Supplementary Material for

Combined BRAF, EGFR, and MEK Inhibition in Patients with *BRAF*^{V600E}-Mutant Colorectal Cancer

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Supplementary Tables S1 – S2

Supplementary Figures S1 – S4

Corcoran et al, Supplementary Table S1. AE summary

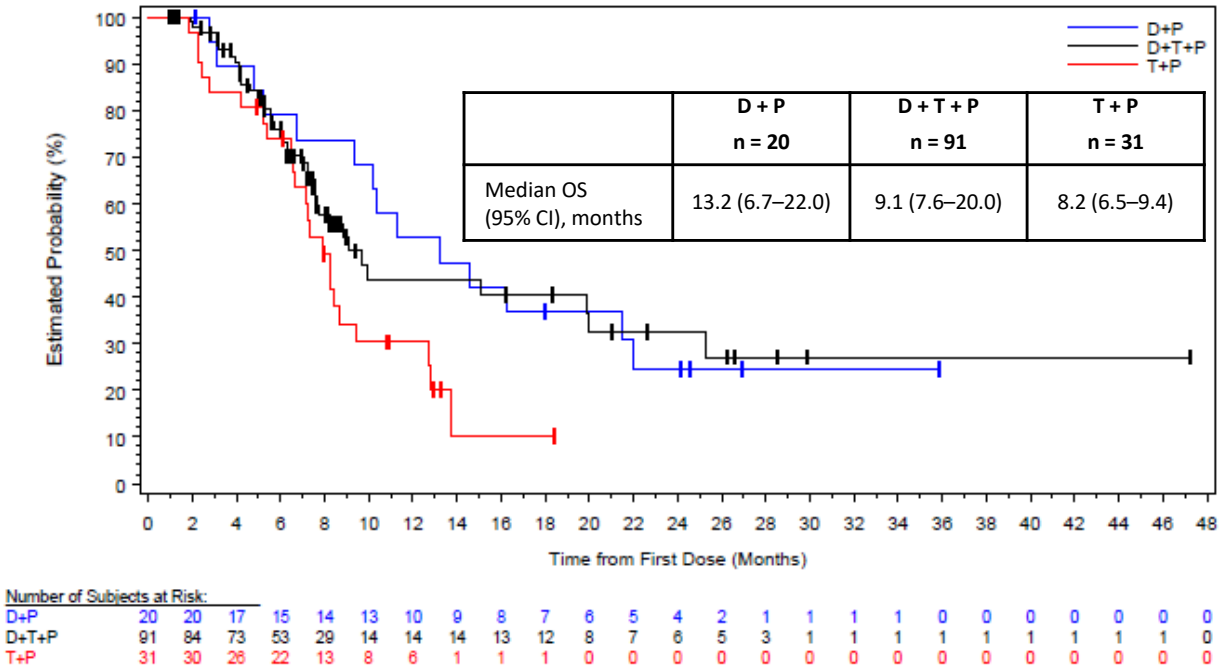
AE, n (%)	D + T + P[a] (n = 91)	D + T + P[b] Part 2B 4.8 mg/kg P (n = 32)	D + T + P[c] Part 2B 6 mg/kg P (n = 24)	T + P (n = 51)	D + P (n = 20)
Any AE	91 (100)	32 (100)	24 (100)	50 (98)	20 (100)
Suspected to be drug related	90 (99)	32 (100)	23 (96)	49 (96)	20 (100)
SAEs	46 (51)	15 (47)	16 (67)	23 (45)	6 (30)
Suspected to be drug related	28 (31)	9 (28)	10 (42)	12 (24)	5 (25)
Fatal SAEs[d]	2 (2)	0	0	0	0
AEs leading to discontinuation	16 (18)	4 (13)	7 (29)	8 (16)	1 (5)
AEs leading to dose reduction	49 (54)	16 (50)	12 (50)	27 (53)	5 (25)
AEs leading to dose interruption/delay	65 (71)	26 (81)	16 (67)	37 (73)	9 (45)

[a] Includes all patients who were treated with triple combination of dabrafenib, trametinib, and panitumumab, which included varying doses of trametinib and panitumumab.
[b] Includes patients who received dabrafenib 150 mg twice daily, trametinib 2 mg once daily, and panitumumab 4.8 mg/kg once every other week in the expansion phase of the trial.
[c] Includes patients who received dabrafenib 150 mg twice daily, trametinib 2 mg once daily, and panitumumab 6 mg/kg once every other week in the expansion phase of the trial.
[d] No fatal SAEs were suspected to be drug related.

Corcoran et al, Supplemental Table S2. Common AEs by dose for the D + T + P arm (≥20%)

AE, n (%)	D + T + P (n = 91)		D + T + P Part 2B 4.8 mg/kg P (n = 32)		D + T + P Part 2B 6 mg/kg P (n = 24)	
	Total	Grade 3/4	Total	Grade 3/4	Total	Grade 3/4
Any AE	91 (100)	64 (70)	32 (100)	20 (63)	24 (100)	19 (79)
Anemia	19 (21)	5 (5)	4 (13)	0	4 (17)	2 (8)
Decreased appetite	36 (40)	2 (2)	13 (41)	0	8 (33)	0
Dermatitis acneiform	54 (59)	9 (10)	21 (66)	4 (13)	13 (54)	2 (8)
Diarrhea	59 (65)	6 (7)	18 (56)	2 (6)	14 (58)	1 (4)
Dry skin	49 (54)	2 (2)	16 (50)	0	15 (63)	1 (4)
Dysgeusia	18 (20)	0	6 (19)	0	2 (8)	0
Fatigue	45 (49)	6 (7)	17 (53)	2 (6)	10 (42)	2 (8)
Hypomagnesemia	26 (29)	1 (1)	7 (22)	0	5 (21)	0
Nausea	51 (56)	2 (2)	21 (66)	1 (3)	12 (50)	0
Edema peripheral	22 (24)	0	7 (22)	0	6 (25)	0
Paronychia	21 (23)	1 (1)	10 (31)	0	3 (13)	0
Pyrexia	44 (48)	4 (4)	15 (47)	1 (3)	12 (50)	3 (13)
Rash	28 (31)	10 (11)	9 (28)	3 (9)	6 (25)	4 (17)
Skin fissures	20 (22)	1 (1)	7 (22)	0	4 (17)	0
Vomiting	39 (43)	2 (2)	15 (47)	0	8 (33)	0

Corcoran et al, Supplemental Figure S1. Overall survival by treatment arm



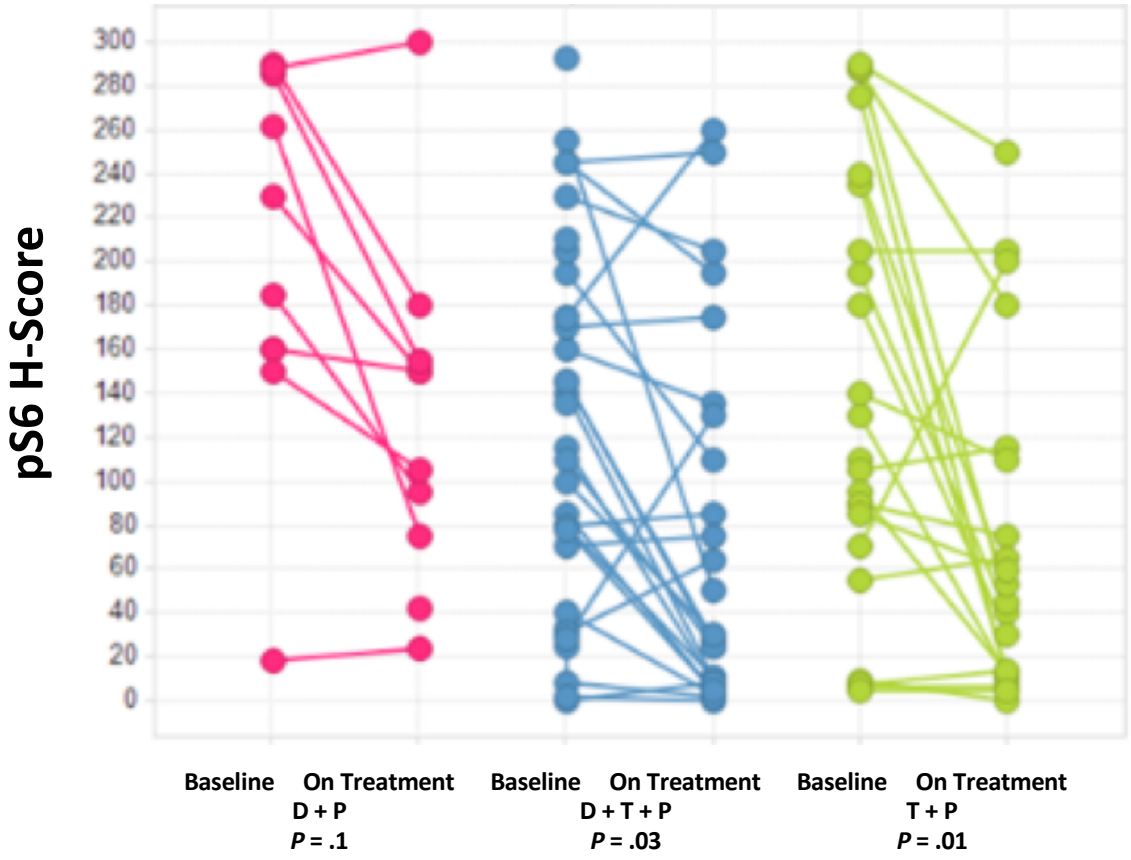
	D + P n = 20	D + T + P n = 91	T + P n = 31
Median OS (95% CI), months	13.2 (6.7–22.0)	9.1 (7.6–20.0)	8.2 (6.5–9.4)

Number of Subjects at Risk:

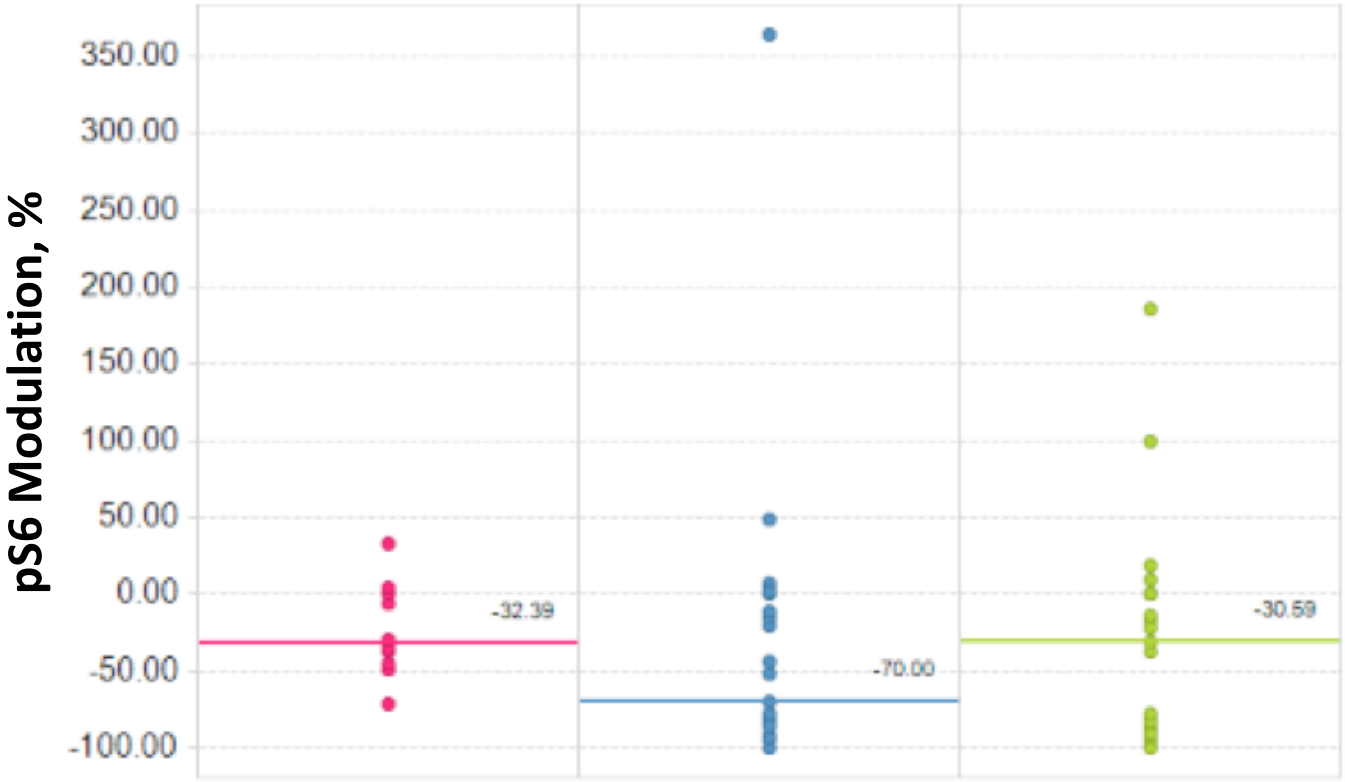
D+P	20	20	17	15	14	13	10	9	8	7	6	5	4	2	1	1	1	1	0	0	0	0	0	0	0
D+T+P	91	84	73	53	29	14	14	14	13	12	8	7	6	5	3	1	1	1	1	1	1	1	1	1	0
T+P	31	30	26	22	13	8	6	1	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Corcoran et al, Supplemental Figure S2. Analysis of pS6 by treatment arm

A

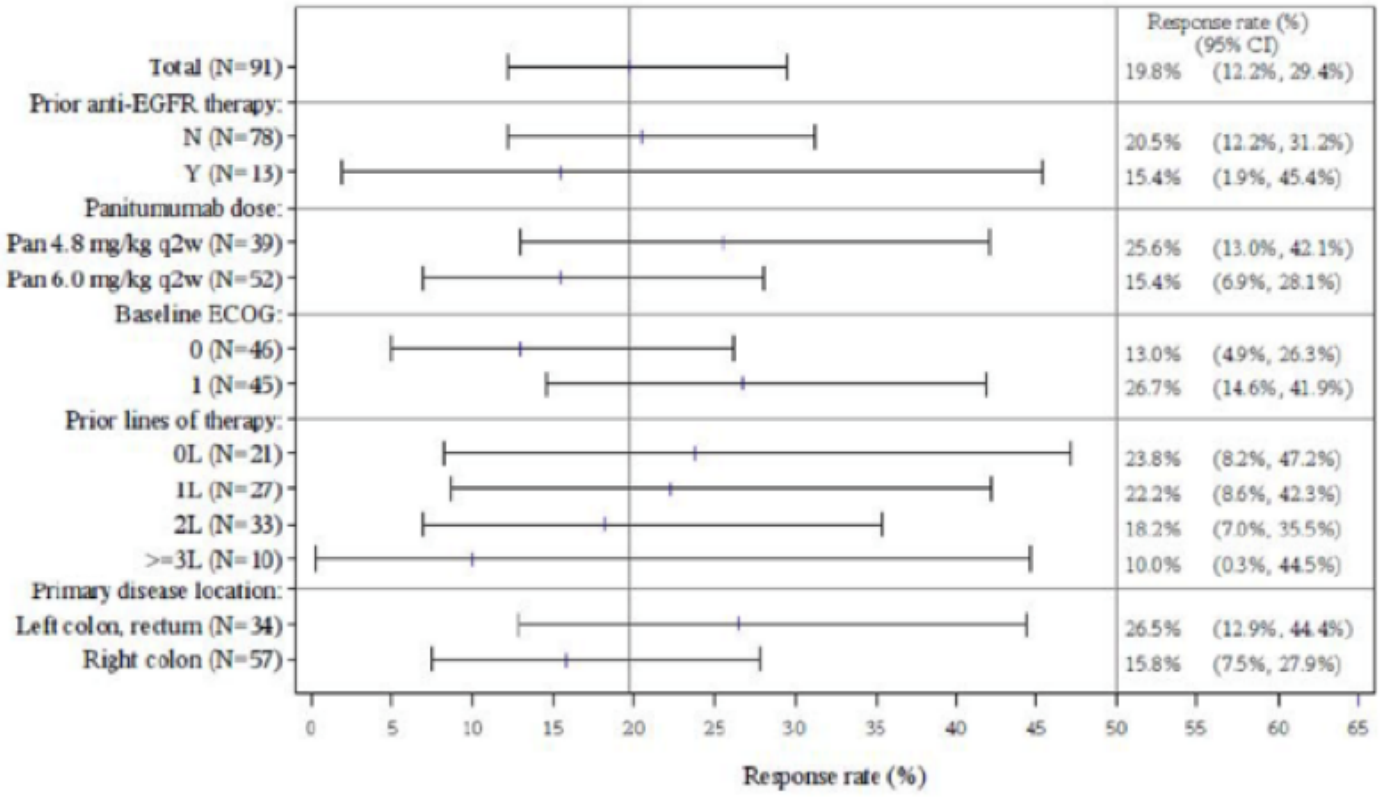


B



	D + P	D + T + P	T + P
n	10	25	21
Median	-32.39	-70.00	-30.59

Corcoran et al, Supplemental Figure S3. Forest plot of response rate for D + T + P



Corcoran et al, Supplemental Figure S4. Efficacy by MSI status: focus on D + T + P arm (n = 78 with known MMR status and evaluable survival data)

A

	MSI-high/dMMR n (%)	MSS/pMMR[a] n (%)
D + P	2 (13)	13 (87)
D + T + P	11 (14)	67 (86)
T + P	3 (12)	22 (88)
Total	16 (14)	102 (86)

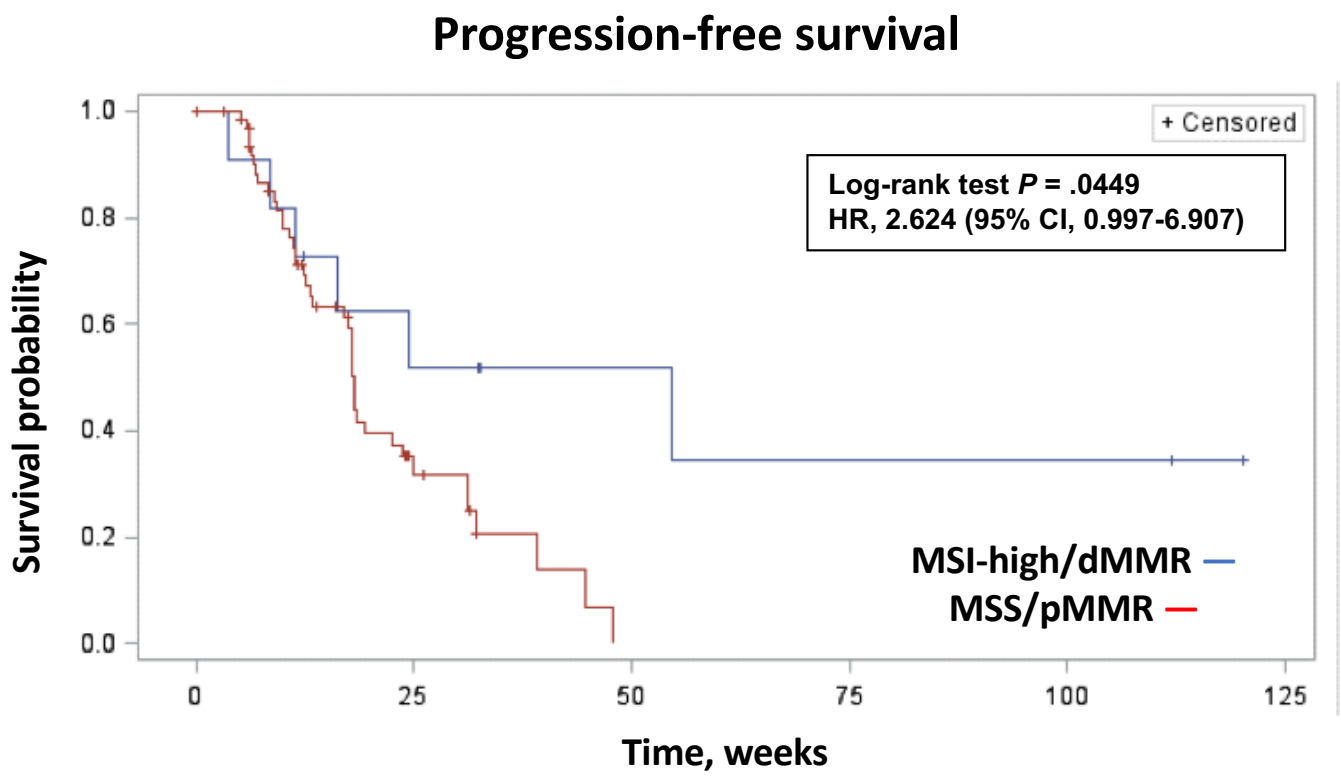
[a]For the subset of patients with insufficient normal DNA available, immunohistochemistry was performed for the following markers: MLH1, MSH2, MSH6, and PMS2. Positive staining for all 4 markers was required for the tumor to be classified as MSS, otherwise the tumor was classified as MSI.

B

Assessment	D + T + P MSI-high/dMMR (n = 11)	D + T + P MSS/pMMR (n = 67)
Best response, n (%)		
CR	1 (9)	0
PR	4 (36)	18 (27)
Stable disease	5 (46)	37 (55)
Non-CR/non-progressive disease (NE)	1 (9)	4 (6)
Progressive disease	0	8 (12)
Response rate, n (%)		
CR + PR	5 (46)	18 (27)
95% CI	17-77	17-39

Corcoran et al, Supplemental Figure S4. Efficacy by MSI status: focus on D + T + P arm (n = 78 with known MMR status and evaluable survival data)

C



MSI-high/dMMR	11	10	7	6	5	3	3	2	2	2	2	2	2	2	2	1
MSS/pMMR	67	51	32	15	6	2	0									