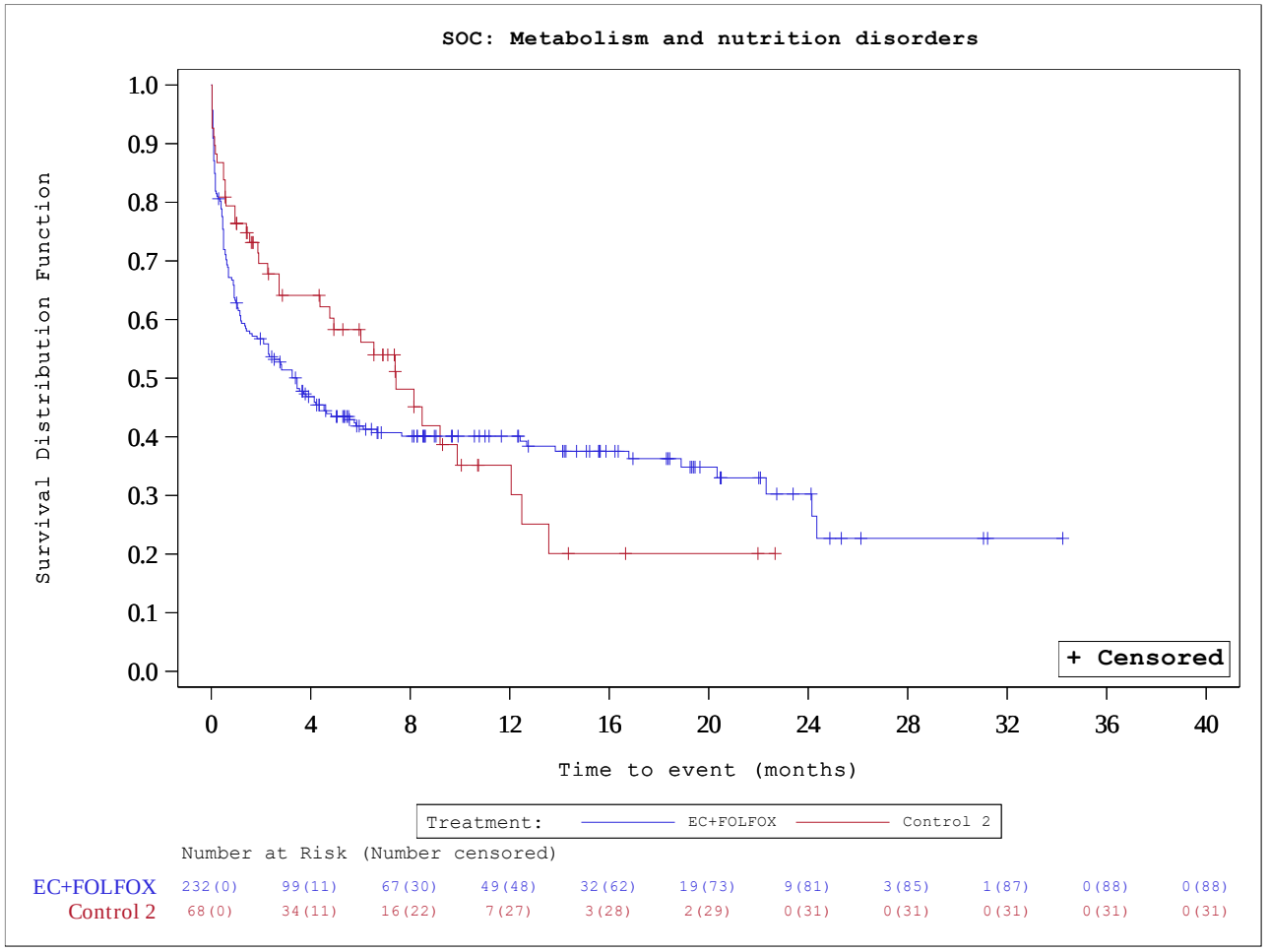

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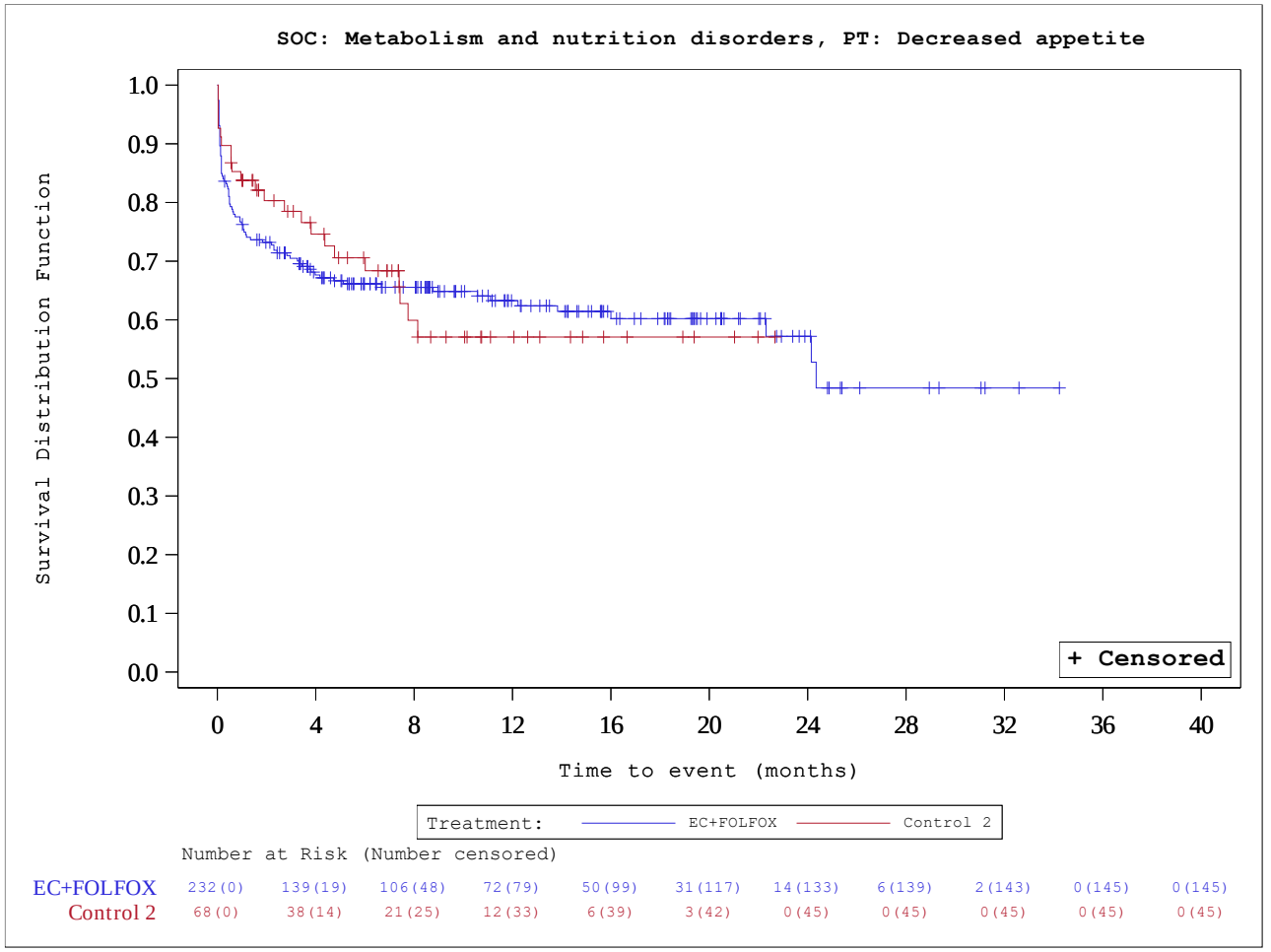

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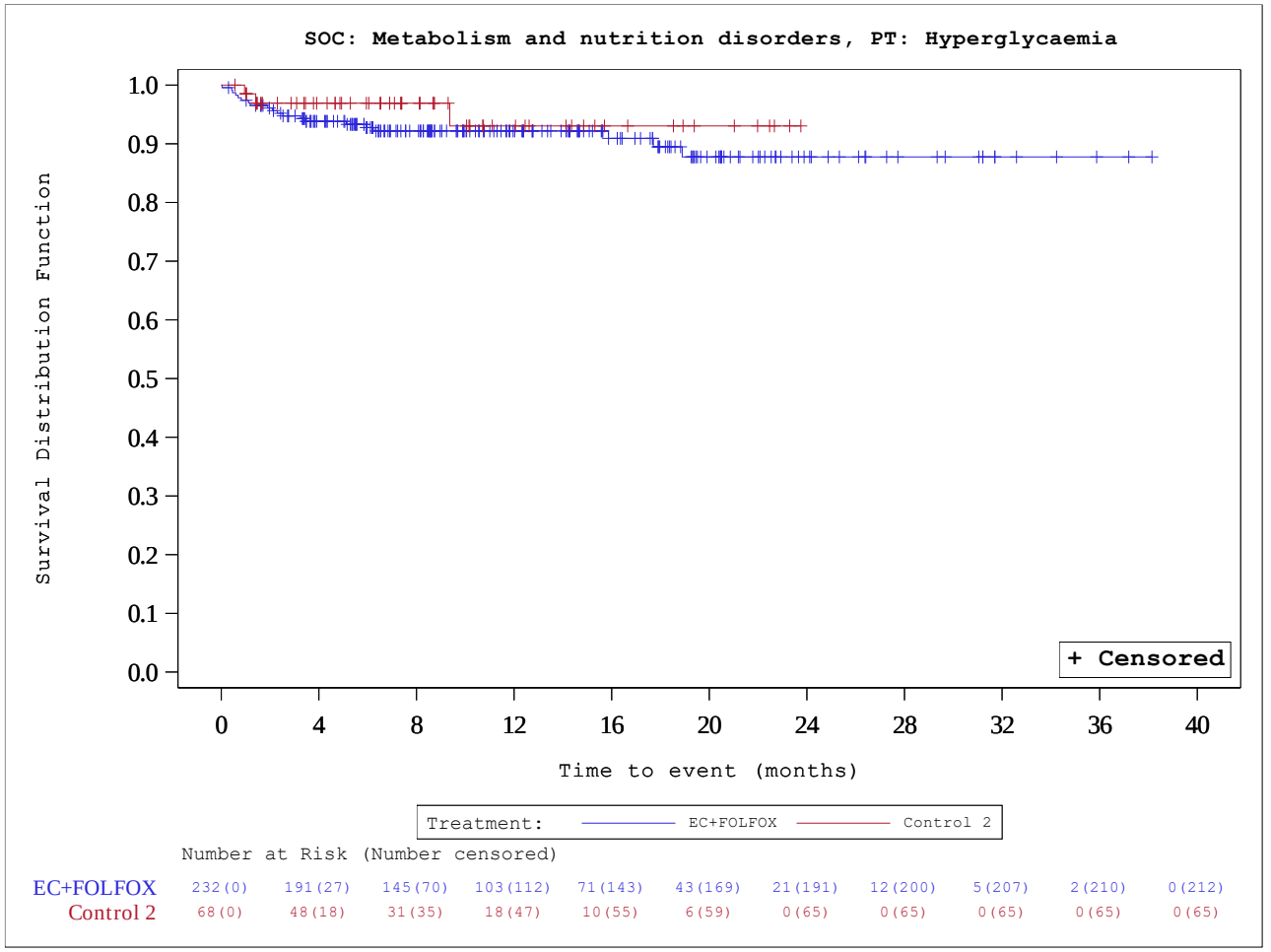

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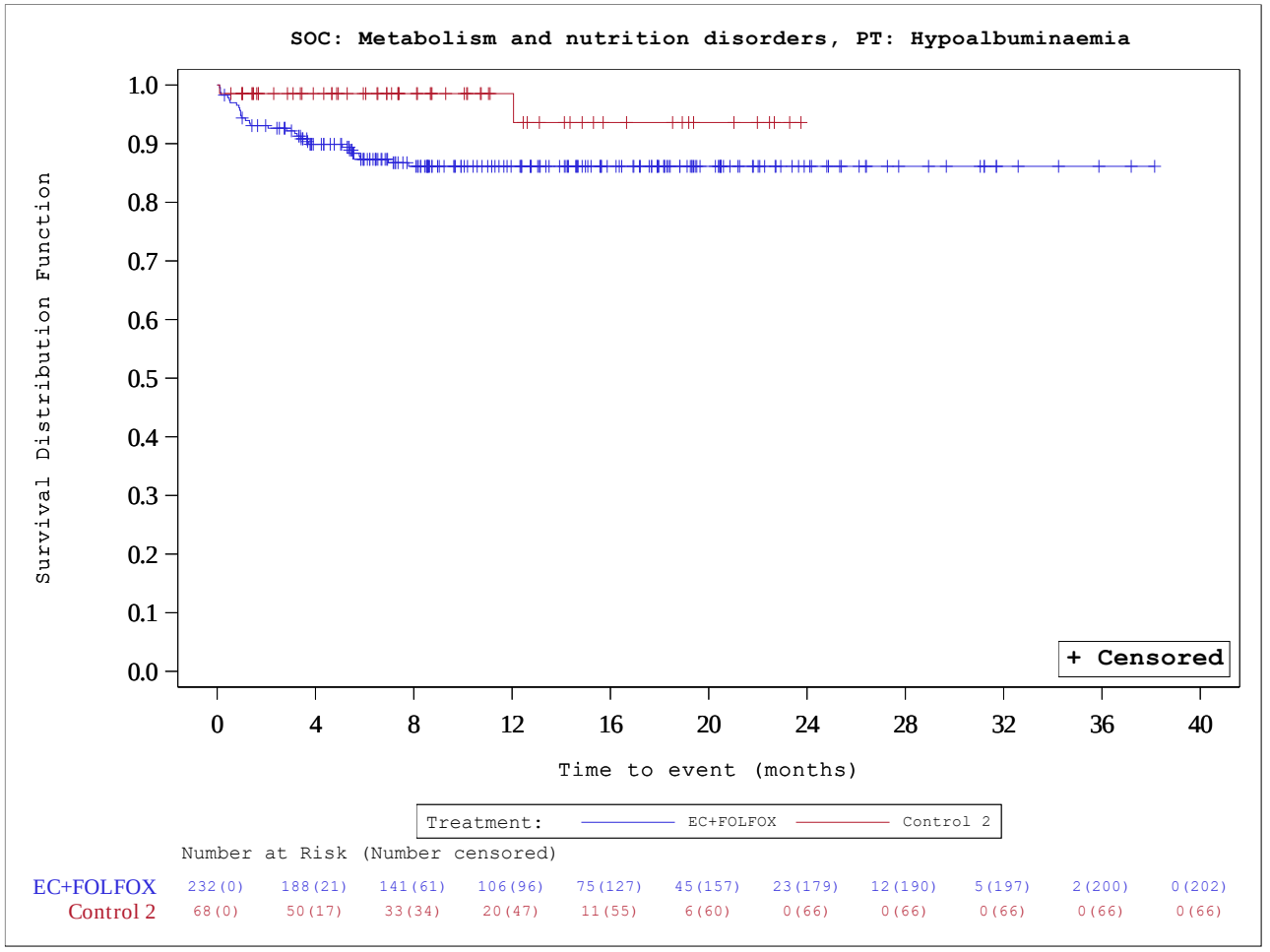

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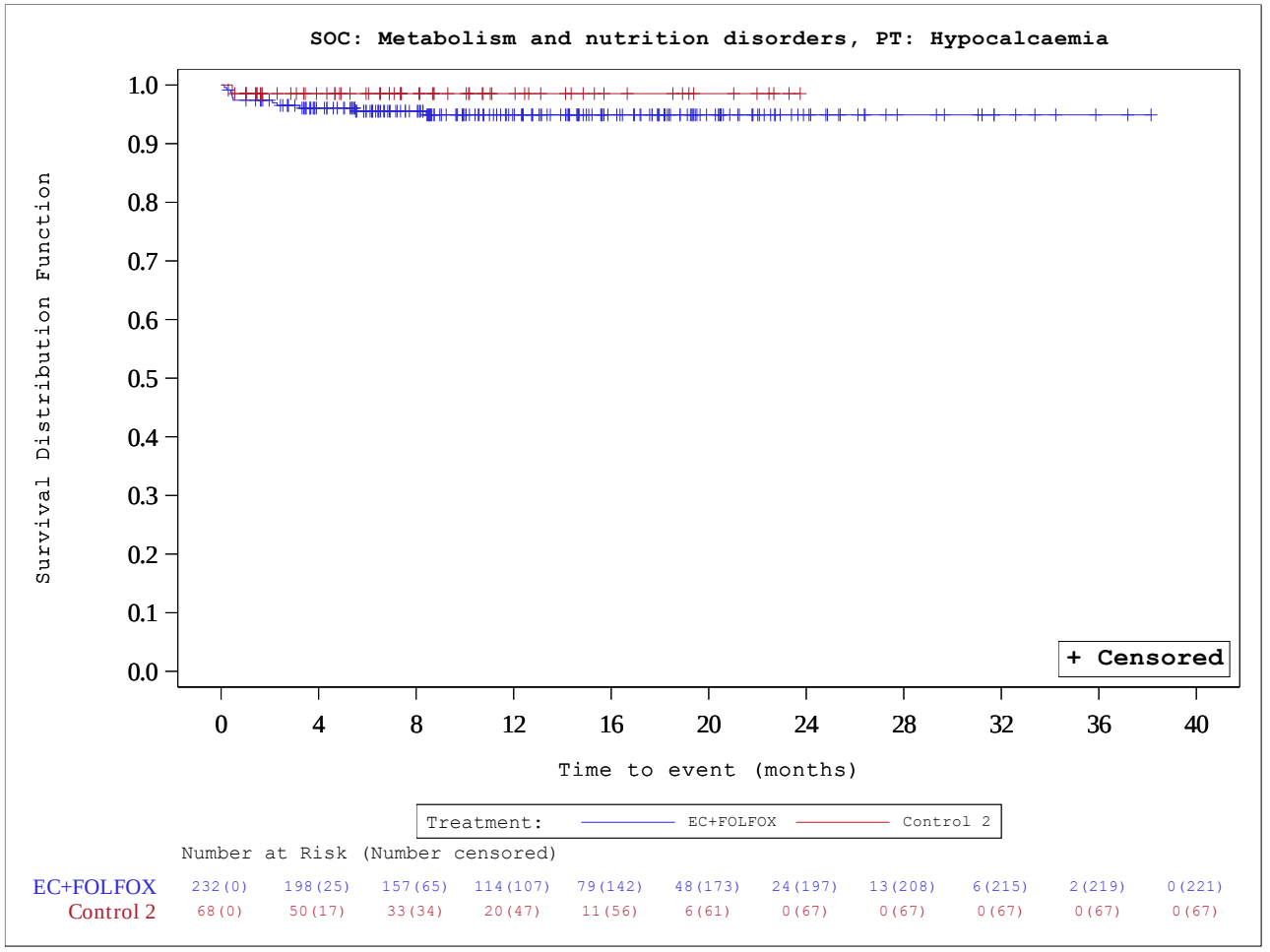

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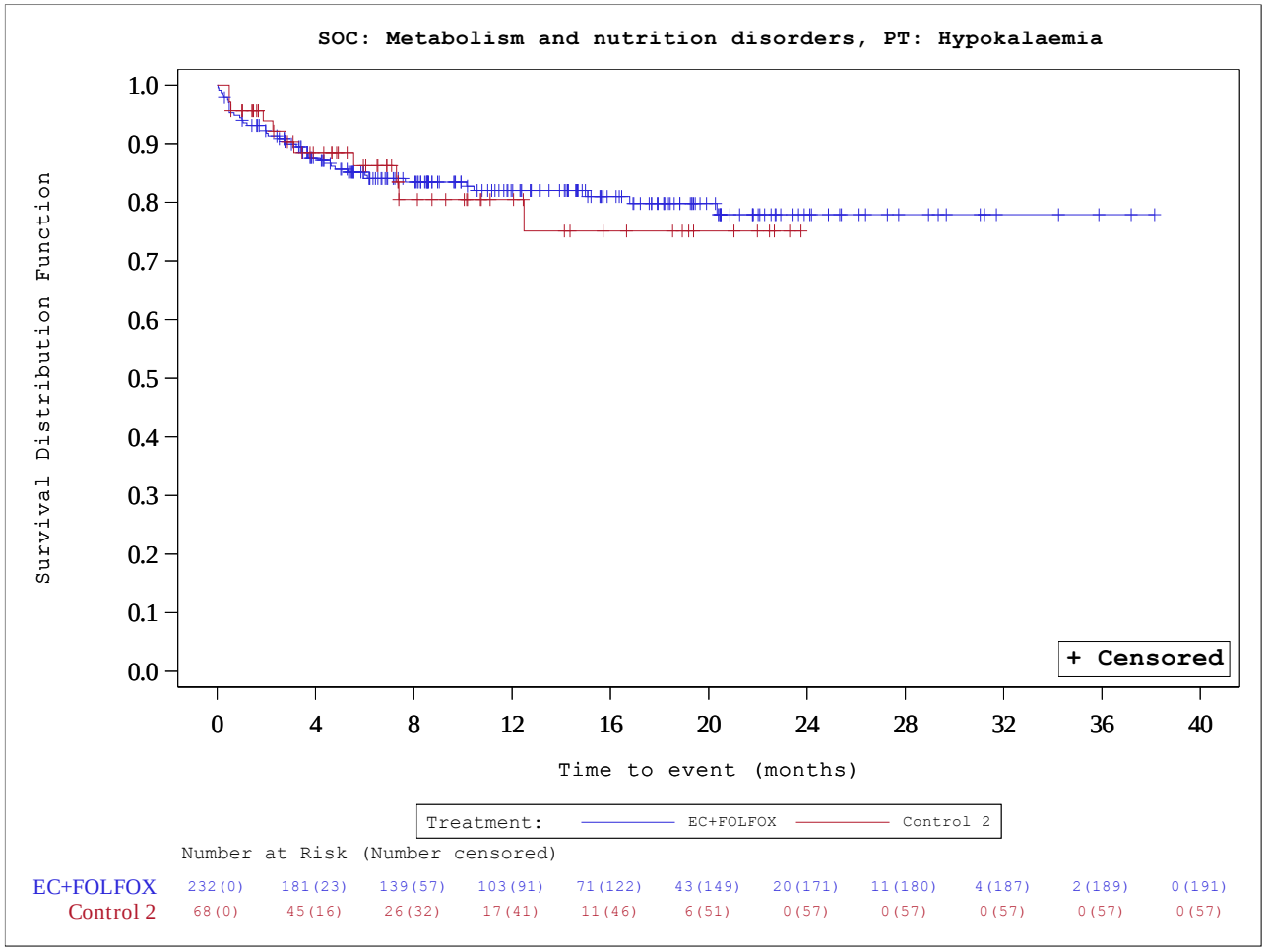

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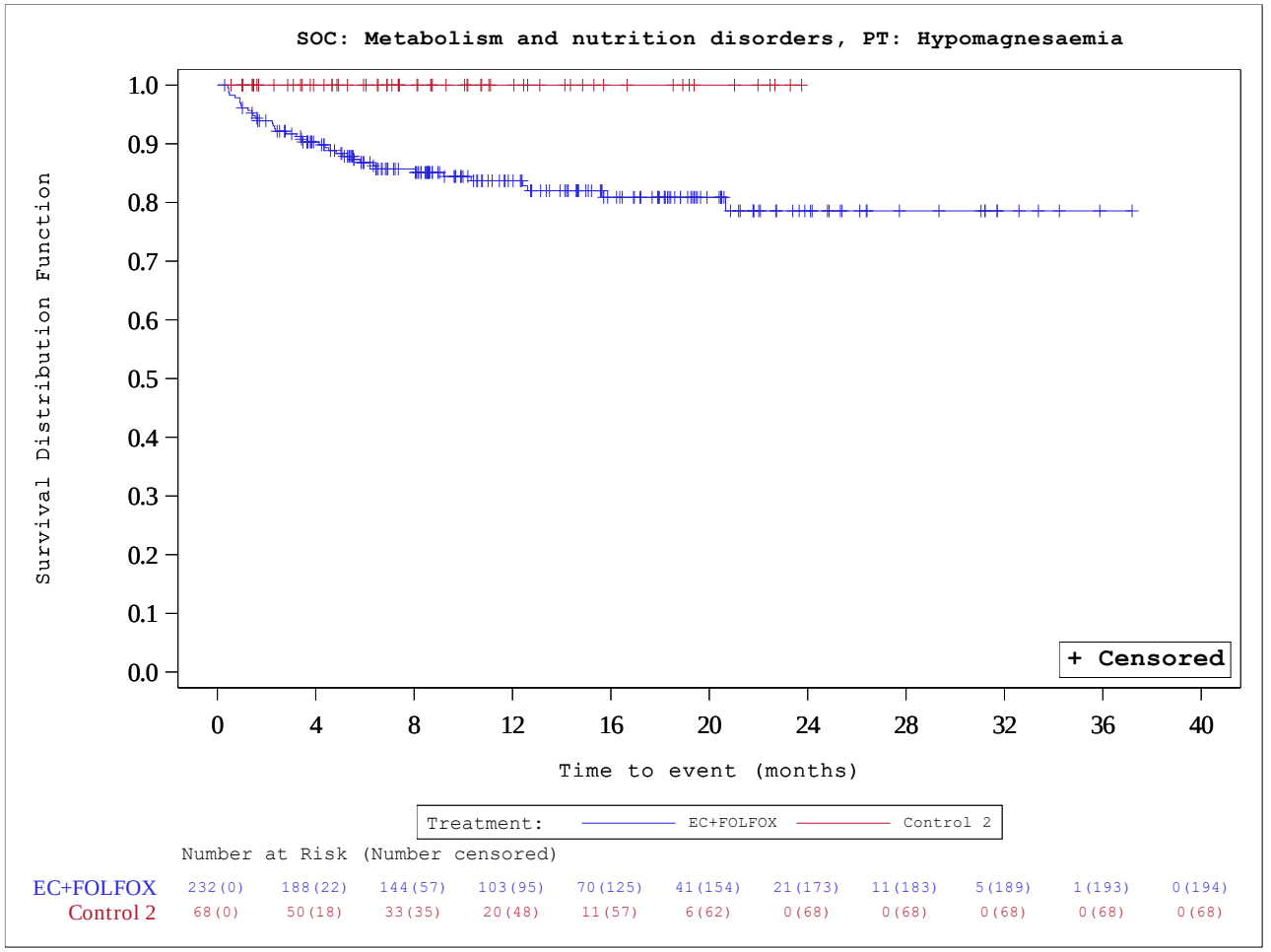

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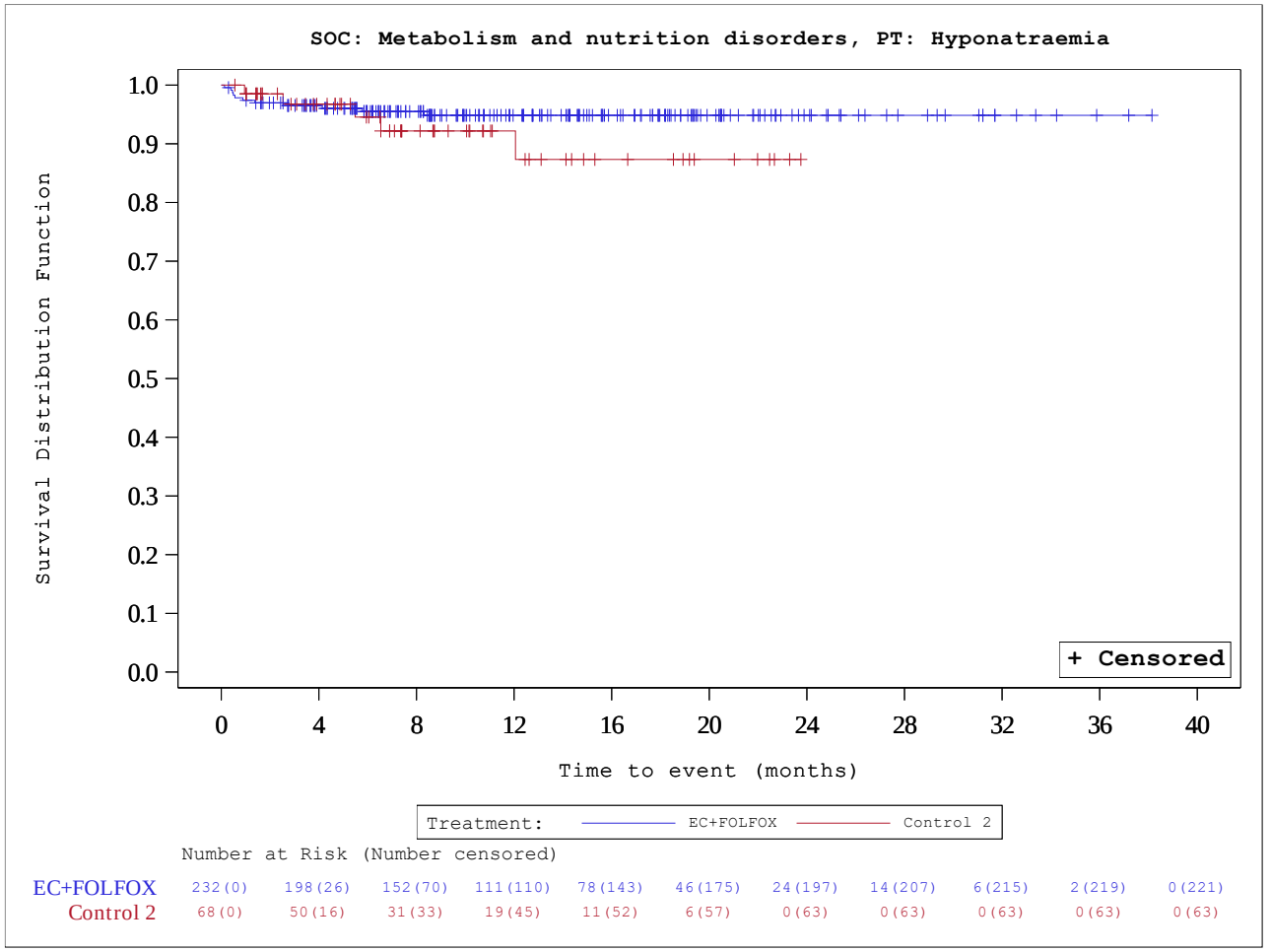

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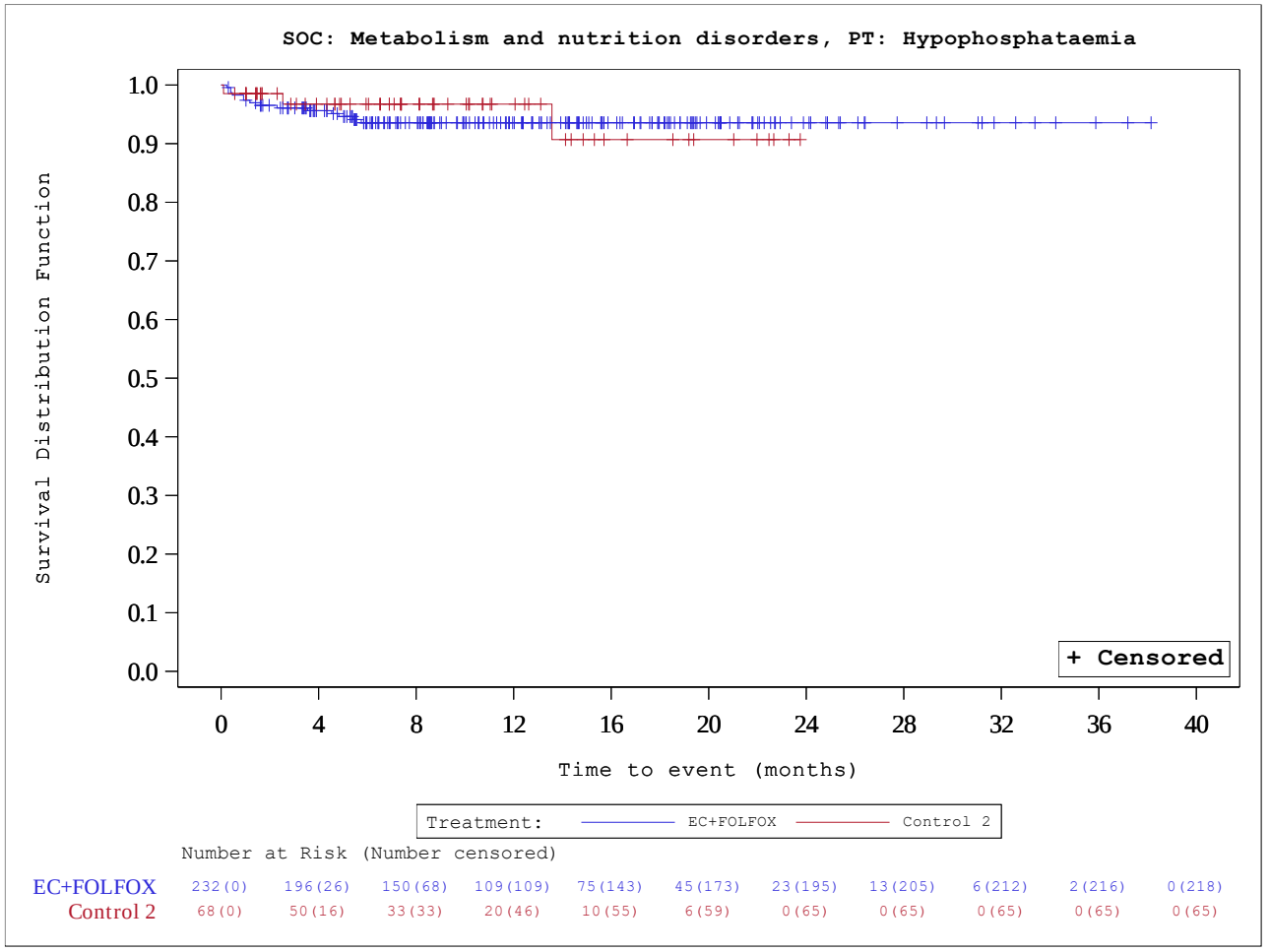

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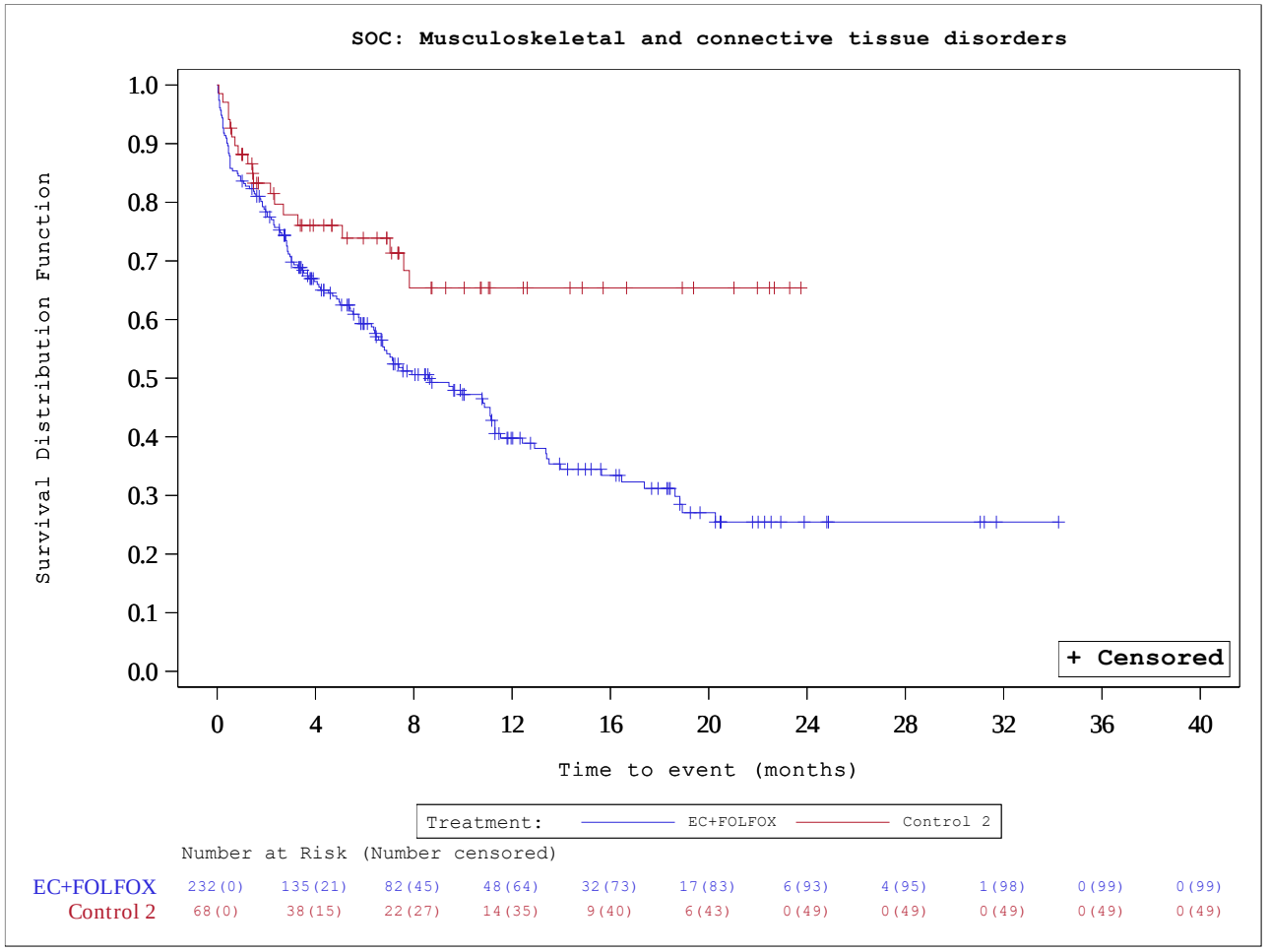

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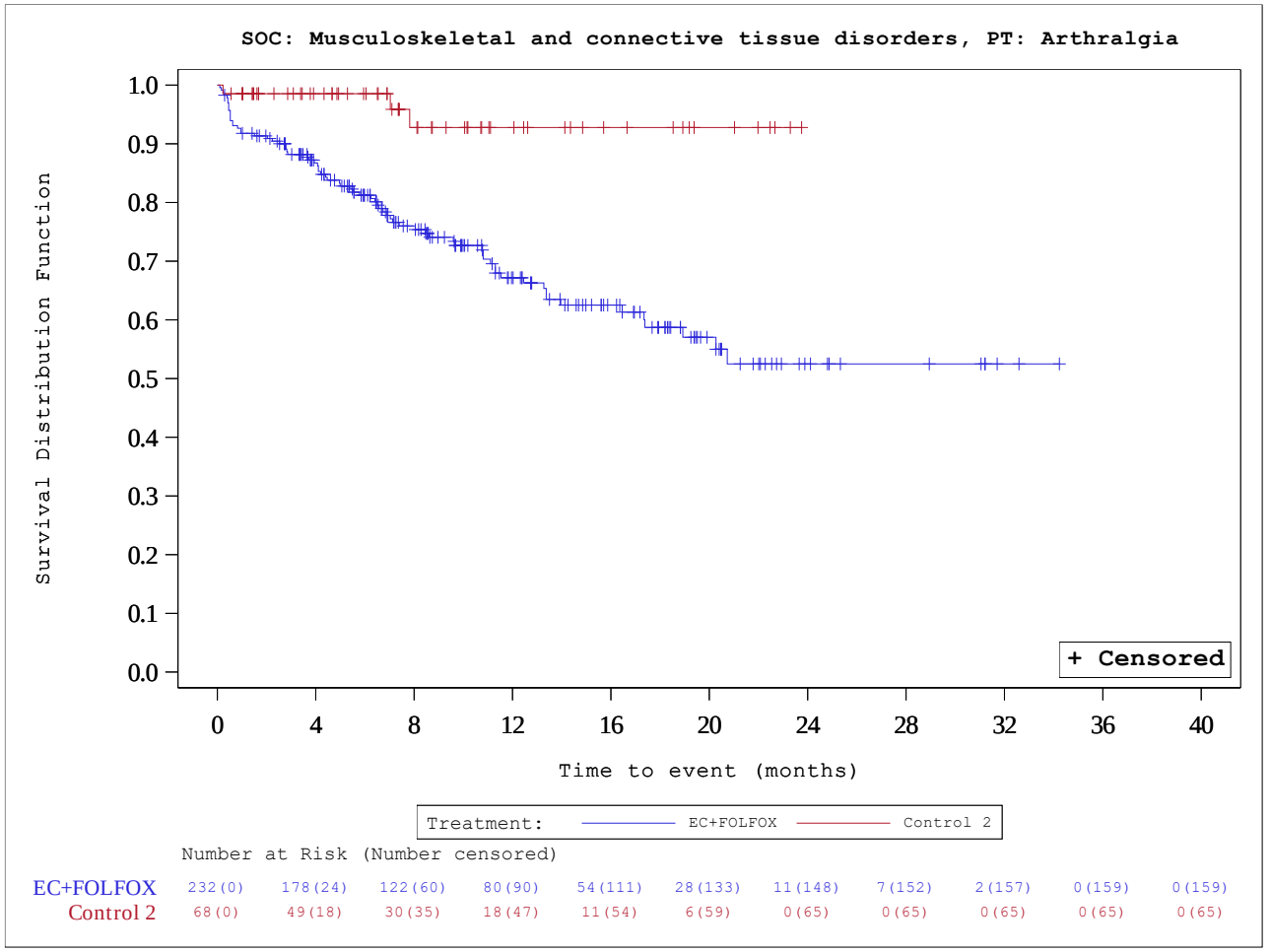

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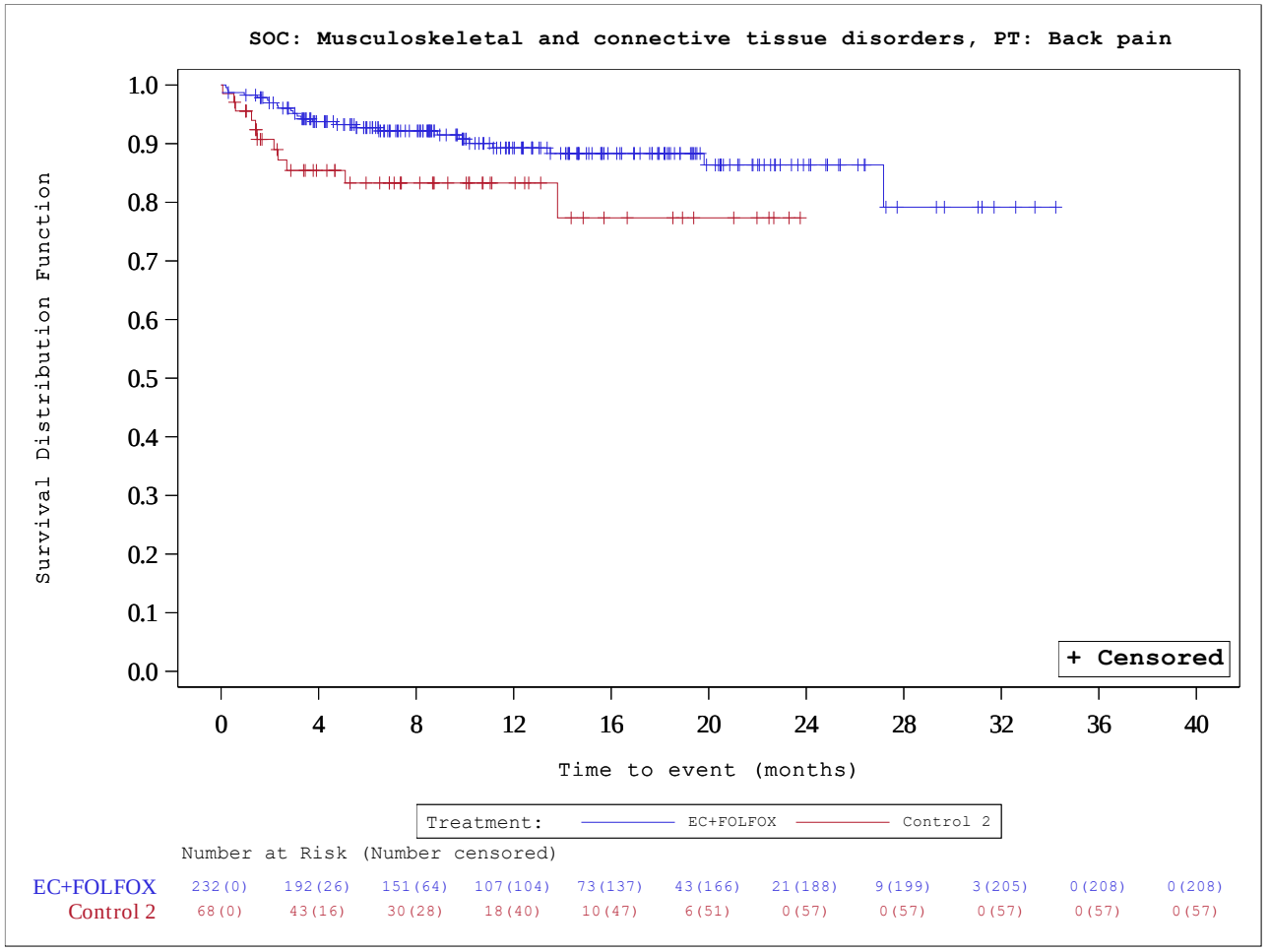

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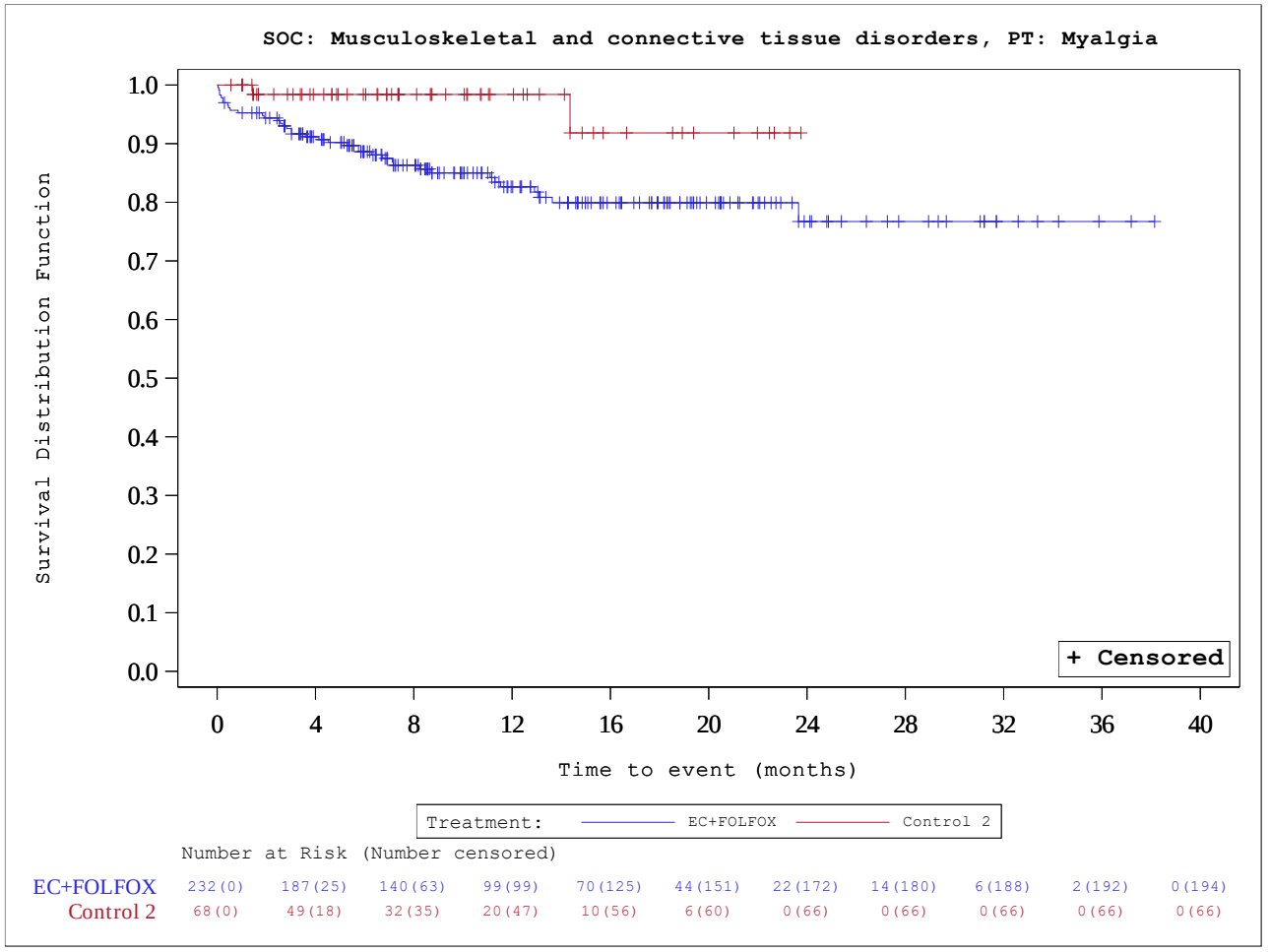

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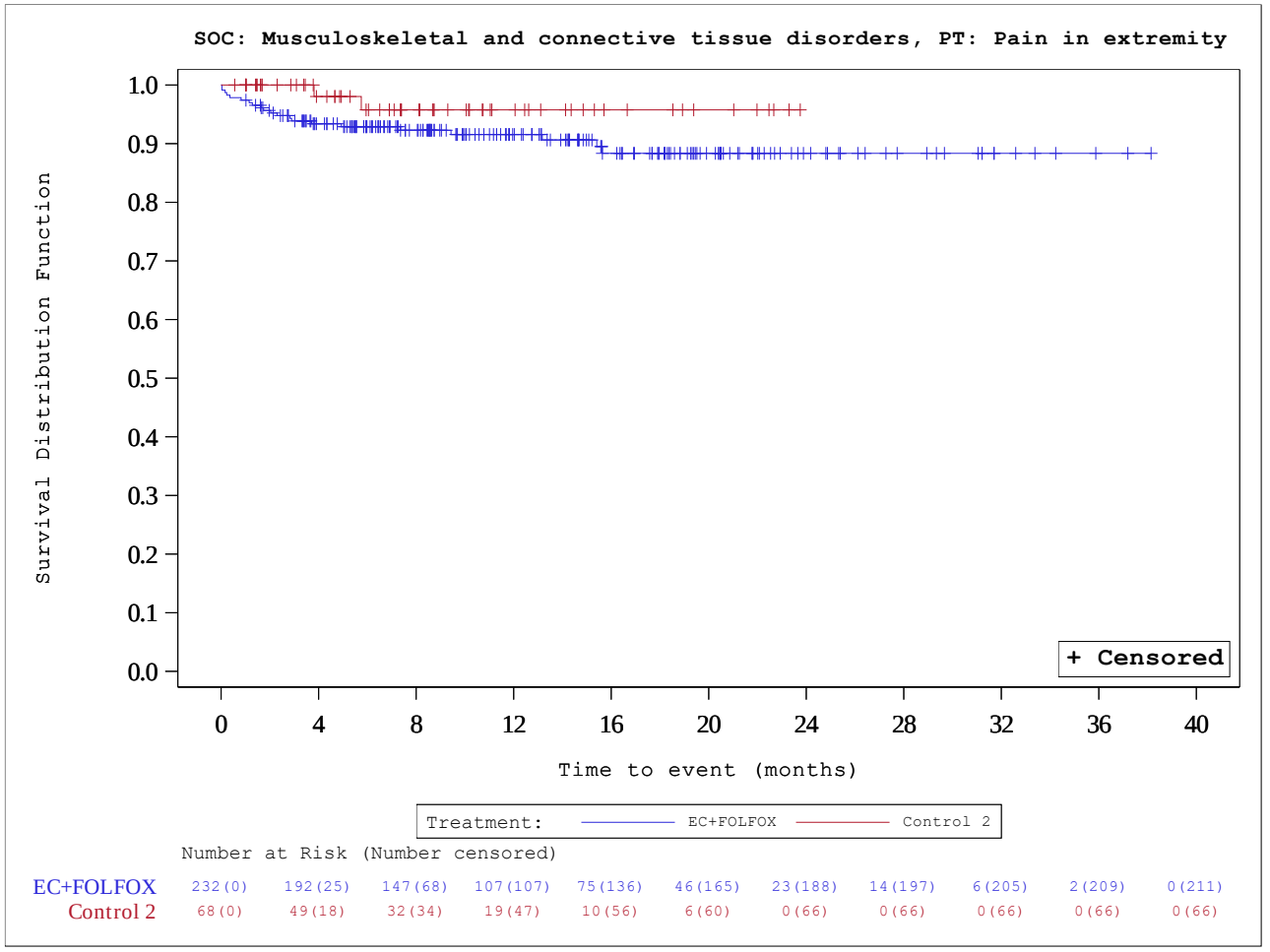

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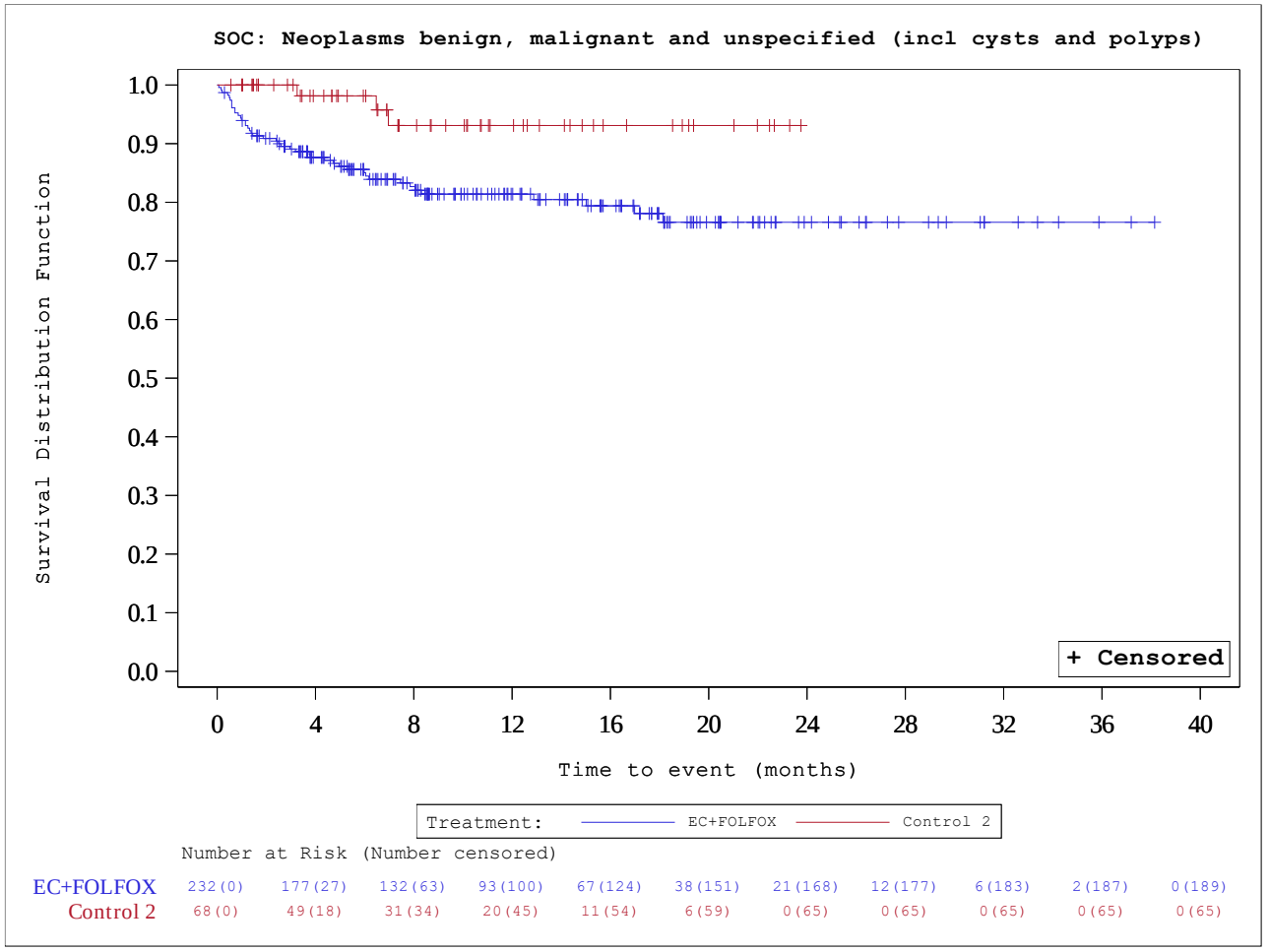

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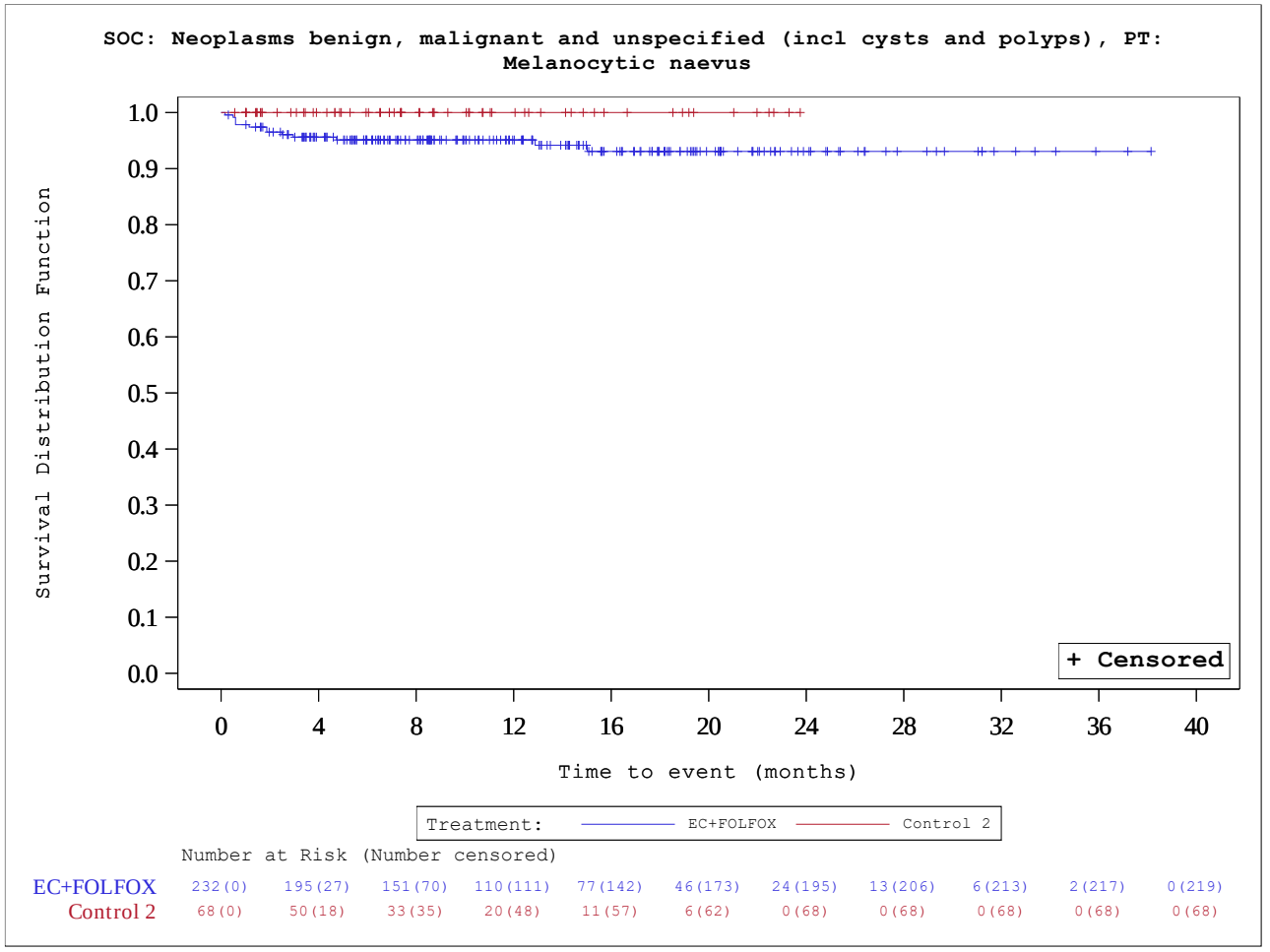

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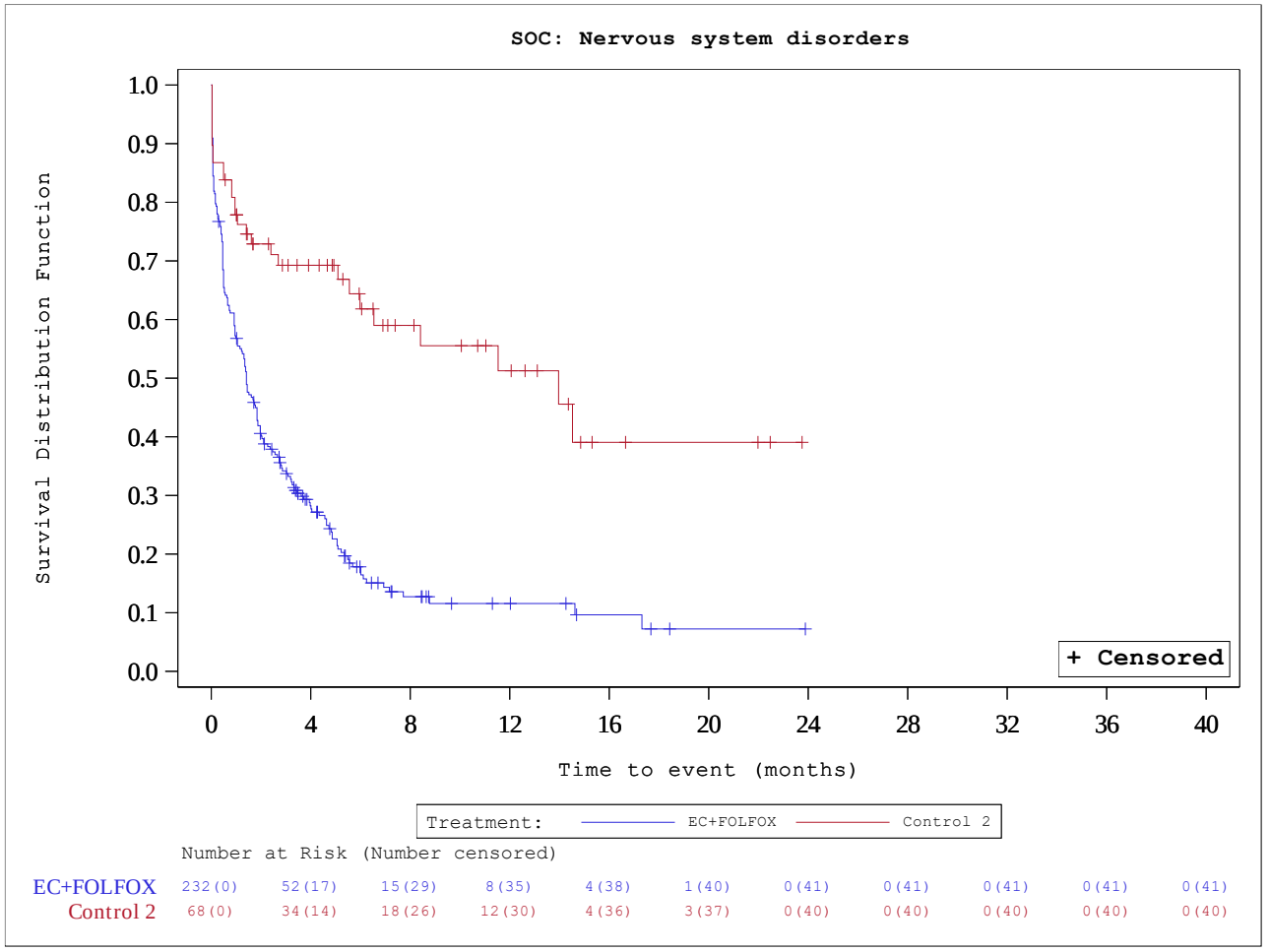

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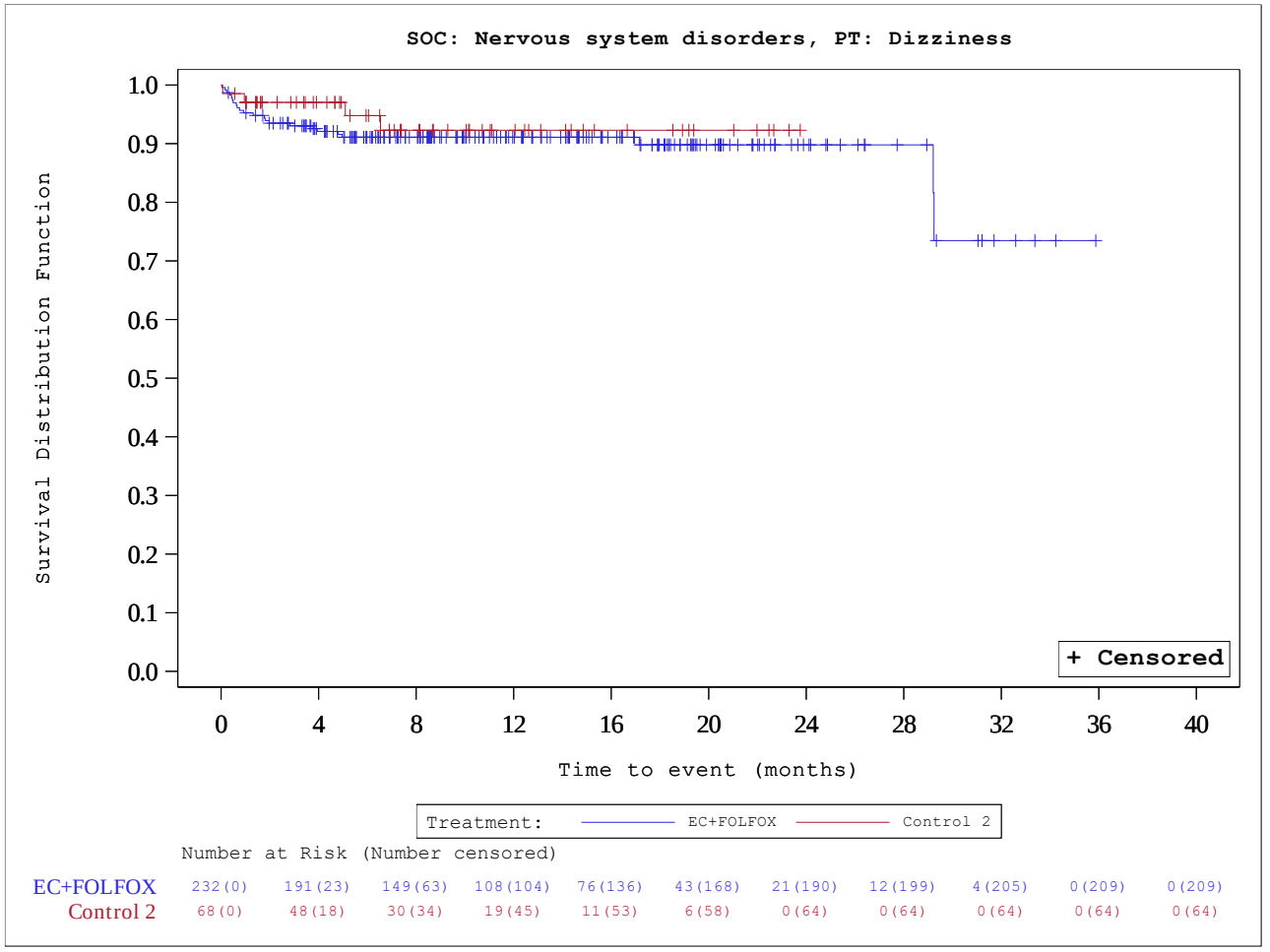

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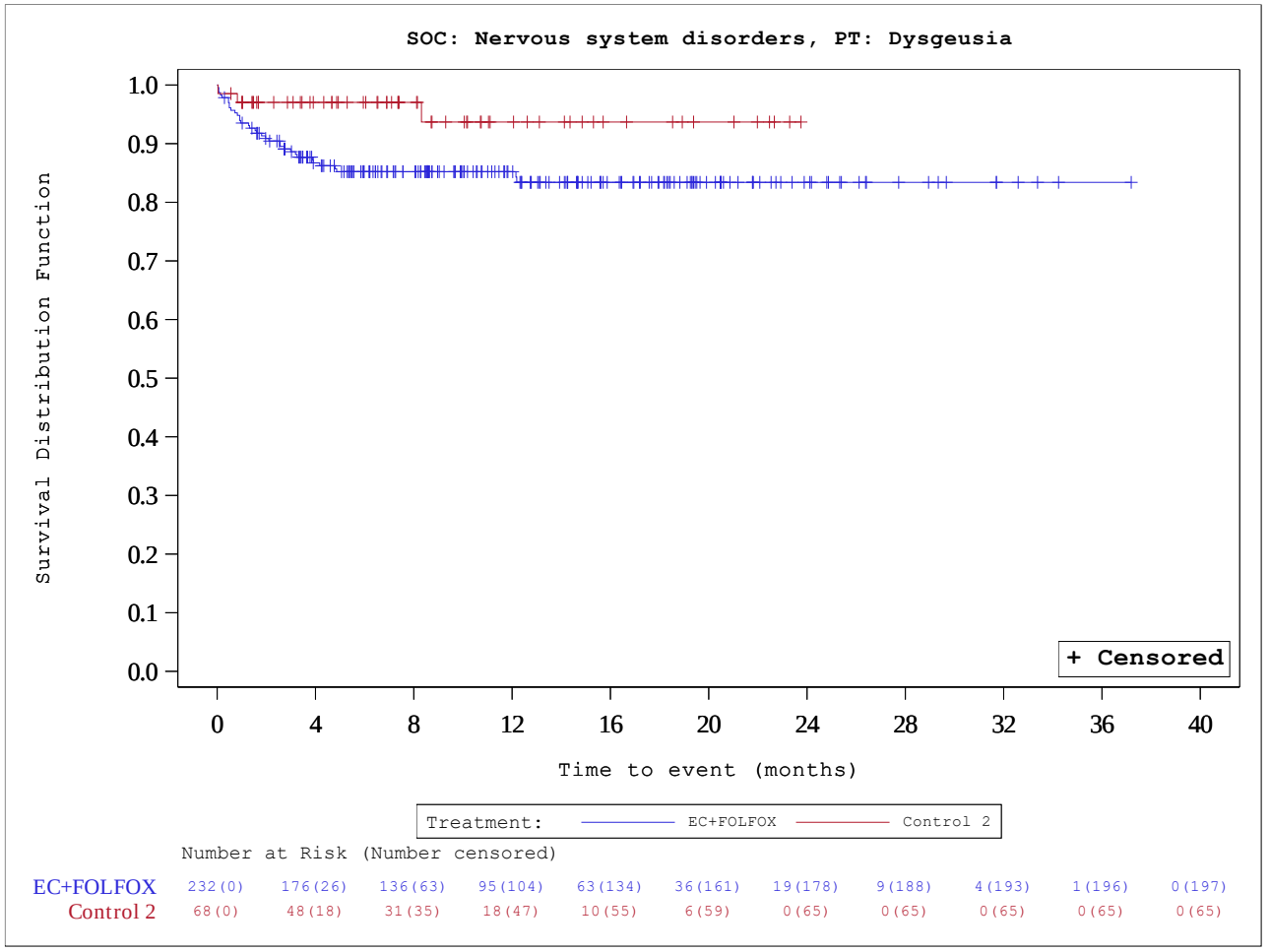

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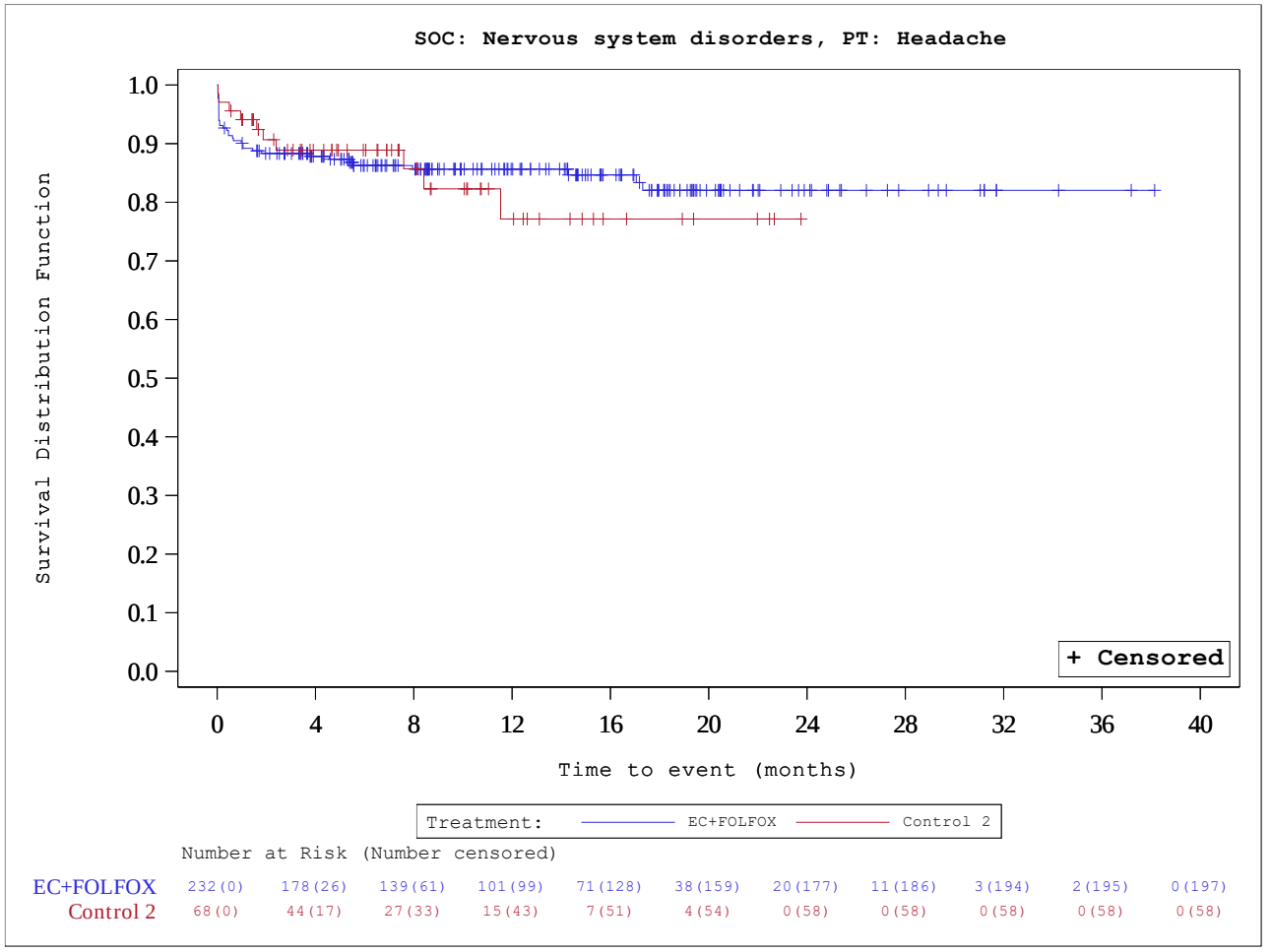

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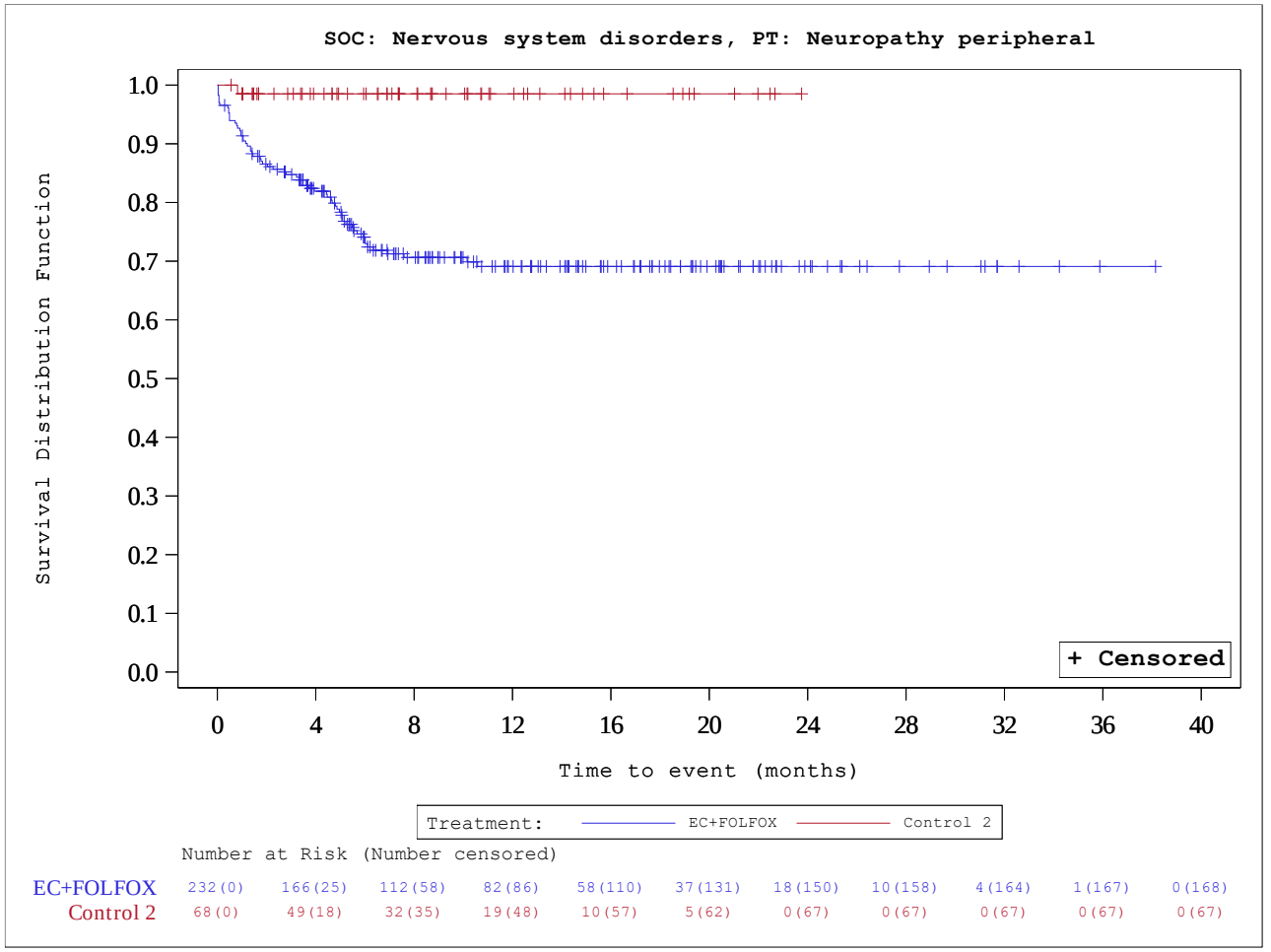

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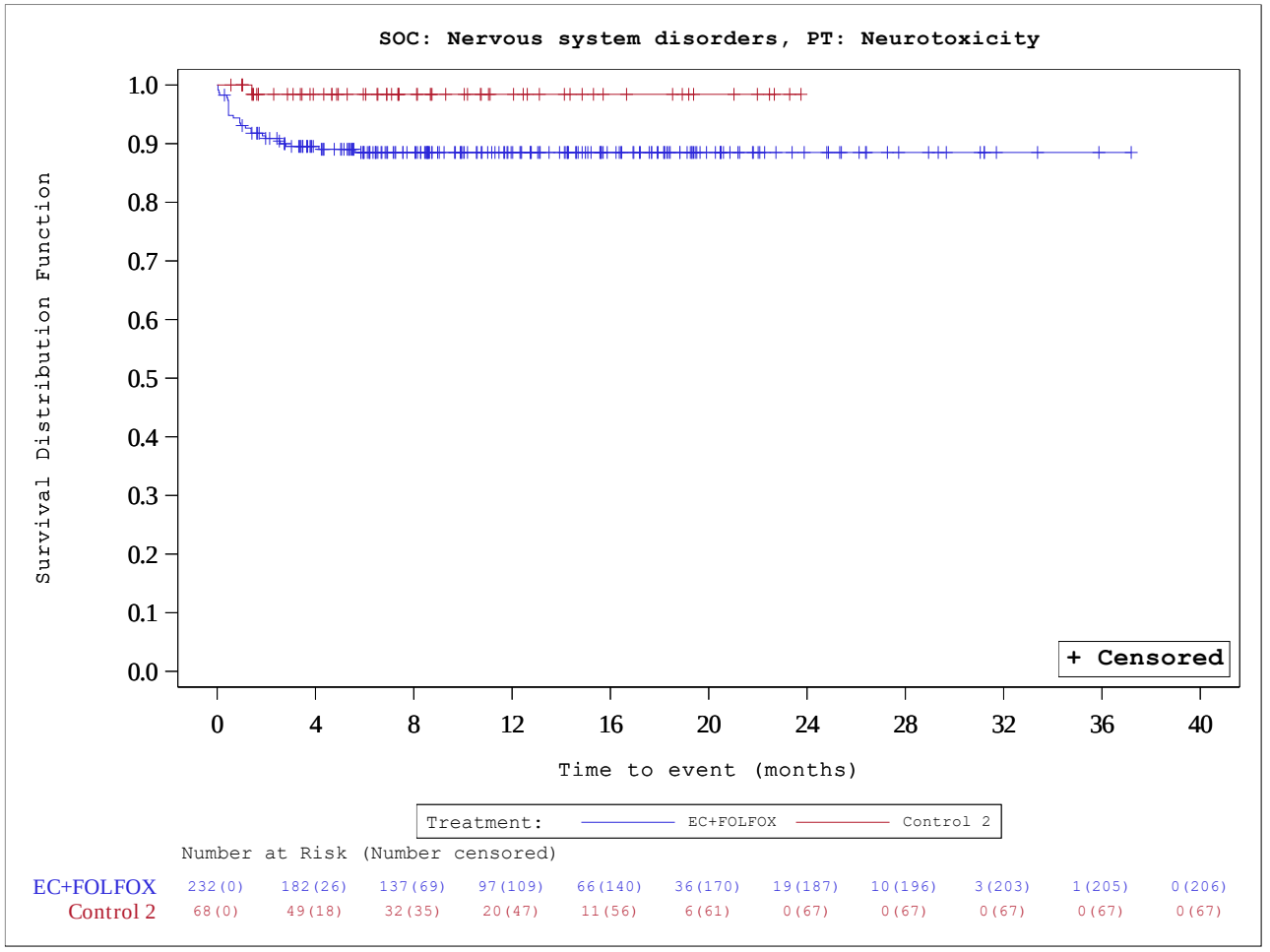

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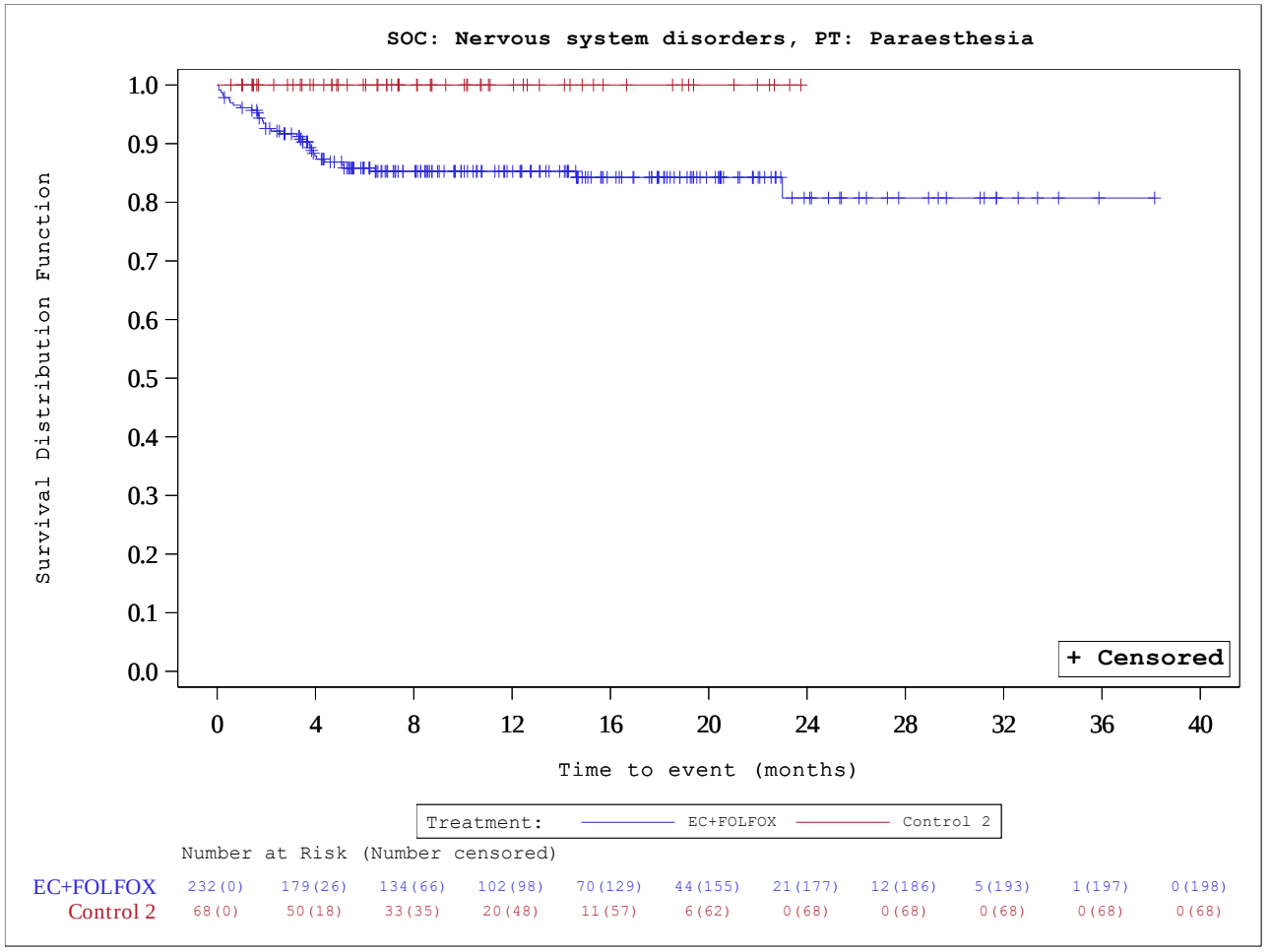

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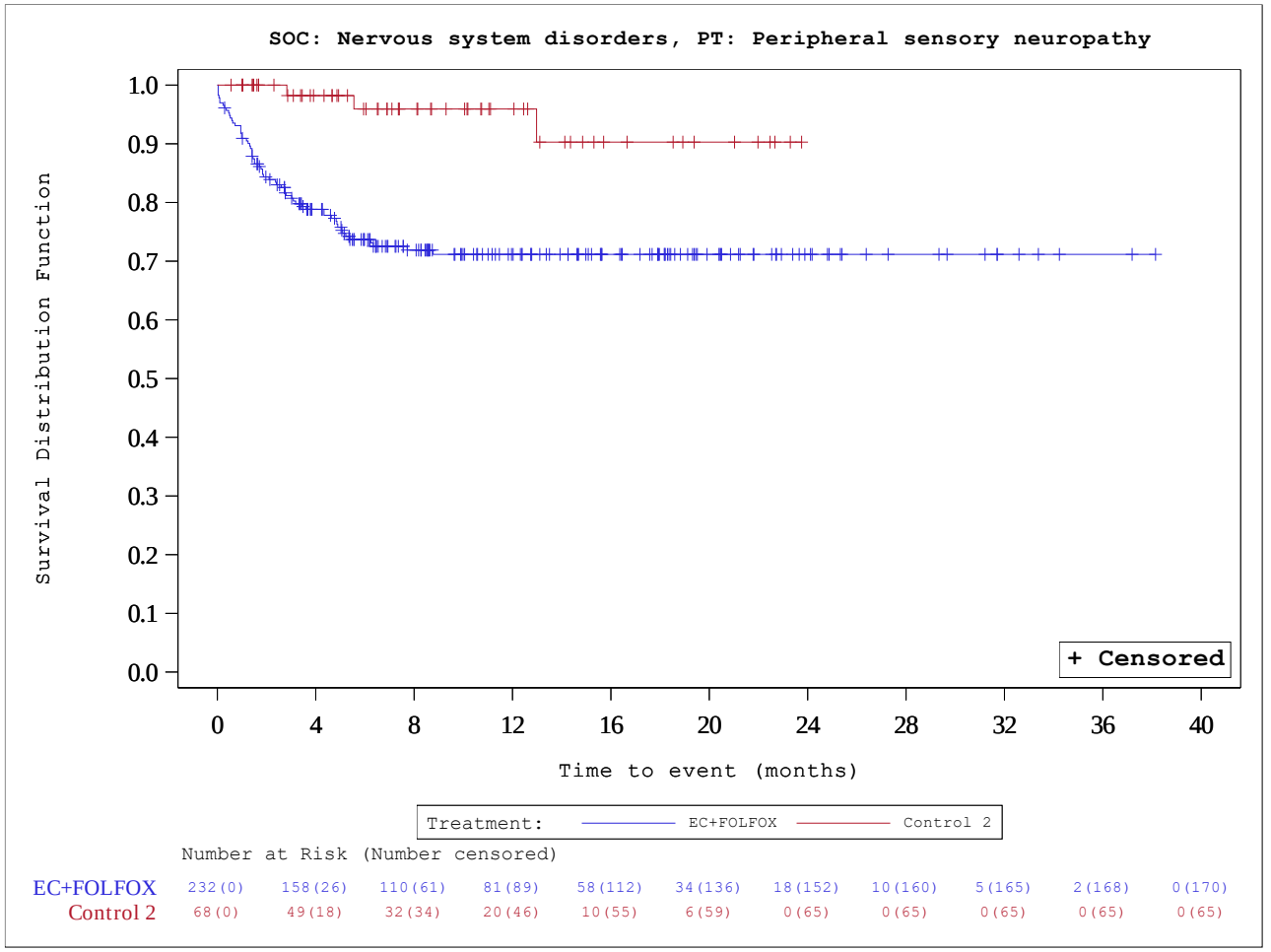

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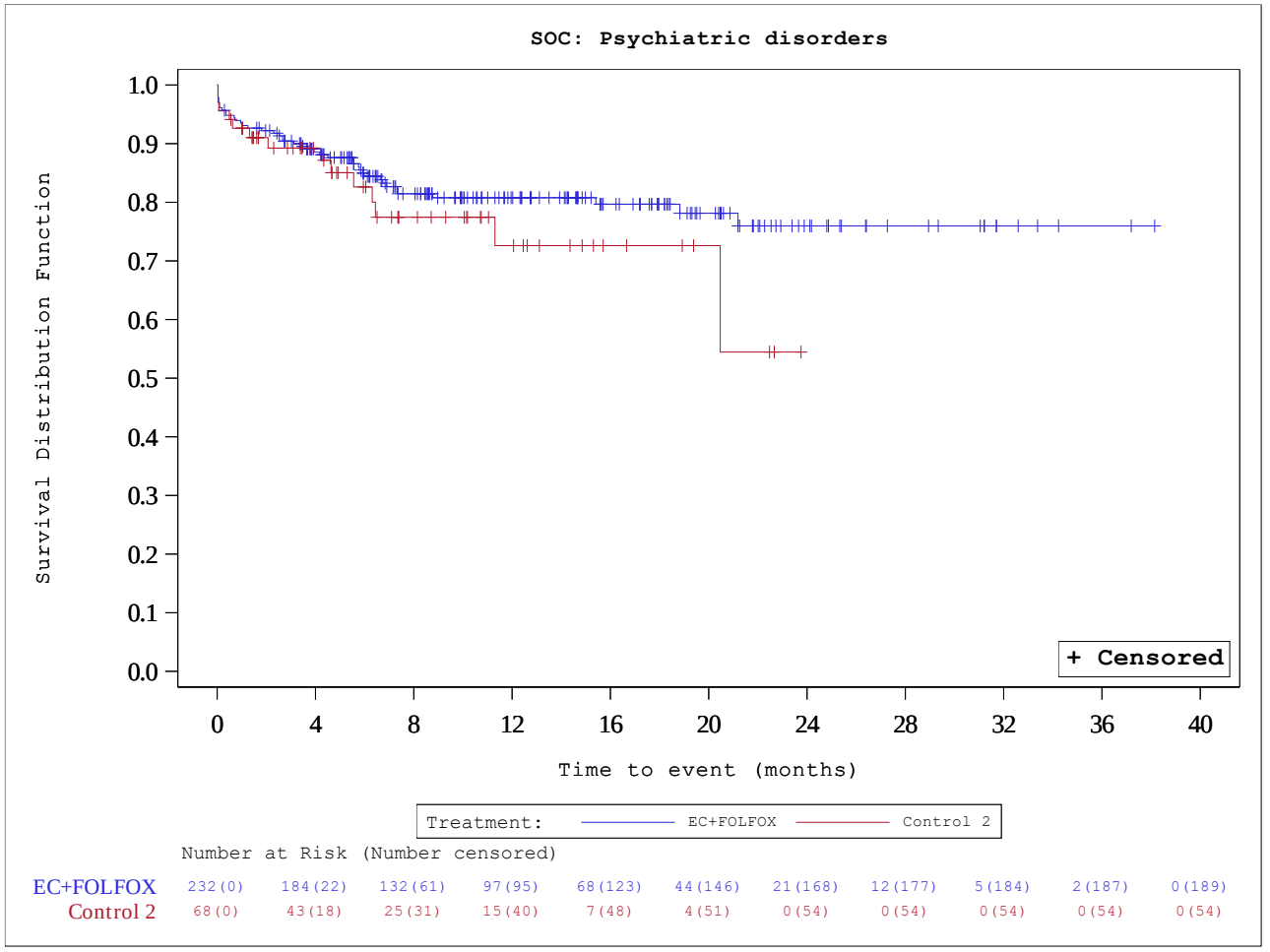

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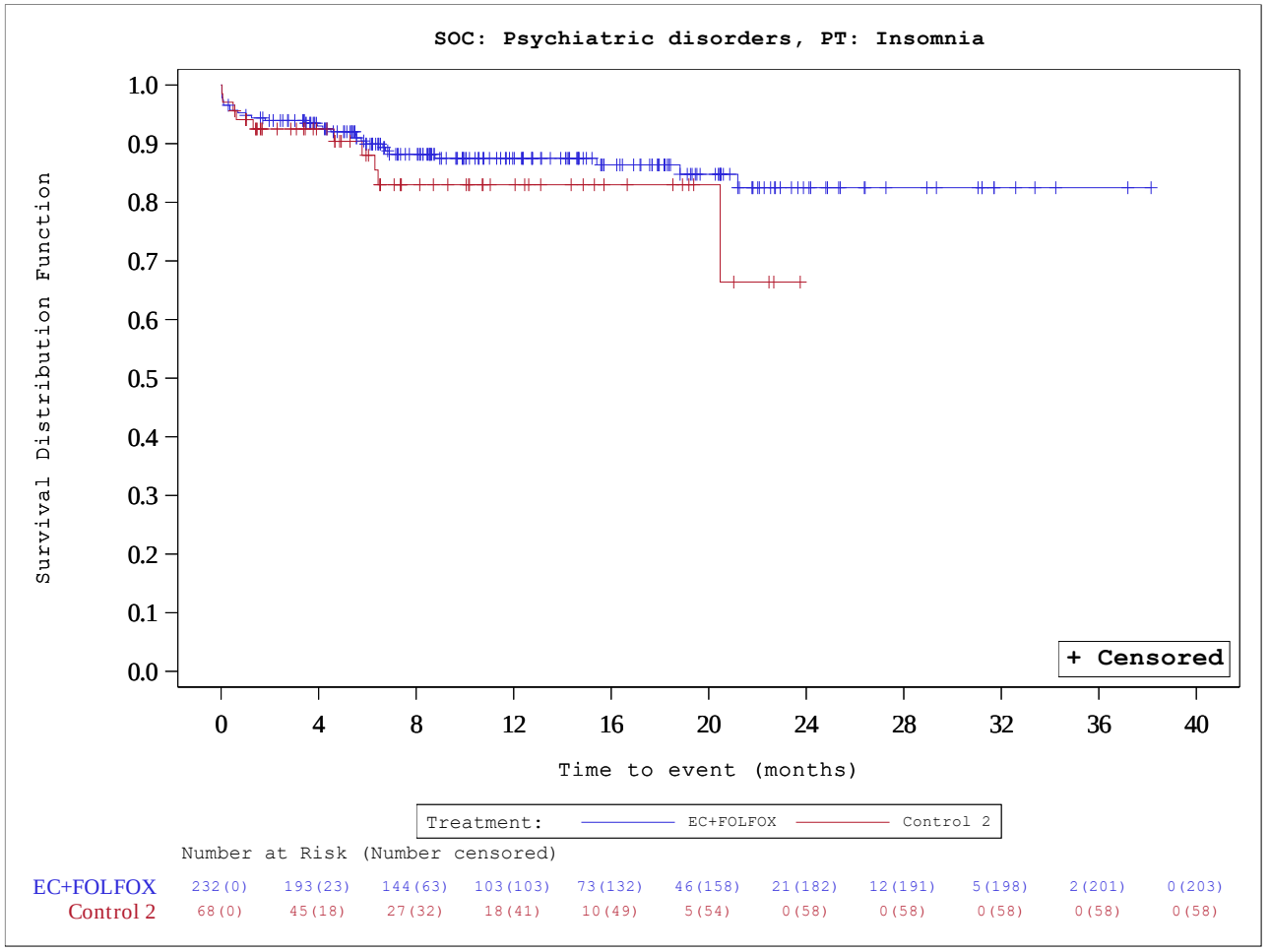

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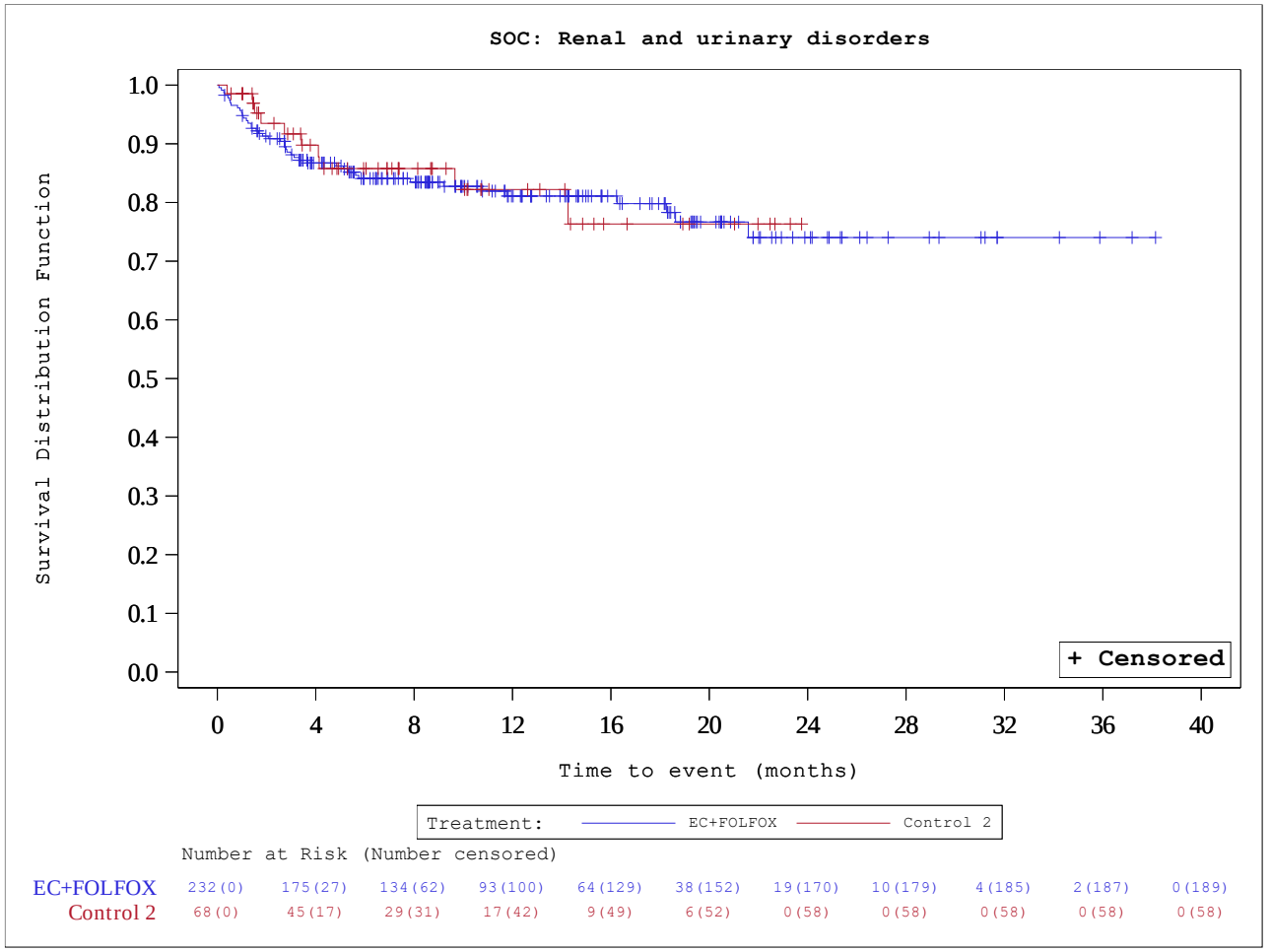

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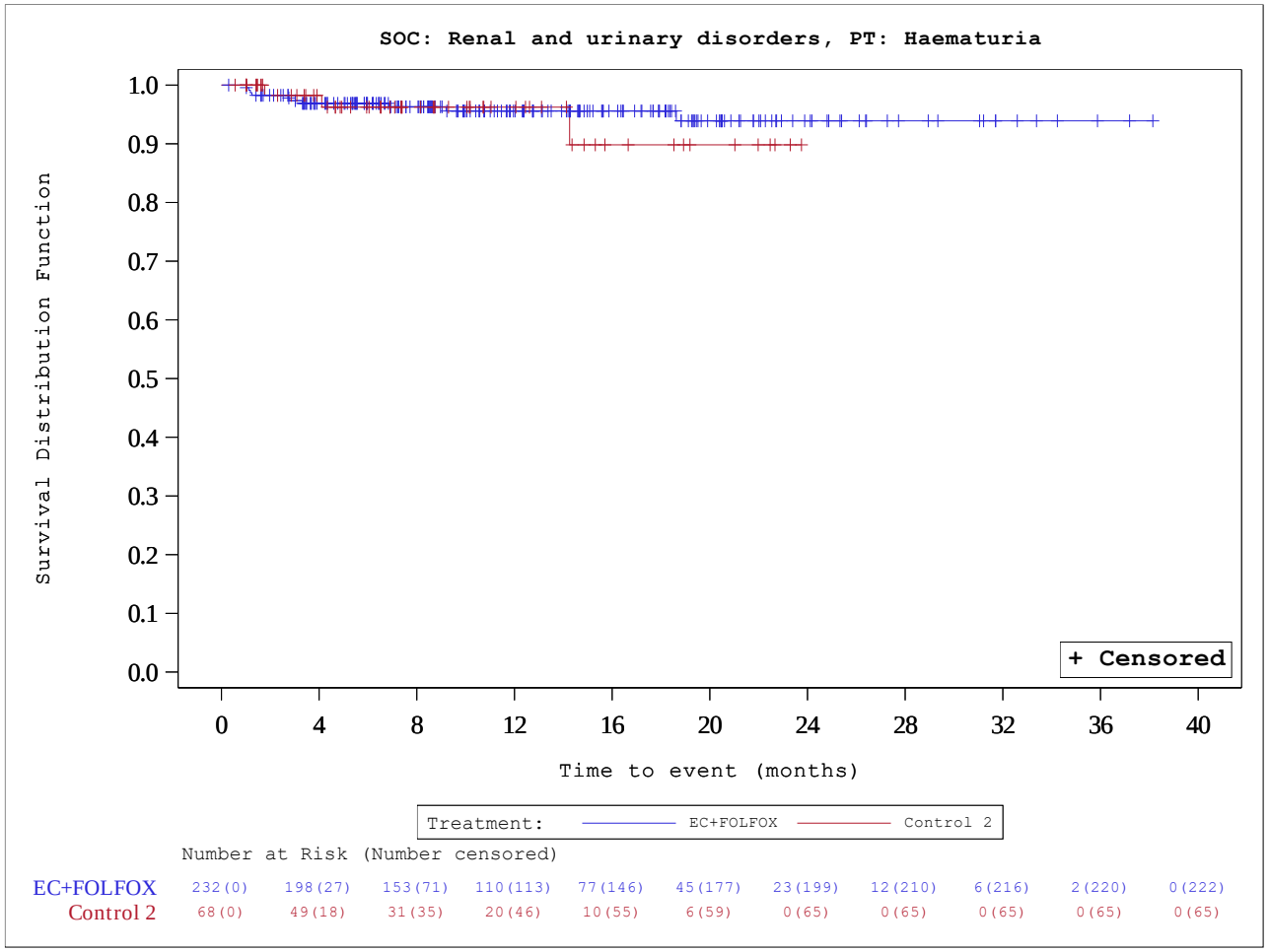

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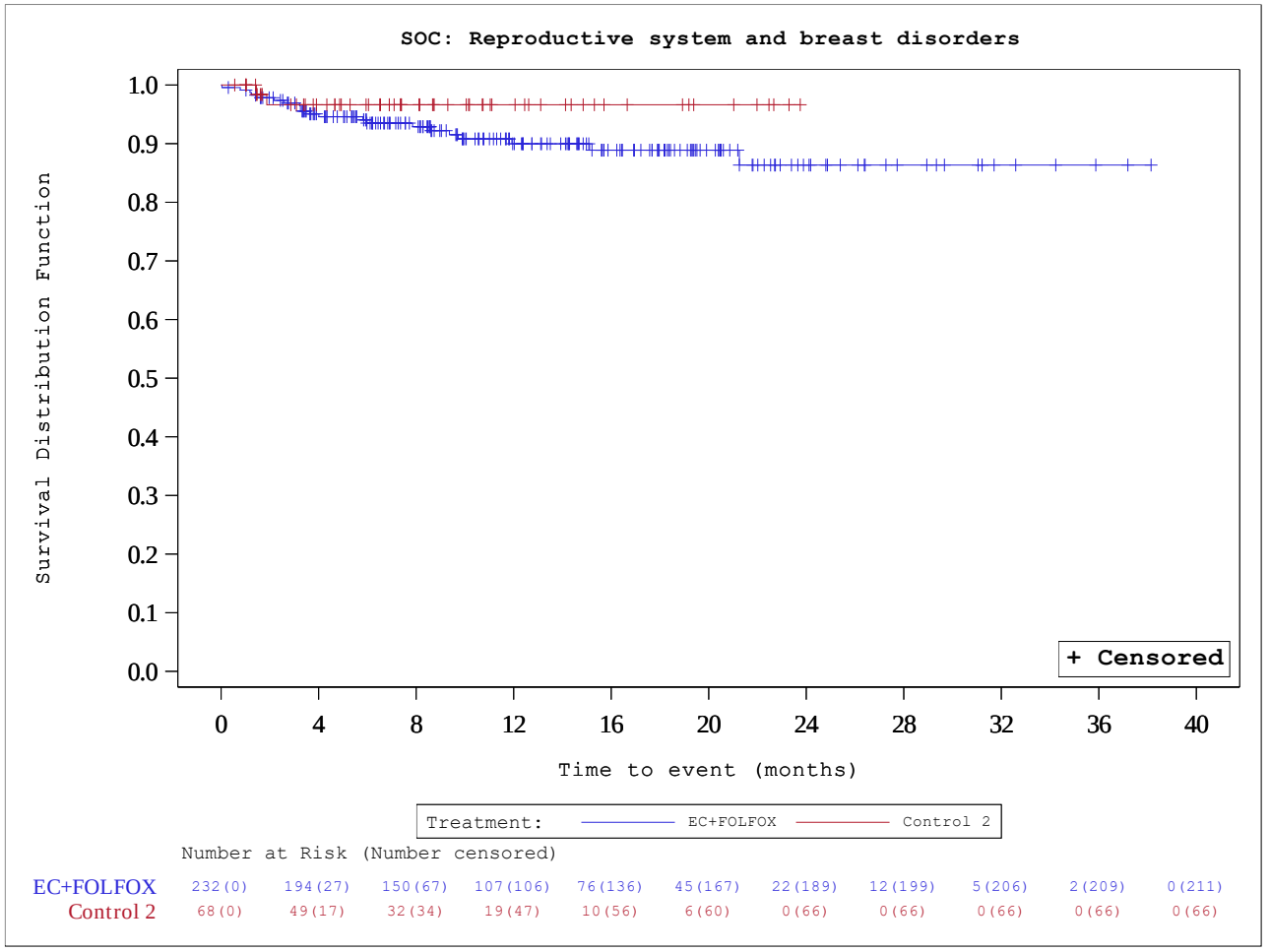

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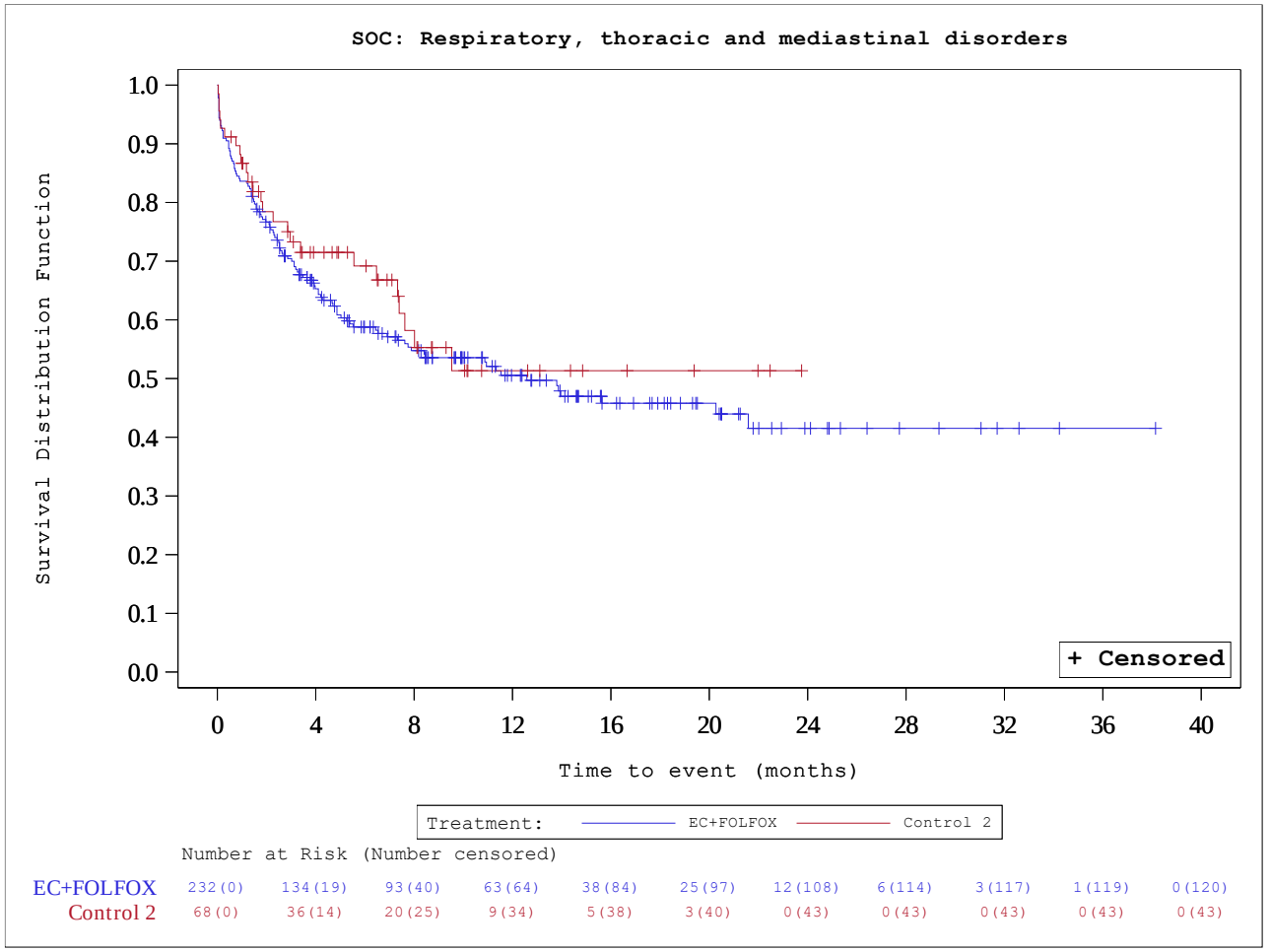

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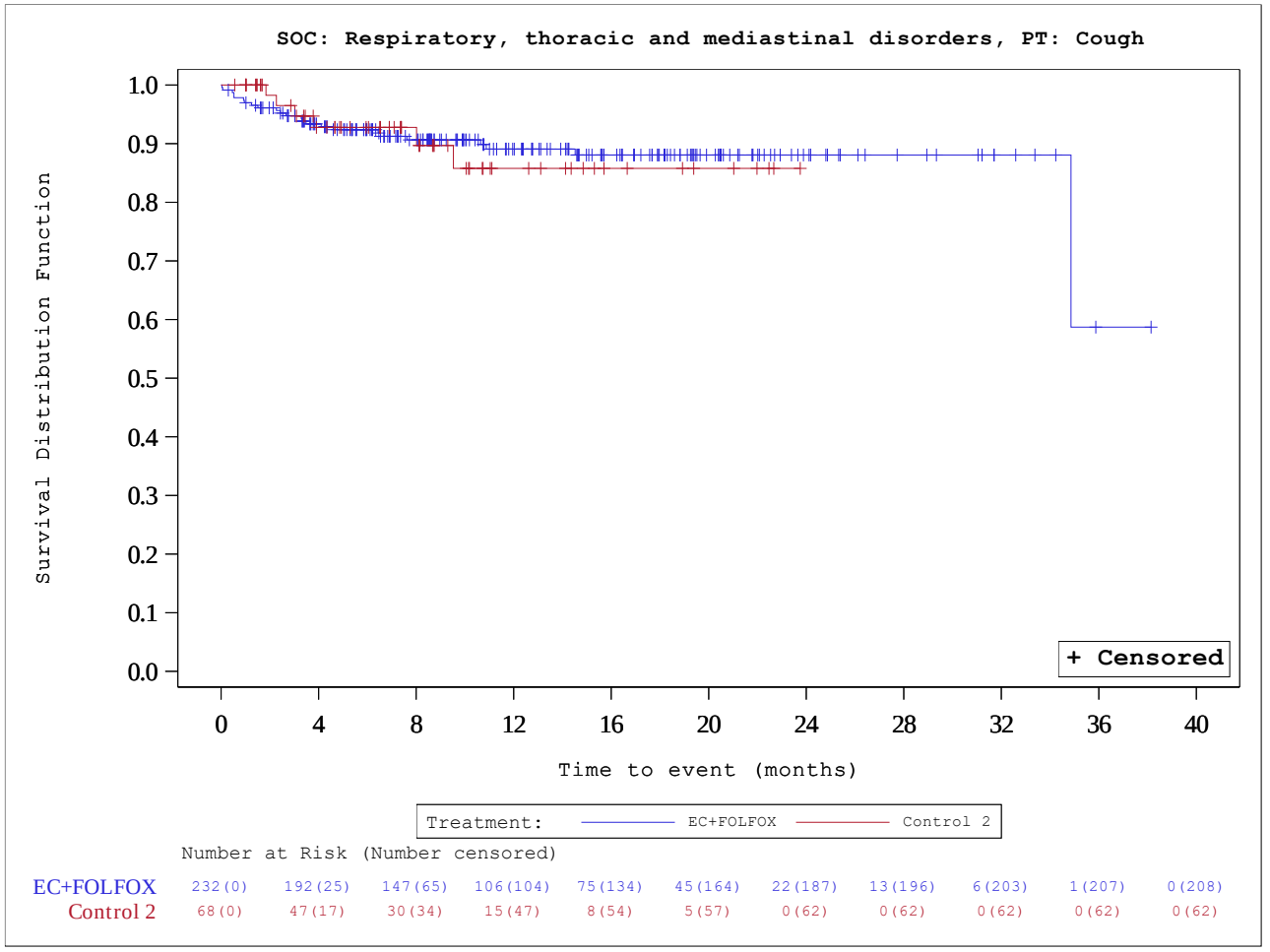

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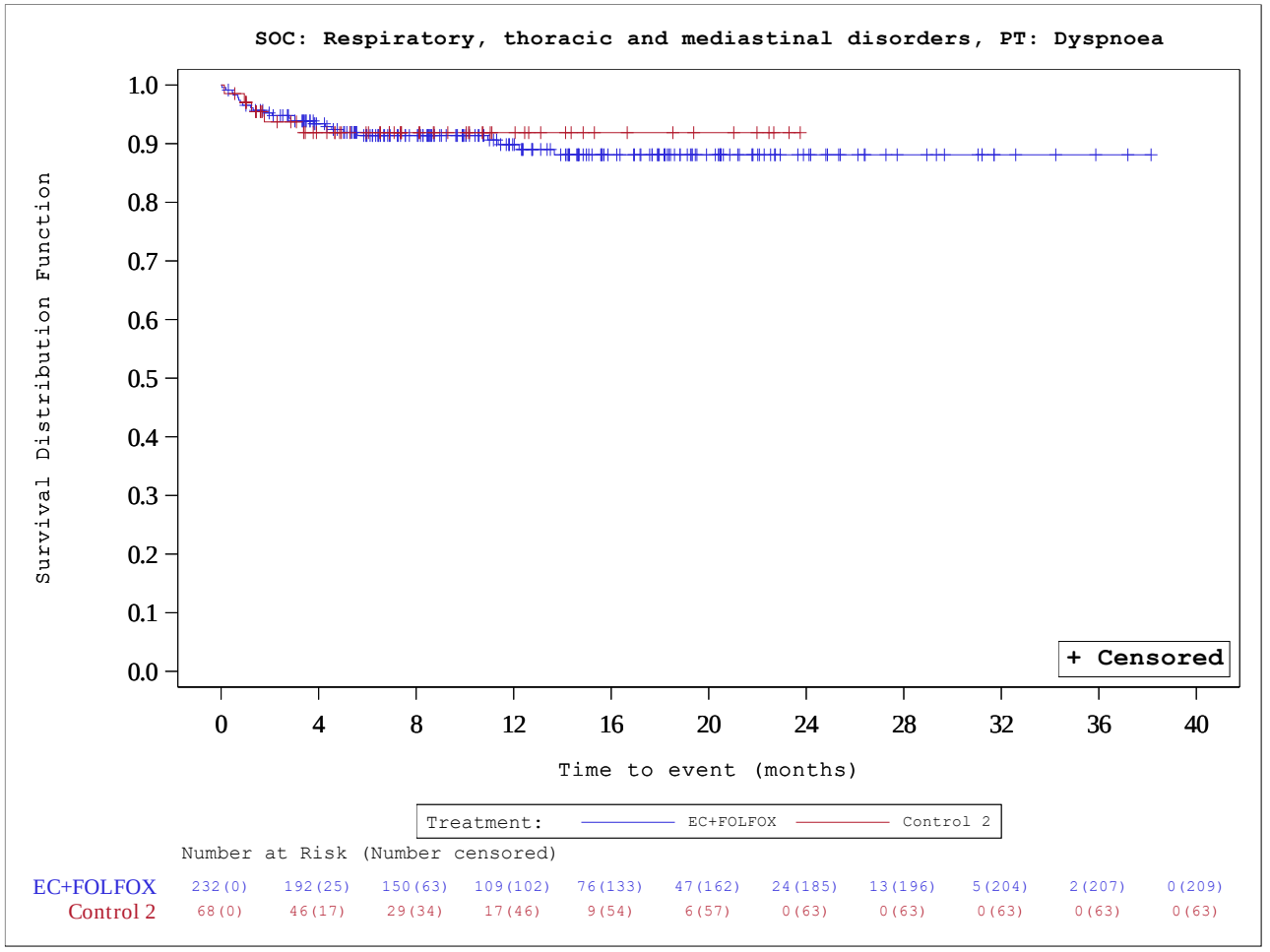

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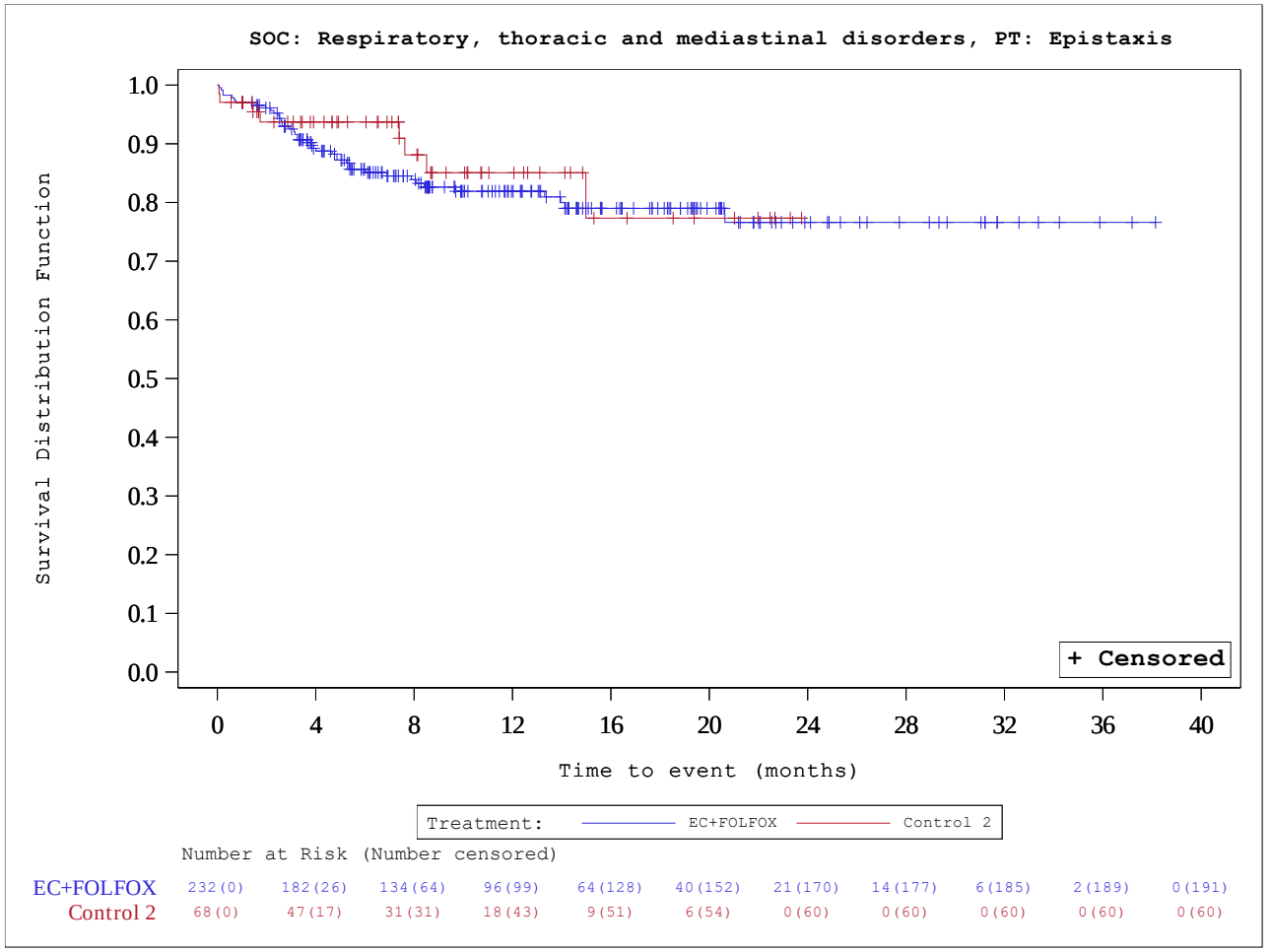

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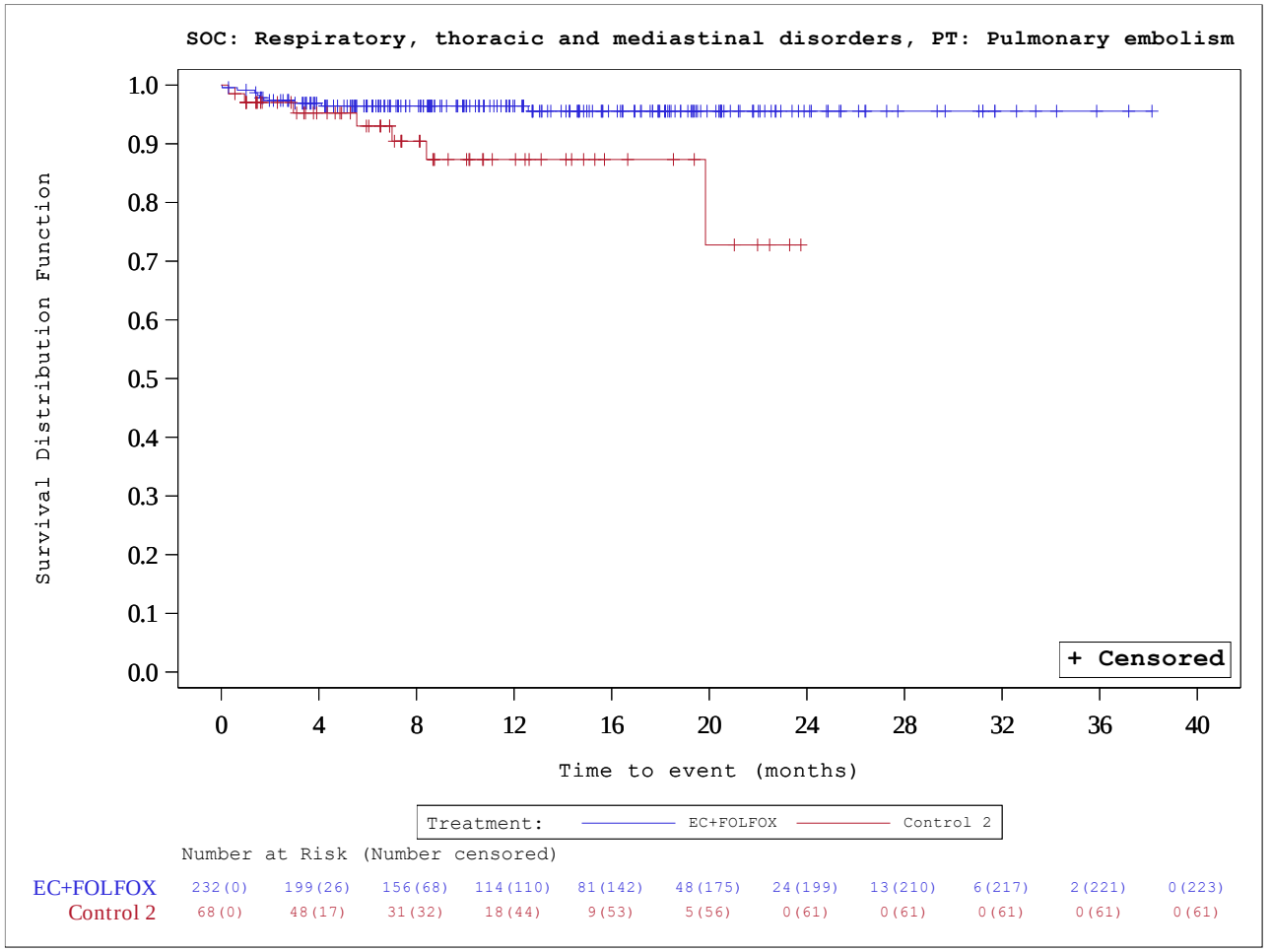

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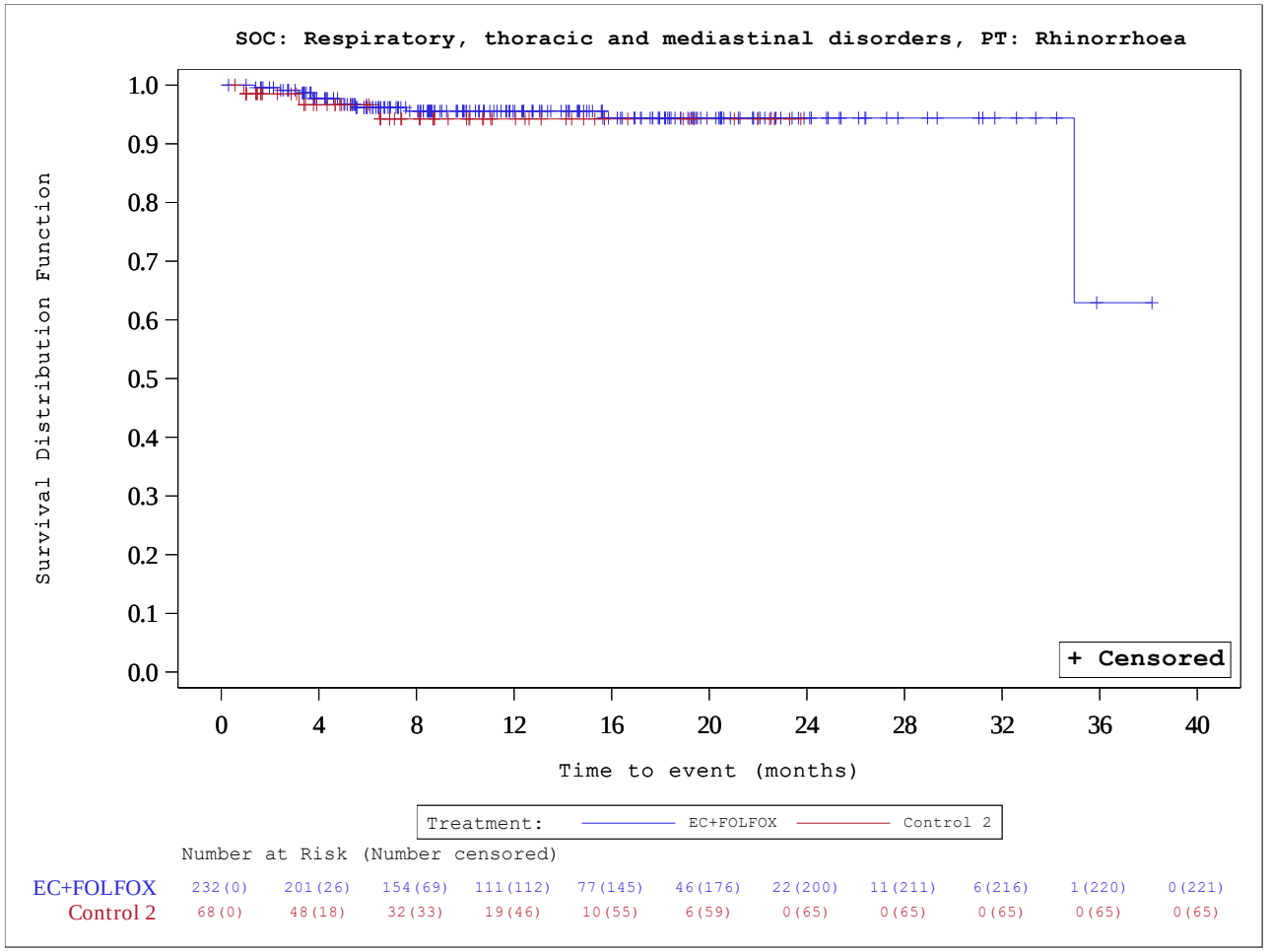

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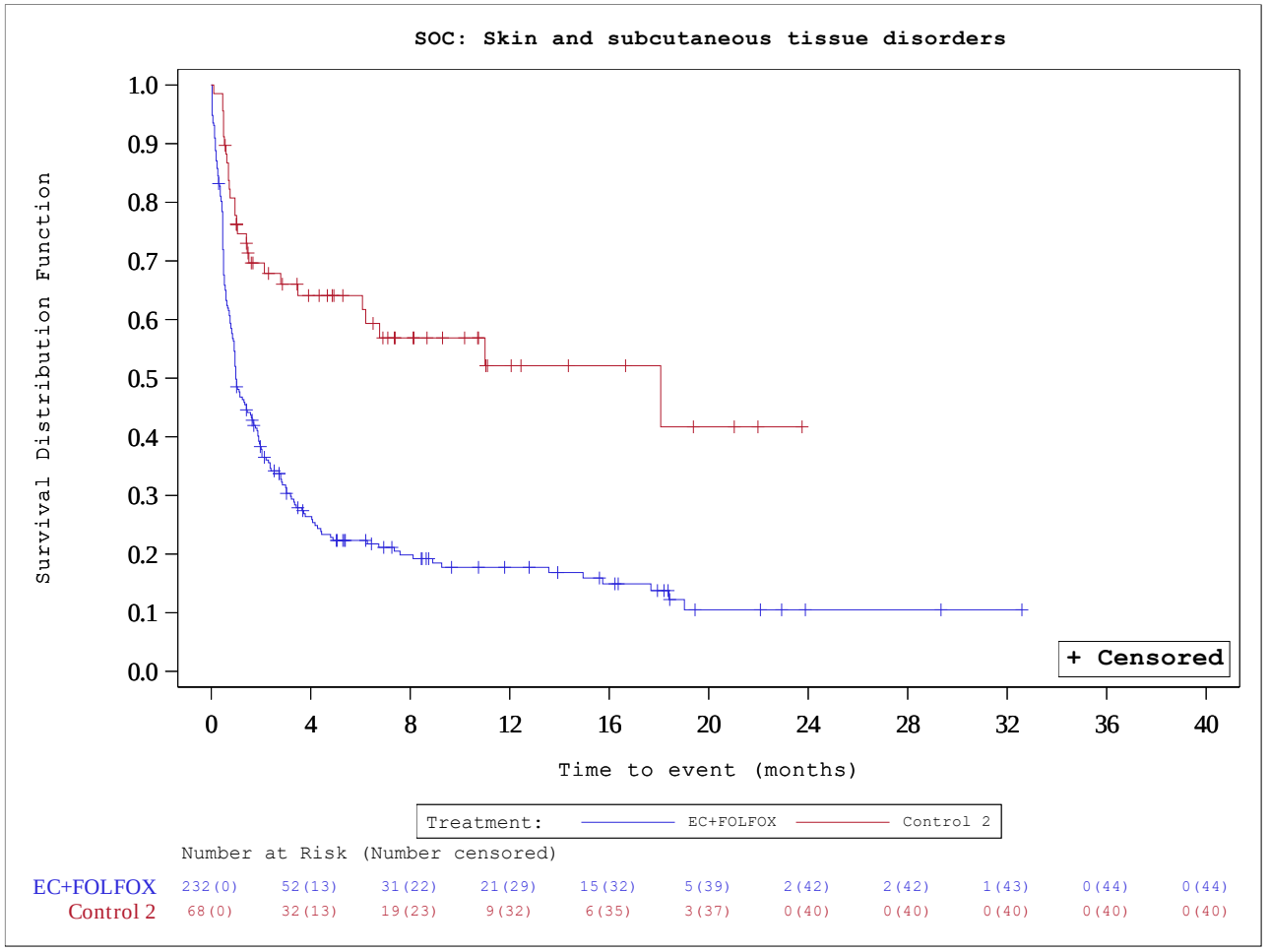

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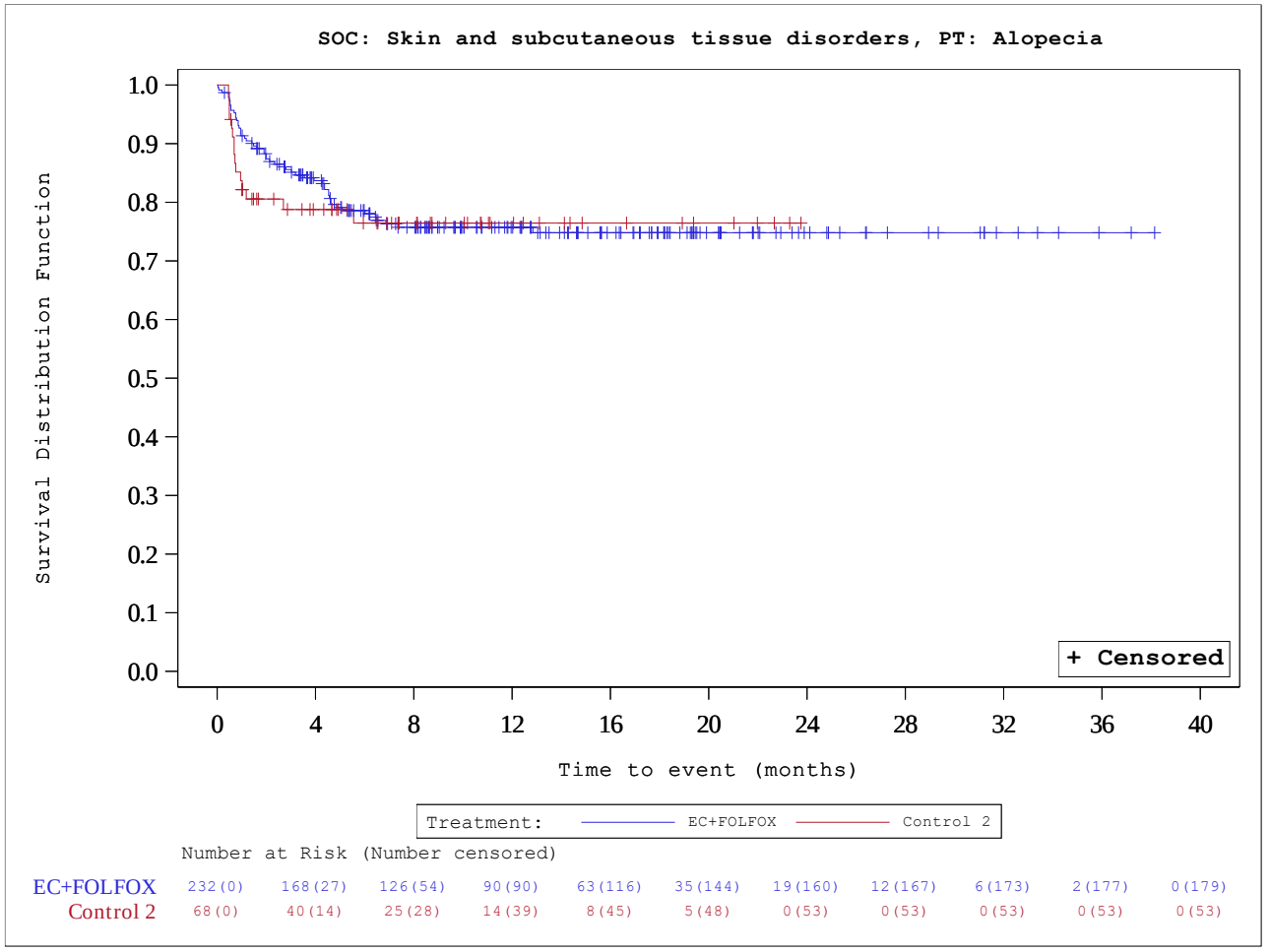

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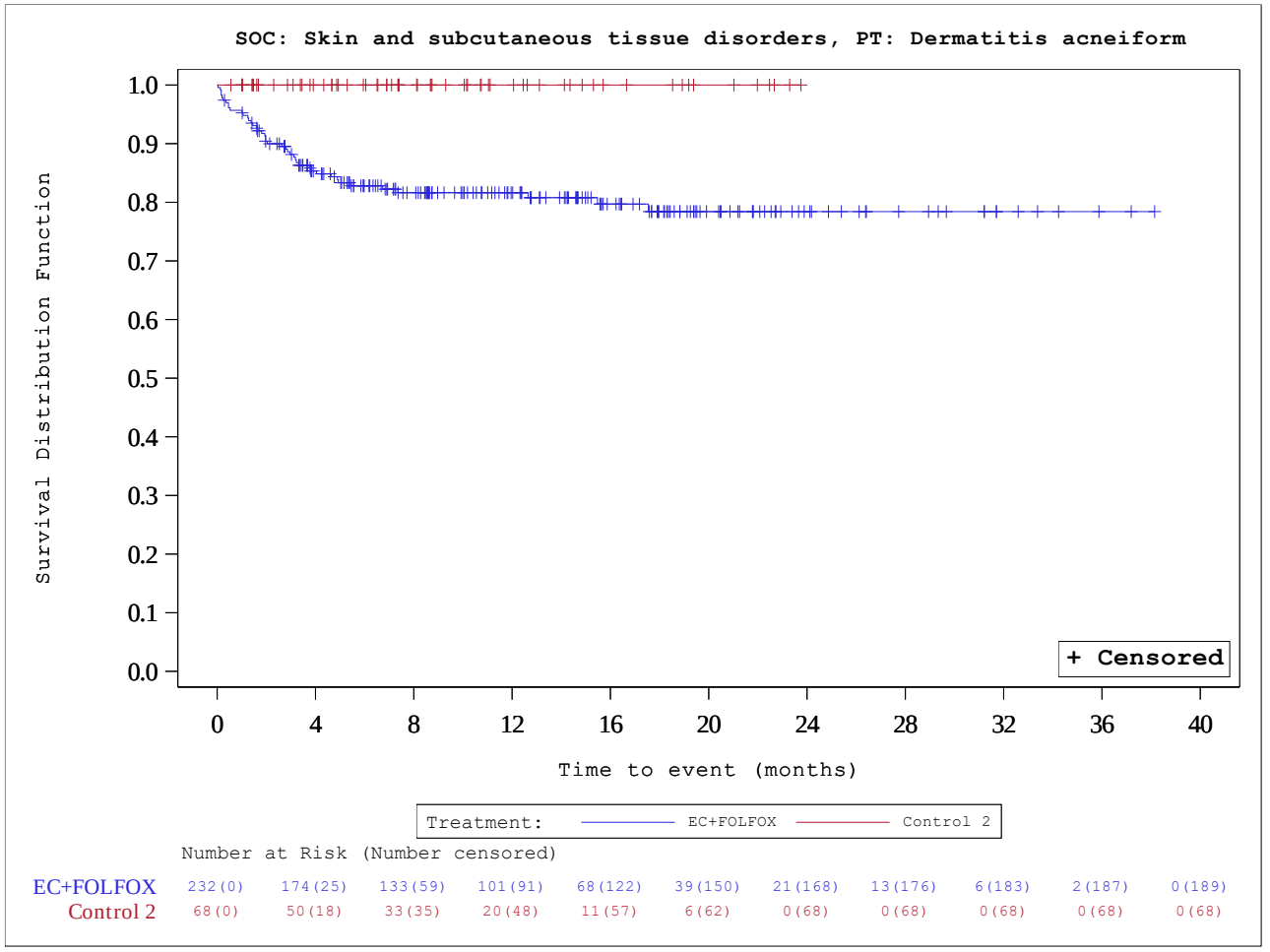

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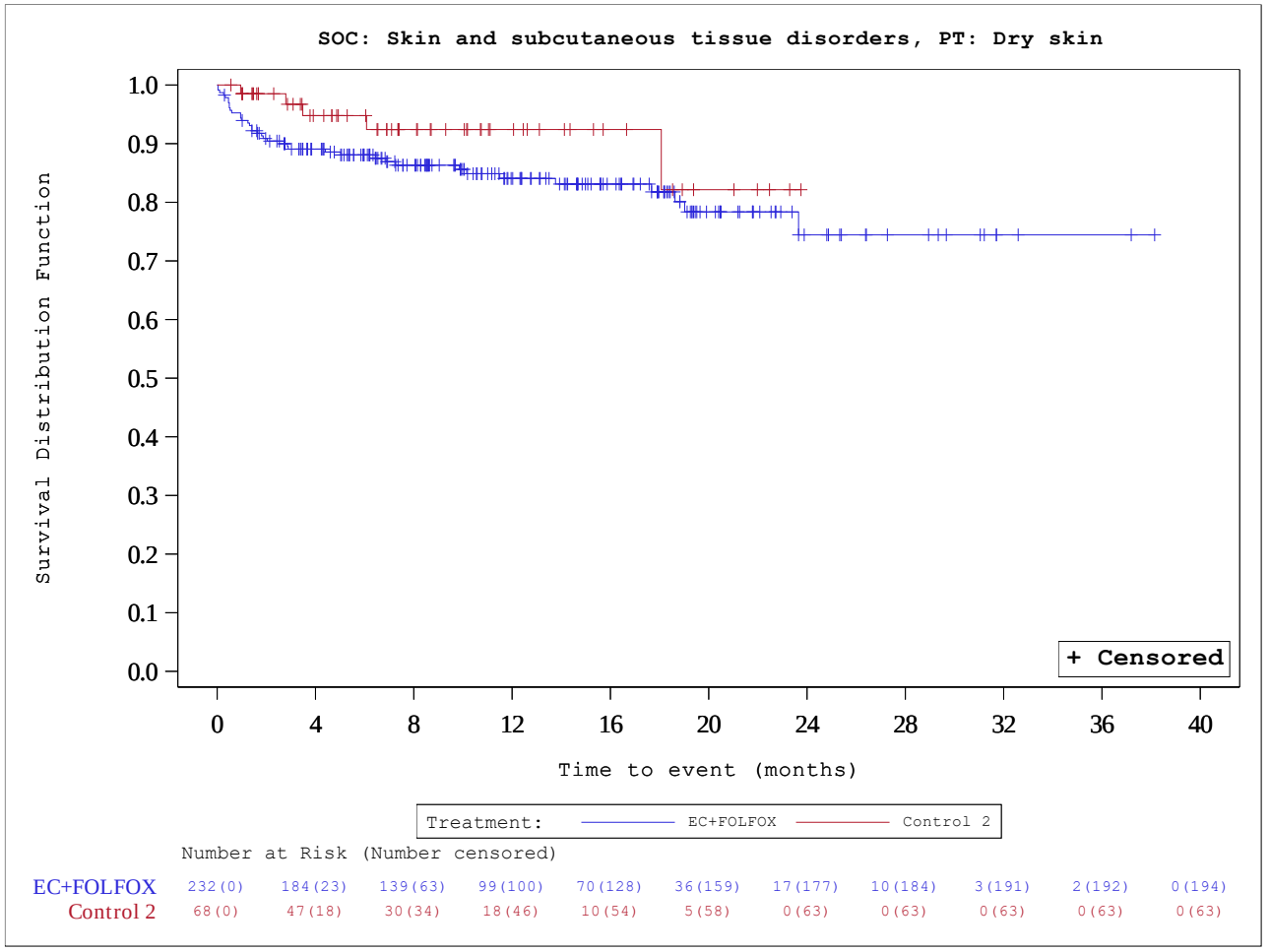

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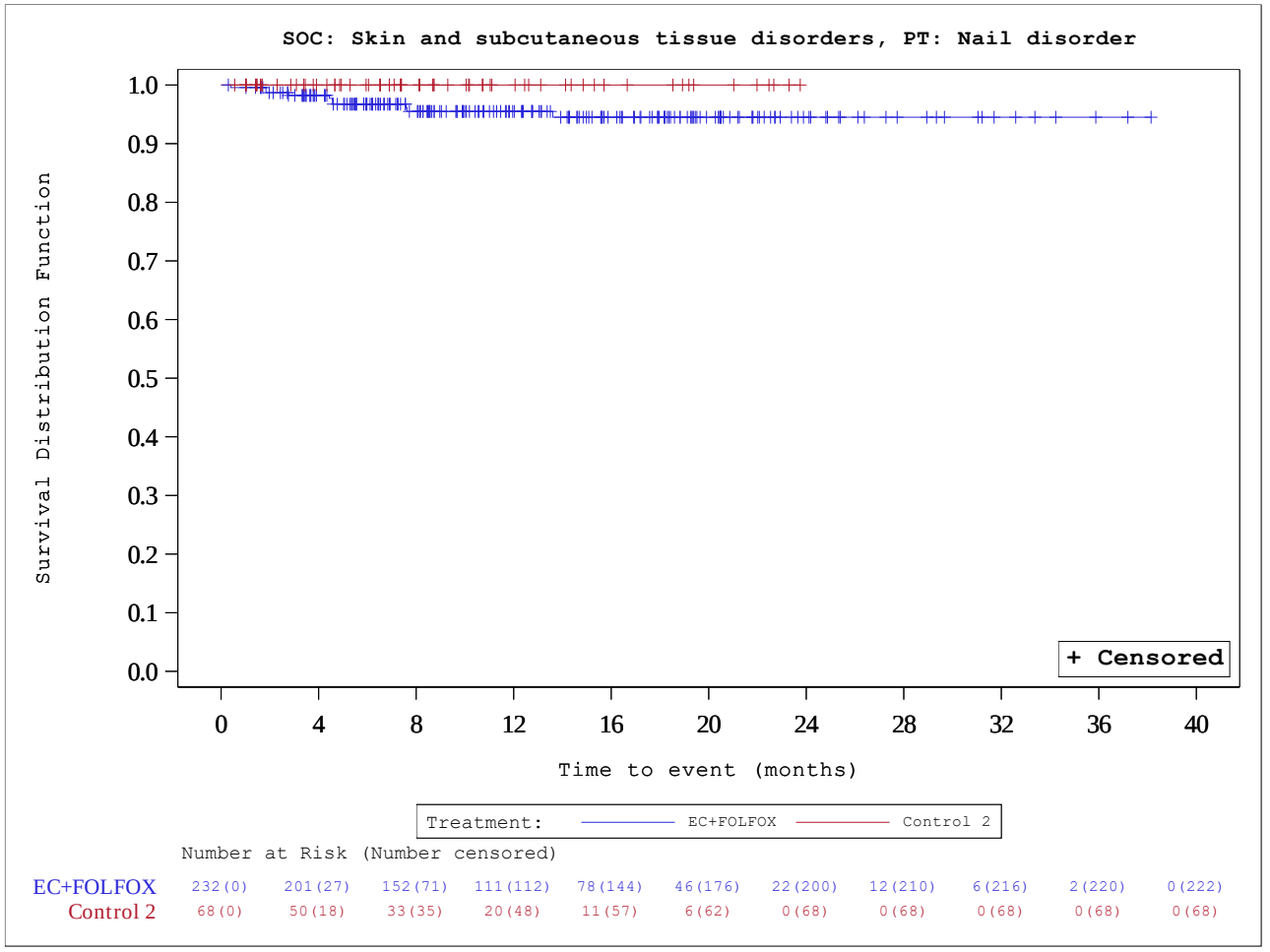

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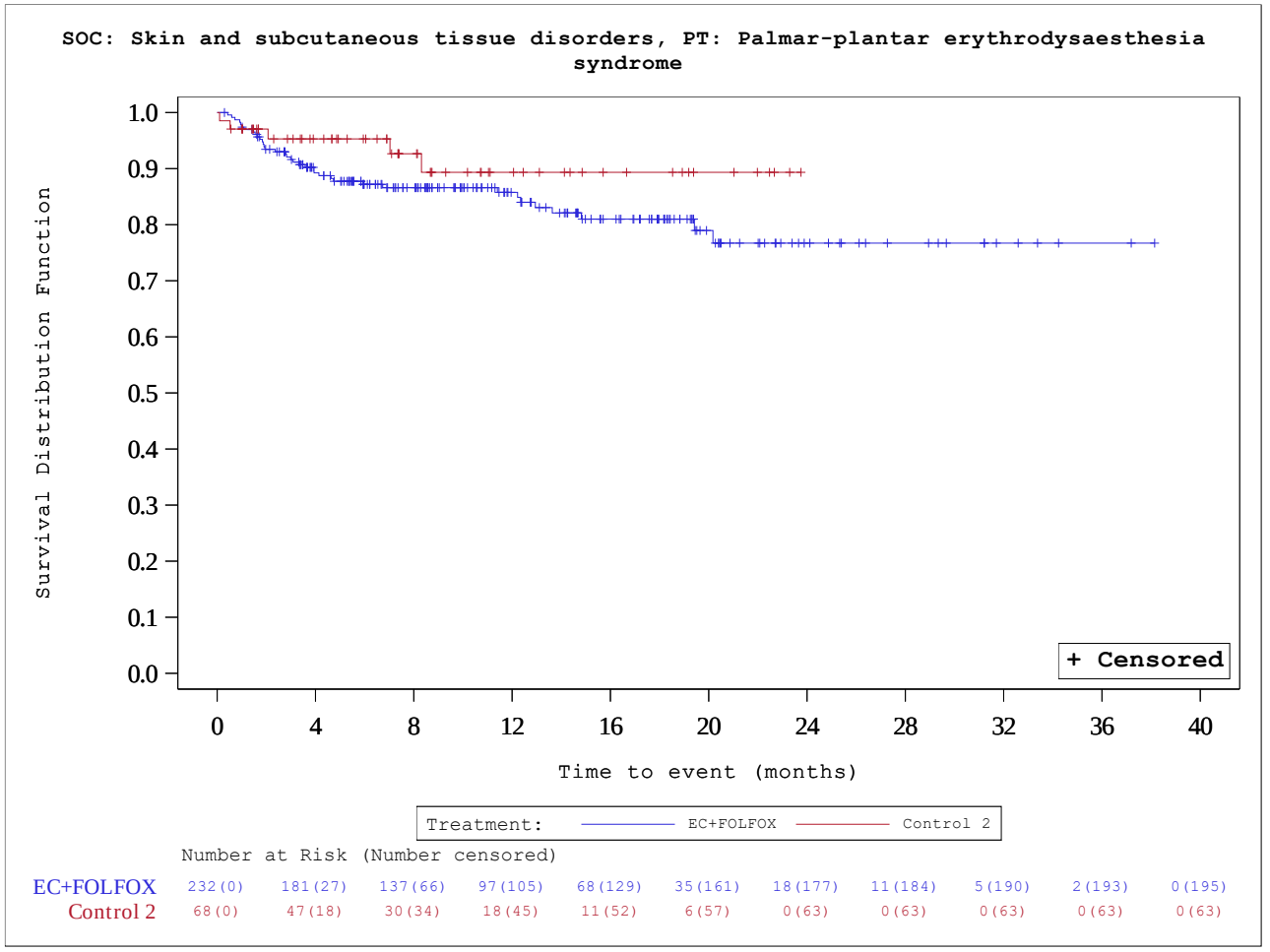

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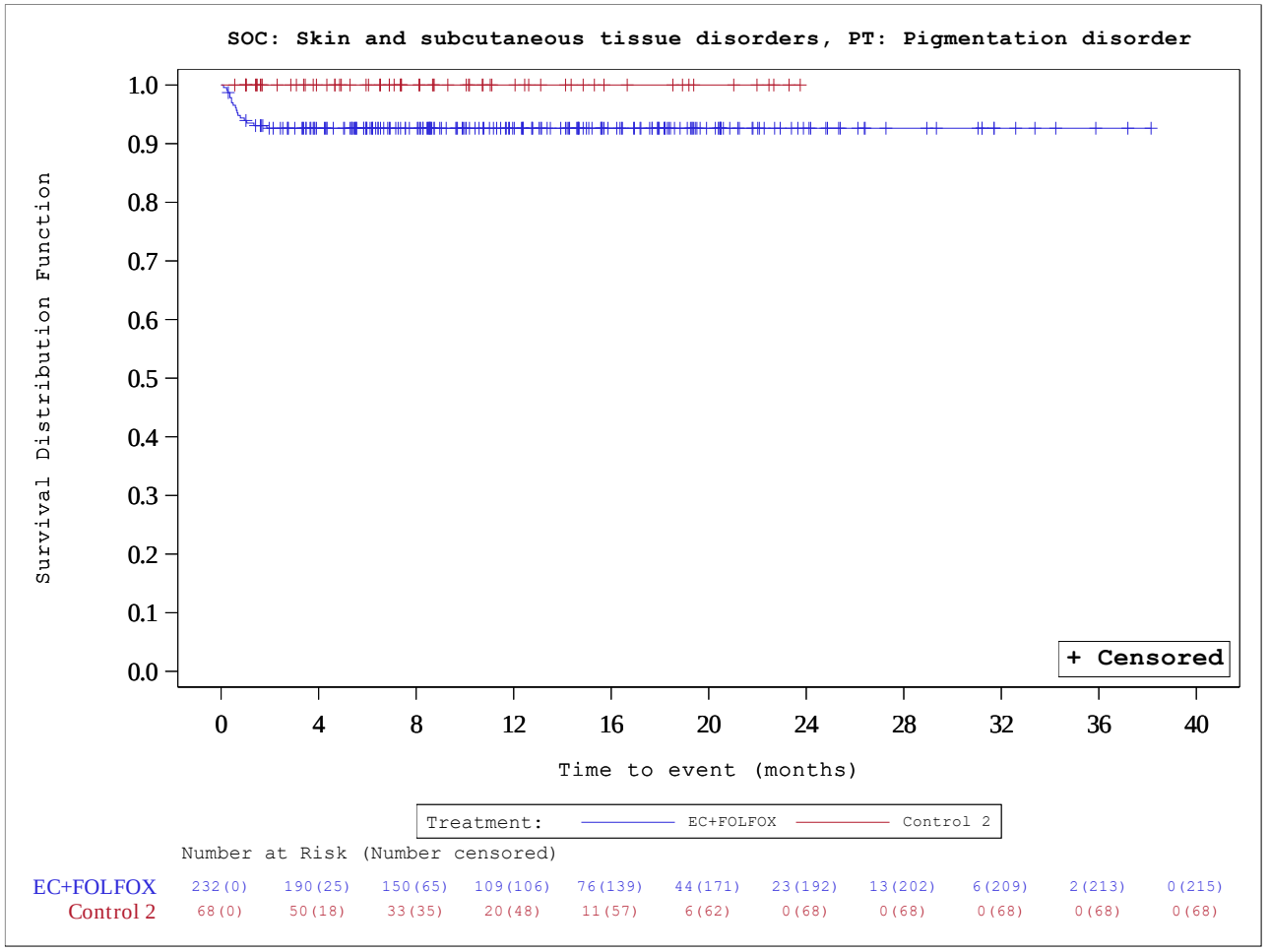

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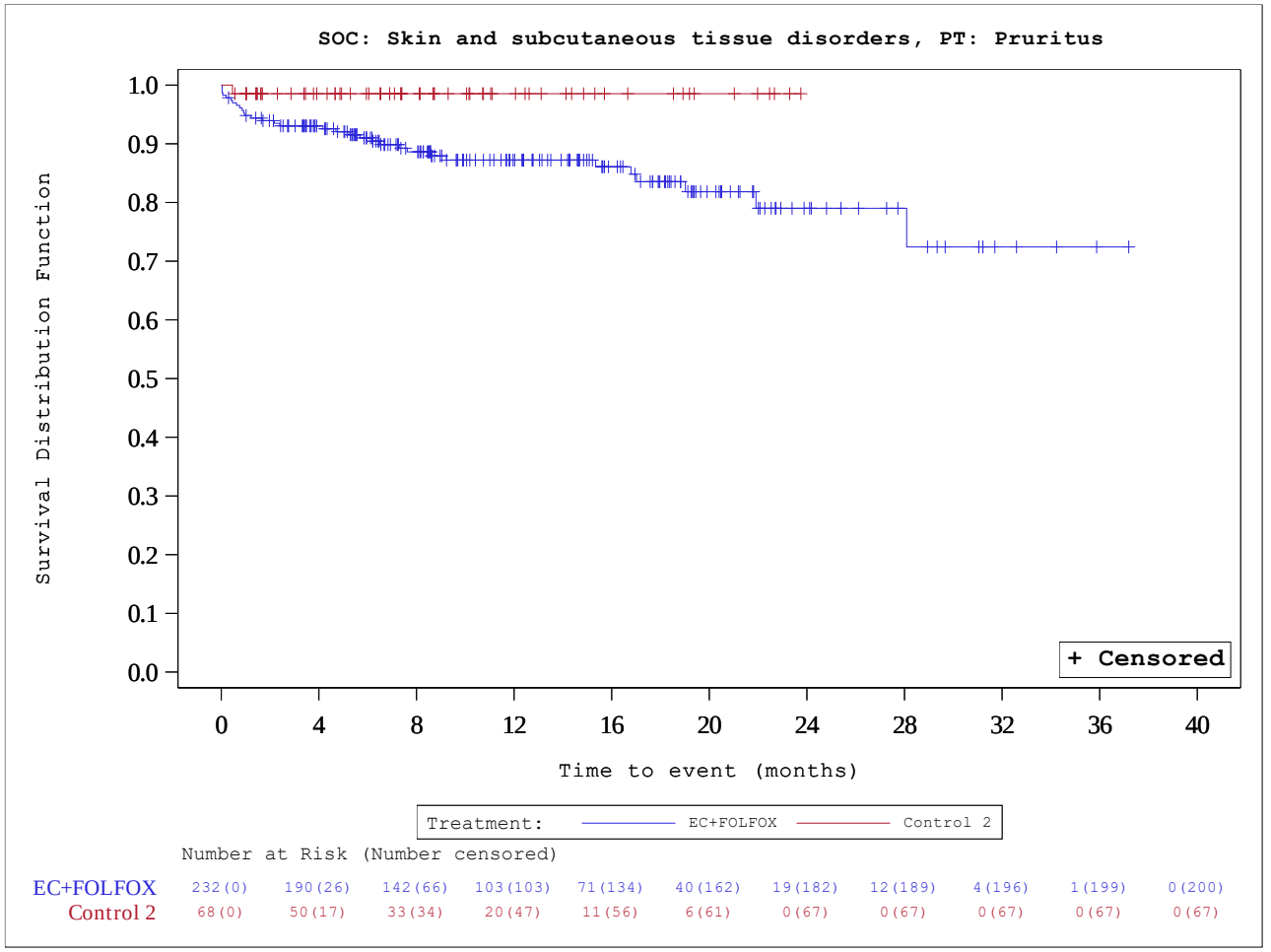

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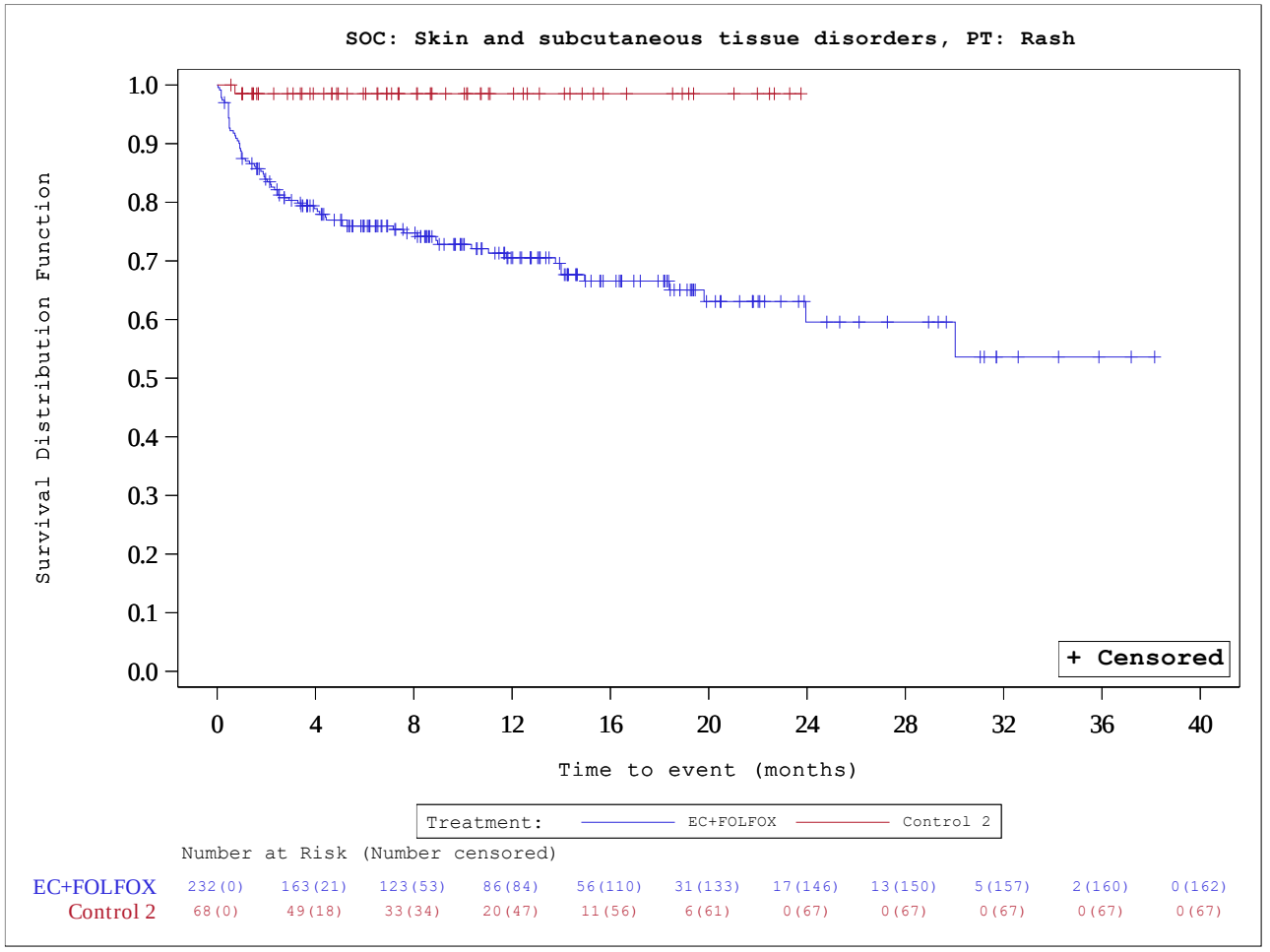

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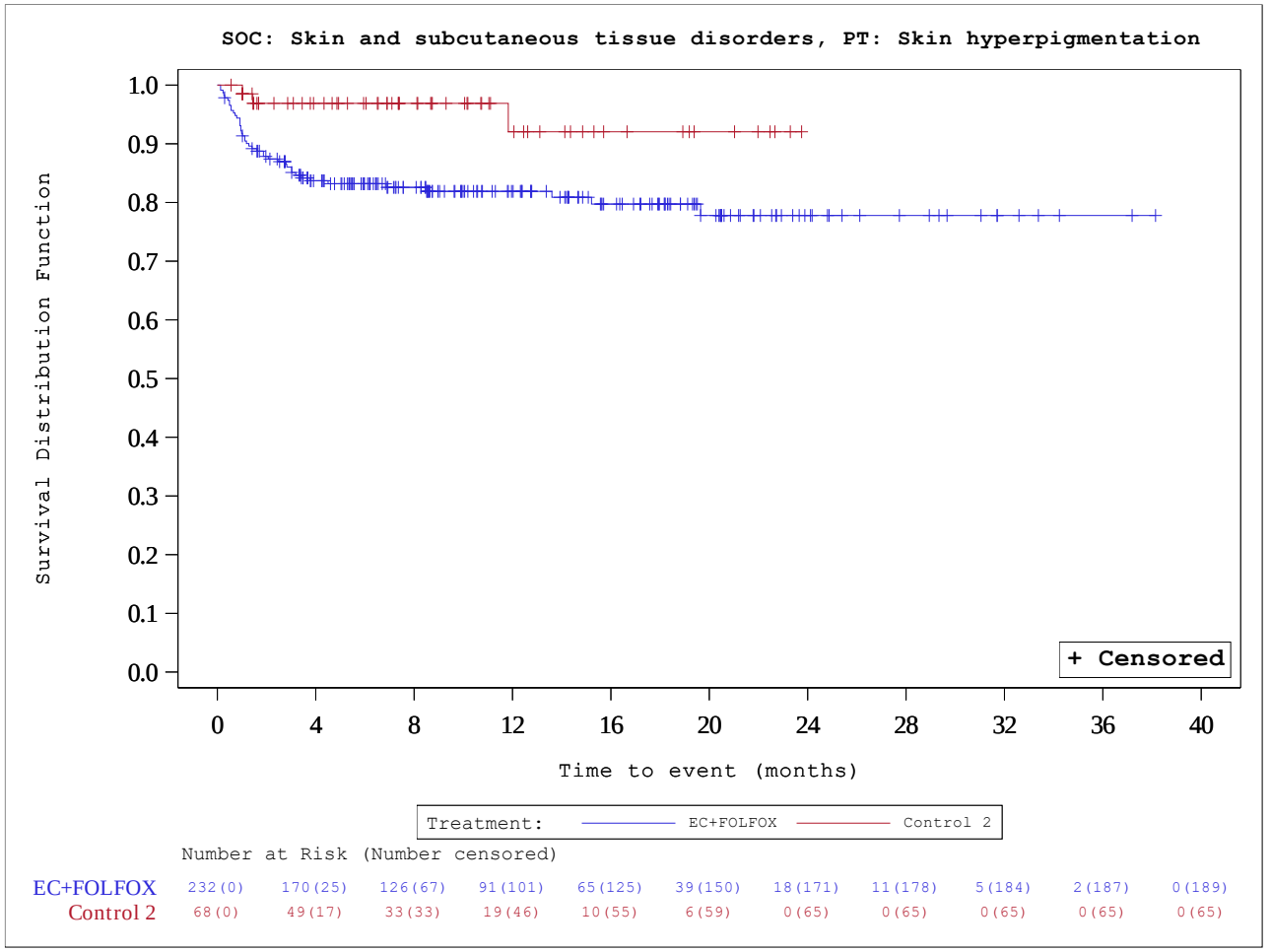

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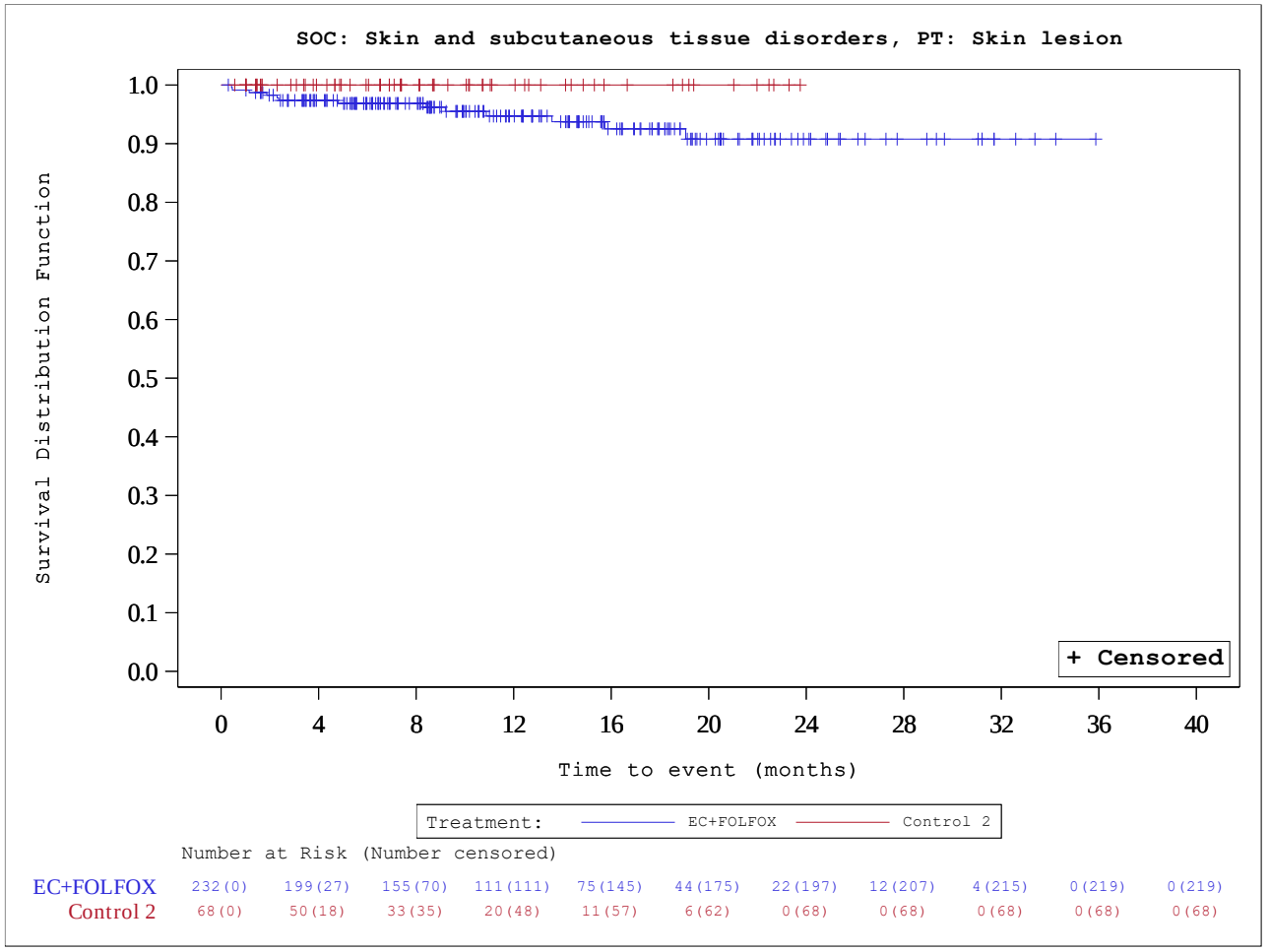

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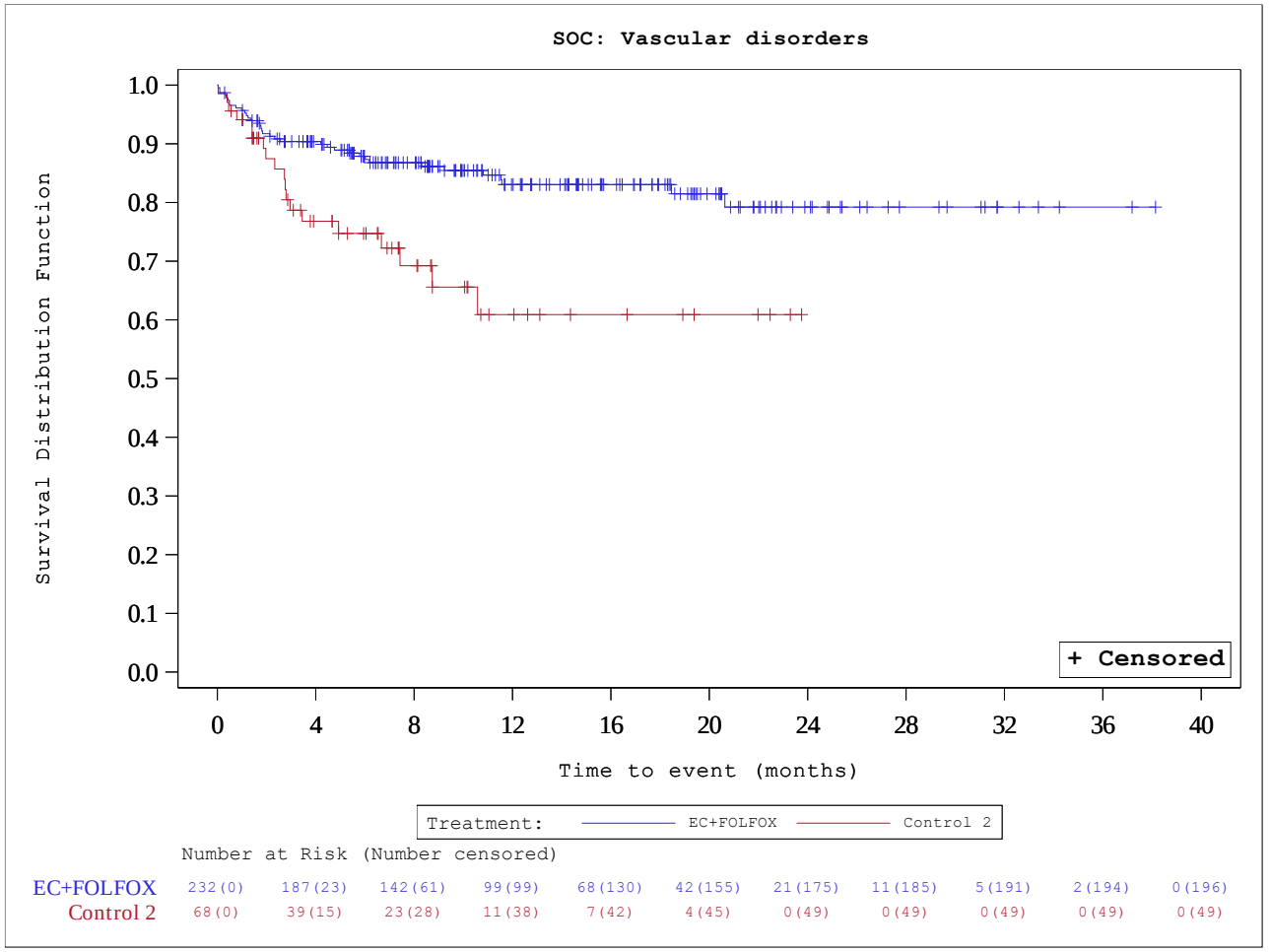

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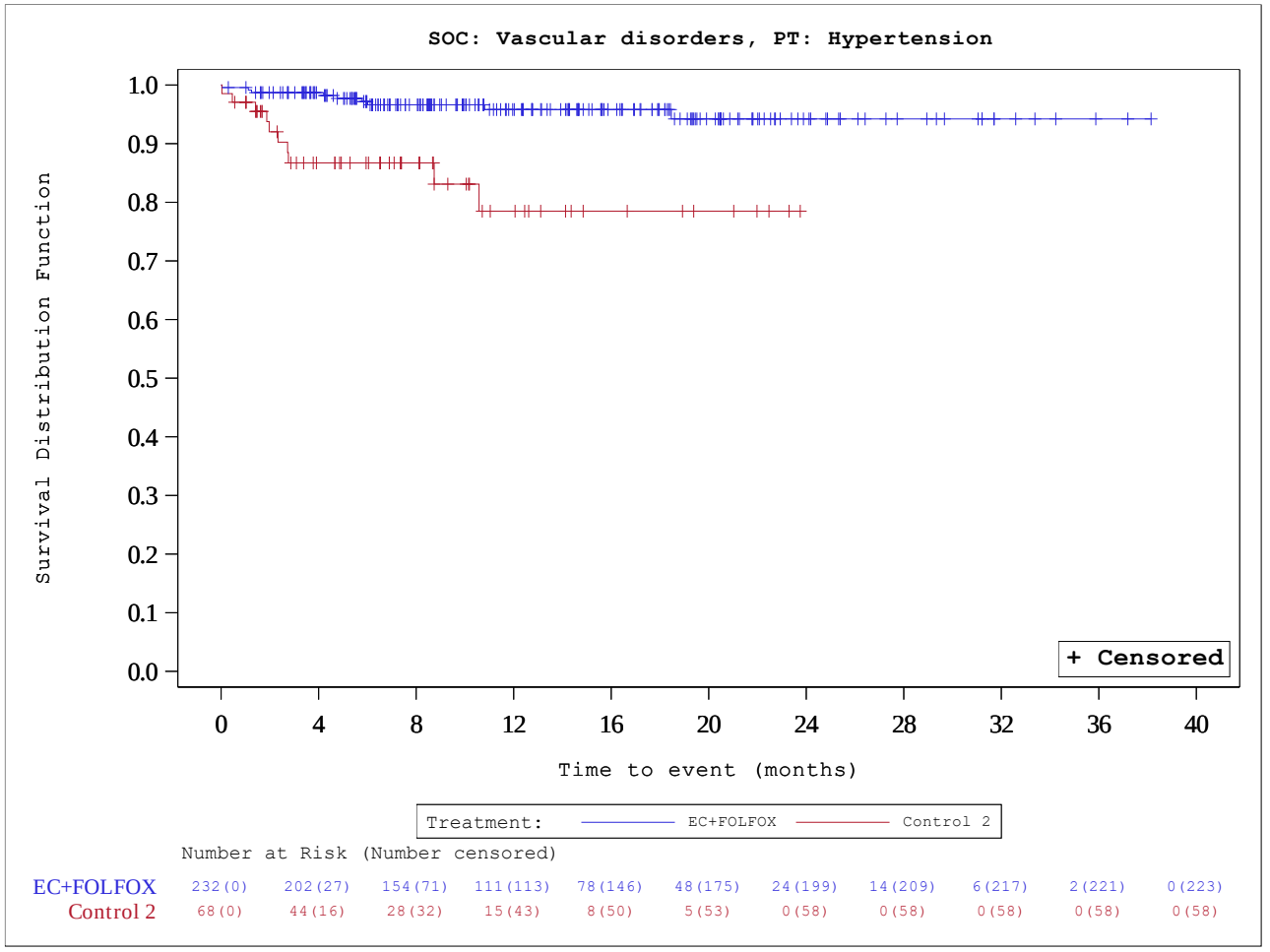

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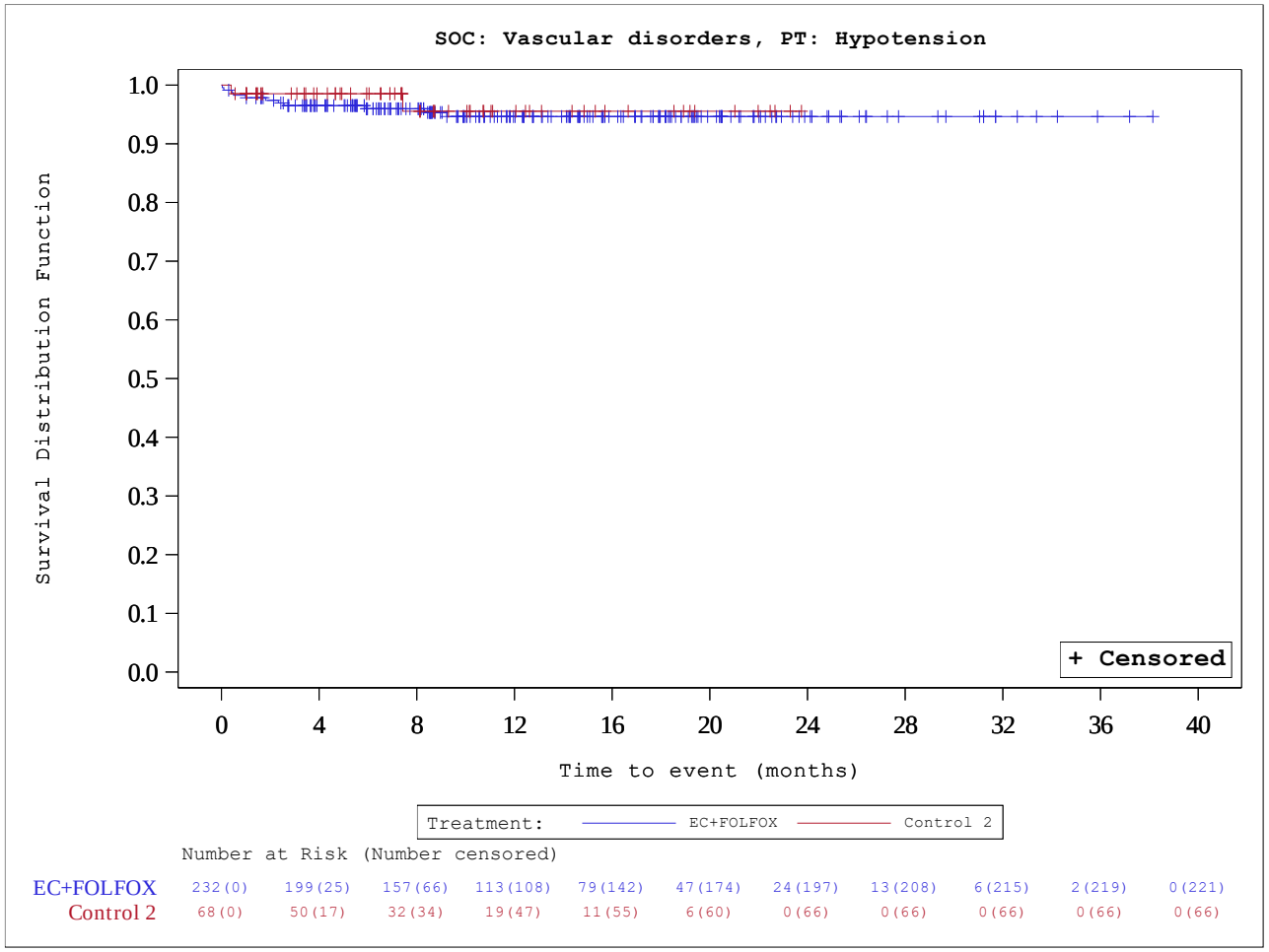

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Subgroup analysis was done for SOCs / PTs with significant overall treatment effect (significant log-rank).
Kaplan-Meier Plots for subgroups only created if p-value for interaction < 0.05.

		EC+FOLFOX (N=232)	Control 2 (N=68)
SOC: Blood and lymphatic system disorders	Number of subjects with events, n (%)	12 (5.2)	0 (0.0)
	Number of censored subjects, n (%)	220 (94.8)	68 (100.0)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Median (95% CI)	NE (NE, NE)	NE (NE, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	NE	
	p-value [3]		

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Frequent Serious AE by SOC, PT (incidence >= 5% or >=10 patients and incidence >= 1%)
Safety Analysis Set

		EC+FOLFOX (N=232)	Control 2 (N=68)
SOC: Gastrointestinal disorders	Number of subjects with events, n (%)	40 (17.2)	15 (22.1)
	Number of censored subjects, n (%)	192 (82.8)	53 (77.9)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	25.4 (14.4, NE)	14.3 (2.7, NE)
	Median (95% CI)	NE (NE, NE)	NE (NE, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	0.61 (0.34, 1.11)	
	p-value [3]	0.1017	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Frequent Serious AE by SOC, PT (incidence >= 5% or >=10 patients and incidence >= 1%)
Safety Analysis Set

		EC+FOLFOX (N=232)	Control 2 (N=68)
SOC: Gastrointestinal disorders, PT: Diarrhoea	Number of subjects with events, n (%)	1 (0.4)	4 (5.9)
	Number of censored subjects, n (%)	231 (99.6)	64 (94.1)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Median (95% CI)	NE (NE, NE)	NE (NE, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	0.06 (0.01, 0.57)	
	p-value [3]	0.0009	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Frequent Serious AE by SOC, PT (incidence >= 5% or >=10 patients and incidence >= 1%)
Safety Analysis Set

		EC+FOLFOX (N=232)	Control 2 (N=68)
SOC: Gastrointestinal disorders, PT: Intestinal obstruction	Number of subjects with events, n (%)	11 (4.7)	5 (7.4)
	Number of censored subjects, n (%)	221 (95.3)	63 (92.6)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	NE (NE, NE)	NE (14.3, NE)
	Median (95% CI)	NE (NE, NE)	NE (NE, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	0.48 (0.16, 1.41)	
	p-value [3]	0.1706	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Frequent Serious AE by SOC, PT (incidence >= 5% or >=10 patients and incidence >= 1%)
Safety Analysis Set

		EC+FOLFOX (N=232)	Control 2 (N=68)
SOC: General disorders and administration site conditions	Number of subjects with events, n (%)	23 (9.9)	2 (2.9)
	Number of censored subjects, n (%)	209 (90.1)	66 (97.1)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Median (95% CI)	NE (NE, NE)	NE (NE, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	2.82 (0.66, 11.99)	
	p-value [3]	0.1415	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.

		EC+FOLFOX (N=232)	Control 2 (N=68)
SOC: Infections and infestations	Number of subjects with events, n (%)	22 (9.5)	4 (5.9)
	Number of censored subjects, n (%)	210 (90.5)	64 (94.1)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Median (95% CI)	NE (NE, NE)	NE (NE, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	1.33 (0.46, 3.87)	
	p-value [3]	0.5963	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Frequent Serious AE by SOC, PT (incidence >= 5% or >=10 patients and incidence >= 1%)
Safety Analysis Set

		EC+FOLFOX (N=232)	Control 2 (N=68)
SOC: Respiratory, thoracic and mediastinal disorders	Number of subjects with events, n (%)	8 (3.4)	4 (5.9)
	Number of censored subjects, n (%)	224 (96.6)	64 (94.1)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Median (95% CI)	NE (NE, NE)	NE (NE, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	0.45 (0.13, 1.49)	
	p-value [3]	0.1791	

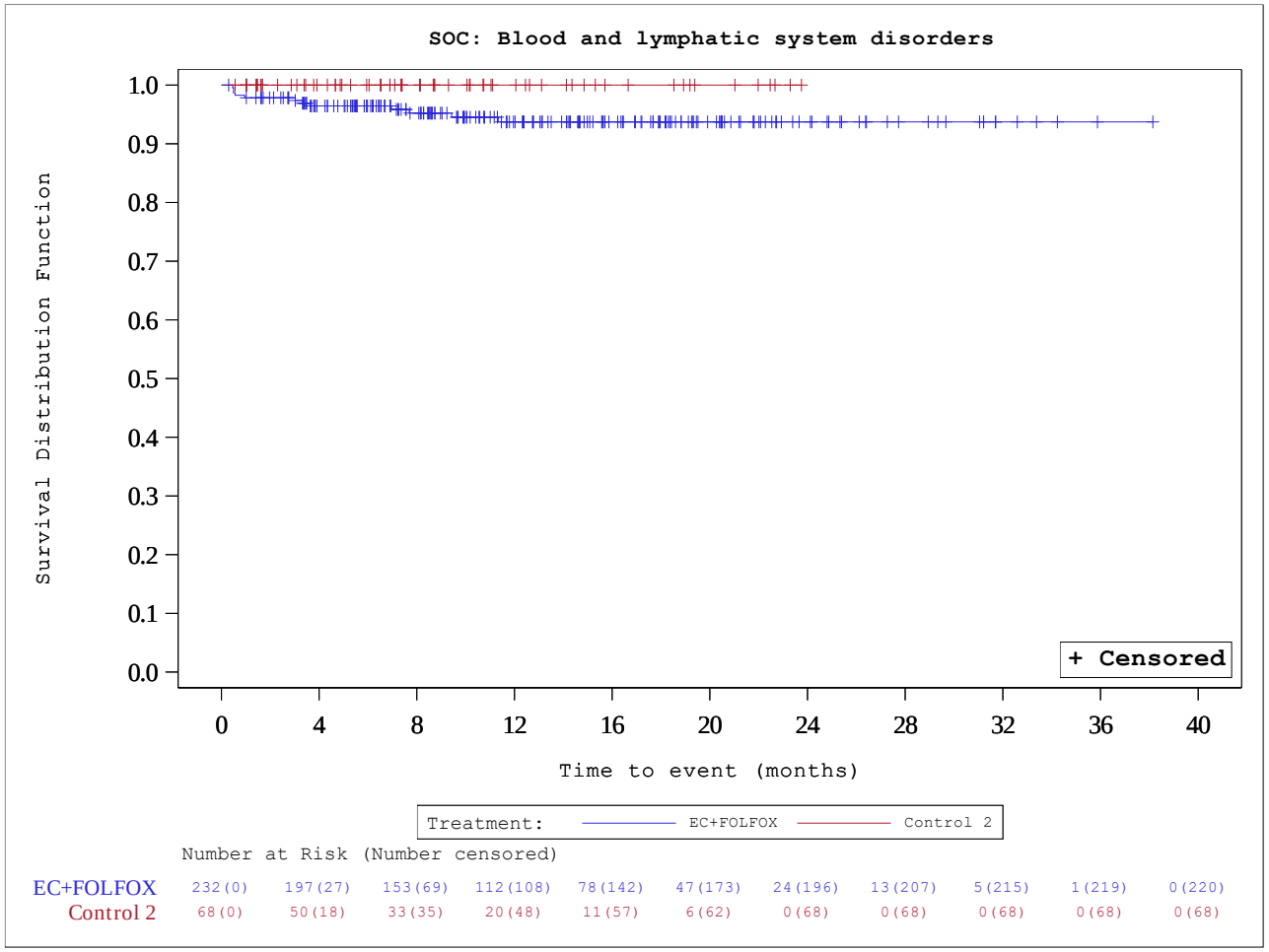
Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Frequent Serious AE by SOC, PT (incidence >= 5% or >=10 patients and incidence >= 1%) - Subgroup analysis
Safety Analysis Set

SOC/PT	Subgroup Level	EC+FOLFOX (N=232) n/ N (%)	EC+FOLFOX (N=232) Median (95% CI)[1]	Control 2 (N=68) n/ N (%)	Control 2 (N=68) Median (95% CI)[1]	Unstratified analysis Hazard Ratio (95% CI)[2]	Unstratified analysis p-Value[3]	Interaction p-Value[4]
SOC: Gastrointestinal disorders, PT: Diarrhoea	Age (Years)							
	< 65	1/ 148 (0.7)		1/ 42 (2.4)				
	>= 65	0/ 84 (0.0)		3/ 26 (11.5)				
	Sex							
	Male	0/ 121 (0.0)		2/ 32 (6.3)				
	Female	1/ 111 (0.9)		2/ 36 (5.6)				
	Region							
	Europe	0/ 108 (0.0)		3/ 38 (7.9)				
	USA/Canada	0/ 15 (0.0)		0/ 7 (0.0)				
	Rest of World	1/ 109 (0.9)		1/ 23 (4.3)				
	ECOG-PS at Randomization							
	0	0/ 130 (0.0)		2/ 44 (4.5)				
	1	1/ 102 (1.0)		2/ 24 (8.3)				
	Number of Organs Involved							
	<= 2	1/ 116 (0.9)		1/ 33 (3.0)				
	>= 3	0/ 116 (0.0)		3/ 35 (8.6)				
	Presence of Liver Metastases							
	Yes	1/ 146 (0.7)		3/ 42 (7.1)				
	No	0/ 86 (0.0)		1/ 26 (3.8)				
	Side of Tumor							
	Left	0/ 88 (0.0)		2/ 33 (6.1)				
	Right	1/ 144 (0.7)		2/ 35 (5.7)				

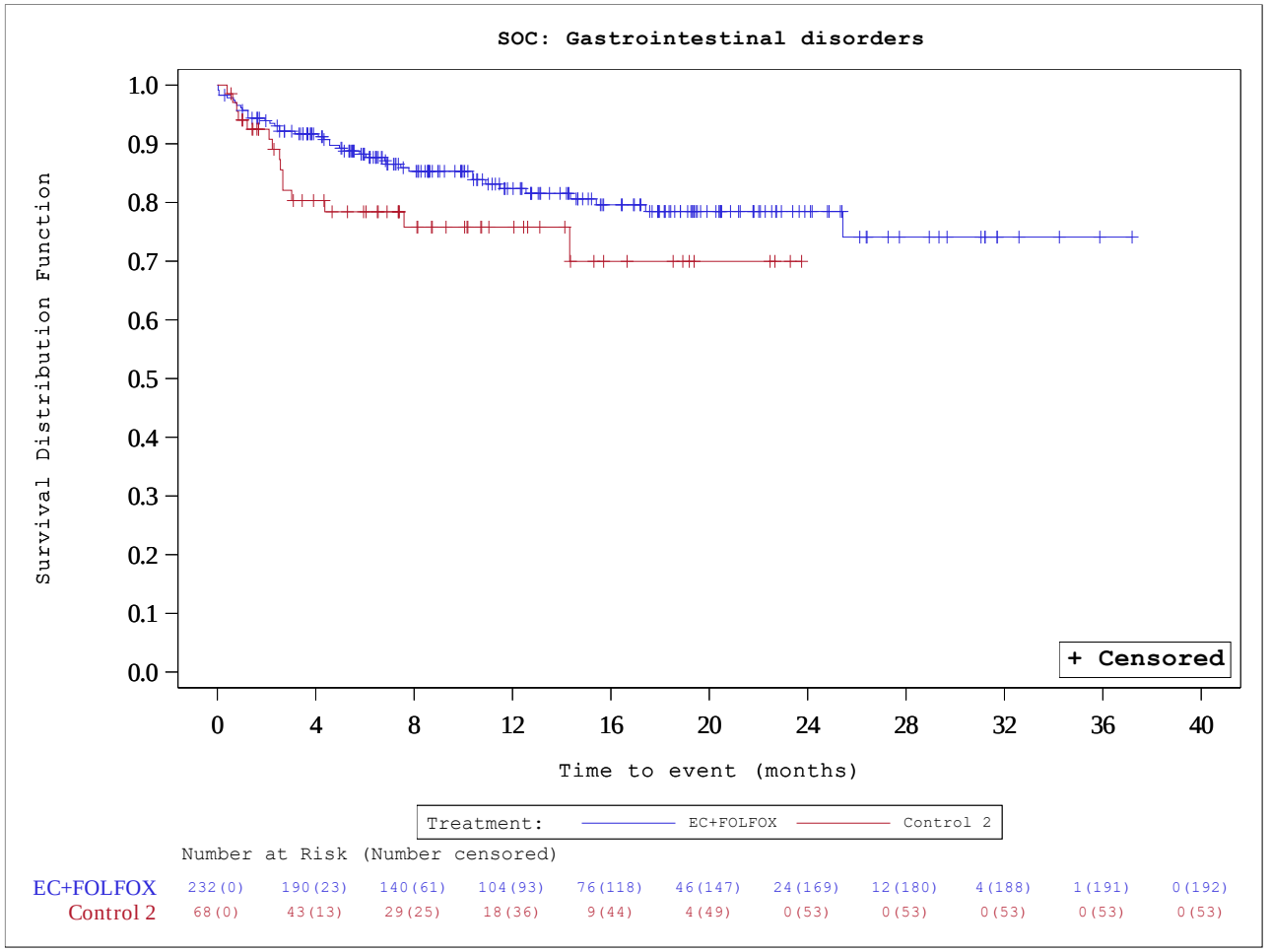
Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
Subgroup analysis was done for SOCs / PTs with significant overall treatment effect (significant log-rank).
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.
[4] P-Value for interaction from Cox proportional hazards model using ties=exact option with treatment, subgroup and treatment*subgroup interaction as covariates.
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Kaplan Meier Plot of frequent Frequent Serious AE by SOC, PT (incidence >= 5% or >=10 patients and incidence >= 1%)
Safety Analysis Set



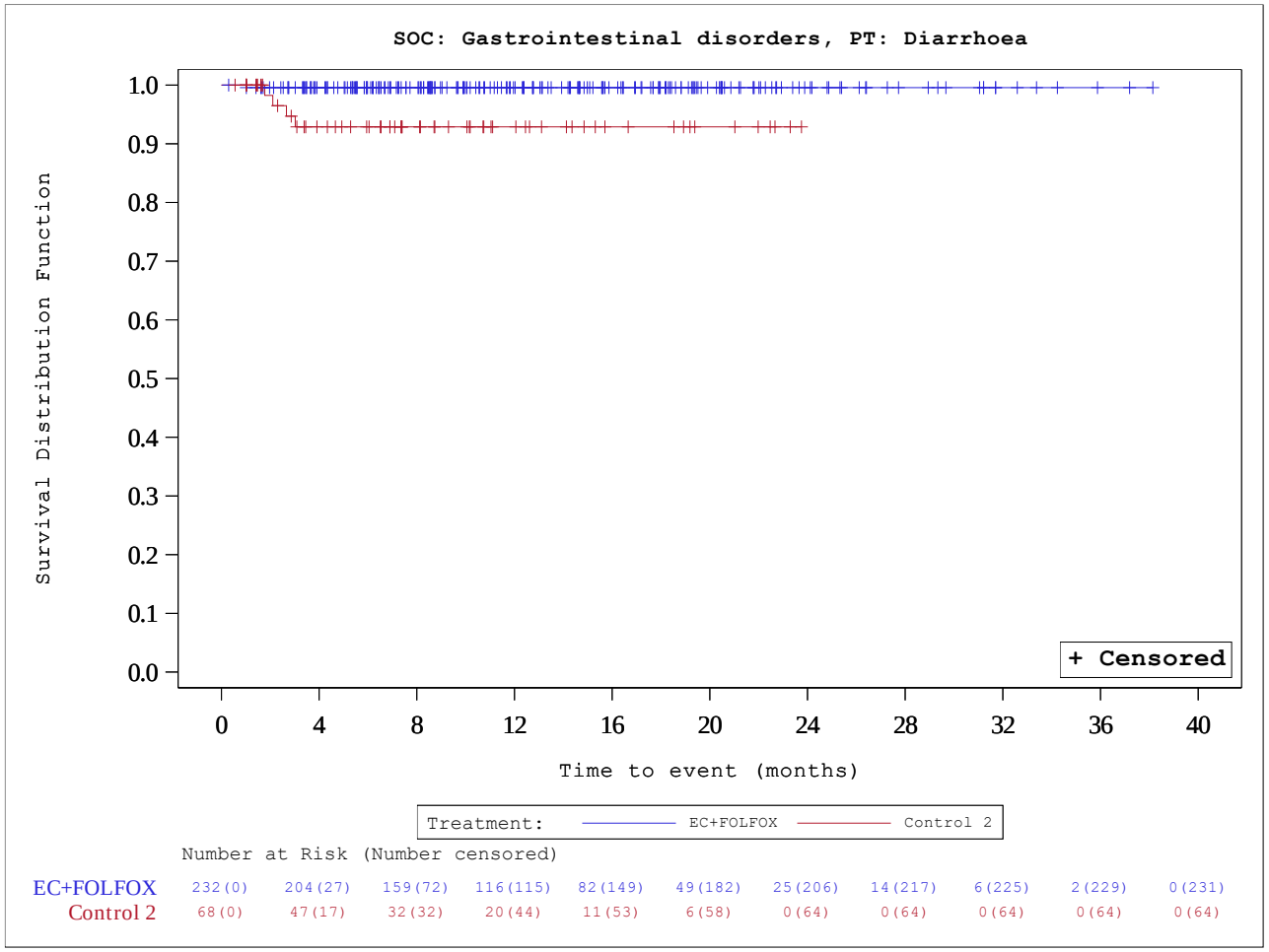
Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
Subgroup analysis was done for SOCs / PTs with significant overall treatment effect (significant log-rank).
Kaplan-Meier Plots for subgroups only created if p-value for interaction < 0.05.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Kaplan Meier Plot of frequent Frequent Serious AE by SOC, PT (incidence >= 5% or >=10 patients and incidence >= 1%)
Safety Analysis Set



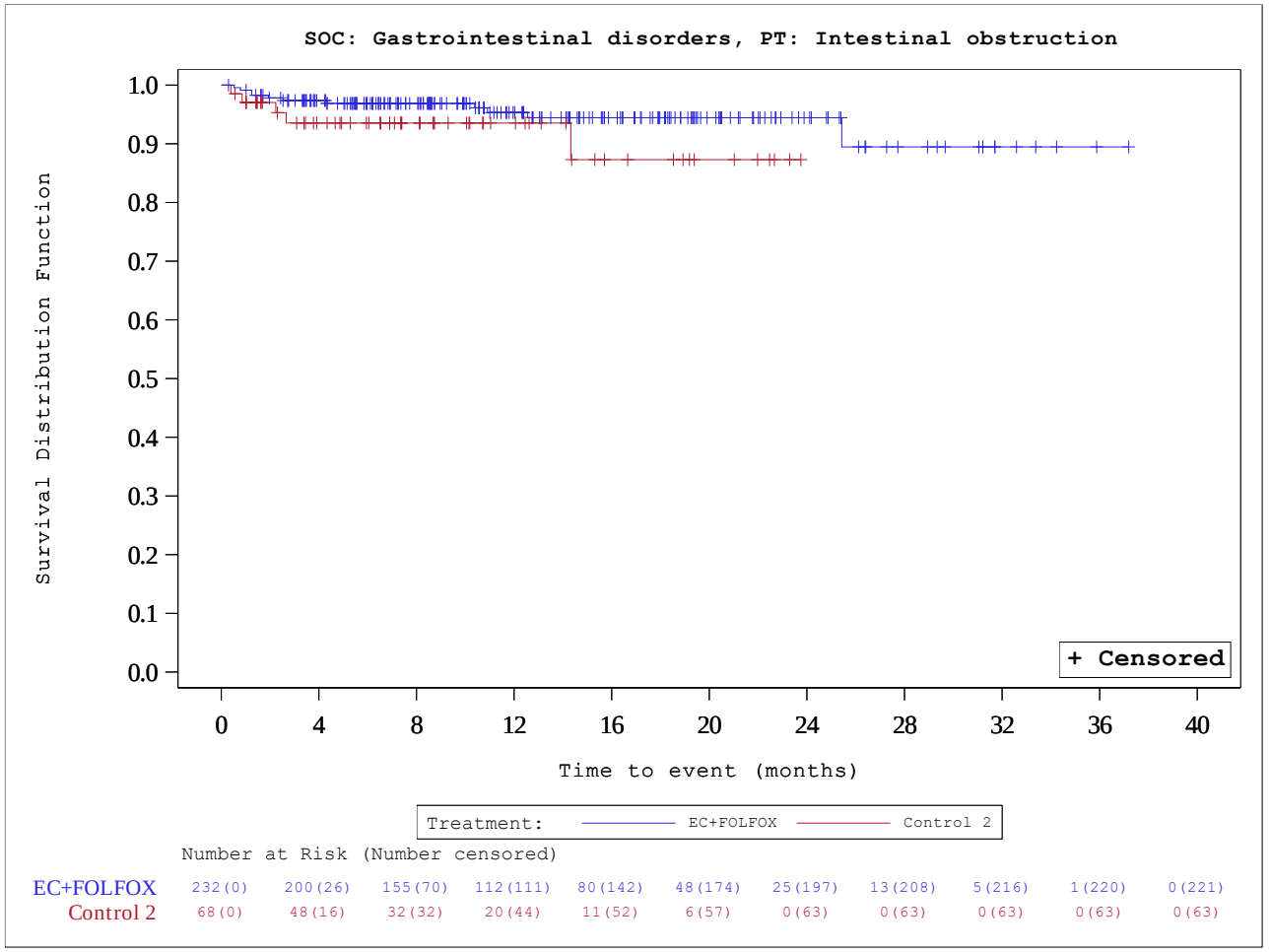
Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
Subgroup analysis was done for SOCs / PTs with significant overall treatment effect (significant log-rank).
Kaplan-Meier Plots for subgroups only created if p-value for interaction < 0.05.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Kaplan Meier Plot of frequent Frequent Serious AE by SOC, PT (incidence >= 5% or >=10 patients and incidence >= 1%)
Safety Analysis Set



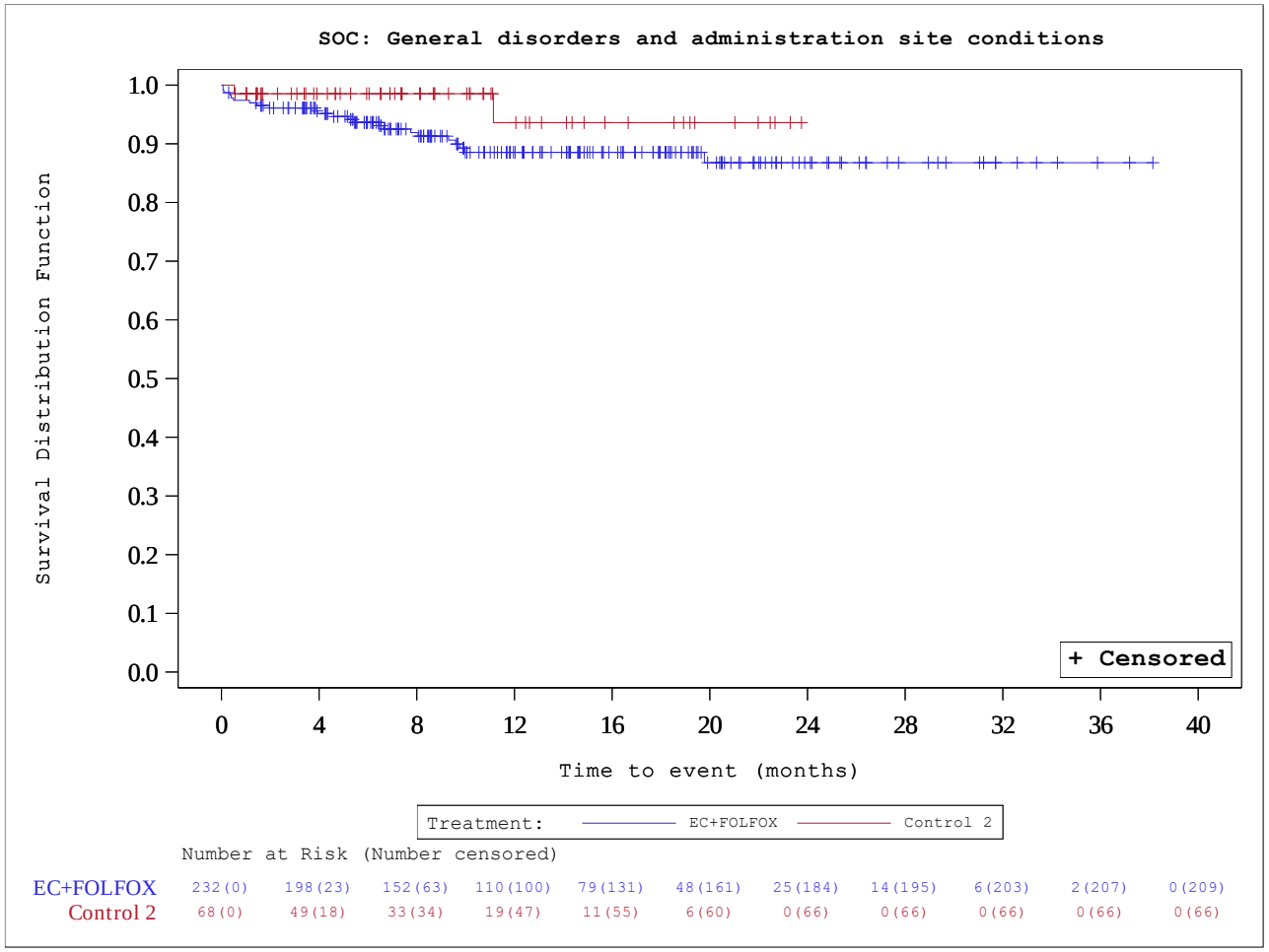
Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
Subgroup analysis was done for SOCs / PTs with significant overall treatment effect (significant log-rank).
Kaplan-Meier Plots for subgroups only created if p-value for interaction < 0.05.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Kaplan Meier Plot of frequent Frequent Serious AE by SOC, PT (incidence >= 5% or >=10 patients and incidence >= 1%)
Safety Analysis Set



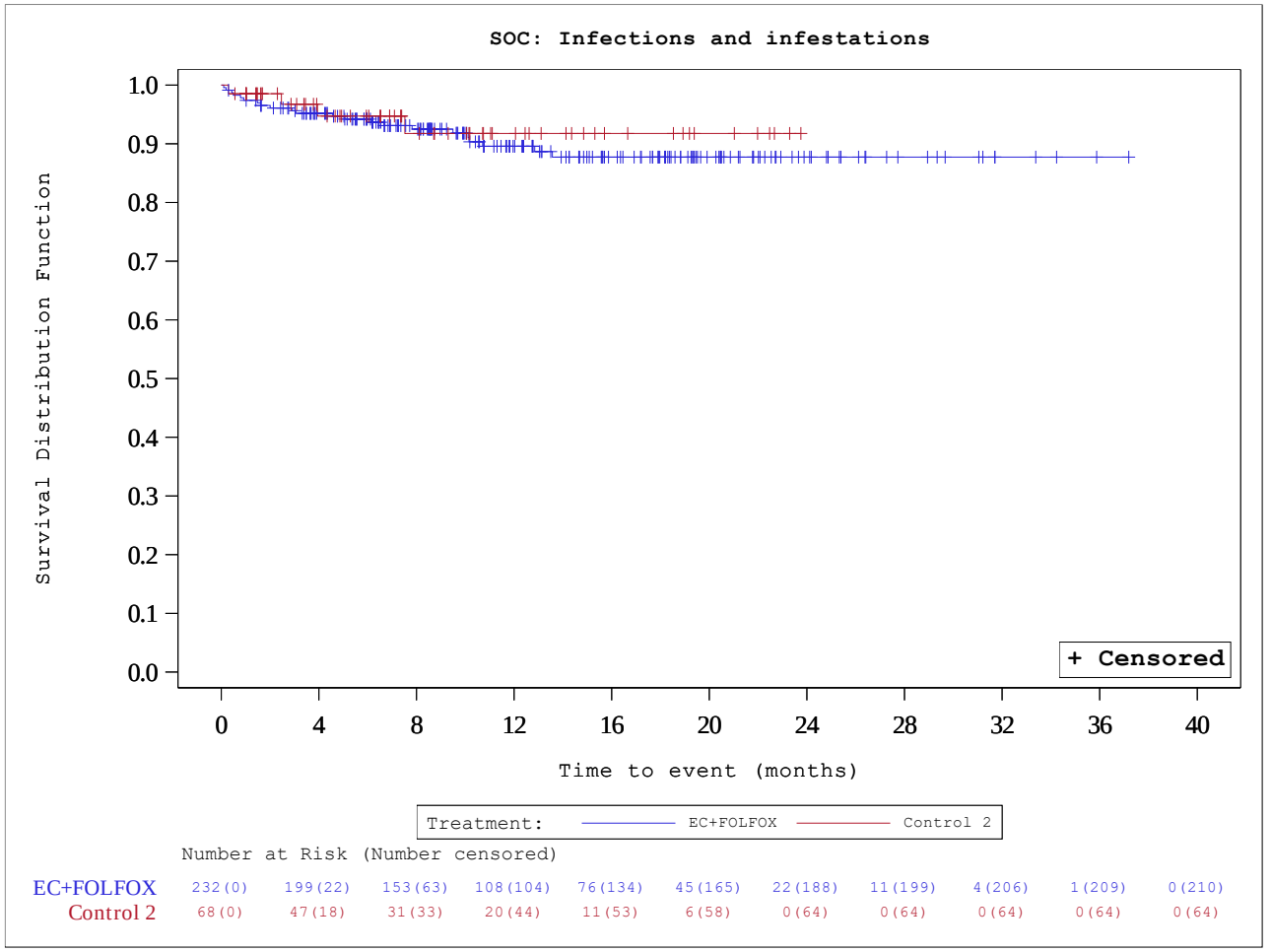
Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
Subgroup analysis was done for SOCs / PTs with significant overall treatment effect (significant log-rank).
Kaplan-Meier Plots for subgroups only created if p-value for interaction < 0.05.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Kaplan Meier Plot of frequent Frequent Serious AE by SOC, PT (incidence >= 5% or >=10 patients and incidence >= 1%)
Safety Analysis Set



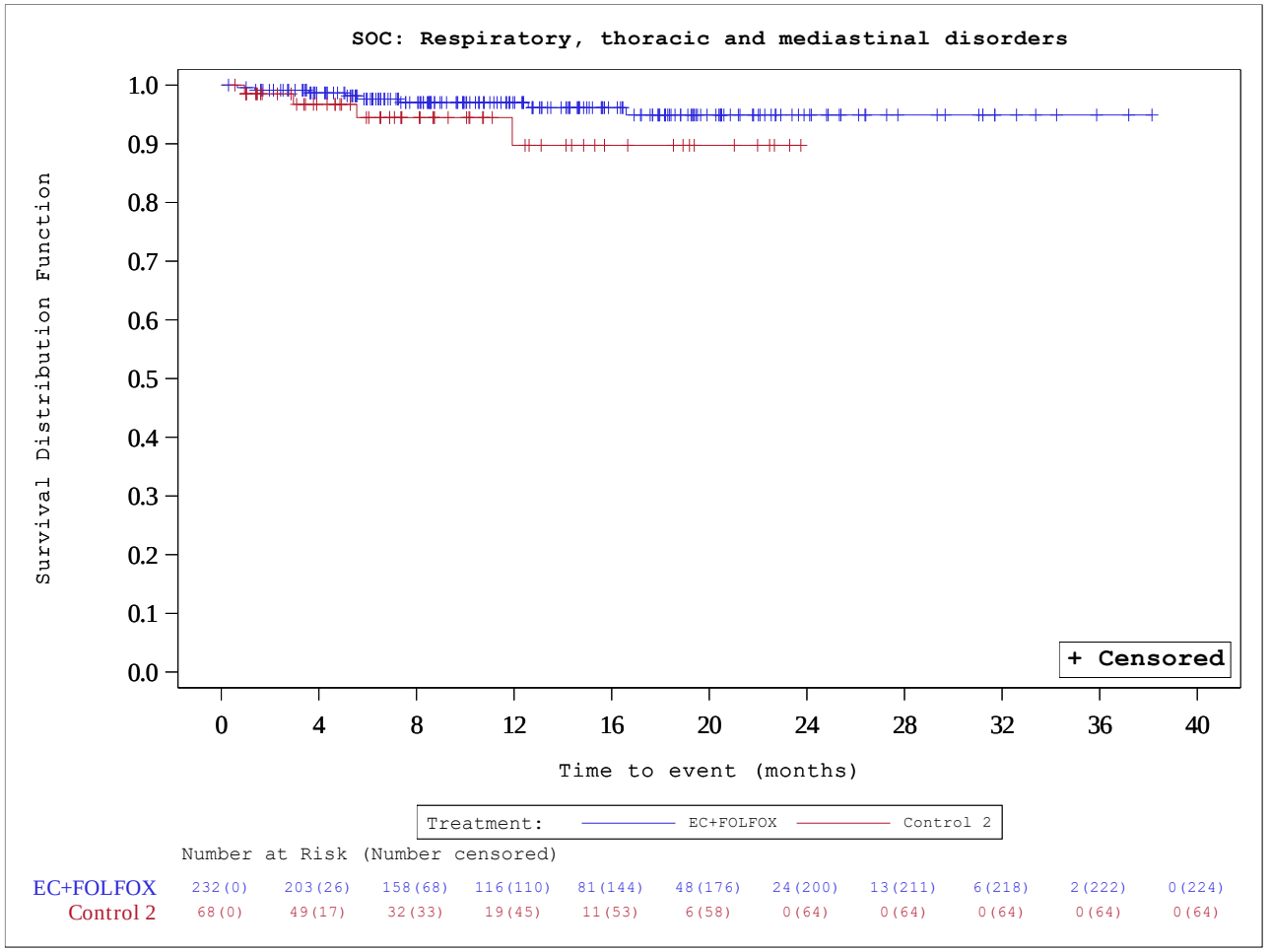
Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
Subgroup analysis was done for SOCs / PTs with significant overall treatment effect (significant log-rank).
Kaplan-Meier Plots for subgroups only created if p-value for interaction < 0.05.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Kaplan Meier Plot of frequent Frequent Serious AE by SOC, PT (incidence >= 5% or >=10 patients and incidence >= 1%)
Safety Analysis Set



Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
Subgroup analysis was done for SOCs / PTs with significant overall treatment effect (significant log-rank).
Kaplan-Meier Plots for subgroups only created if p-value for interaction < 0.05.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Kaplan Meier Plot of frequent Frequent Serious AE by SOC, PT (incidence >= 5% or >=10 patients and incidence >= 1%)
Safety Analysis Set



Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
Subgroup analysis was done for SOCs / PTs with significant overall treatment effect (significant log-rank).
Kaplan-Meier Plots for subgroups only created if p-value for interaction < 0.05.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Frequent Severe AE by SOC, PT (incidence >= 5% or >=10 patients and incidence >= 1%)
Safety Analysis Set

		EC+FOLFOX (N=232)	Control 2 (N=68)
SOC: Blood and lymphatic system disorders	Number of subjects with events, n (%)	67 (28.9)	9 (13.2)
	Number of censored subjects, n (%)	165 (71.1)	59 (86.8)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	6.2 (3.6, 13.8)	NE (10.9, NE)
	Median (95% CI)	NE (NE, NE)	NE (NE, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	2.05 (1.02, 4.12)	
	p-value [3]	0.0380	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.

		EC+FOLFOX (N=232)	Control 2 (N=68)
SOC: Blood and lymphatic system disorders, PT: Anaemia	Number of subjects with events, n (%)	35 (15.1)	1 (1.5)
	Number of censored subjects, n (%)	197 (84.9)	67 (98.5)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	NE (14.3, NE)	NE (NE, NE)
	Median (95% CI)	NE (NE, NE)	NE (NE, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	8.50 (1.16, 62.07)	
	p-value [3]	0.0113	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Frequent Severe AE by SOC, PT (incidence >= 5% or >=10 patients and incidence >= 1%)
Safety Analysis Set

		EC+FOLFOX (N=232)	Control 2 (N=68)
SOC: Blood and lymphatic system disorders, PT: Neutropenia	Number of subjects with events, n (%)	35 (15.1)	8 (11.8)
	Number of censored subjects, n (%)	197 (84.9)	60 (88.2)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	NE (NE, NE)	NE (10.9, NE)
	Median (95% CI)	NE (NE, NE)	NE (NE, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	1.22 (0.56, 2.63)	
	p-value [3]	0.6173	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.

		EC+FOLFOX (N=232)	Control 2 (N=68)
SOC: Gastrointestinal disorders	Number of subjects with events, n (%)	53 (22.8)	20 (29.4)
	Number of censored subjects, n (%)	179 (77.2)	48 (70.6)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	17.4 (10.4, NE)	5.3 (2.5, 14.3)
	Median (95% CI)	NE (NE, NE)	NE (11.8, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	0.63 (0.37, 1.05)	
	p-value [3]	0.0732	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Frequent Severe AE by SOC, PT (incidence >= 5% or >=10 patients and incidence >= 1%)
Safety Analysis Set

		EC+FOLFOX (N=232)	Control 2 (N=68)
SOC: Gastrointestinal disorders, PT: Abdominal pain	Number of subjects with events, n (%)	11 (4.7)	1 (1.5)
	Number of censored subjects, n (%)	221 (95.3)	67 (98.5)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Median (95% CI)	NE (NE, NE)	NE (NE, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	2.57 (0.33, 20.00)	
	p-value [3]	0.3486	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.

		EC+FOLFOX (N=232)	Control 2 (N=68)
SOC: Gastrointestinal disorders, PT: Diarrhoea	Number of subjects with events, n (%)	3 (1.3)	6 (8.8)
	Number of censored subjects, n (%)	229 (98.7)	62 (91.2)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Median (95% CI)	NE (NE, NE)	NE (NE, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	0.12 (0.03, 0.48)	
	p-value [3]	0.0003	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.

		EC+FOLFOX (N=232)	Control 2 (N=68)
SOC: Gastrointestinal disorders, PT: Intestinal obstruction	Number of subjects with events, n (%)	12 (5.2)	5 (7.4)
	Number of censored subjects, n (%)	220 (94.8)	63 (92.6)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	NE (NE, NE)	NE (14.3, NE)
	Median (95% CI)	NE (NE, NE)	NE (NE, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	0.50 (0.17, 1.44)	
	p-value [3]	0.1870	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.

		EC+FOLFOX (N=232)	Control 2 (N=68)
SOC: General disorders and administration site conditions	Number of subjects with events, n (%)	36 (15.5)	11 (16.2)
	Number of censored subjects, n (%)	196 (84.5)	57 (83.8)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	NE (19.7, NE)	11.1 (7.0, NE)
	Median (95% CI)	NE (NE, NE)	NE (NE, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	0.77 (0.39, 1.51)	
	p-value [3]	0.4408	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.

		EC+FOLFOX (N=232)	Control 2 (N=68)
SOC: General disorders and administration site conditions, PT: Asthenia	Number of subjects with events, n (%)	12 (5.2)	3 (4.4)
	Number of censored subjects, n (%)	220 (94.8)	65 (95.6)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Median (95% CI)	NE (NE, NE)	NE (NE, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	0.95 (0.27, 3.39)	
	p-value [3]	0.9386	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.

		EC+FOLFOX (N=232)	Control 2 (N=68)
SOC: Infections and infestations	Number of subjects with events, n (%)	29 (12.5)	3 (4.4)
	Number of censored subjects, n (%)	203 (87.5)	65 (95.6)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	28.8 (23.5, NE)	NE (NE, NE)
	Median (95% CI)	NE (30.0, NE)	NE (NE, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	2.03 (0.61, 6.72)	
	p-value [3]	0.2387	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.

		EC+FOLFOX (N=232)	Control 2 (N=68)
SOC: Injury, poisoning and procedural complications	Number of subjects with events, n (%)	4 (1.7)	4 (5.9)
	Number of censored subjects, n (%)	228 (98.3)	64 (94.1)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	NE (NE, NE)	NE (13.8, NE)
	Median (95% CI)	NE (NE, NE)	NE (NE, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	0.24 (0.06, 0.95)	
	p-value [3]	0.0273	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.

		EC+FOLFOX (N=232)	Control 2 (N=68)
SOC: Investigations	Number of subjects with events, n (%)	88 (37.9)	22 (32.4)
	Number of censored subjects, n (%)	144 (62.1)	46 (67.6)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	1.1 (0.6, 2.0)	5.1 (2.3, 14.1)
	Median (95% CI)	NE (NE, NE)	19.5 (11.3, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (19.5, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	1.22 (0.76, 1.94)	
	p-value [3]	0.4206	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.

		EC+FOLFOX (N=232)	Control 2 (N=68)
SOC: Investigations, PT: Lipase increased	Number of subjects with events, n (%)	40 (17.2)	4 (5.9)
	Number of censored subjects, n (%)	192 (82.8)	64 (94.1)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Median (95% CI)	NE (NE, NE)	NE (NE, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	2.87 (1.03, 8.01)	
	p-value [3]	0.0355	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.

		EC+FOLFOX (N=232)	Control 2 (N=68)
SOC: Investigations, PT: Neutrophil count decreased	Number of subjects with events, n (%)	44 (19.0)	14 (20.6)
	Number of censored subjects, n (%)	188 (81.0)	54 (79.4)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	NE (NE, NE)	19.5 (2.8, NE)
	Median (95% CI)	NE (NE, NE)	NE (19.5, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	0.91 (0.50, 1.65)	
	p-value [3]	0.7352	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.

		EC+FOLFOX (N=232)	Control 2 (N=68)
SOC: Investigations, PT: White blood cell count decreased	Number of subjects with events, n (%)	13 (5.6)	2 (2.9)
	Number of censored subjects, n (%)	219 (94.4)	66 (97.1)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	NE (NE, NE)	NE (19.5, NE)
	Median (95% CI)	NE (NE, NE)	NE (NE, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	1.83 (0.41, 8.12)	
	p-value [3]	0.4202	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.

		EC+FOLFOX (N=232)	Control 2 (N=68)
SOC: Metabolism and nutrition disorders	Number of subjects with events, n (%)	23 (9.9)	6 (8.8)
	Number of censored subjects, n (%)	209 (90.1)	62 (91.2)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	NE (30.1, NE)	NE (NE, NE)
	Median (95% CI)	NE (NE, NE)	NE (NE, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	0.91 (0.37, 2.24)	
	p-value [3]	0.8315	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.

		EC+FOLFOX (N=232)	Control 2 (N=68)
SOC: Nervous system disorders	Number of subjects with events, n (%)	61 (26.3)	5 (7.4)
	Number of censored subjects, n (%)	171 (73.7)	63 (92.6)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	6.5 (5.7, NE)	NE (14.5, NE)
	Median (95% CI)	NE (NE, NE)	NE (NE, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	3.33 (1.34, 8.29)	
	p-value [3]	0.0060	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.

		EC+FOLFOX (N=232)	Control 2 (N=68)
SOC: Nervous system disorders, PT: Neuropathy peripheral	Number of subjects with events, n (%)	18 (7.8)	0 (0.0)
	Number of censored subjects, n (%)	214 (92.2)	68 (100.0)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Median (95% CI)	NE (NE, NE)	NE (NE, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	NE	
	p-value [3]		

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Frequent Severe AE by SOC, PT (incidence >= 5% or >=10 patients and incidence >= 1%)
Safety Analysis Set

		EC+FOLFOX (N=232)	Control 2 (N=68)
SOC: Nervous system disorders, PT: Neurotoxicity	Number of subjects with events, n (%)	13 (5.6)	0 (0.0)
	Number of censored subjects, n (%)	219 (94.4)	68 (100.0)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Median (95% CI)	NE (NE, NE)	NE (NE, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	NE	
	p-value [3]		

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.

		EC+FOLFOX (N=232)	Control 2 (N=68)
SOC: Nervous system disorders, PT: Paraesthesia	Number of subjects with events, n (%)	10 (4.3)	0 (0.0)
	Number of censored subjects, n (%)	222 (95.7)	68 (100.0)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Median (95% CI)	NE (NE, NE)	NE (NE, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	NE	
	p-value [3]		

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Frequent Severe AE by SOC, PT (incidence >= 5% or >=10 patients and incidence >= 1%)
Safety Analysis Set

		EC+FOLFOX (N=232)	Control 2 (N=68)
SOC: Nervous system disorders, PT: Peripheral sensory neuropathy	Number of subjects with events, n (%)	16 (6.9)	1 (1.5)
	Number of censored subjects, n (%)	216 (93.1)	67 (98.5)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Median (95% CI)	NE (NE, NE)	NE (NE, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	3.90 (0.52, 29.39)	
	p-value [3]	0.1547	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.

		EC+FOLFOX (N=232)	Control 2 (N=68)
SOC: Respiratory, thoracic and mediastinal disorders	Number of subjects with events, n (%)	12 (5.2)	8 (11.8)
	Number of censored subjects, n (%)	220 (94.8)	60 (88.2)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	NE (NE, NE)	19.8 (11.9, NE)
	Median (95% CI)	NE (NE, NE)	NE (19.8, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	0.33 (0.13, 0.82)	
	p-value [3]	0.0116	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Frequent Severe AE by SOC, PT (incidence >= 5% or >=10 patients and incidence >= 1%)
Safety Analysis Set

		EC+FOLFOX (N=232)	Control 2 (N=68)
SOC: Respiratory, thoracic and mediastinal disorders, PT: Pulmonary embolism	Number of subjects with events, n (%)	6 (2.6)	7 (10.3)
	Number of censored subjects, n (%)	226 (97.4)	61 (89.7)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	NE (NE, NE)	19.8 (19.8, NE)
	Median (95% CI)	NE (NE, NE)	NE (19.8, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	0.19 (0.06, 0.58)	
	p-value [3]	0.0011	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.

		EC+FOLFOX (N=232)	Control 2 (N=68)
SOC: Skin and subcutaneous tissue disorders	Number of subjects with events, n (%)	16 (6.9)	0 (0.0)
	Number of censored subjects, n (%)	216 (93.1)	68 (100.0)
	Kaplan-Meier estimates of Time to Event (months) [1]		
	25%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Median (95% CI)	NE (NE, NE)	NE (NE, NE)
	75%-ile (95% CI)	NE (NE, NE)	NE (NE, NE)
	Unstratified analysis		
	Hazard Ratio (95% CI) [2]	NE	
	p-value [3]		

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Frequent Severe AE by SOC, PT (incidence >= 5% or >=10 patients and incidence >= 1%) - Subgroup analysis
Safety Analysis Set

SOC/PT	Subgroup Level	EC+FOLFOX (N=232) n/ N (%)	EC+FOLFOX (N=232) Median (95% CI)[1]	Control 2 (N=68) n/ N (%)	Control 2 (N=68) Median (95% CI)[1]	Unstratified analysis Hazard Ratio (95% CI)[2]	Unstratified analysis p-Value[3]	Interaction p-Value[4]
SOC: Blood and lymphatic system disorders	Age (Years)							0.2946
	< 65	36/ 148 (24.3)	NE (NE , NE)	3/ 42 (7.1)	NE (NE , NE)	3.27 (1.01, 10.62)	0.0362	
	>= 65	31/ 84 (36.9)	NE (10.6, NE)	6/ 26 (23.1)	NE (10.9, NE)	1.46 (0.61, 3.52)	0.3876	
	Sex							0.2118
	Male	22/ 121 (18.2)	NE (NE , NE)	4/ 32 (12.5)	NE (NE , NE)	1.24 (0.42, 3.59)	0.6949	
	Female	45/ 111 (40.5)	NE (9.7, NE)	5/ 36 (13.9)	NE (NE , NE)	3.06 (1.21, 7.70)	0.0124	
	Region							0.8148
	Europe	33/ 108 (30.6)	NE (NE , NE)	6/ 38 (15.8)	NE (NE , NE)	1.83 (0.77, 4.37)	0.1626	
	USA/Canada	5/ 15 (33.3)	NE (6.3, NE)	1/ 7 (14.3)	NE (NE , NE)	2.40 (0.28, 20.56)	0.4125	
	Rest of World	29/ 109 (26.6)	NE (NE , NE)	2/ 23 (8.7)	NE (NE , NE)	2.80 (0.67, 11.77)	0.1410	
	ECOG-PS at Randomization							0.6091
	0	32/ 130 (24.6)	NE (NE , NE)	6/ 44 (13.6)	NE (NE , NE)	1.66 (0.69, 3.97)	0.2470	
	1	35/ 102 (34.3)	NE (10.6, NE)	3/ 24 (12.5)	NE (NE , NE)	2.58 (0.79, 8.41)	0.1001	
	Number of Organs Involved							0.6117
	<= 2	34/ 116 (29.3)	NE (NE , NE)	4/ 33 (12.1)	NE (NE , NE)	2.48 (0.88, 6.98)	0.0754	
	>= 3	33/ 116 (28.4)	NE (NE , NE)	5/ 35 (14.3)	NE (NE , NE)	1.73 (0.67, 4.46)	0.2437	
	Presence of Liver Metastases							0.9836
	Yes	49/ 146 (33.6)	NE (13.8, NE)	9/ 42 (21.4)	NE (10.9, NE)	1.41 (0.69, 2.88)	0.3336	
	No	18/ 86 (20.9)	NE (NE , NE)	0/ 26 (0.0)	NE (NE , NE)	NE		
	Side of Tumor							0.5414
	Left	23/ 88 (26.1)	NE (NE , NE)	3/ 33 (9.1)	NE (NE , NE)	2.65 (0.79, 8.83)	0.0994	
	Right	44/ 144 (30.6)	NE (NE , NE)	6/ 35 (17.1)	NE (NE , NE)	1.69 (0.72, 3.98)	0.2171	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
Subgroup analysis was done for SOCs / PTs with significant overall treatment effect (significant log-rank).
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.
[4] P-Value for interaction from Cox proportional hazards model using ties=exact option with treatment, subgroup and treatment*subgroup interaction as covariates.
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Frequent Severe AE by SOC, PT (incidence >= 5% or >=10 patients and incidence >= 1%) - Subgroup analysis
Safety Analysis Set

SOC/PT	Subgroup Level	EC+FOLFOX (N=232) n/ N (%)	EC+FOLFOX (N=232) Median (95% CI)[1]	Control 2 (N=68) n/ N (%)	Control 2 (N=68) Median (95% CI)[1]	Unstratified analysis Hazard Ratio (95% CI)[2]	Unstratified analysis p-Value[3]	Interaction p-Value[4]
SOC: Blood and lymphatic system disorders, PT: Anaemia	Age (Years)							0.9907
	< 65	19/ 148 (12.8)	NE (NE , NE)	1/ 42 (2.4)	NE (NE , NE)	4.40 (0.59, 32.87)	0.1146	
	>= 65	16/ 84 (19.0)	NE (NE , NE)	0/ 26 (0.0)	NE (NE , NE)	NE		
	Sex							0.9880
	Male	12/ 121 (9.9)	NE (NE , NE)	1/ 32 (3.1)	NE (NE , NE)	2.47 (0.32, 19.06)	0.3681	
	Female	23/ 111 (20.7)	NE (NE , NE)	0/ 36 (0.0)	NE (NE , NE)	NE		
	Region							0.9999
	Europe	12/ 108 (11.1)	NE (NE , NE)	1/ 38 (2.6)	NE (NE , NE)	3.24 (0.42, 25.00)	0.2323	
	USA/Canada	2/ 15 (13.3)	NE (NE , NE)	0/ 7 (0.0)	NE (NE , NE)	NE		
	Rest of World	21/ 109 (19.3)	NE (NE , NE)	0/ 23 (0.0)	NE (NE , NE)	NE		
	ECOG-PS at Randomization							0.9881
	0	13/ 130 (10.0)	NE (NE , NE)	0/ 44 (0.0)	NE (NE , NE)	NE		
	1	22/ 102 (21.6)	NE (NE , NE)	1/ 24 (4.2)	NE (NE , NE)	3.87 (0.52, 28.80)	0.1547	
	Number of Organs Involved							0.9885
	<= 2	14/ 116 (12.1)	NE (NE , NE)	0/ 33 (0.0)	NE (NE , NE)	NE		
	>= 3	21/ 116 (18.1)	NE (NE , NE)	1/ 35 (2.9)	NE (NE , NE)	4.41 (0.59, 32.99)	0.1137	
	Presence of Liver Metastases							0.9906
	Yes	26/ 146 (17.8)	NE (NE , NE)	1/ 42 (2.4)	NE (NE , NE)	5.98 (0.81, 44.09)	0.0458	
	No	9/ 86 (10.5)	NE (NE , NE)	0/ 26 (0.0)	NE (NE , NE)	NE		
	Side of Tumor							0.9897
	Left	12/ 88 (13.6)	NE (NE , NE)	0/ 33 (0.0)	NE (NE , NE)	NE		
	Right	23/ 144 (16.0)	NE (NE , NE)	1/ 35 (2.9)	NE (NE , NE)	4.76 (0.64, 35.29)	0.0915	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
Subgroup analysis was done for SOCs / PTs with significant overall treatment effect (significant log-rank).
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.
[4] P-Value for interaction from Cox proportional hazards model using ties=exact option with treatment, subgroup and treatment*subgroup interaction as covariates.
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

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Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Frequent Severe AE by SOC, PT (incidence >= 5% or >=10 patients and incidence >= 1%) - Subgroup analysis
Safety Analysis Set

SOC/PT	Subgroup Level	EC+FOLFOX (N=232) n/ N (%)	EC+FOLFOX (N=232) Median (95% CI)[1]	Control 2 (N=68) n/ N (%)	Control 2 (N=68) Median (95% CI)[1]	Unstratified analysis Hazard Ratio (95% CI)[2]	Unstratified analysis p-Value[3]	Interaction p-Value[4]
SOC: Gastrointestinal disorders, PT: Diarrhoea	Age (Years)							
	< 65	2/ 148 (1.4)		3/ 42 (7.1)				
	>= 65	1/ 84 (1.2)		3/ 26 (11.5)				
	Sex							
	Male	2/ 121 (1.7)		3/ 32 (9.4)				
	Female	1/ 111 (0.9)		3/ 36 (8.3)				
	Region							
	Europe	0/ 108 (0.0)		5/ 38 (13.2)				
	USA/Canada	1/ 15 (6.7)		0/ 7 (0.0)				
	Rest of World	2/ 109 (1.8)		1/ 23 (4.3)				
	ECOG-PS at Randomization							
	0	1/ 130 (0.8)		2/ 44 (4.5)				
	1	2/ 102 (2.0)		4/ 24 (16.7)				
	Number of Organs Involved							
	<= 2	2/ 116 (1.7)		2/ 33 (6.1)				
	>= 3	1/ 116 (0.9)		4/ 35 (11.4)				
	Presence of Liver Metastases							
	Yes	3/ 146 (2.1)		4/ 42 (9.5)				
	No	0/ 86 (0.0)		2/ 26 (7.7)				
	Side of Tumor							
	Left	0/ 88 (0.0)		3/ 33 (9.1)				
	Right	3/ 144 (2.1)		3/ 35 (8.6)				

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
Subgroup analysis was done for SOCs / PTs with significant overall treatment effect (significant log-rank).
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.
[4] P-Value for interaction from Cox proportional hazards model using ties=exact option with treatment, subgroup and treatment*subgroup interaction as covariates.
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

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Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Frequent Severe AE by SOC, PT (incidence >= 5% or >=10 patients and incidence >= 1%) - Subgroup analysis
Safety Analysis Set

SOC/PT	Subgroup Level	EC+FOLFOX (N=232) n/ N (%)	EC+FOLFOX (N=232) Median (95% CI)[1]	Control 2 (N=68) n/ N (%)	Control 2 (N=68) Median (95% CI)[1]	Unstratified analysis Hazard Ratio (95% CI)[2]	Unstratified analysis p-Value[3]	Interaction p-Value[4]
SOC: Injury, poisoning and procedural complications	Age (Years)							
	< 65	1/ 148 (0.7)		3/ 42 (7.1)				
	>= 65	3/ 84 (3.6)		1/ 26 (3.8)				
	Sex							
	Male	4/ 121 (3.3)		2/ 32 (6.3)				
	Female	0/ 111 (0.0)		2/ 36 (5.6)				
	Region							
	Europe	0/ 108 (0.0)		3/ 38 (7.9)				
	USA/Canada	0/ 15 (0.0)		0/ 7 (0.0)				
	Rest of World	4/ 109 (3.7)		1/ 23 (4.3)				
	ECOG-PS at Randomization							
	0	1/ 130 (0.8)		4/ 44 (9.1)				
	1	3/ 102 (2.9)		0/ 24 (0.0)				
	Number of Organs Involved							
	<= 2	3/ 116 (2.6)		2/ 33 (6.1)				
	>= 3	1/ 116 (0.9)		2/ 35 (5.7)				
	Presence of Liver Metastases							
	Yes	3/ 146 (2.1)		2/ 42 (4.8)				
	No	1/ 86 (1.2)		2/ 26 (7.7)				
	Side of Tumor							
	Left	1/ 88 (1.1)		3/ 33 (9.1)				
	Right	3/ 144 (2.1)		1/ 35 (2.9)				

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
Subgroup analysis was done for SOCs / PTs with significant overall treatment effect (significant log-rank).
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.
[4] P-Value for interaction from Cox proportional hazards model using ties=exact option with treatment, subgroup and treatment*subgroup interaction as covariates.
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Frequent Severe AE by SOC, PT (incidence >= 5% or >=10 patients and incidence >= 1%) - Subgroup analysis
Safety Analysis Set

SOC/PT	Subgroup Level	EC+FOLFOX (N=232) n/ N (%)	EC+FOLFOX (N=232) Median (95% CI)[1]	Control 2 (N=68) n/ N (%)	Control 2 (N=68) Median (95% CI)[1]	Unstratified analysis Hazard Ratio (95% CI)[2]	Unstratified analysis p-Value[3]	Interaction p-Value[4]
SOC: Investigations, PT: Lipase increased	Age (Years)							0.6314
	< 65	26/ 148 (17.6)	NE (NE , NE)	3/ 42 (7.1)	NE (NE , NE)	2.39 (0.72, 7.88)	0.1416	
	>= 65	14/ 84 (16.7)	NE (NE , NE)	1/ 26 (3.8)	NE (NE , NE)	4.19 (0.55, 31.89)	0.1322	
	Sex							0.3651
	Male	23/ 121 (19.0)	NE (NE , NE)	3/ 32 (9.4)	NE (NE , NE)	1.85 (0.55, 6.16)	0.3100	
	Female	17/ 111 (15.3)	NE (NE , NE)	1/ 36 (2.8)	NE (NE , NE)	5.64 (0.75, 42.40)	0.0575	
	Region							0.9895
	Europe	16/ 108 (14.8)	NE (NE , NE)	2/ 38 (5.3)	NE (NE , NE)	2.59 (0.60, 11.27)	0.1884	
	USA/Canada	3/ 15 (20.0)	NE (NE , NE)	0/ 7 (0.0)	NE (NE , NE)	NE		
	Rest of World	21/ 109 (19.3)	NE (NE , NE)	2/ 23 (8.7)	NE (11.3, NE)	2.28 (0.53, 9.73)	0.2527	
	ECOG-PS at Randomization							0.6691
	0	22/ 130 (16.9)	NE (NE , NE)	3/ 44 (6.8)	NE (NE , NE)	2.41 (0.72, 8.06)	0.1397	
	1	18/ 102 (17.6)	NE (NE , NE)	1/ 24 (4.2)	NE (NE , NE)	4.15 (0.55, 31.06)	0.1328	
	Number of Organs Involved							0.2333
	<= 2	22/ 116 (19.0)	NE (NE , NE)	1/ 33 (3.0)	NE (NE , NE)	6.66 (0.90, 49.38)	0.0320	
	>= 3	18/ 116 (15.5)	NE (NE , NE)	3/ 35 (8.6)	NE (NE , NE)	1.59 (0.47, 5.43)	0.4515	
	Presence of Liver Metastases							0.8494
	Yes	23/ 146 (15.8)	NE (NE , NE)	2/ 42 (4.8)	NE (NE , NE)	3.16 (0.74, 13.40)	0.0994	
	No	17/ 86 (19.8)	NE (NE , NE)	2/ 26 (7.7)	NE (NE , NE)	2.56 (0.59, 11.08)	0.1930	
	Side of Tumor							0.4654
	Left	14/ 88 (15.9)	NE (NE , NE)	1/ 33 (3.0)	NE (NE , NE)	5.04 (0.66, 38.34)	0.0822	
	Right	26/ 144 (18.1)	NE (NE , NE)	3/ 35 (8.6)	NE (NE , NE)	2.09 (0.63, 6.92)	0.2162	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
Subgroup analysis was done for SOCs / PTs with significant overall treatment effect (significant log-rank).
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.
[4] P-Value for interaction from Cox proportional hazards model using ties=exact option with treatment, subgroup and treatment*subgroup interaction as covariates.
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

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Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Frequent Severe AE by SOC, PT (incidence >= 5% or >=10 patients and incidence >= 1%) - Subgroup analysis
Safety Analysis Set

SOC/PT	Subgroup Level	EC+FOLFOX (N=232) n/ N (%)	EC+FOLFOX (N=232) Median (95% CI)[1]	Control 2 (N=68) n/ N (%)	Control 2 (N=68) Median (95% CI)[1]	Unstratified analysis Hazard Ratio (95% CI)[2]	Unstratified analysis p-Value[3]	Interaction p-Value[4]
SOC: Nervous system disorders	Age (Years)							0.0887
	< 65	40/ 148 (27.0)	NE (NE , NE)	1/ 42 (2.4)	NE (NE , NE)	10.63 (1.46, 77.37)	0.0035	
	>= 65	21/ 84 (25.0)	NE (NE , NE)	4/ 26 (15.4)	NE (14.5, NE)	1.48 (0.51, 4.33)	0.4682	
	Sex							0.7442
	Male	27/ 121 (22.3)	NE (NE , NE)	2/ 32 (6.3)	NE (14.5, NE)	2.81 (0.67, 11.83)	0.1396	
	Female	34/ 111 (30.6)	NE (NE , NE)	3/ 36 (8.3)	NE (NE , NE)	3.93 (1.21, 12.79)	0.0142	
	Region							0.1730
	Europe	39/ 108 (36.1)	NE (8.5, NE)	1/ 38 (2.6)	NE (NE , NE)	13.27 (1.82, 96.60)	0.0009	
	USA/Canada	5/ 15 (33.3)	NE (4.6, NE)	2/ 7 (28.6)	NE (6.5, NE)	1.33 (0.26, 6.98)	0.7316	
	Rest of World	17/ 109 (15.6)	NE (NE , NE)	2/ 23 (8.7)	NE (14.5, NE)	1.63 (0.38, 7.04)	0.5125	
	ECOG-PS at Randomization							0.6300
	0	35/ 130 (26.9)	NE (NE , NE)	4/ 44 (9.1)	NE (NE , NE)	2.87 (1.02, 8.09)	0.0361	
	1	26/ 102 (25.5)	NE (NE , NE)	1/ 24 (4.2)	NE (NE , NE)	5.04 (0.68, 37.16)	0.0774	
	Number of Organs Involved							0.2969
	<= 2	29/ 116 (25.0)	NE (NE , NE)	4/ 33 (12.1)	NE (NE , NE)	2.24 (0.79, 6.39)	0.1199	
	>= 3	32/ 116 (27.6)	NE (NE , NE)	1/ 35 (2.9)	NE (NE , NE)	7.40 (1.01, 54.12)	0.0205	
	Presence of Liver Metastases							0.9030
	Yes	32/ 146 (21.9)	NE (NE , NE)	2/ 42 (4.8)	NE (NE , NE)	3.79 (0.91, 15.83)	0.0490	
	No	29/ 86 (33.7)	NE (9.1, NE)	3/ 26 (11.5)	NE (14.5, NE)	3.28 (1.00, 10.79)	0.0380	
	Side of Tumor							0.3803
	Left	20/ 88 (22.7)	NE (NE , NE)	1/ 33 (3.0)	NE (NE , NE)	6.59 (0.88, 49.08)	0.0336	
	Right	41/ 144 (28.5)	NE (NE , NE)	4/ 35 (11.4)	NE (14.5, NE)	2.41 (0.86, 6.72)	0.0836	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
Subgroup analysis was done for SOCs / PTs with significant overall treatment effect (significant log-rank).
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.
[4] P-Value for interaction from Cox proportional hazards model using ties=exact option with treatment, subgroup and treatment*subgroup interaction as covariates.
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Frequent Severe AE by SOC, PT (incidence >= 5% or >=10 patients and incidence >= 1%) - Subgroup analysis
Safety Analysis Set

SOC/PT	Subgroup Level	EC+FOLFOX (N=232) n/ N (%)	EC+FOLFOX (N=232) Median (95% CI)[1]	Control 2 (N=68) n/ N (%)	Control 2 (N=68) Median (95% CI)[1]	Unstratified analysis Hazard Ratio (95% CI)[2]	Unstratified analysis p-Value[3]	Interaction p-Value[4]
SOC: Respiratory, thoracic and mediastinal disorders	Age (Years)							0.2340
	< 65	6/ 148 (4.1)	NE (NE , NE)	6/ 42 (14.3)	NE (19.8, NE)	0.20 (0.07, 0.64)	0.0025	
	>= 65	6/ 84 (7.1)	NE (NE , NE)	2/ 26 (7.7)	NE (NE , NE)	0.78 (0.16, 3.90)	0.7654	
	Sex							0.9969
	Male	7/ 121 (5.8)	NE (NE , NE)	4/ 32 (12.5)	19.8 (19.8, NE)	0.32 (0.09, 1.11)	0.0593	
	Female	5/ 111 (4.5)	NE (NE , NE)	4/ 36 (11.1)	NE (NE , NE)	0.33 (0.09, 1.22)	0.0809	
	Region							0.1002
	Europe	8/ 108 (7.4)	NE (NE , NE)	2/ 38 (5.3)	19.8 (19.8, NE)	1.07 (0.22, 5.09)	0.9346	
	USA/Canada	3/ 15 (20.0)	NE (NE , NE)	3/ 7 (42.9)	NE (7.0, NE)	0.51 (0.10, 2.59)	0.4124	
	Rest of World	1/ 109 (0.9)	NE (NE , NE)	3/ 23 (13.0)	NE (11.9, NE)	0.04 (0.00, 0.44)	0.0001	
	ECOG-PS at Randomization							0.5375
	0	6/ 130 (4.6)	NE (NE , NE)	4/ 44 (9.1)	NE (19.8, NE)	0.37 (0.10, 1.31)	0.1082	
	1	6/ 102 (5.9)	NE (NE , NE)	4/ 24 (16.7)	NE (11.9, NE)	0.26 (0.07, 0.93)	0.0260	
	Number of Organs Involved							0.2162
	<= 2	7/ 116 (6.0)	NE (NE , NE)	3/ 33 (9.1)	NE (NE , NE)	0.61 (0.16, 2.37)	0.4735	
	>= 3	5/ 116 (4.3)	NE (NE , NE)	5/ 35 (14.3)	19.8 (19.8, NE)	0.19 (0.05, 0.67)	0.0041	
	Presence of Liver Metastases							0.6885
	Yes	7/ 146 (4.8)	NE (NE , NE)	5/ 42 (11.9)	19.8 (19.8, NE)	0.27 (0.08, 0.86)	0.0183	
	No	5/ 86 (5.8)	NE (NE , NE)	3/ 26 (11.5)	NE (NE , NE)	0.44 (0.10, 1.83)	0.2436	
	Side of Tumor							0.8083
	Left	3/ 88 (3.4)	NE (NE , NE)	3/ 33 (9.1)	NE (11.9, NE)	0.25 (0.05, 1.26)	0.0698	
	Right	9/ 144 (6.3)	NE (NE , NE)	5/ 35 (14.3)	NE (19.8, NE)	0.35 (0.12, 1.05)	0.0510	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
Subgroup analysis was done for SOCs / PTs with significant overall treatment effect (significant log-rank).
[1] Based on the Brookmeyer and Crowley method.
[2] Hazard ratio based on Cox proportional hazards model using ties=exact option; under proportional hazards, hazard ratio < 1 indicates reduction in hazard rate in favor of EC+FOLFOX compared to Control 2.
[3] P-value from 2-sided log-rank test.
[4] P-Value for interaction from Cox proportional hazards model using ties=exact option with treatment, subgroup and treatment*subgroup interaction as covariates.
Effect measures are calculated if each subgroup level comprises at least 10 patients and at least 10 events occurred in one of the subgroup levels.

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Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Frequent Severe AE by SOC, PT (incidence >= 5% or >=10 patients and incidence >= 1%) - Subgroup analysis
Safety Analysis Set

SOC/PT	Subgroup Level	EC+FOLFOX (N=232) n/ N (%)	EC+FOLFOX (N=232) Median (95% CI)[1]	Control 2 (N=68) n/ N (%)	Control 2 (N=68) Median (95% CI)[1]	Unstratified analysis Hazard Ratio (95% CI)[2]	Unstratified analysis p-Value[3]	Interaction p-Value[4]
SOC: Respiratory, thoracic and mediastinal disorders, PT: Pulmonary embolism	Age (Years)							
	< 65	4/ 148 (2.7)		5/ 42 (11.9)				
	>= 65	2/ 84 (2.4)		2/ 26 (7.7)				
	Sex							
	Male	4/ 121 (3.3)		4/ 32 (12.5)				
	Female	2/ 111 (1.8)		3/ 36 (8.3)				
	Region							
	Europe	3/ 108 (2.8)		2/ 38 (5.3)				
	USA/Canada	2/ 15 (13.3)		3/ 7 (42.9)				
	Rest of World	1/ 109 (0.9)		2/ 23 (8.7)				
	ECOG-PS at Randomization							
	0	3/ 130 (2.3)		4/ 44 (9.1)				
	1	3/ 102 (2.9)		3/ 24 (12.5)				
	Number of Organs Involved							
	<= 2	4/ 116 (3.4)		2/ 33 (6.1)				
	>= 3	2/ 116 (1.7)		5/ 35 (14.3)				
	Presence of Liver Metastases							
	Yes	4/ 146 (2.7)		5/ 42 (11.9)				
	No	2/ 86 (2.3)		2/ 26 (7.7)				
	Side of Tumor							0.8032
	Left	1/ 88 (1.1)	NE (NE , NE)	2/ 33 (6.1)	NE (NE , NE)	0.14 (0.01, 1.52)	0.0581	
	Right	5/ 144 (3.5)	NE (NE , NE)	5/ 35 (14.3)	NE (19.8, NE)	0.20 (0.06, 0.69)	0.0047	

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
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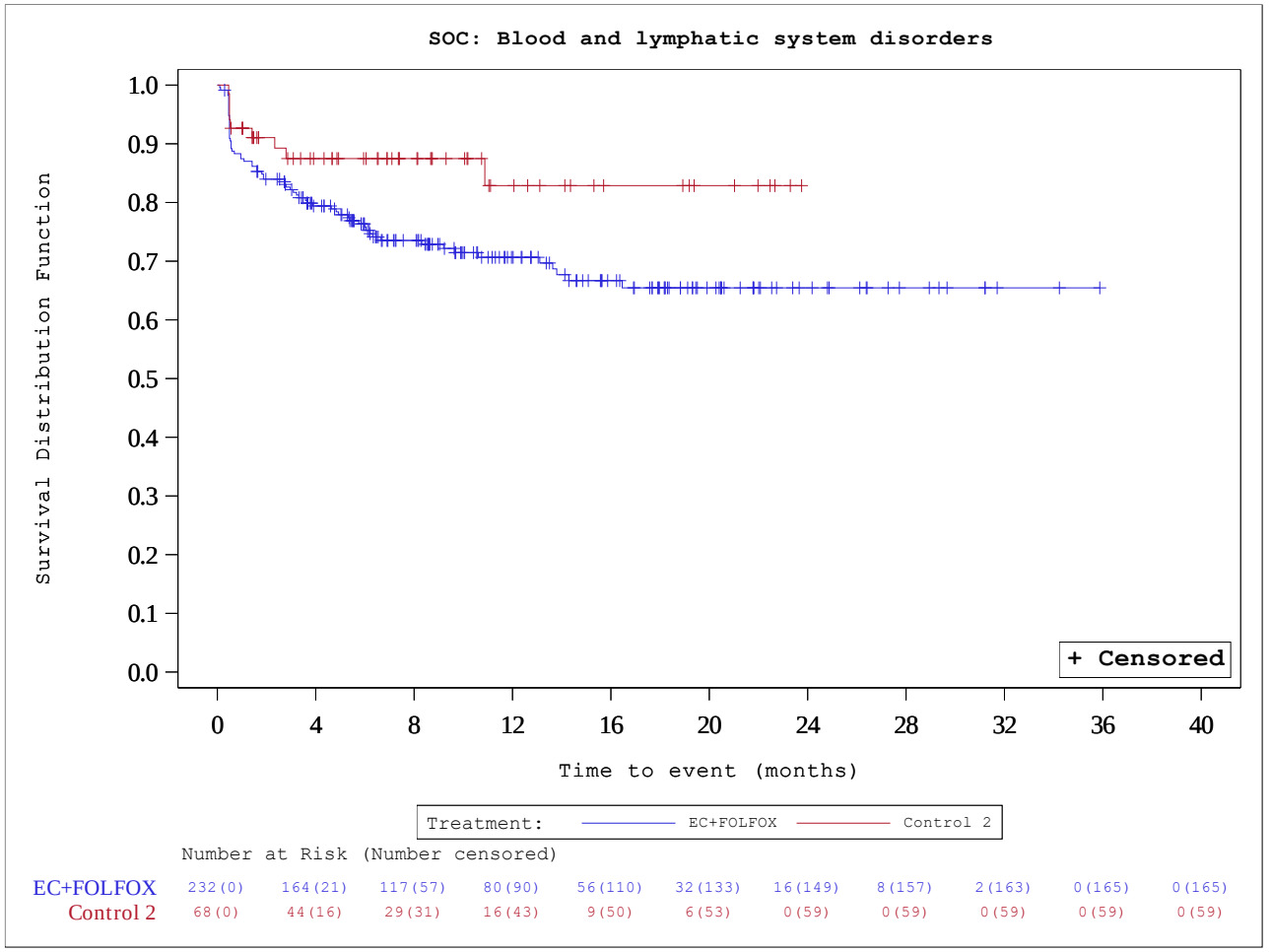
Safety Analysis Set



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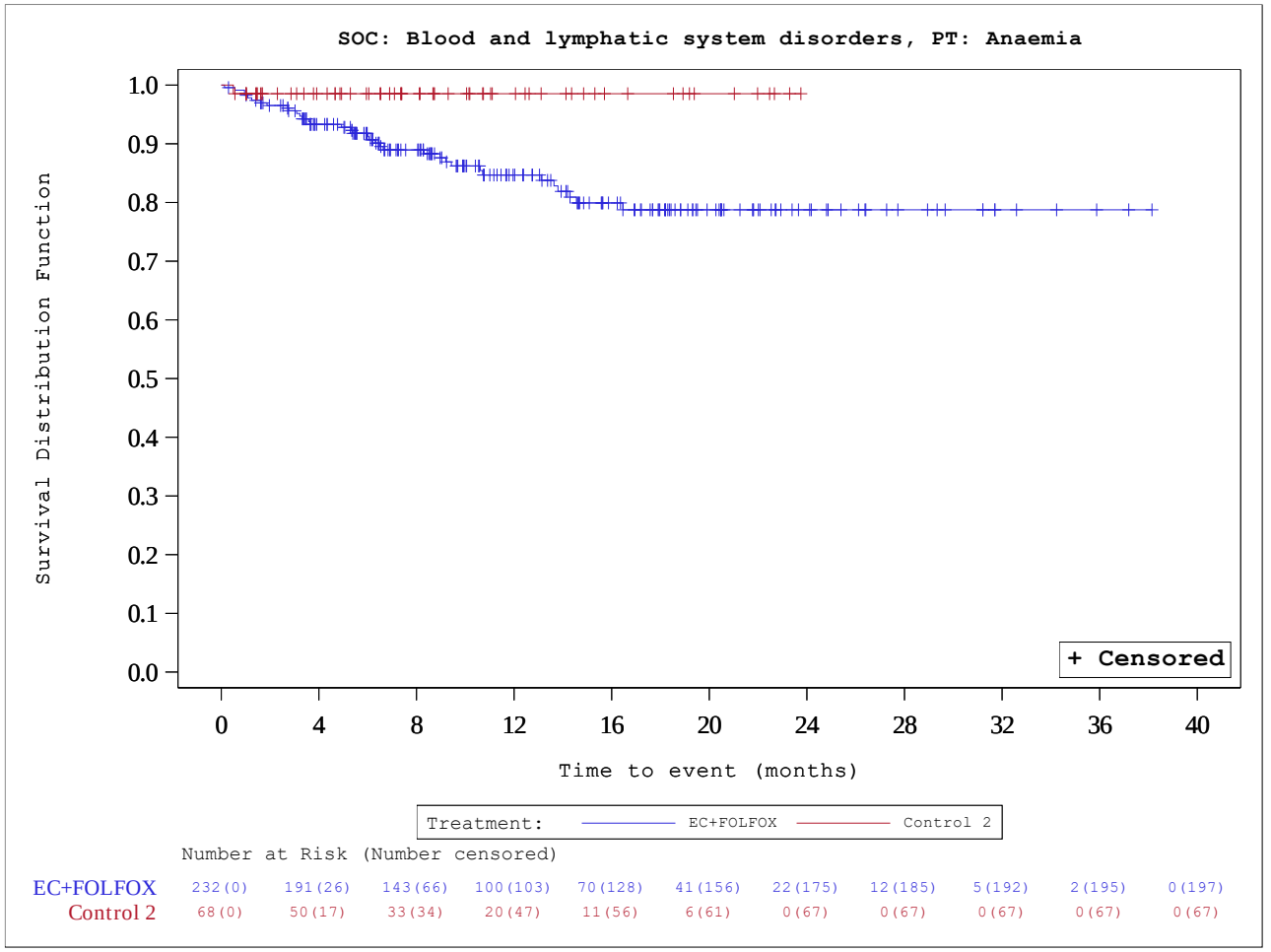

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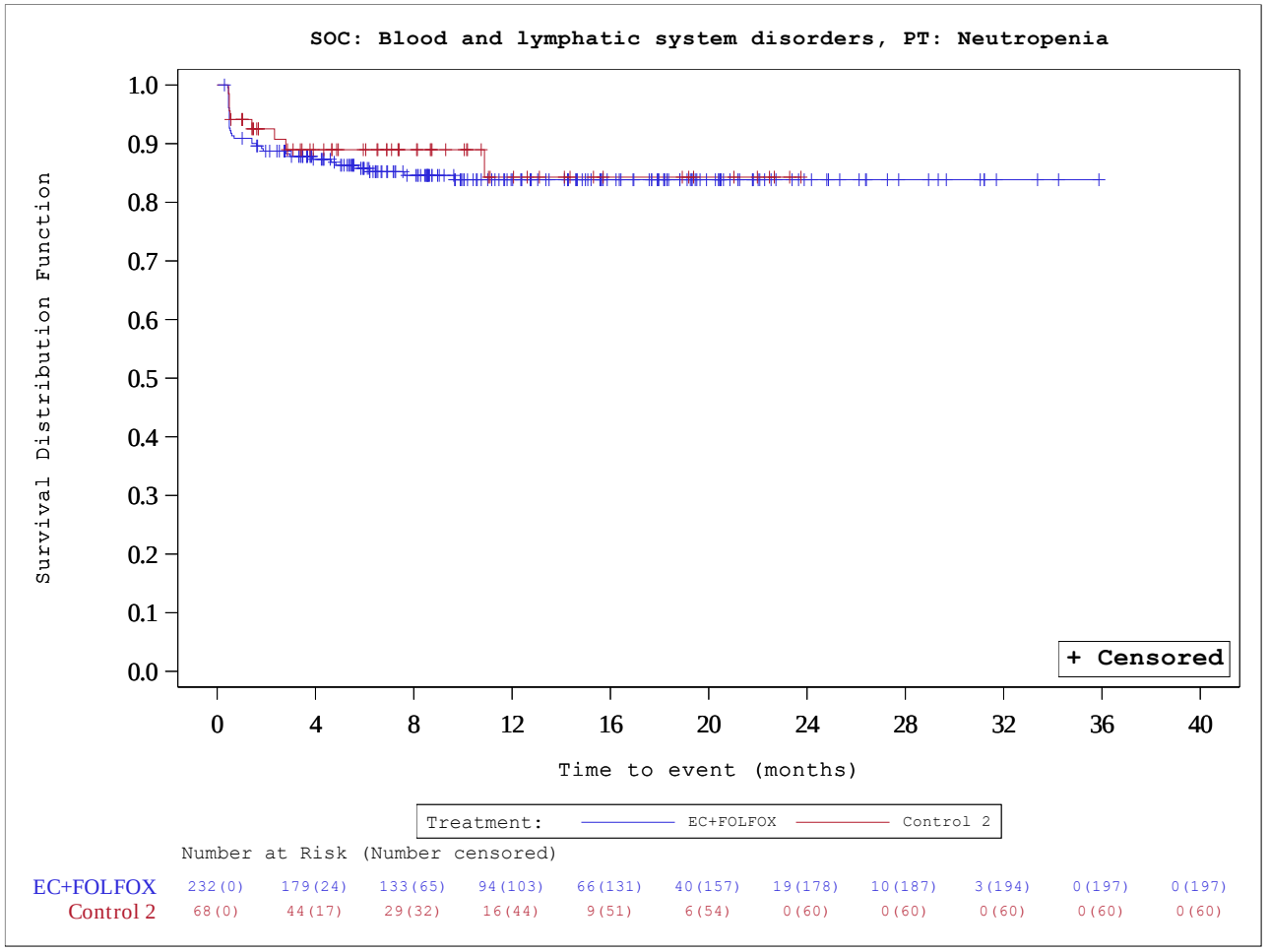

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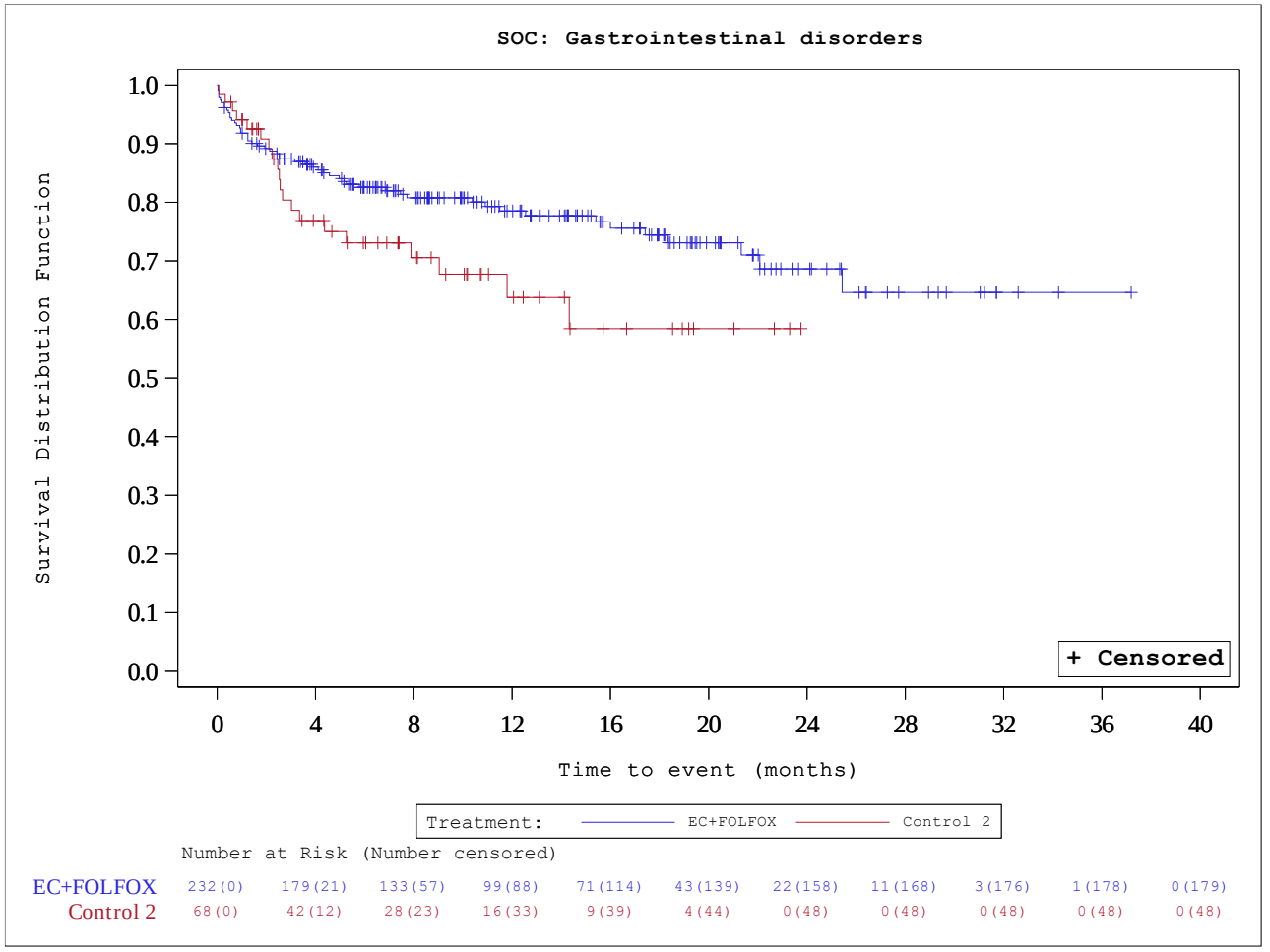

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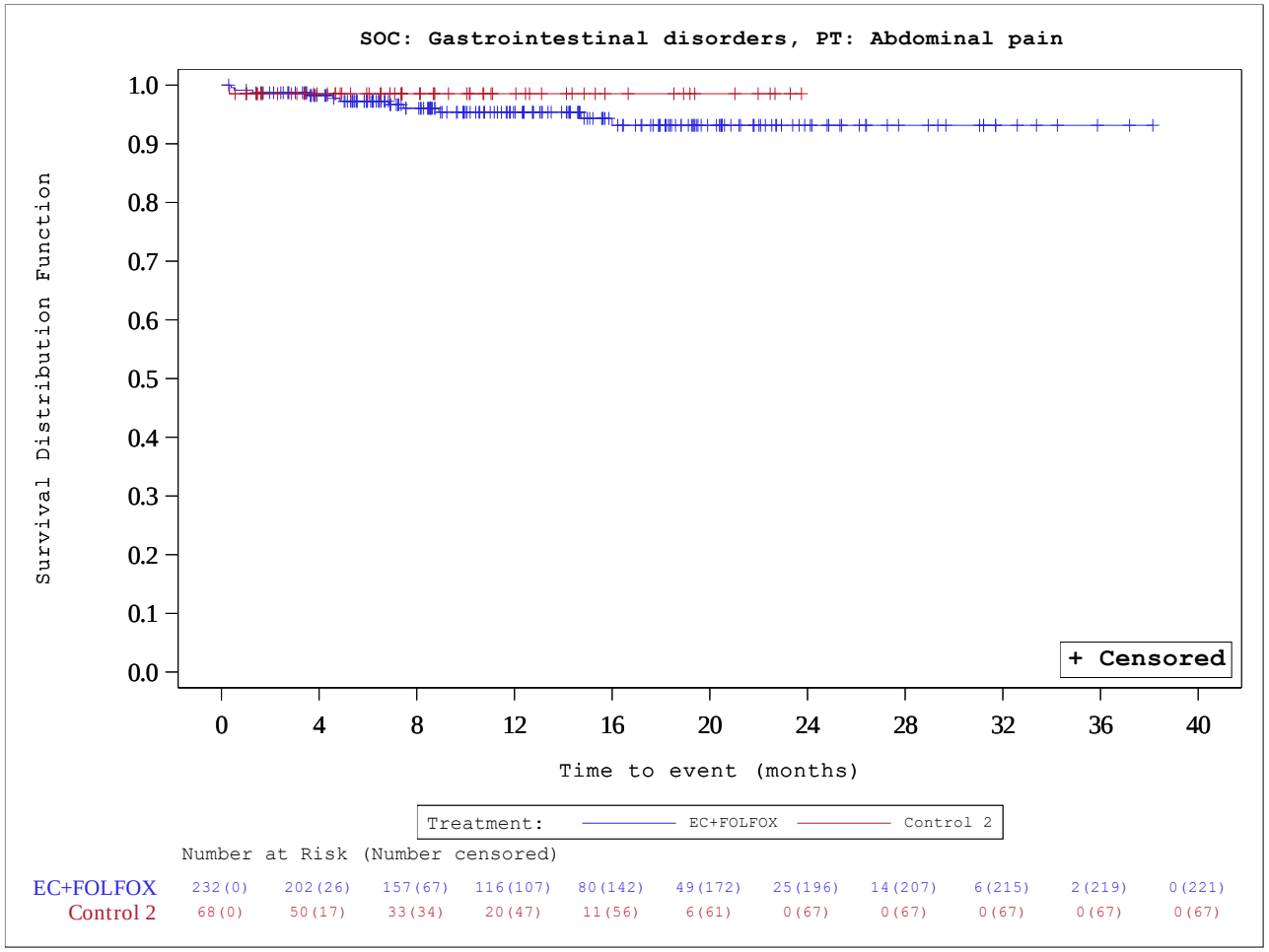

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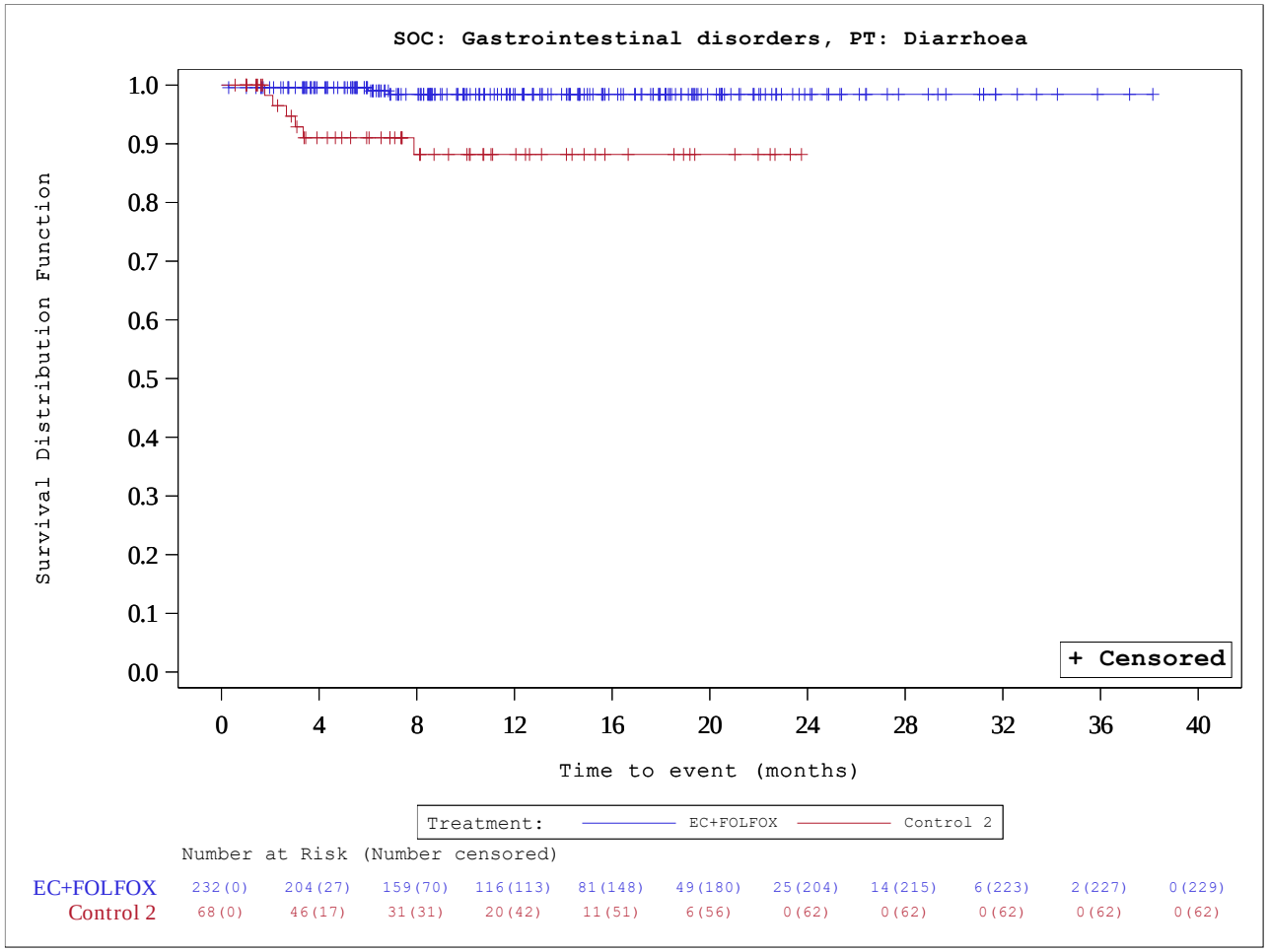

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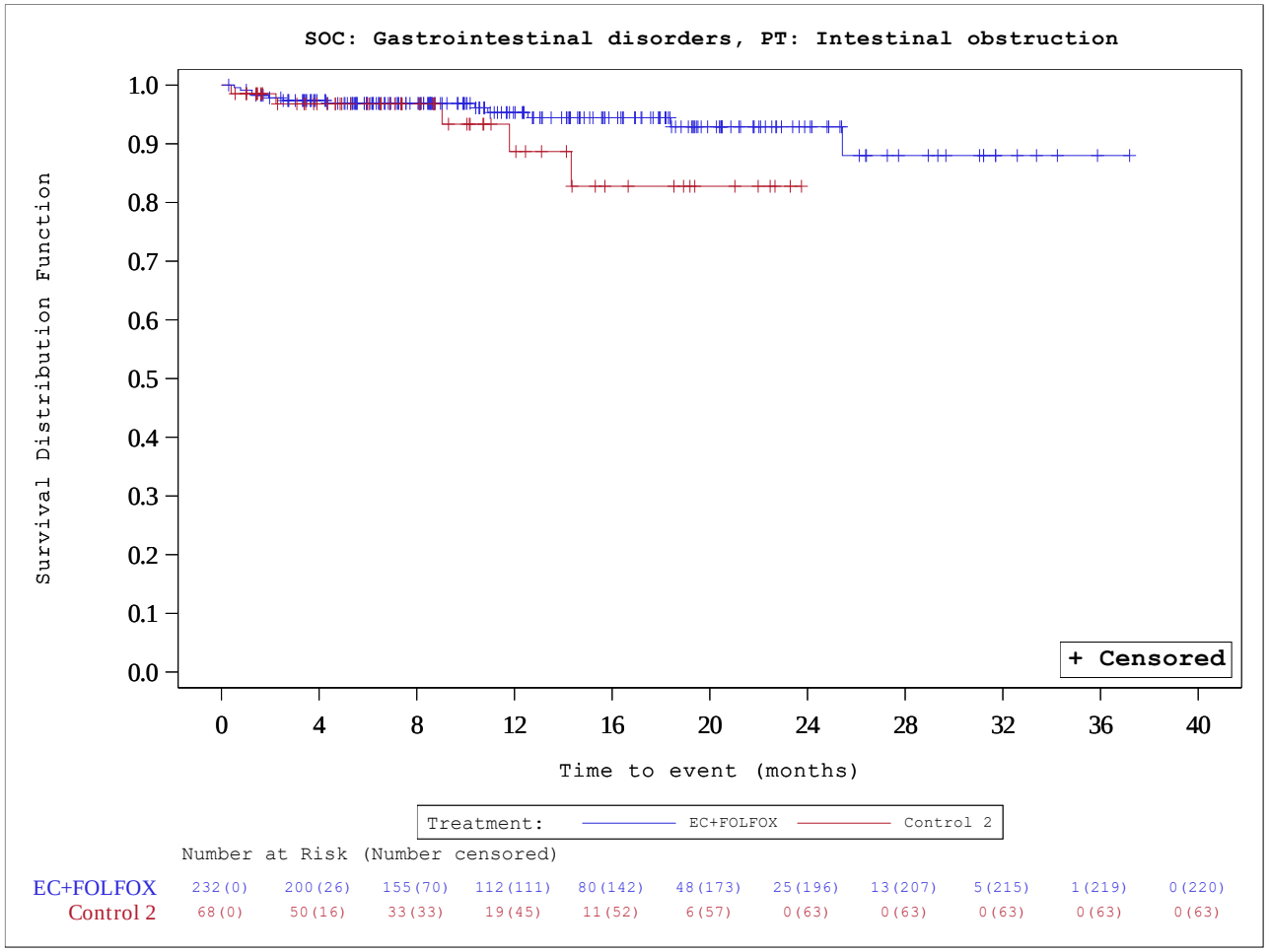

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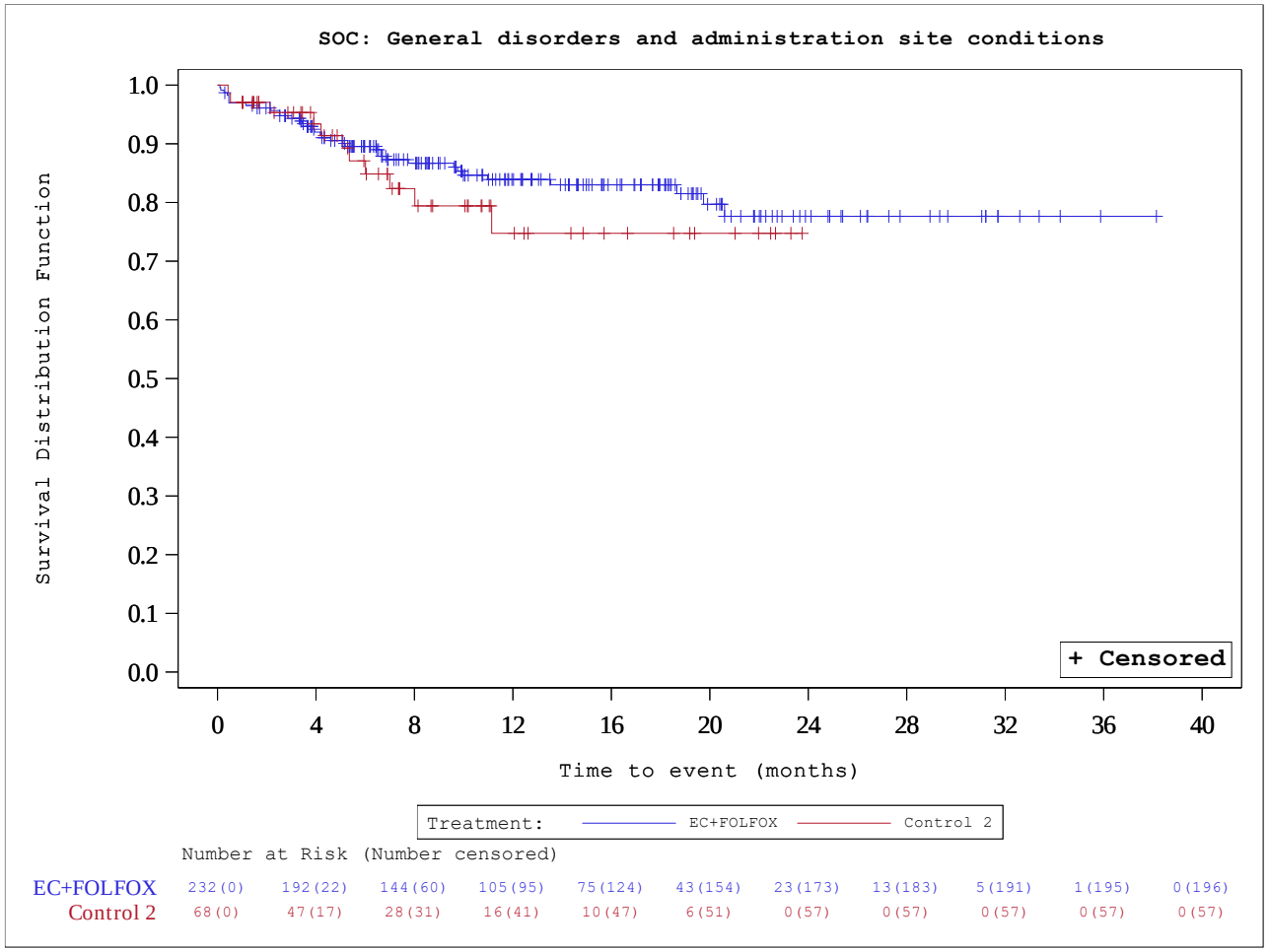

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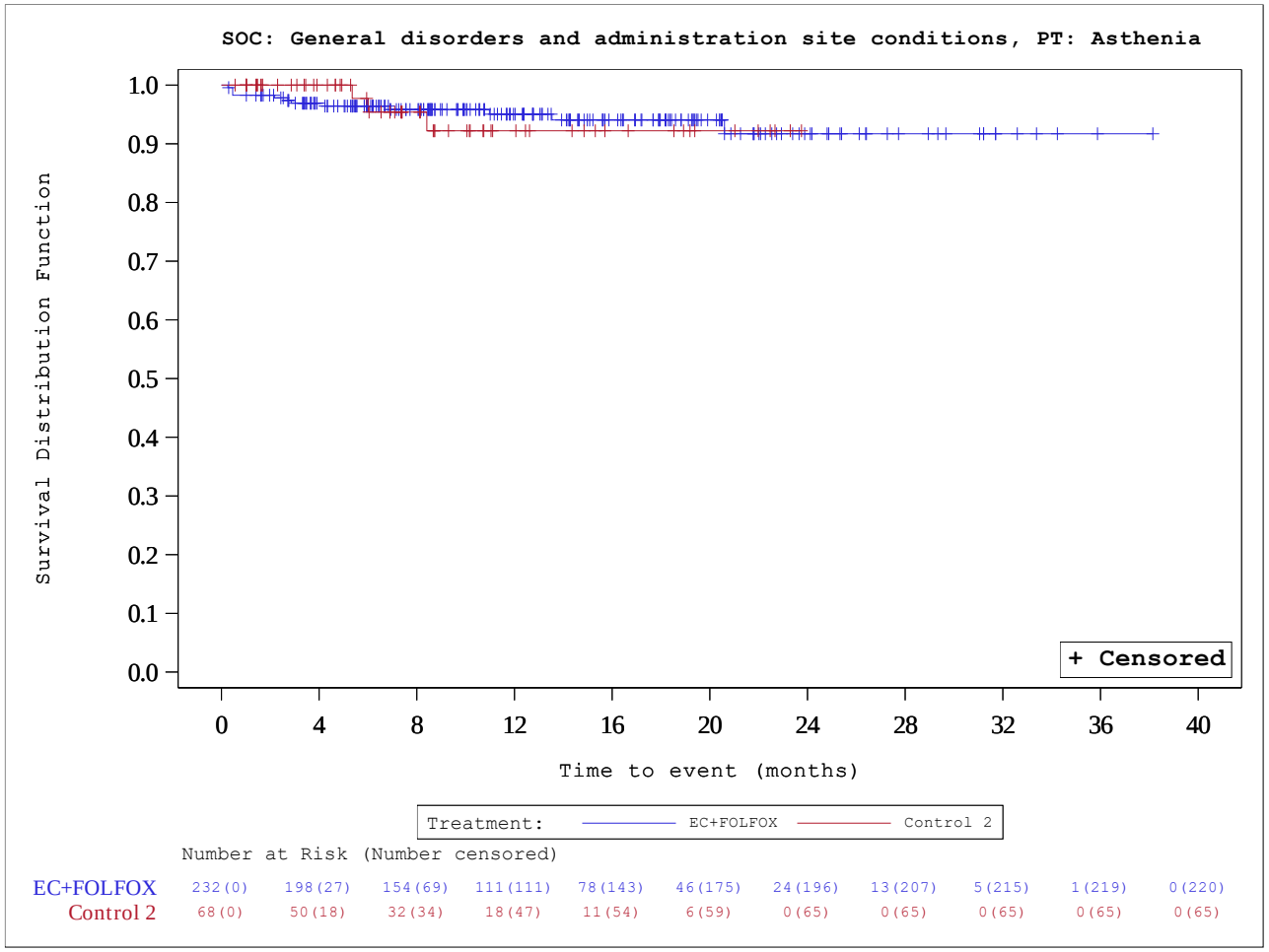

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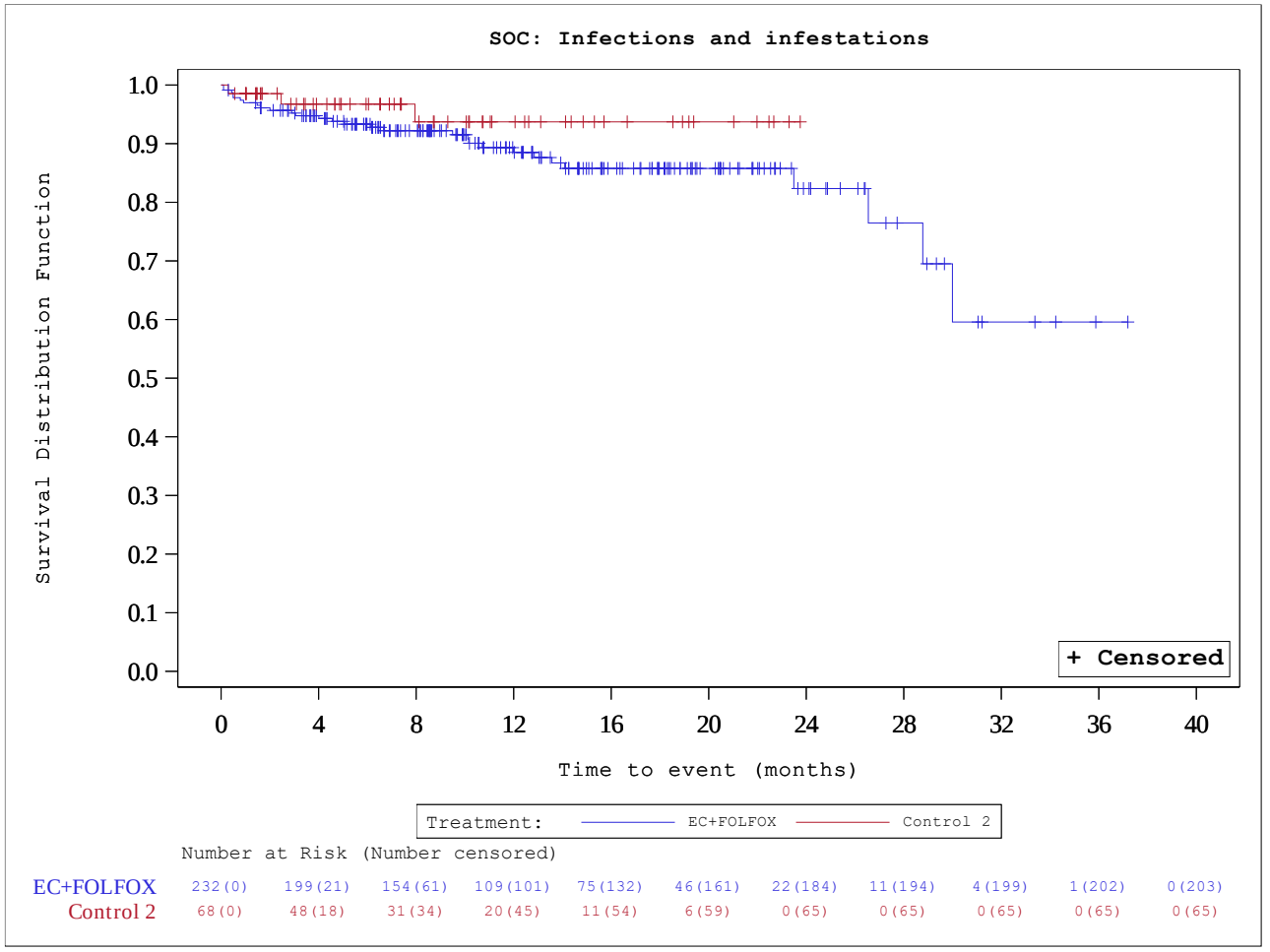

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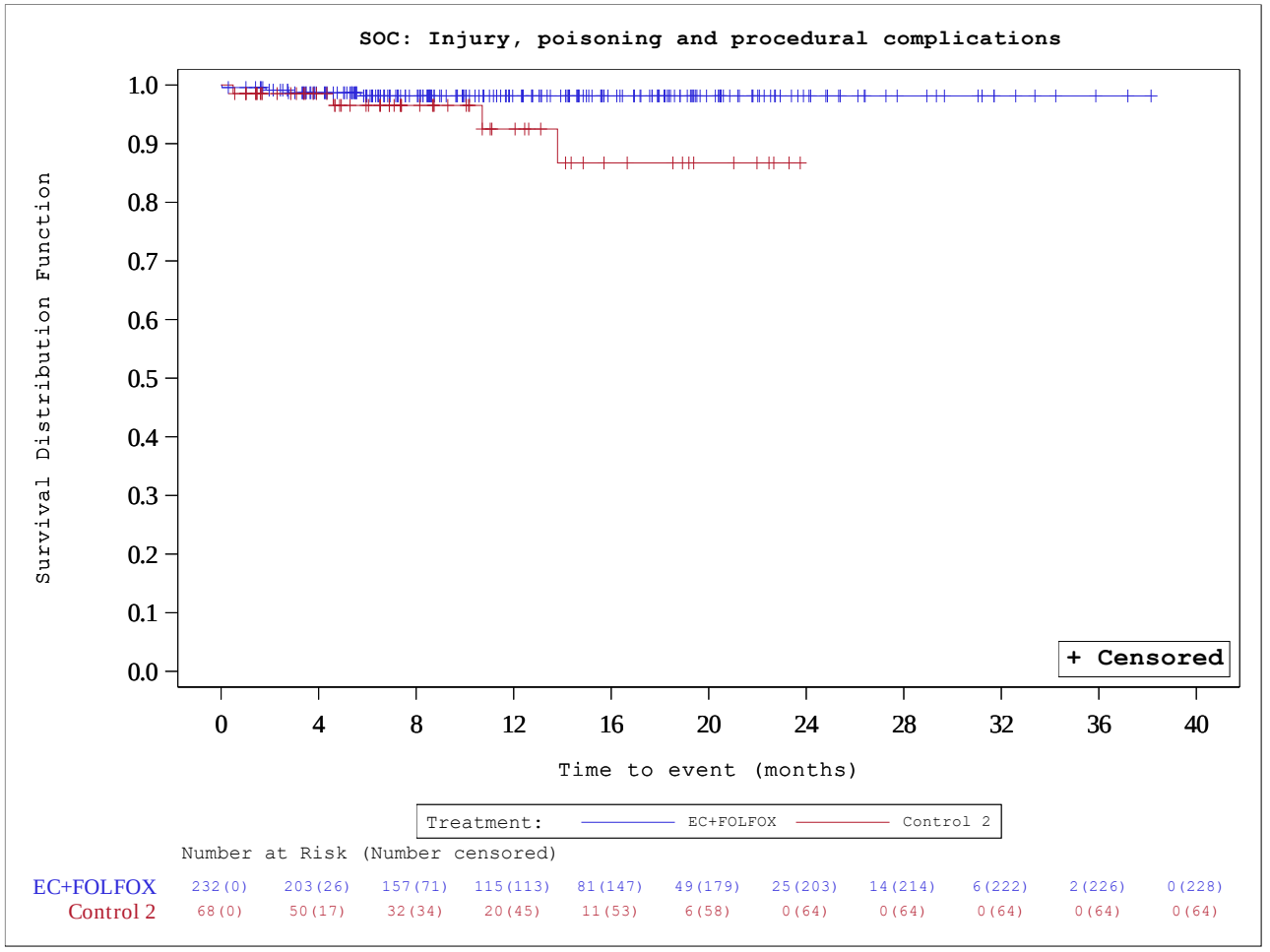

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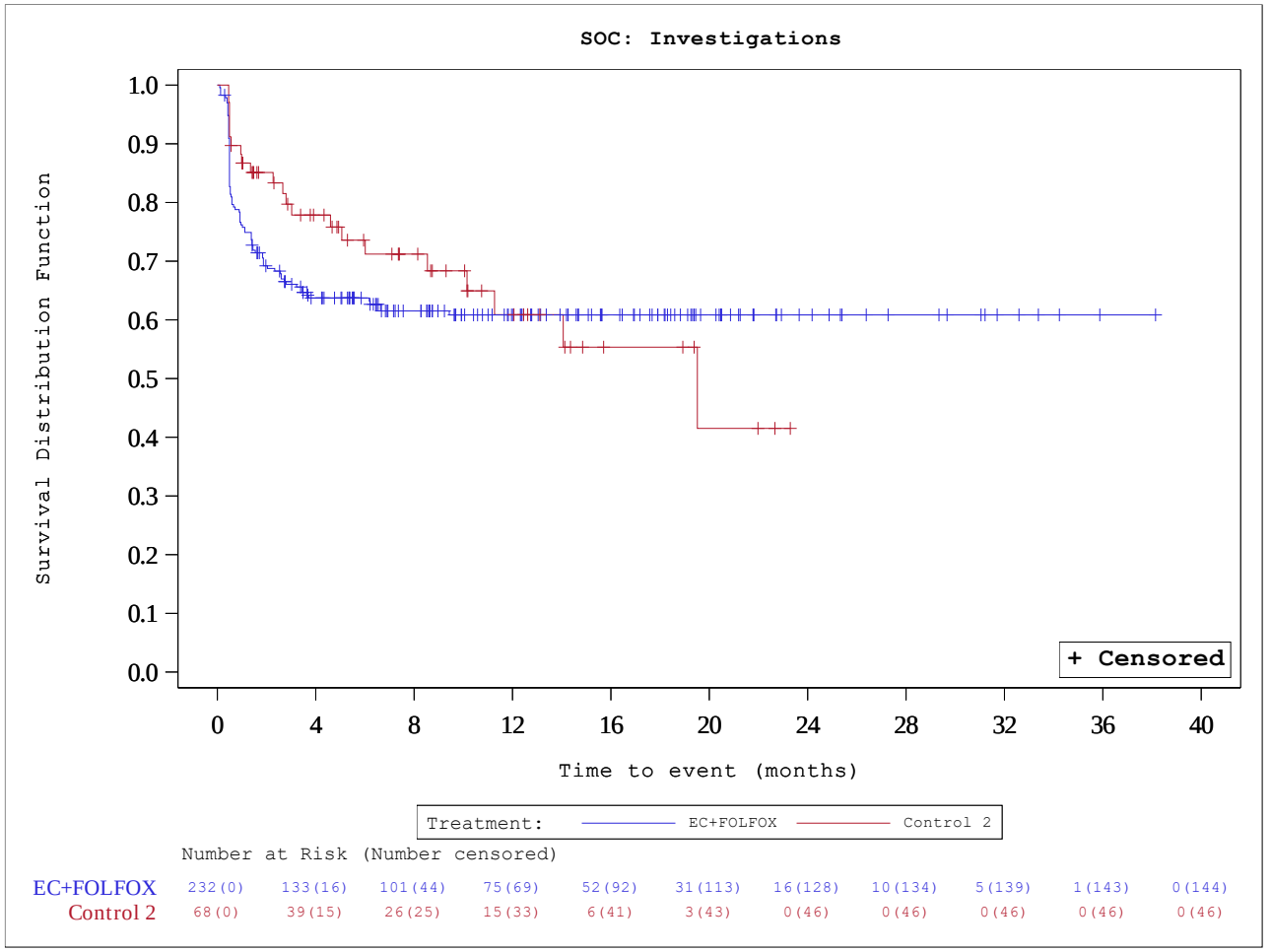

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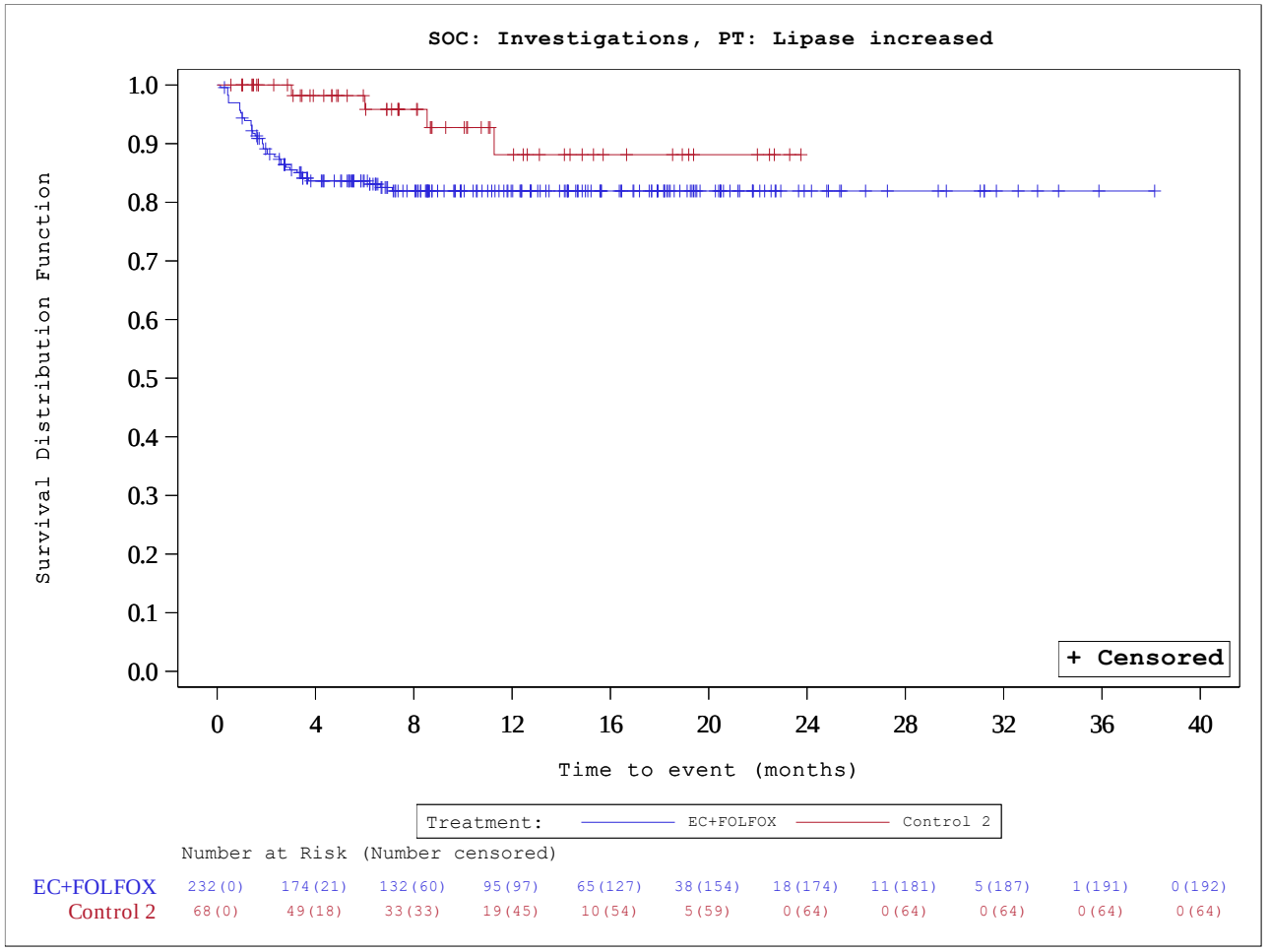

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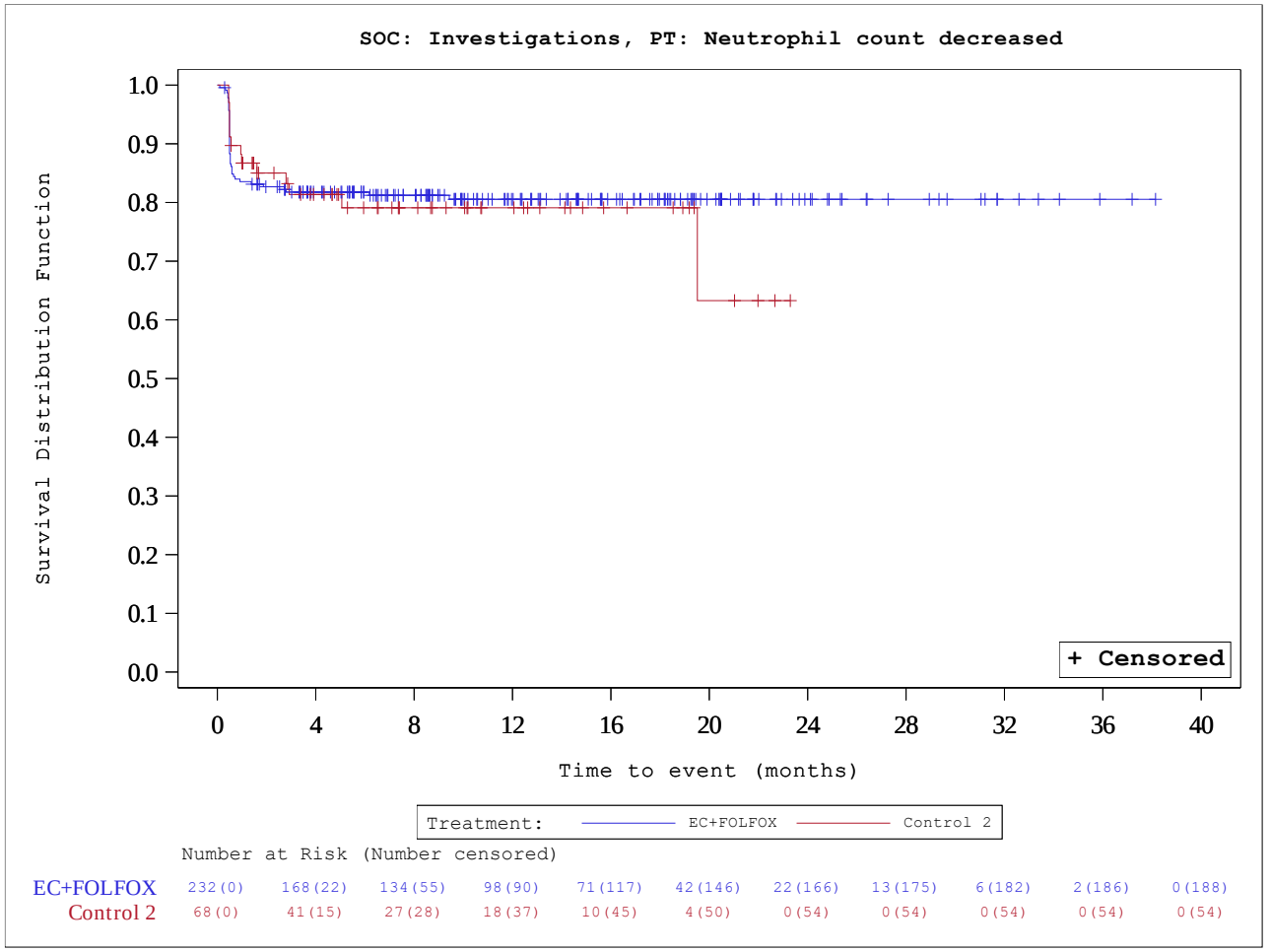

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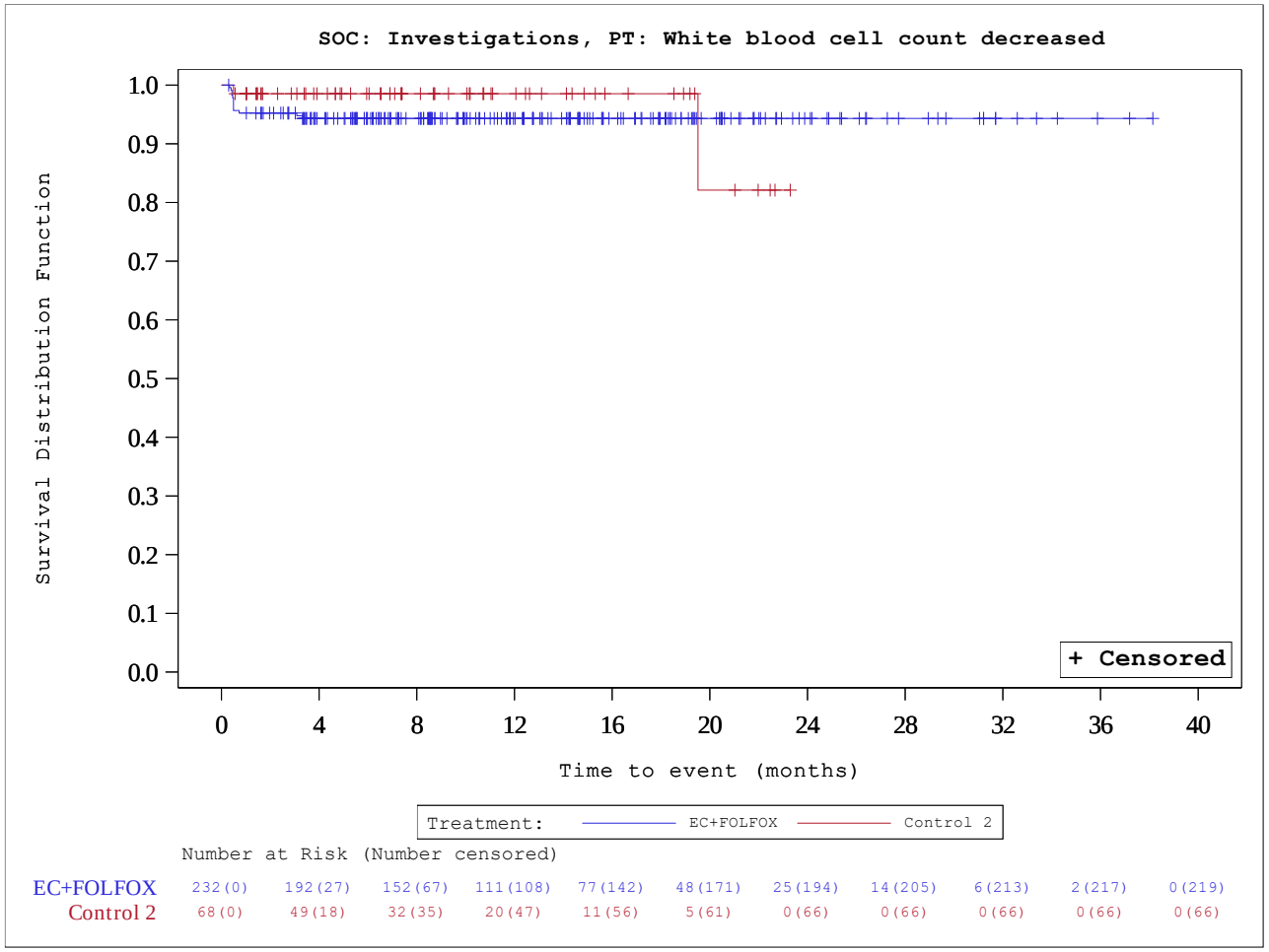

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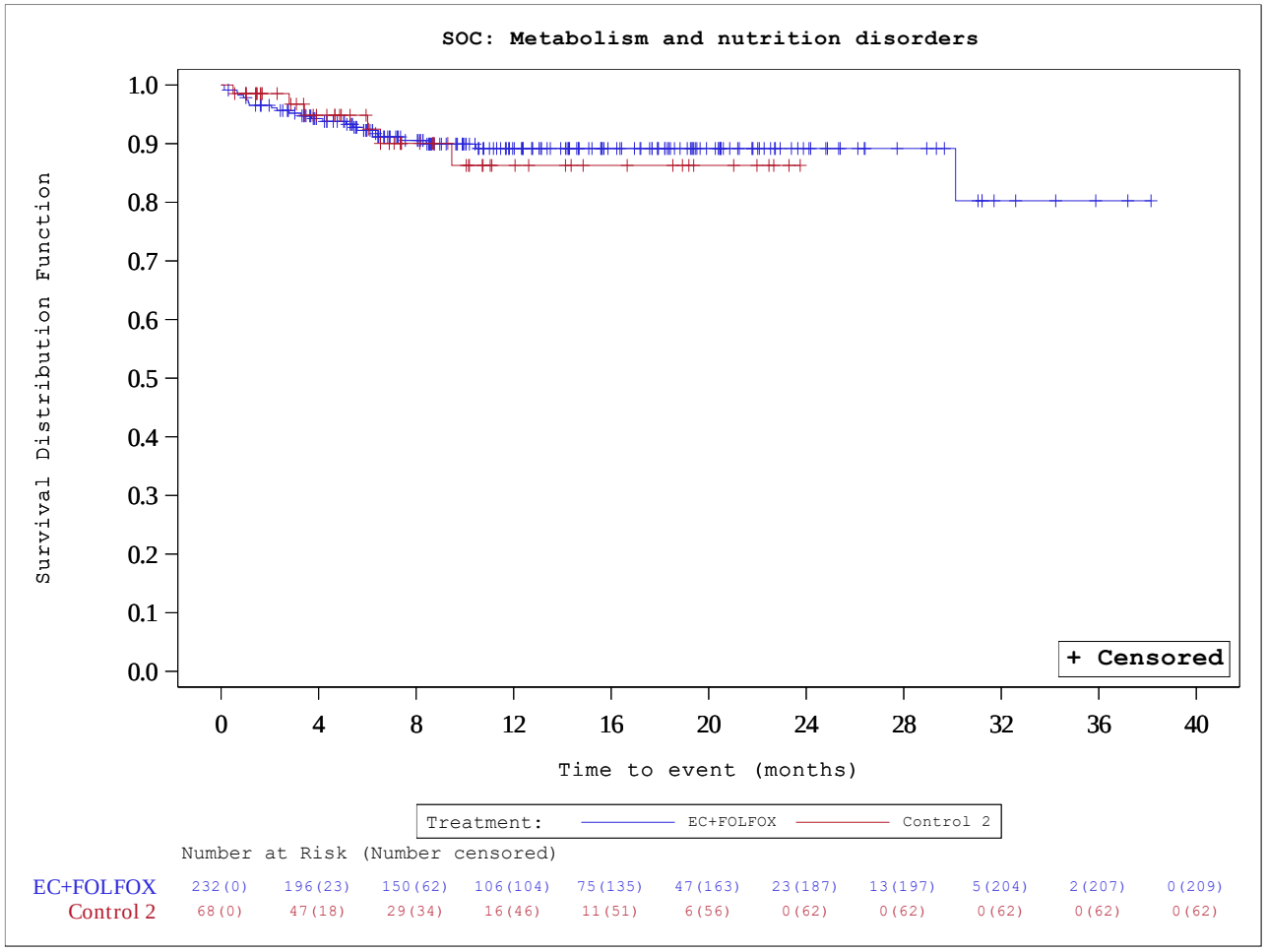

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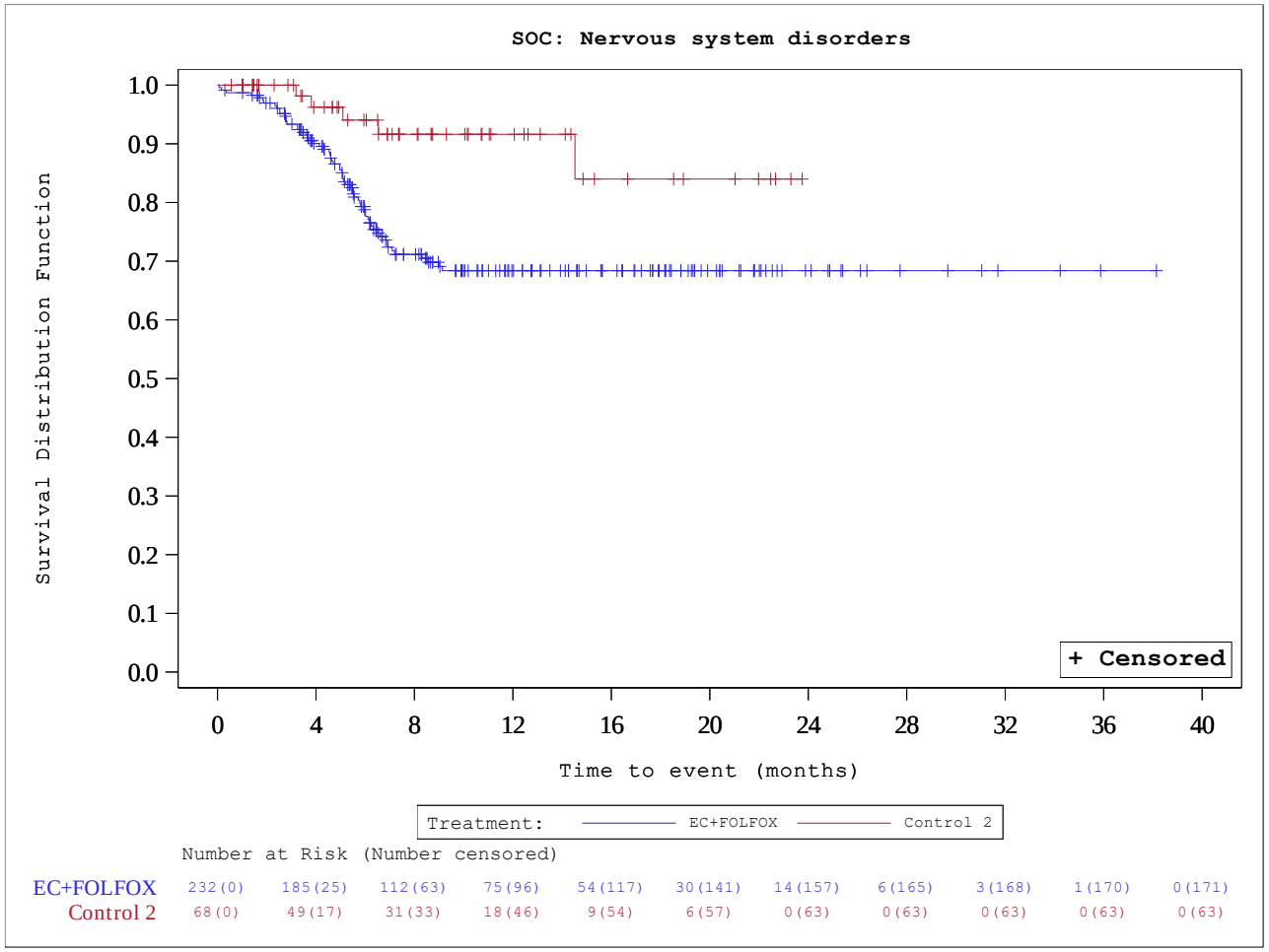

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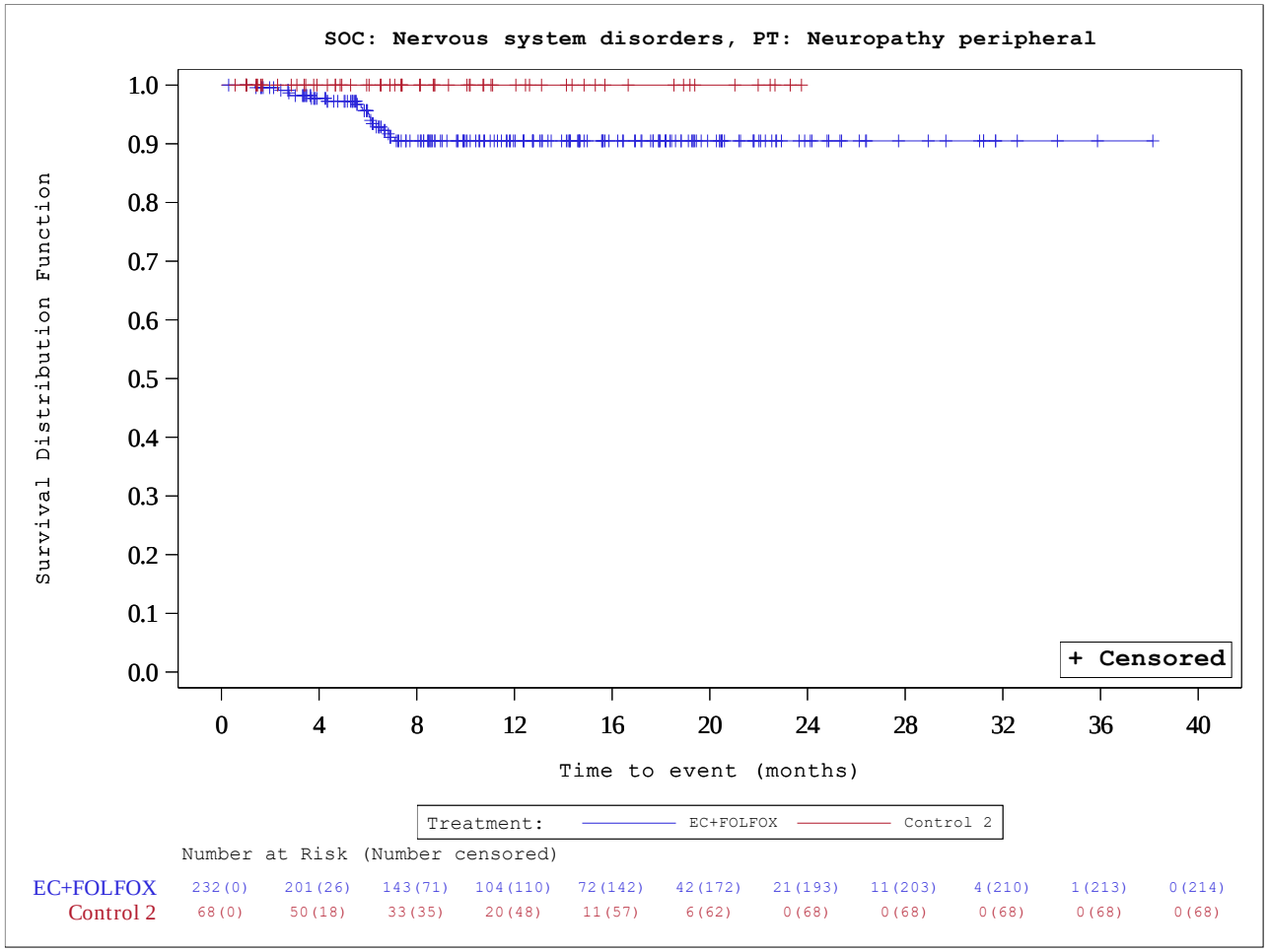

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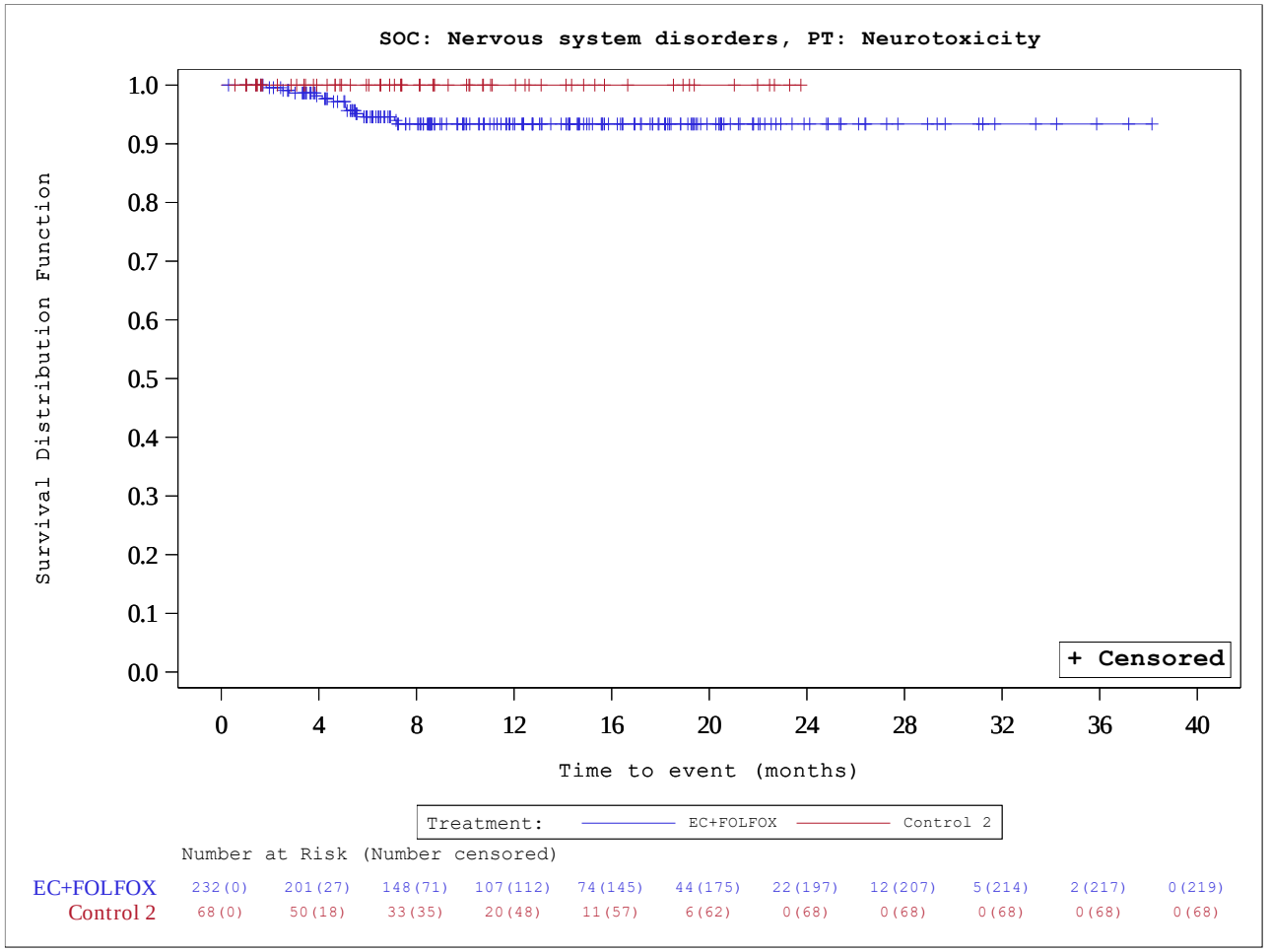

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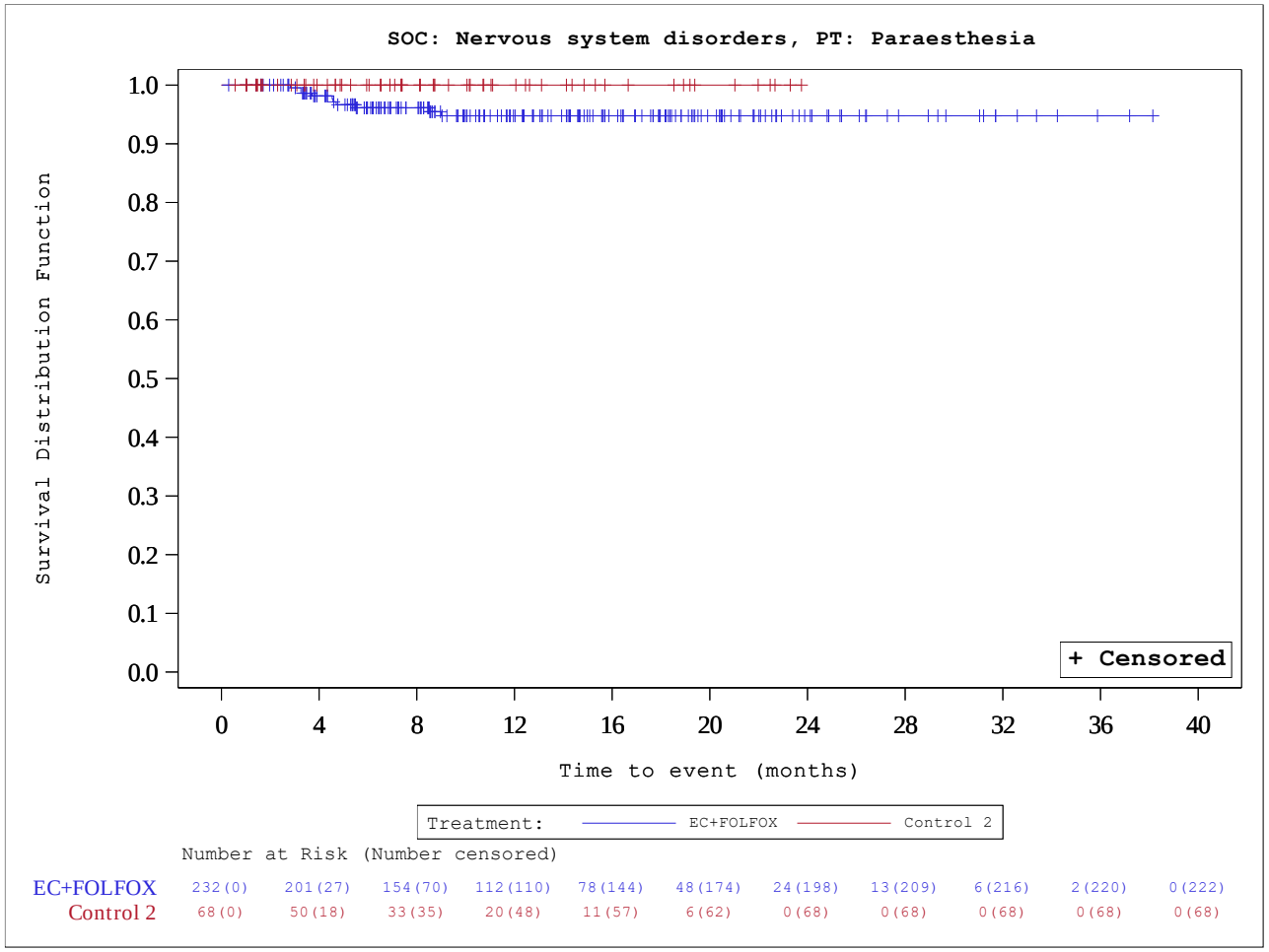
Subgroup analysis was done for SOCs / PTs with significant overall treatment effect (significant log-rank).
Kaplan-Meier Plots for subgroups only created if p-value for interaction < 0.05.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Kaplan Meier Plot of frequent Frequent Severe AE by SOC, PT (incidence >= 5% or >=10 patients and incidence >= 1%)
Safety Analysis Set



Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
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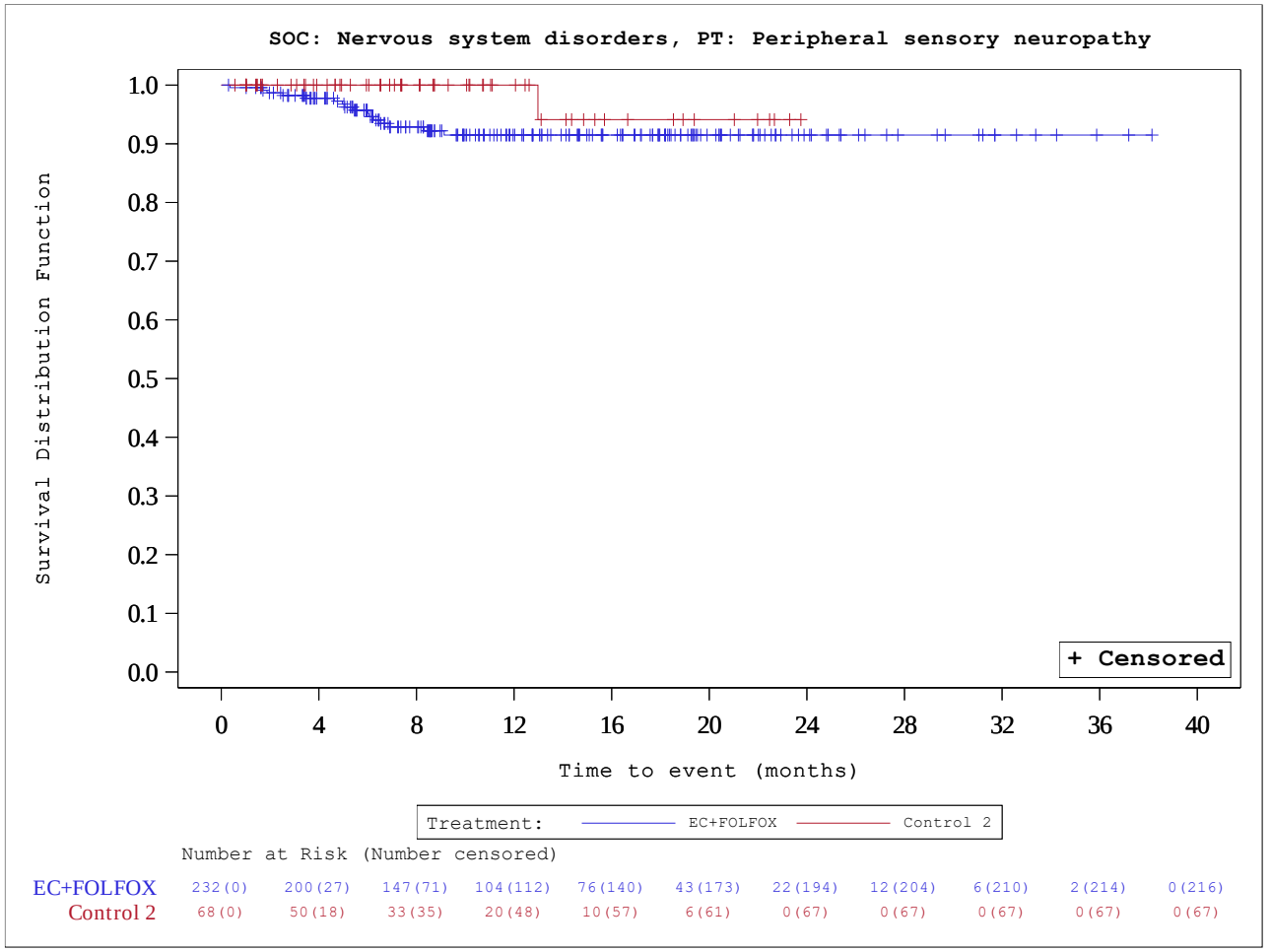
Kaplan-Meier Plots for subgroups only created if p-value for interaction < 0.05.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Kaplan Meier Plot of frequent Frequent Severe AE by SOC, PT (incidence >= 5% or >=10 patients and incidence >= 1%)
Safety Analysis Set



Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
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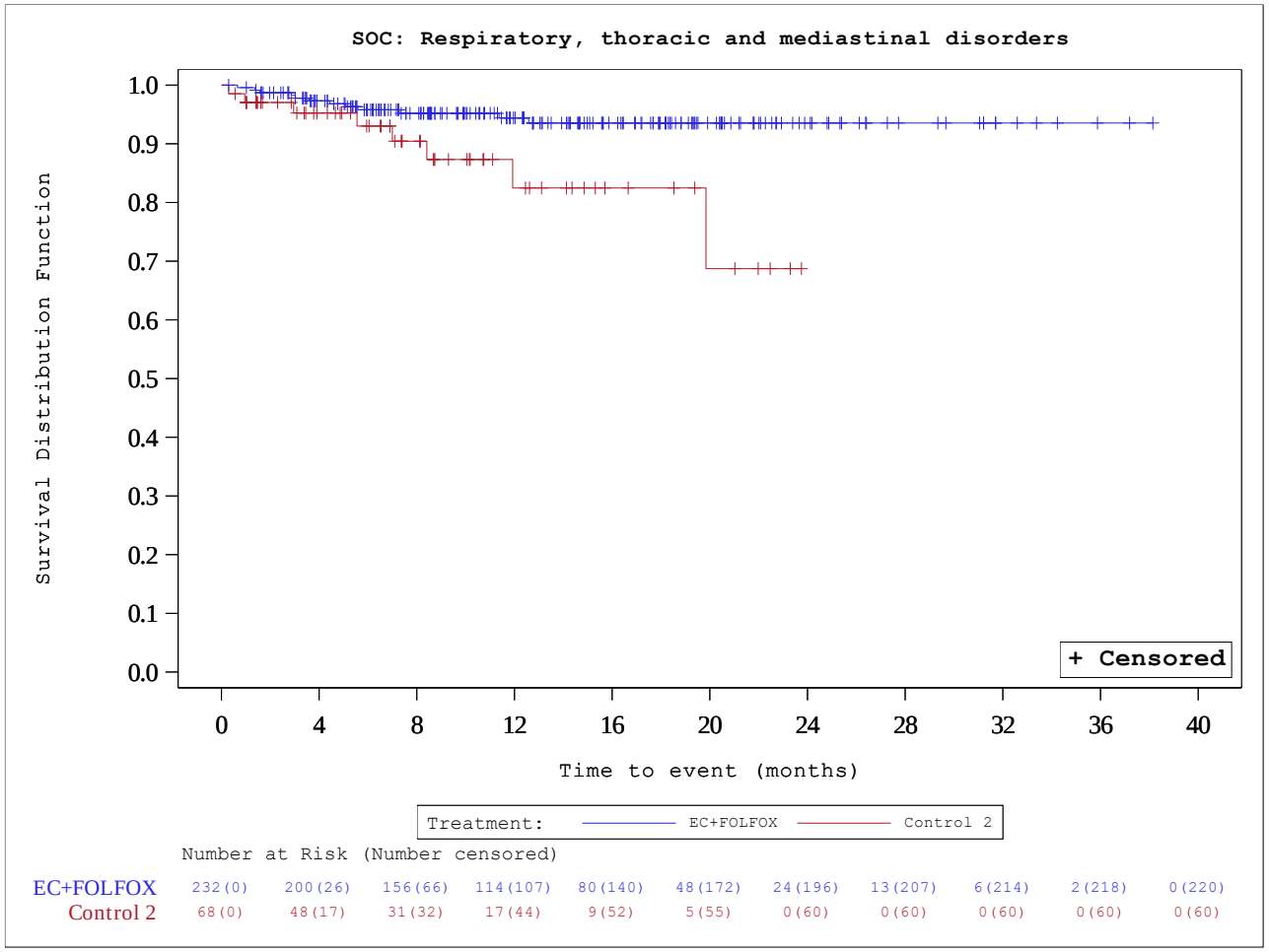
Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Kaplan Meier Plot of frequent Frequent Severe AE by SOC, PT (incidence >= 5% or >=10 patients and incidence >= 1%)
Safety Analysis Set



Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
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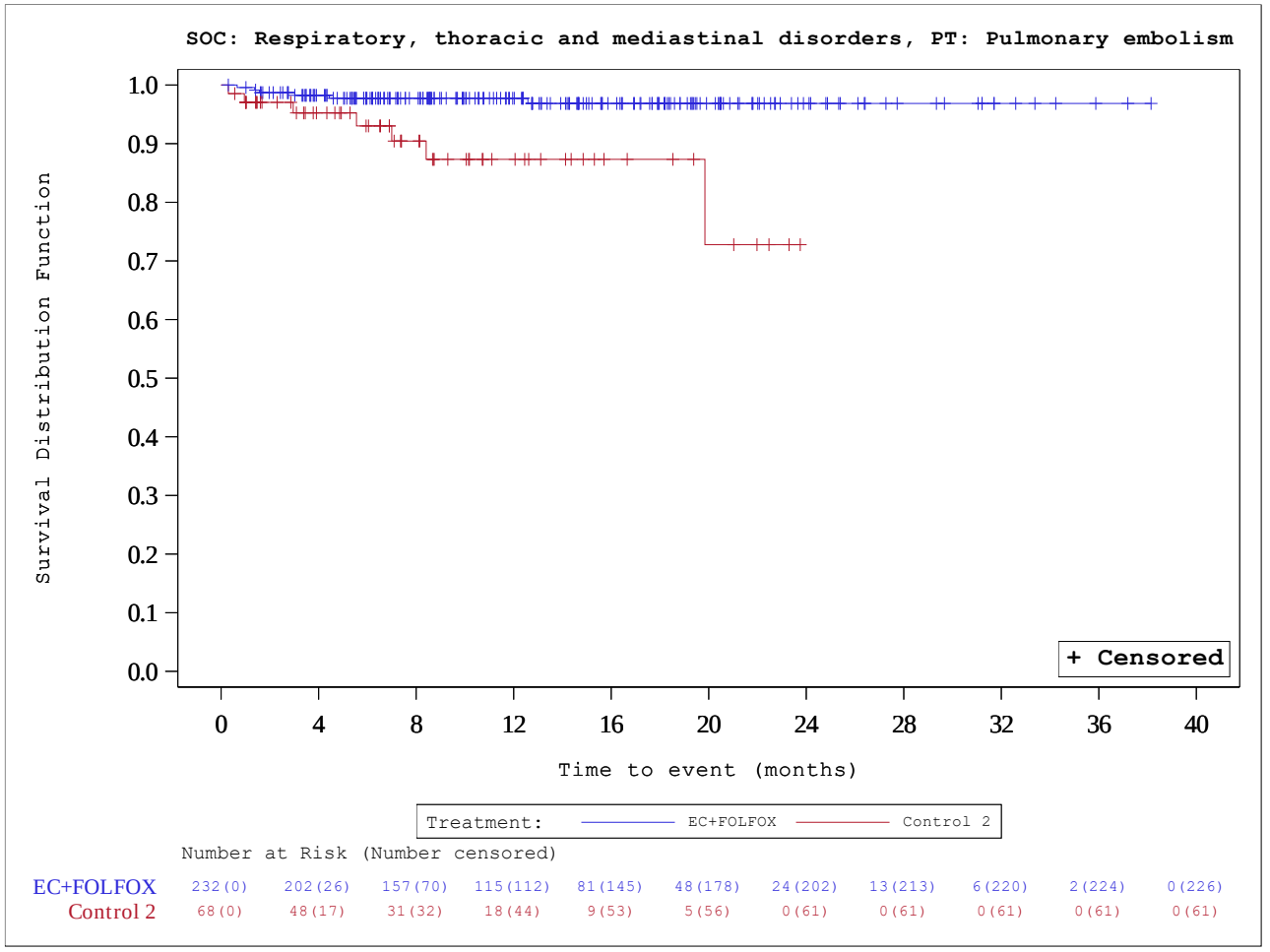
Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Kaplan Meier Plot of frequent Frequent Severe AE by SOC, PT (incidence >= 5% or >=10 patients and incidence >= 1%)
Safety Analysis Set



Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
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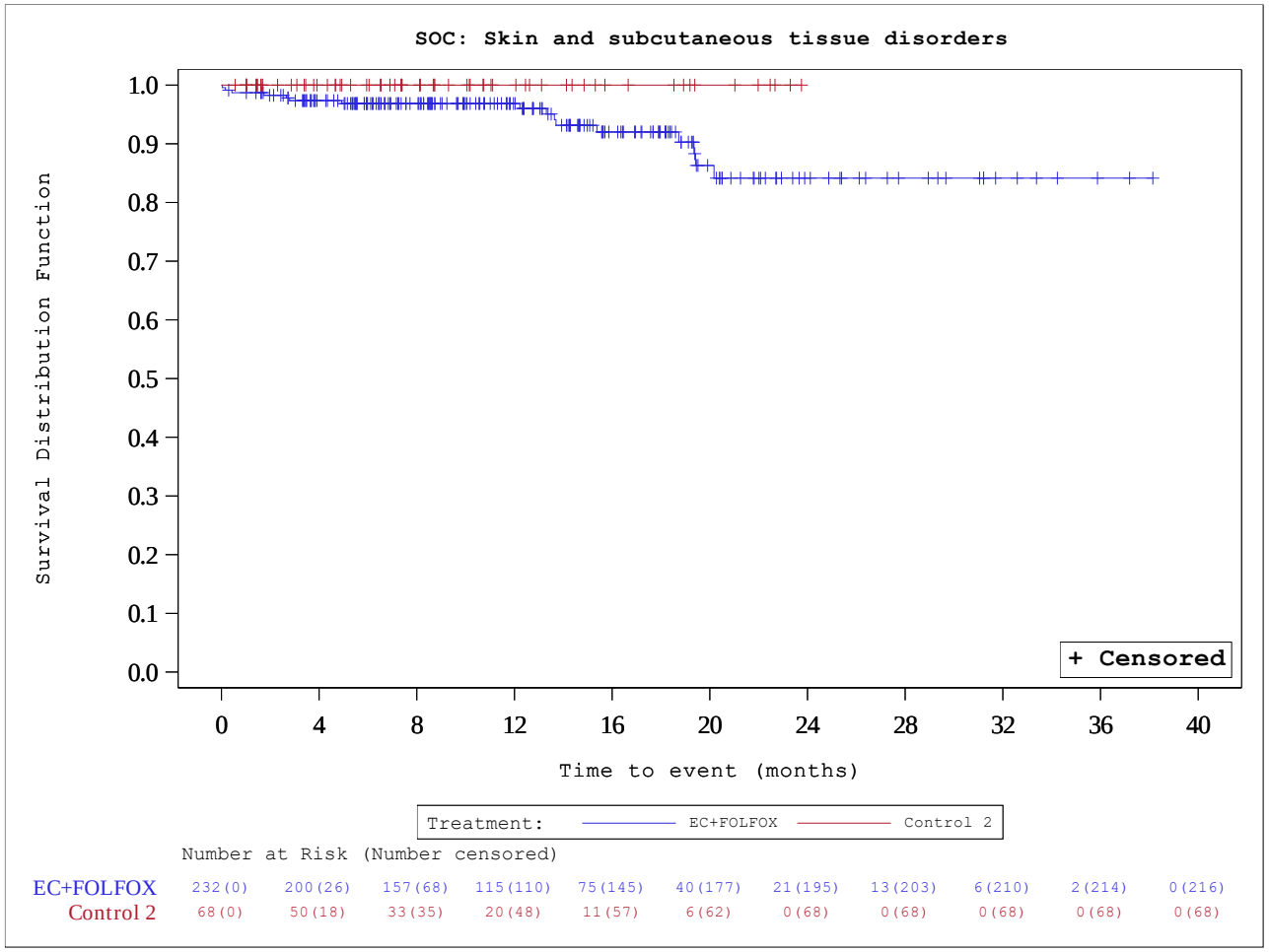
Kaplan-Meier Plots for subgroups only created if p-value for interaction < 0.05.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Kaplan Meier Plot of frequent Frequent Severe AE by SOC, PT (incidence >= 5% or >=10 patients and incidence >= 1%)
Safety Analysis Set



Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
Subgroup analysis was done for SOCs / PTs with significant overall treatment effect (significant log-rank).
Kaplan-Meier Plots for subgroups only created if p-value for interaction < 0.05.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Duration of frequent significant AE (months)
Safety Analysis Set

SOC - PT		EC+FOLFOX (N=232)	Control 2 (N=68)
Blood and lymphatic system disorders - Thrombocytopenia	n (missing)	32 (0)	2 (0)
	Mean (SD)	1.08 (2.126)	1.07 (0.813)
	Median	0.48	1.07
	Q1, Q3	0.30, 0.95	0.49, 1.64
	Min, Max	0.2, 12.2	0.5, 1.6
Gastrointestinal disorders - Diarrhoea	n (missing)	97 (0)	34 (0)
	Mean (SD)	1.66 (4.254)	1.83 (3.152)
	Median	0.13	0.33
	Q1, Q3	0.07, 0.56	0.10, 2.46
	Min, Max	0.0, 23.0	0.0, 13.6
General disorders and administration site conditions - Asthenia	n (missing)	68 (0)	8 (0)
	Mean (SD)	2.13 (3.887)	8.04 (7.843)
	Median	0.57	6.82
	Q1, Q3	0.25, 1.87	0.85, 14.31
	Min, Max	0.0, 18.1	0.2, 20.1
General disorders and administration site conditions - Fatigue	n (missing)	61 (0)	27 (0)
	Mean (SD)	5.72 (6.736)	7.18 (7.127)
	Median	3.38	3.61
	Q1, Q3	0.46, 9.36	0.82, 14.06
	Min, Max	0.1, 30.3	0.1, 20.0
General disorders and administration site conditions - Pyrexia	n (missing)	67 (0)	6 (0)
	Mean (SD)	0.26 (0.601)	0.07 (0.042)
	Median	0.07	0.05
	Q1, Q3	0.03, 0.23	0.03, 0.10
	Min, Max	0.0, 4.1	0.0, 0.1
Investigations	n (missing)	164 (0)	36 (0)
	Mean (SD)	1.30 (2.236)	1.19 (2.814)
	Median	0.49	0.46
	Q1, Q3	0.26, 1.17	0.23, 0.80
	Min, Max	0.0, 14.5	0.0, 16.6
Investigations - Lipase increased	n (missing)	52 (0)	4 (0)
	Mean (SD)	1.62 (2.402)	0.50 (0.354)
	Median	0.92	0.57
	Q1, Q3	0.46, 1.56	0.23, 0.77
	Min, Max	0.0, 14.6	0.0, 0.8
Investigations - Platelet count decreased	n (missing)	53 (0)	4 (0)
	Mean (SD)	1.52 (3.432)	0.32 (0.183)
	Median	0.49	0.33
	Q1, Q3	0.46, 1.18	0.16, 0.48
	Min, Max	0.1, 21.1	0.1, 0.5
Metabolism and nutrition disorders - Hypoalbuminaemia	n (missing)	30 (0)	2 (0)
	Mean (SD)	1.47 (2.622)	0.99 (0.186)
	Median	0.49	0.99
	Q1, Q3	0.36, 1.28	0.85, 1.12
	Min, Max	0.1, 12.2	0.9, 1.1

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
Duration is defined as the time from AE onset to AE end date + 1.
Division by 30.4375 for day-to-month calculation.
Significant denotes to SOCs / PTs with p-value from 2-sided log-rank test < 0.05.
Frequent indicates SOCs / PTs with criteria: incidence >= 10% or >=10 patients and incidence >= 1%.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Duration of frequent significant AE (months)
Safety Analysis Set

SOC - PT		EC+FOLFOX (N=232)	Control 2 (N=68)
Musculoskeletal and connective tissue disorders	n (missing)	133 (0)	19 (0)
	Mean (SD)	4.74 (6.059)	2.29 (4.418)
	Median	2.10	0.62
	Q1, Q3	0.46, 6.83	0.26, 1.45
	Min, Max	0.0, 28.8	0.0, 17.9
Musculoskeletal and connective tissue disorders - Arthralgia	n (missing)	73 (0)	3 (0)
	Mean (SD)	4.95 (6.654)	6.26 (10.112)
	Median	2.10	0.62
	Q1, Q3	0.46, 6.41	0.23, 17.94
	Min, Max	0.1, 28.8	0.2, 17.9
Musculoskeletal and connective tissue disorders - Back pain	n (missing)	24 (0)	11 (0)
	Mean (SD)	3.10 (3.525)	2.16 (3.940)
	Median	1.99	0.62
	Q1, Q3	0.28, 5.26	0.26, 1.41
	Min, Max	0.1, 13.7	0.1, 13.1
Musculoskeletal and connective tissue disorders - Myalgia	n (missing)	38 (0)	2 (0)
	Mean (SD)	4.89 (4.321)	0.20 (0.232)
	Median	3.71	0.20
	Q1, Q3	1.05, 7.26	0.03, 0.36
	Min, Max	0.0, 14.3	0.0, 0.4
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	n (missing)	43 (0)	3 (0)
	Mean (SD)	6.96 (6.978)	1.72 (1.428)
	Median	3.75	2.27
	Q1, Q3	0.85, 13.40	0.10, 2.79
	Min, Max	0.0, 19.8	0.1, 2.8
Nervous system disorders	n (missing)	191 (0)	28 (0)
	Mean (SD)	4.67 (6.288)	2.00 (4.175)
	Median	1.81	0.26
	Q1, Q3	0.33, 5.91	0.03, 1.17
	Min, Max	0.0, 26.5	0.0, 18.1
Nervous system disorders - Dysgeusia	n (missing)	35 (0)	3 (0)
	Mean (SD)	10.25 (9.489)	13.37 (4.170)
	Median	7.33	11.60
	Q1, Q3	2.30, 18.07	10.38, 18.14
	Min, Max	0.2, 34.9	10.4, 18.1
Nervous system disorders - Neuropathy peripheral	n (missing)	64 (0)	1 (0)
	Mean (SD)	5.02 (5.695)	0.26 (-)
	Median	2.64	0.26
	Q1, Q3	0.71, 6.77	0.26, 0.26
	Min, Max	0.1, 22.8	0.3, 0.3
Nervous system disorders - Neurotoxicity	n (missing)	26 (0)	1 (0)
	Mean (SD)	1.84 (2.704)	0.92 (-)
	Median	0.95	0.92
	Q1, Q3	0.46, 2.33	0.92, 0.92
	Min, Max	0.0, 13.3	0.9, 0.9

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
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Significant denotes to SOCs / PTs with p-value from 2-sided log-rank test < 0.05.
Frequent indicates SOCs / PTs with criteria: incidence >= 10% or >=10 patients and incidence >= 1%.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Duration of frequent significant AE (months)
Safety Analysis Set

SOC - PT		EC+FOLFOX (N=232)	Control 2 (N=68)
Nervous system disorders - Peripheral sensory neuropathy	n (missing)	62 (0)	3 (0)
	Mean (SD)	7.41 (7.766)	1.11 (0.934)
	Median	4.29	1.38
	Q1, Q3	1.31, 13.90	0.07, 1.87
	Min, Max	0.1, 34.4	0.1, 1.9
Respiratory, thoracic and mediastinal disorders - Pulmonary embolism	n (missing)	9 (0)	7 (0)
	Mean (SD)	1.93 (2.315)	2.10 (1.872)
	Median	0.95	1.64
	Q1, Q3	0.30, 2.69	0.36, 4.11
	Min, Max	0.1, 6.5	0.2, 5.2
Skin and subcutaneous tissue disorders	n (missing)	188 (0)	28 (0)
	Mean (SD)	8.33 (8.043)	7.23 (6.054)
	Median	6.23	6.60
	Q1, Q3	1.18, 13.39	1.38, 10.45
	Min, Max	0.0, 34.0	0.0, 21.1
Skin and subcutaneous tissue disorders - Pruritus	n (missing)	32 (0)	1 (0)
	Mean (SD)	4.29 (5.983)	0.76 (-)
	Median	1.82	0.76
	Q1, Q3	0.46, 5.83	0.76, 0.76
	Min, Max	0.0, 25.1	0.8, 0.8
Skin and subcutaneous tissue disorders - Rash	n (missing)	70 (0)	1 (0)
	Mean (SD)	5.61 (7.090)	6.70 (-)
	Median	2.22	6.70
	Q1, Q3	0.49, 9.07	6.70, 6.70
	Min, Max	0.0, 26.7	6.7, 6.7
Skin and subcutaneous tissue disorders - Skin hyperpigmentation	n (missing)	43 (0)	3 (0)
	Mean (SD)	13.28 (7.659)	4.57 (1.453)
	Median	12.42	4.04
	Q1, Q3	6.24, 18.66	3.45, 6.21
	Min, Max	1.3, 34.0	3.4, 6.2
Vascular disorders	n (missing)	36 (0)	19 (0)
	Mean (SD)	3.38 (6.152)	4.88 (5.366)
	Median	0.49	3.25
	Q1, Q3	0.21, 2.18	0.49, 8.94
	Min, Max	0.0, 21.7	0.0, 19.0
Vascular disorders - Hypertension	n (missing)	9 (0)	10 (0)
	Mean (SD)	0.57 (0.541)	3.75 (6.144)
	Median	0.46	0.82
	Q1, Q3	0.30, 0.53	0.49, 3.25
	Min, Max	0.0, 1.9	0.1, 19.0

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
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Frequent indicates SOCs / PTs with criteria: incidence >= 10% or >=10 patients and incidence >= 1%.

SOC - PT		EC+FOLFOX (N=232)	Control 2 (N=68)
Gastrointestinal disorders - Diarrhoea	n (missing)	1 (0)	4 (0)
	Mean (SD)	0.10 (-)	0.30 (0.123)
	Median	0.10	0.31
	Q1, Q3	0.10, 0.10	0.21, 0.38
	Min, Max	0.1, 0.1	0.1, 0.4

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
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Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Duration of frequent significant severe AE (months)
Safety Analysis Set

SOC - PT		EC+FOLFOX (N=232)	Control 2 (N=68)
Blood and lymphatic system disorders	n (missing)	67 (0)	9 (0)
	Mean (SD)	0.37 (0.354)	0.28 (0.131)
	Median	0.26	0.26
	Q1, Q3	0.20, 0.46	0.23, 0.26
	Min, Max	0.0, 2.0	0.1, 0.5
Blood and lymphatic system disorders - Anaemia	n (missing)	35 (0)	1 (0)
	Mean (SD)	0.41 (0.395)	0.26 (-)
	Median	0.30	0.26
	Q1, Q3	0.16, 0.49	0.26, 0.26
	Min, Max	0.0, 2.0	0.3, 0.3
Gastrointestinal disorders - Diarrhoea	n (missing)	3 (0)	6 (0)
	Mean (SD)	0.10 (0.000)	0.27 (0.127)
	Median	0.10	0.31
	Q1, Q3	0.10, 0.10	0.13, 0.33
	Min, Max	0.1, 0.1	0.1, 0.4
Injury, poisoning and procedural complications	n (missing)	4 (0)	4 (0)
	Mean (SD)	0.15 (0.166)	0.76 (0.548)
	Median	0.08	0.74
	Q1, Q3	0.05, 0.25	0.30, 1.22
	Min, Max	0.0, 0.4	0.2, 1.3
Investigations - Lipase increased	n (missing)	40 (0)	4 (0)
	Mean (SD)	1.48 (1.472)	0.45 (0.381)
	Median	0.95	0.48
	Q1, Q3	0.49, 1.74	0.13, 0.77
	Min, Max	0.1, 6.4	0.0, 0.8
Nervous system disorders	n (missing)	61 (0)	5 (0)
	Mean (SD)	5.25 (6.049)	0.07 (0.054)
	Median	2.07	0.03
	Q1, Q3	0.46, 8.31	0.03, 0.13
	Min, Max	0.0, 23.4	0.0, 0.1
Respiratory, thoracic and mediastinal disorders	n (missing)	12 (0)	8 (0)
	Mean (SD)	2.21 (4.784)	1.99 (1.759)
	Median	0.36	1.46
	Q1, Q3	0.23, 0.74	0.80, 2.99
	Min, Max	0.1, 16.3	0.2, 5.2
Respiratory, thoracic and mediastinal disorders - Pulmonary embolism	n (missing)	6 (0)	7 (0)
	Mean (SD)	4.08 (6.470)	2.10 (1.872)
	Median	0.66	1.64
	Q1, Q3	0.30, 6.54	0.36, 4.11
	Min, Max	0.1, 16.3	0.2, 5.2

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
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Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Resolved and unresolved events of frequent significant Any AE
Safety Analysis Set

SOC PT or SOC - PT	EC+FOLFOX (N=232)				Control 2 (N=68)			
	Patients with event	Any event	Resolved event	Unresolved event	Patients with event	Any event	Resolved event	Unresolved event
Blood and lymphatic system disorders - Thrombocytopenia	32 (13.8)	67	60 (89.6)	7 (10.4)	2 (2.9)	3	3 (100.0)	0
Gastrointestinal disorders - Diarrhoea	97 (41.8)	204	186 (91.2)	18 (8.8)	34 (50.0)	81	71 (87.7)	10 (12.3)
General disorders and administration site conditions - Asthenia	68 (29.3)	214	182 (85.0)	32 (15.0)	8 (11.8)	16	9 (56.3)	7 (43.8)
Fatigue	61 (26.3)	129	92 (71.3)	37 (28.7)	27 (39.7)	58	38 (65.5)	20 (34.5)
Pyrexia	67 (28.9)	123	120 (97.6)	3 (2.4)	6 (8.8)	7	7 (100.0)	0
Investigations	164 (70.7)	1153	1053 (91.3)	100 (8.7)	36 (52.9)	323	304 (94.1)	19 (5.9)
Lipase increased	52 (22.4)	168	156 (92.9)	12 (7.1)	4 (5.9)	10	9 (90.0)	1 (10.0)
Platelet count decreased	53 (22.8)	184	177 (96.2)	7 (3.8)	4 (5.9)	20	20 (100.0)	0
Metabolism and nutrition disorders - Hypoalbuminaemia	30 (12.9)	67	59 (88.1)	8 (11.9)	2 (2.9)	3	1 (33.3)	2 (66.7)
Musculoskeletal and connective tissue disorders	133 (57.3)	328	213 (64.9)	115 (35.1)	19 (27.9)	42	34 (81.0)	8 (19.0)
Arthralgia	73 (31.5)	138	89 (64.5)	49 (35.5)	3 (4.4)	5	3 (60.0)	2 (40.0)
Back pain	24 (10.3)	31	24 (77.4)	7 (22.6)	11 (16.2)	18	14 (77.8)	4 (22.2)
Myalgia	38 (16.4)	49	28 (57.1)	21 (42.9)	2 (2.9)	3	2 (66.7)	1 (33.3)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	43 (18.5)	62	35 (56.5)	27 (43.5)	3 (4.4)	5	3 (60.0)	2 (40.0)
Nervous system disorders	191 (82.3)	650	446 (68.6)	204 (31.4)	28 (41.2)	53	38 (71.7)	15 (28.3)
Dysgeusia	35 (15.1)	44	21 (47.7)	23 (52.3)	3 (4.4)	3	0	3 (100.0)
Neuropathy peripheral	64 (27.6)	147	92 (62.6)	55 (37.4)	1 (1.5)	1	1 (100.0)	0
Neurotoxicity	26 (11.2)	91	75 (82.4)	16 (17.6)	1 (1.5)	3	2 (66.7)	1 (33.3)
Peripheral sensory neuropathy	62 (26.7)	132	79 (59.8)	53 (40.2)	3 (4.4)	4	2 (50.0)	2 (50.0)
Respiratory, thoracic and mediastinal disorders - Pulmonary embolism	9 (3.9)	14	9 (64.3)	5 (35.7)	7 (10.3)	8	6 (75.0)	2 (25.0)
Skin and subcutaneous tissue disorders	188 (81.0)	627	346 (55.2)	281 (44.8)	28 (41.2)	46	20 (43.5)	26 (56.5)
Pruritus	32 (13.8)	42	31 (73.8)	11 (26.2)	1 (1.5)	1	1 (100.0)	0
Rash	70 (30.2)	101	64 (63.4)	37 (36.6)	1 (1.5)	1	0	1 (100.0)
Skin hyperpigmentation	43 (18.5)	46	6 (13.0)	40 (87.0)	3 (4.4)	3	1 (33.3)	2 (66.7)
Vascular disorders	36 (15.5)	62	47 (75.8)	15 (24.2)	19 (27.9)	40	29 (72.5)	11 (27.5)
Hypertension	9 (3.9)	20	18 (90.0)	2 (10.0)	10 (14.7)	29	23 (79.3)	6 (20.7)

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
Significant denotes to SOCs / PTs with p-value from 2-sided log-rank test < 0.05.
Frequent indicates SOCs / PTs with criteria: incidence >= 10% or >=10 patients and incidence >= 1%.

SOC PT or SOC - PT	EC+FOLFOX (N=232)				Control 2 (N=68)			
	Patients with event	Any event	Resolved event	Unresolved event	Patients with event	Any event	Resolved event	Unresolved event
Gastrointestinal disorders - Diarrhoea	1 (0.4)	1	1 (100.0)	0	4 (5.9)	4	4 (100.0)	0

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
Significant denotes to SOCs / PTs with p-value from 2-sided log-rank test < 0.05.
Frequent indicates SOCs / PTs with criteria: incidence >= 5% or >=10 patients and incidence >= 1%.

Pierre Fabre Pharma GmbH: Final
Encorafenib (PF-07263896) Protocol C4221015
Population: arm B vs. arm E
Datacut: EC+FOLFOX: 06JAN2025 + Control 2: 06JAN2026
Resolved and unresolved events of frequent significant severe AE
Safety Analysis Set

SOC PT or SOC - PT	EC+FOLFOX (N=232) Patients with event	Any event	Resolved event	Unresolved event	Control 2 (N=68) Patients with event	Any event	Resolved event	Unresolved event
Blood and lymphatic system disorders	67 (28.9)	115	113 (98.3)	2 (1.7)	9 (13.2)	10	10 (100.0)	0
Anaemia	35 (15.1)	66	64 (97.0)	2 (3.0)	1 (1.5)	1	1 (100.0)	0
Gastrointestinal disorders - Diarrhoea	3 (1.3)	4	4 (100.0)	0	6 (8.8)	8	7 (87.5)	1 (12.5)
Injury, poisoning and procedural complications	4 (1.7)	4	4 (100.0)	0	4 (5.9)	5	5 (100.0)	0
Investigations - Lipase increased	40 (17.2)	66	62 (93.9)	4 (6.1)	4 (5.9)	5	4 (80.0)	1 (20.0)
Nervous system disorders	61 (26.3)	73	47 (64.4)	26 (35.6)	5 (7.4)	7	7 (100.0)	0
Respiratory, thoracic and mediastinal disorders	12 (5.2)	13	10 (76.9)	3 (23.1)	8 (11.8)	9	7 (77.8)	2 (22.2)
Pulmonary embolism	6 (2.6)	7	5 (71.4)	2 (28.6)	7 (10.3)	7	6 (85.7)	1 (14.3)

Analysis based on Treatment-Emergent Adverse Events (TEAEs). TEAEs are those events if the event starts on or after the first dosing day and time, but before the last dose +28 days. Or date of new anti-cancer therapy - 1 day. Whichever occured earlier.
Significant denotes to SOCs / PTs with p-value from 2-sided log-rank test < 0.05.
Frequent indicates SOCs / PTs with the criteria: incidence >= 5% or >=10 patients and incidence >= 1%.