

SUPPLEMENTARY TABLES:

Systemic chemotherapies retain anti-tumor activity in desmoid tumors independent of specific mutations in *CTNNB1* or *APC*: A multi-institutional retrospective study.

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Table S1. Cox proportional hazard analysis of first-line RECIST PFS by mutation status.

Variable		All	HR (univariable) (95% CI, p value)	HR (multivariable) (95% CI, p value)
Sex	Female	55 (100)	-	-
	Male	44 (100)	1.2 (0.55-2.6, p=0.65)	0.61 (0.21-1.8, p=0.38)
Age	Mean (SD)	41 (14)	1.0 (0.99-1.0, p=0.37)	1.1 (0.99-1.1, p=0.085)
Number of Treatment Lines	1	60 (100)	-	-
	2	22 (100)	2.0 (0.74-5.2, p=0.17)	0.75 (0.16-3.5, p=0.72)
	3+	17 (100)	4.5 (1.8-11.2, p=0.001)	3.9 (1.1-13.9, p=0.033)
Mutation subtype	T41A	24 (100)	-	-
	S45F	15 (100)	0.73 (0.14-3.6, p=0.70)	0.64 (0.13-3.2, p=0.59)
	APC	7 (100)	3.5 (0.97-13, p=0.055)	2.4 (0.58-10, p=0.23)
	Other	10 (100)	0.87 (0.25-3.0, p=0.83)	1.4 (0.30-6.9, p=0.65)

Table S2. Cox proportional hazard analysis of second-line RECIST PFS by mutation status.

Variable		All	HR (univariable) (95% CI, p value)	HR (multivariable) (95% CI, p value)
Sex	Female	55 (100)	-	-
	Male	23 (100)	1.1 (0.42-2.9, p=0.84)	1.9 (0.58-6.4, p=0.28)
Age	Mean (SD)	35 (13)	0.98 (0.94-1.0, p=0.23)	0.98 (0.94-1.0, p=0.49)
Time to 2 nd line therapy	Mean (SD)	15 (21)	1.00 (0.97-1.0, p=0.97)	0.99 (0.95-1.0, p=0.65)
# of Treatment Lines	1	N/A	N/A	N/A
	2	46 (100)	-	-
	3+	32 (100)	3.7 (1.4-9.8, p=0.008)	2.8 (0.74-10, p=0.13)
Mutation subtype	T41A	23 (100)	-	-
	S45F	14 (100)	1.8 (0.44-7.0, p=0.43)	1.9 (0.40-8.7, p=0.43)
	APC	6 (100.0)	3.5 (0.77-15, p=0.11)	2.3 (0.41-13, p=0.34)
	Other	15 (100.0)	2.6 (0.74-9.3, p=0.14)	1.7 (0.36-7.7, p=0.52)

Table S3. Cox proportional hazard analysis for first-line time to next treatment by mutation subtype.

Variable		All	HR (univariable) (95% CI, p value)	HR (multivariable) (95% CI, p value)
Sex	Female	156 (100)	-	-
	Male	77 (100)	0.79 (0.56-1.1, p=0.18)	0.73 (0.46-1.2, p=0.17)
Race	Caucasian	133 (100)	-	-
	Hispanic/Latino	34 (100)	0.89 (0.56-1.4, p=0.64)	0.82 (0.43-1.6, p=0.55)
	African-American	18 (100)	0.80 (0.44-1.5, p=0.46)	0.77 (0.39-1.5, p=0.45)
	Asian	10 (100)	1.2 (0.57-2.7, p=0.60)	1.2 (0.46-2.9, p=0.76)
	Other/Unknown	9 (100)	0.93 (0.41-2.1, p=0.87)	1.5 (0.34-6.6, p=0.60)
Age	Mean (SD)	37 (15)	0.99 (0.98-1.0, p=0.013)	0.99 (0.98-1.0, p=0.26)
Mutation subtype	T41A	59 (100)	-	-
	S45F	41 (100)	1.1 (0.65-1.8, p=0.80)	1.0 (0.60-1.8, p=0.91)
	APC	10 (100)	1.4 (0.64-3.0, p=0.41)	1.3 (0.59-2.8, p=0.53)
	Other	40 (100)	0.92 (0.58-1.5, p=0.73)	0.87 (0.52-1.5, p=0.60)

Table S4. Cox proportional hazard analysis for second-line time to next treatment by mutation subtype.

Variable		All	HR (univariable) (95% CI, p value)	HR (multivariable) (95% CI, p value)
Sex	Female	110 (100)	-	-
	Male	53 (100)	0.89 (0.57-1.4, p=0.62)	0.86 (0.47-1.6, p=0.61)
Race	Caucasian	98 (100)	-	-
	Hispanic/Latino	22 (100)	1.5 (0.82-2.6, p=0.20)	1.1 (0.54-2.3, p=0.78)
	African-American	13 (100)	0.74 (0.32-1.7, p=0.48)	0.63 (0.22-1.8, p=0.39)
	Asian	6 (100)	1.2 (0.37-3.8, p=0.79)	1.6 (0.37-6.9, p=0.53)
	Other/Unknown	6 (100)	2.1 (0.77-6.0, p=0.15)	3.1 (0.61-16.0, p=0.17)
Age	Mean (SD)	345 (14)	0.98 (0.97-1.0, p=0.016)	0.99 (0.96-1.0, p=0.16)
Time to 2 nd line treatment	Mean (SD)	17 (21)	1.0 (0.99-1.0, p=0.91)	1.0 (0.99-1.0, p=0.53)
Mutation subtype	T41A	48 (100)	-	-
	S45F	28 (100)	1.0 (0.54-2.0, p=0.92)	1.0 (0.49-2.1, p=0.98)
	APC	7 (100)	2.1 (0.79-5.6, p=0.14)	2.0 (0.71-5.5, p=0.19)
	Other	34 (100)	1.6 (0.90-2.8, p=0.11)	1.4 (0.73-2.8, p=0.29)

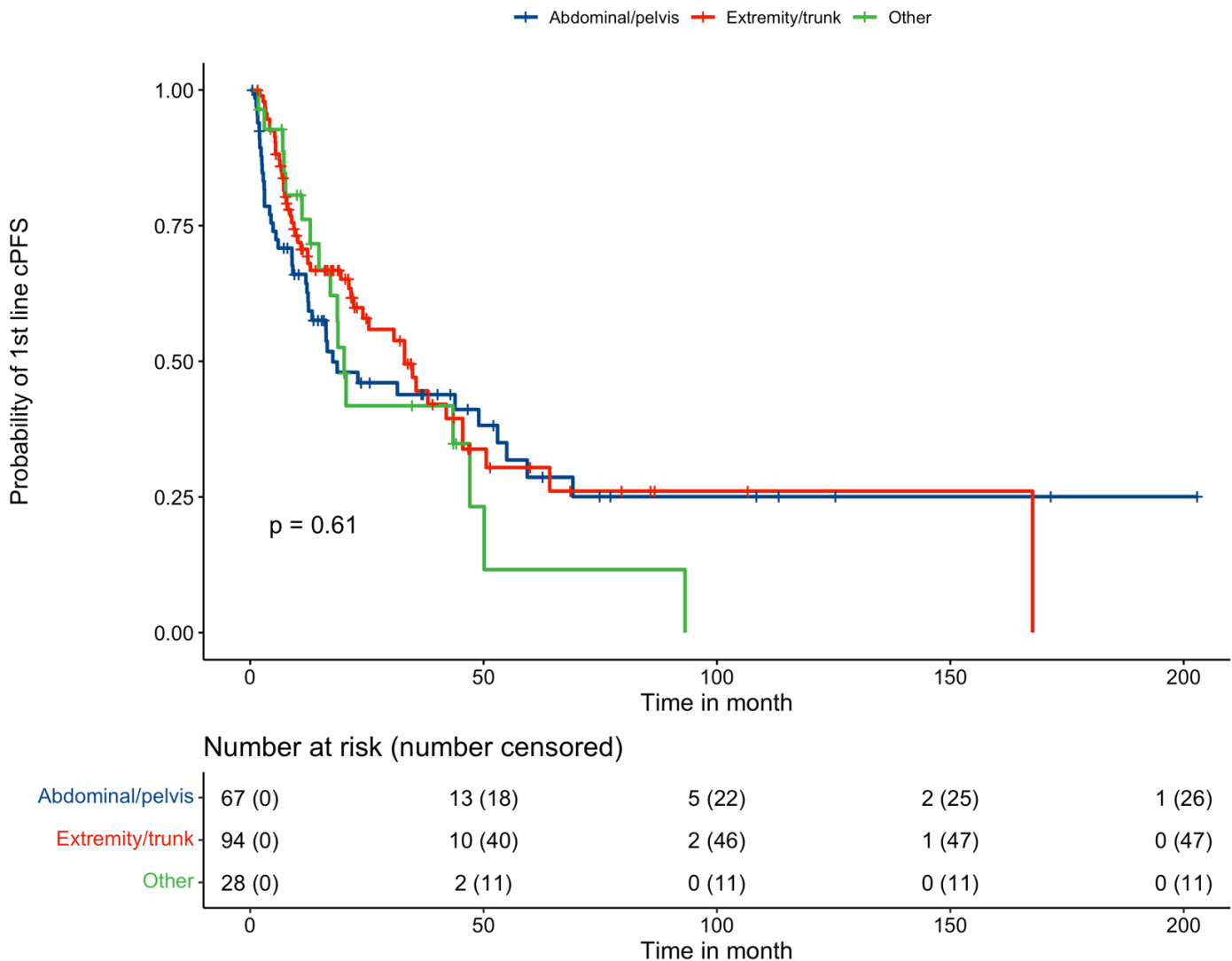
Table S5. Kaplan Meier and Cox proportional hazard analysis of first-line clinical PFS by desmoid location.**A. Kaplan-Meier – Median cPFS time by desmoid tumor location**

	N	events	median	95% CI Lower Limit	95% CI Upper Limit
Abdominal/pelvis	67	40	18	13	55
Extremity/trunk	94	47	33	22	51
Other	28	17	20	17	Not Reached

B. Kaplan-Meier 1-year cPFS by desmoid tumor location

	N at risk	events	1-year survival	95% CI Lower Limit	95% CI Upper Limit
Abdominal/pelvis	38	23	0.64	0.54	0.77
Extremity/trunk	55	26	0.71	0.62	0.81
Other	17	6	0.76	0.61	0.95

The log-rank test suggests that the 1st line treatment cPFS is not significantly different by desmoid fibromatosis locations (Chi-squared statistic = 0.98, df = 2, p-value = 0.61).



C. Cox proportional hazard analysis

Variable		All	HR (univariable) (95% CI, p value)	HR (multivariable) (95% CI, p value)
Sex	Female	125 (100)	-	-
	Male	64 (100)	0.75 (0.49-1.2, p=0.19)	0.91 (0.56-1.5, p=0.70)
Race	Caucasian	115 (100)	-	-
	Hispanic/Latino	23 (100)	0.91 (0.48-1.7, p=0.78)	1.3 (0.68-2.6, p=0.42)
	African-American	15 (100)	1.1 (0.54-2.2, p=0.83)	0.75 (0.35-1.6, p=0.44)
	Asian	8 (100)	0.77 (0.24-2.5, p=0.66)	1.0 (0.31-3.4, p=0.97)
	Other/Unknown	7 (100)	0.94 (0.34-2.6, p=0.91)	1.2 (0.40-3.5, p=0.75)
Age	Mean (SD)	37 (15)	0.99 (0.97-1.0, p=0.10)	1.0 (0.99-1.0, p=0.55)
History FAP	No	141 (100)	-	-
	Yes	37 (100)	1.1 (0.70-1.7, p=0.71)	0.70 (0.38-1.3, p=0.25)
# of Treatment Lines	1	73 (100)	-	-
	2	45 (100)	6.7 (3.4-13, p<0.001)	8.4 (3.6-20, p<0.001)
	3+	71 (100)	8.6 (4.5-16.4, p<0.001)	12 (5.2-27.2, p<0.001)
Desmoid Location	Abdominal/pelvis	67 (10)	-	-
	Extremity/trunk	94 (100)	0.86 (0.56-1.3, p=0.50)	0.59 (0.35-0.99, p=0.047)
	Other	28 (100)	1.1 (0.63-2.0, p=0.71)	0.84 (0.45-1.6, p=0.58)

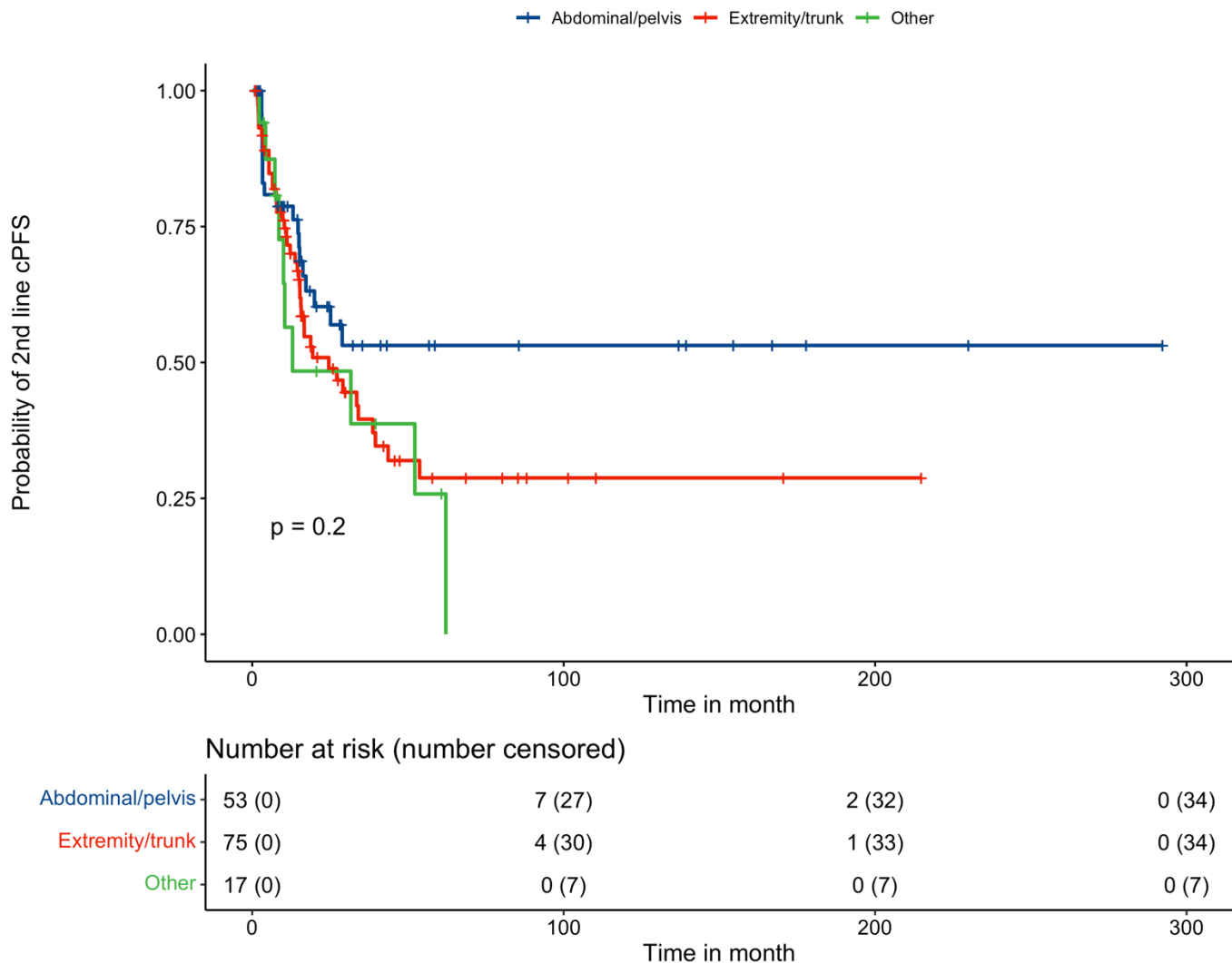
Table S6. Kaplan Meier and Cox proportional hazard analysis of second-line clinical PFS by desmoid location.**A. Kaplan-Meier – Median cPFS time by desmoid tumor location**

	N	events	median	95% CI Lower Limit	95% CI Upper Limit
Abdominal/pelvis	53	19	Not Reached	20	Not Reached
Extremity/trunk	75	41	25	16	44
Other	17	10	13	10	Not Reached

B. Kaplan-Meier 1-year cPFS by desmoid tumor location

	N at risk	events	1-year survival	95% CI Lower Limit	95% CI Upper Limit
Abdominal/pelvis	32	10	0.79	0.68	0.91
Extremity/trunk	46	20	0.72	0.62	0.83
Other	7	6	0.57	0.35	0.91

The log-rank test suggests that the 2nd line treatment cPFS is not significantly different by desmoid fibromatosis locations (Chi-squared statistic = 3.2, df = 2, p-value = 0.20).



C. Cox proportional hazard analysis

Variable		All	HR (univariable) (95% CI, p value)	HR (multivariable) (95% CI, p value)
Sex	Female	99 (100)	-	-
	Male	46 (100)	0.90 (0.54-1.5, p=0.69)	0.96 (0.52-1.8, p=0.89)
Age	Mean (SD)	35 (14)	0.98 (0.97-1.0, p=0.065)	0.99 (0.97-1.0, p=0.56)
Time to 2 nd line therapy	Mean (SD)	16 (21)	1.00 (0.98-1.0, p=0.57)	0.99 (0.98-1.0, p=0.48)
History FAP	No		-	-
	Yes		1.5 (0.87-2.6, p=0.14)	1.6 (0.79-3.4, p=0.18)
# of Treatment Lines	1	N/A	N/A	N/A
	2	68 (100)	-	-
	3+	77 (100)	5.4 (3.0-9.7, p<0.001)	7.9 (3.5-17.8, p<0.001)
Desmoid Location	Abdominal/pelvis	45 (100)	-	-
	Extremity/trunk	28 (100)	1.5 (0.88-2.6, p=0.13)	1.2 (0.60-2.3, p=0.64)
	Other	29 (100)	1.8 (0.85-4.0, p=0.12)	0.77 (0.30-2.0, p=0.59)

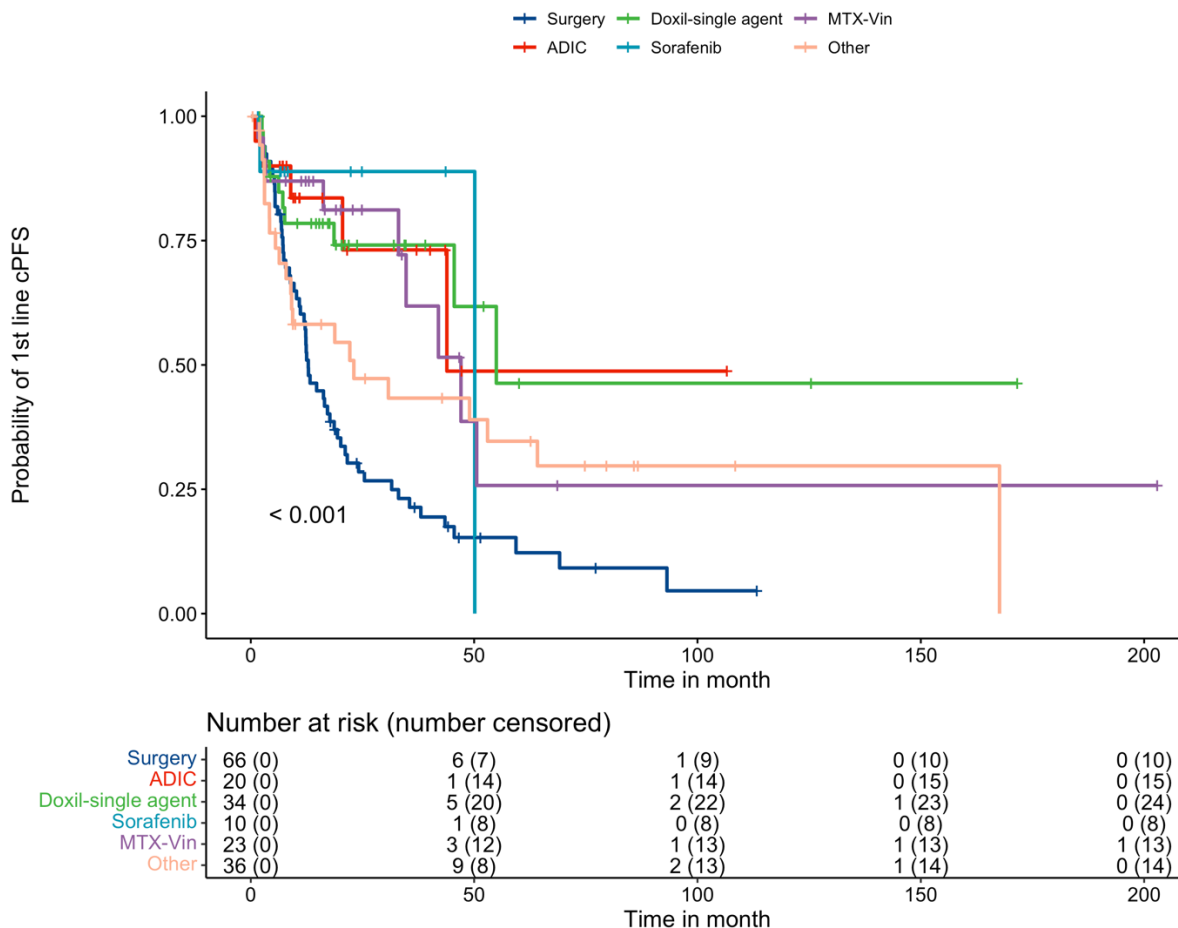
Table S7. Kaplan Meier and Cox proportional hazard analysis for first-line clinical PFS by treatment type.**A. Kaplan-Meier – Median cPFS time by treatment type**

	N	events	median	95% CI Lower Limit	95% CI Upper Limit
Surgery	66	56	13	11	19
ADIC	20	5	44	44	Not Reached
Doxil-single agent	34	10	55	46	Not Reached
Sorafenib	10	2	50	Not Reached	Not Reached
MTX-Vin	23	9	47	35	Not Reached
Other	36	22	23	9.0	Not Reached

B. Kaplan-Meier 1-year cPFS by treatment type

	N at risk	events	1-year survival	95% CI Lower Limit	95% CI Upper Limit
Surgery	38	27	0.59	0.48	0.72
ADIC	9	3	0.84	0.68	1.00
Doxil-single agent	24	7	0.79	0.66	0.94
Sorafenib	4	1	0.89	0.71	1.00
MTX-Vin	18	3	0.87	0.74	1.00
Other	17	14	0.58	0.44	0.78

The log-rank test suggests that the 1st line treatment cPFS is significantly different by 1st line treatment (Chi-squared statistic = 27, df = 5, p-value <0.001).



C. Cox proportional hazard analysis

Variable		All	HR (univariable) (95% CI, p value)	HR (multivariable) (95% CI, p value)
Sex	Female	125 (100)	-	-
	Male	64 (100)	0.75 (0.49-1.2, p=0.19)	0.94 (0.58-1.5, p=0.79)
Race	Caucasian	115 (100)	-	-
	Hispanic/Latino	23 (100)	0.91 (0.48-1.7, p=0.78)	1.4 (0.72-2.8, p=0.32)
	African-American	15 (100)	1.1 (0.54-2.2, p=0.83)	0.90 (0.43-1.9, p=0.78)
	Asian	8 (100)	0.77 (0.24-2.5, p=0.66)	1.1 (0.35-3.8, p=0.83)
	Other/Unknown	7 (100)	0.94 (0.34-2.6, p=0.91)	1.4 (0.46-4.2, p=0.56)
Age	Mean (SD)	37 (15)	0.99 (0.97-1.0, p=0.098)	1.0 (0.99-1.0, p=0.20)
History FAP	No	141 (100)	-	-
	Yes	37 (100)	1.1 (0.70-1.7, p=0.71)	0.98 (0.58-1.7, p=0.94)
# of Treatment Lines	1	73 (100)	-	-
	2	45 (100)	6.7 (3.4-13, p<0.001)	8.7 (3.6-21, p<0.001)
	3+	71 (100)	8.6 (4.5-16, p<0.001)	9.7 (4.1-23, p<0.001)
First-line treatment	Surgery	66 (100)	-	-
	ADIC	20 (100)	0.29 (0.12-0.72, p=0.008)	0.30 (0.11-0.77, p=0.013)
	Doxorubicin single agent	34 (100)	0.29 (0.15-0.57, p<0.001)	0.50 (0.24-1.1, p=0.075)
	Sorafenib	10 (100)	0.28 (0.07-1.1, p=0.074)	0.84 (0.20-3.6, p=0.81)
	MTX/Vinca	23 (100)	0.35 (0.17-0.71, p=0.004)	0.50 (0.21-1.2, p=0.13)
	Other	36 (100)	0.60 (0.36-0.99, p=0.045)	1.0 (0.58-1.9, p=0.90)

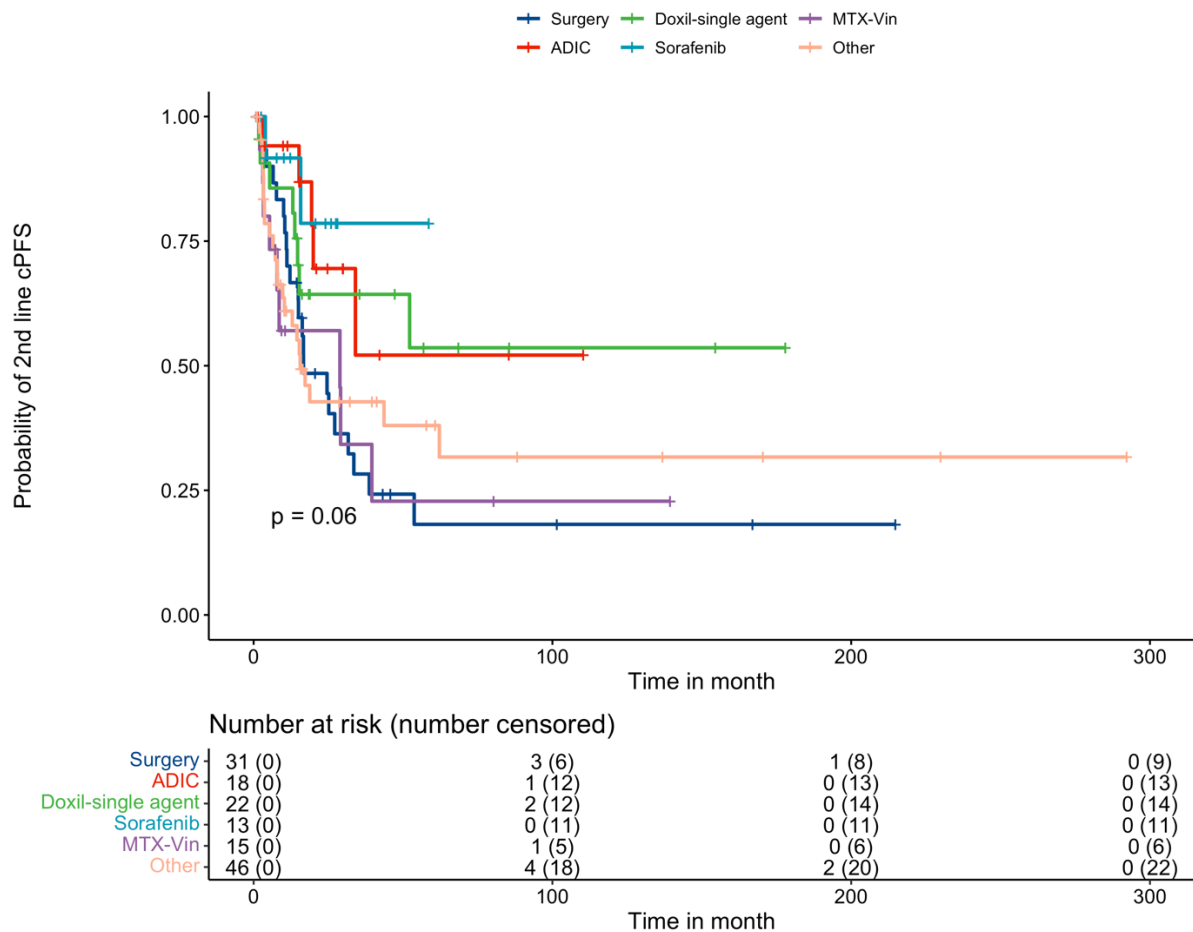
Table S8. Kaplan Meier and Cox proportional hazard analysis for second-line clinical PFS by treatment type.**A. Kaplan-Meier – Median cPFS time by treatment type**

	N	events	median	95% CI Lower Limit	95% CI Upper Limit
Surgery	31	22	17	15	39
ADIC	18	5	Not Reached	20	Not Reached
Doxil-single agent	22	8	Not Reached	15	Not Reached
Sorafenib	13	2	Not Reached	Not Reached	Not Reached
MTX-Vin	15	9	29	7.8	Not Reached
Other	46	24	16	10	Not Reached

B. Kaplan-Meier 1-year cPFS by treatment type

	N at risk	events	1-year survival	95% CI Lower Limit	95% CI Upper Limit
Surgery	21	9	0.70	0.55	0.89
ADIC	13	1	0.94	0.84	1.000
Doxil-single agent	17	3	0.86	0.72	1.000
Sorafenib	8	1	0.92	0.77	1.000
MTX-Vin	5	6	0.57	0.36	0.91
Other	21	16	0.61	0.48	0.78

The log-rank test suggests that the 2nd line treatment cPFS is not significantly different by 2nd line treatment (Chi-squared statistic = 11, df = 5, p-value = 0.060).



C. Cox proportional hazard analysis

Variable		All	HR (univariable) (95% CI, p value)	HR (multivariable) (95% CI, p value)
Sex	Female	99 (100)	-	-
	Male	46 (100)	0.90 (0.54-1.5, p=0.70)	0.84 (0.44-1.6, p=0.61)
Age	Mean (SD)	35 (14)	0.98 (0.97-1.0, p=0.065)	0.99 (0.96-1.0, p=0.24)
	Time to 2 nd line therapy	Mean (SD)	16 (21)	1.0 (0.98-1.0, p=0.57)
History FAP	No		-	-
	Yes		1.5 (0.87-2.6, p=0.14)	1.3 (0.66-2.6, p=0.44)
# of Treatment Lines	1	N/A	N/A	N/A
	2	68 (100)	-	-
	3+	77 (100)	5.4 (3.0-9.7, p<0.001)	7.1 (3.1-16, p<0.001)
First-line treatment	Surgery	45 (100)	-	-
	ADIC	28 (100)	0.38 (0.14-1.0, p=0.049)	0.39 (0.14-1.0, p=0.063)
	Doxorubicin single agent	7 (100)	0.49 (0.22-1.1, p=0.080)	0.54 (0.21-1.4, p=0.20)
	Sorafenib	29 (100)	0.25 (0.06-1.07, p=0.063)	0.48 (0.06-3.8, p=0.49)
	MTX/Vinca		1.08 (0.50-2.35, p=0.844)	1.3 (0.56-3.0, p=0.54)
	Other		0.90 (0.50-1.61, p=0.723)	1.2 (0.59-2.3, p=0.66)

Table S9. Kaplan Meier and Cox proportional hazard analysis for clinical PFS, all treatment episodes by treatment type.

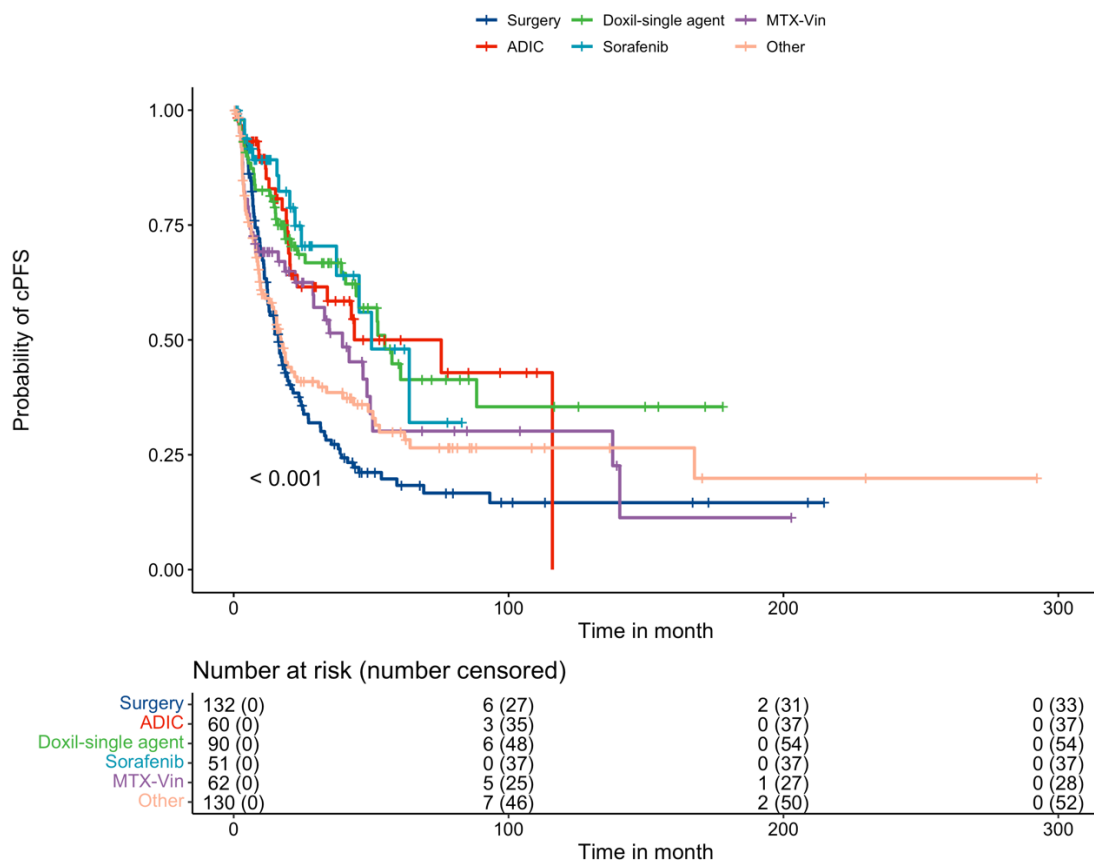
A. Kaplan-Meier – Median cPFS time by treatment type

	N	events	median	95% CI Lower Limit	95% CI Upper Limit
Surgery	132	99	16	13	20
ADIC	60	23	76	23	Not Reached
Doxil-single agent	90	36	55	45	Not Reached
Sorafenib	51	14	50	37	Not Reached
MTX-Vin	62	34	40	29	138
Other	130	78	17	13	34

B. Kaplan-Meier 1-year cPFS rate by treatment type

	N at risk	events	1-year survival	95% CI Lower Limit	95% CI Upper Limit
Surgery	78	48	0.63	0.55	0.72
ADIC	39	8	0.85	0.76	0.95
Doxil-single agent	69	15	0.83	0.75	0.91
Sorafenib	30	5	0.89	0.81	0.99
MTX-Vin	36	19	0.69	0.59	0.82
Other	63	49	0.59	0.51	0.69

The log-rank test suggests that cPFS is significantly different by treatment type (Chi-squared statistic = 36, df = 5, p-value <0.001).



C. Cox proportional hazard analysis

Variable		All	HR (univariable) (95% CI, p value)	HR (multivariable) (95% CI, p value)
Sex	Female	362 (100)	-	-
	Male	163 (100)	0.96 (0.75-1.2, p=0.76)	1.0 (0.71-1.4, p=0.97)
Race	Caucasian	326 (100)	-	-
	Hispanic/Latino	64 (100)	0.98 (0.67-1.4, p=0.92)	0.97 (0.60-1.6, p=0.90)
	African-American	45 (100)	1.3 (0.84-1.9, p=0.27)	1.3 (0.79-2.2, p=0.29)
	Asian	16 (100)	0.27 (0.08-0.83, p=0.023)	0.35 (0.09-1.3, p=0.12)
	Other/Unknown	24 (100)	1.2 (0.72-2.1, p=0.44)	1.2 (0.62-2.4, p=0.55)
Age	Mean (SD)	35 (14)	0.99 (0.98-1.0, p=0.011)	0.98 (0.97-0.99, p=0.002)
Frailty (ID)		-	-	-
History FAP	No	395 (100)	-	-
	Yes	109 (100)	1.4 (1.0-1.8, p=0.027)	1.3 (0.85-1.8, p=0.25)
# of Treatment Lines	1	189 (100)	-	-
	2	145 (100)	0.86 (0.64-1.2, p=0.34)	0.90 (0.64-1.3, p=0.55)
	3+	191 (100)	0.92 (0.70-1.2, p=0.53)	0.79 (0.57-1.1, p=0.14)
First-line treatment	Surgery	132 (100)	-	-
	ADIC	60 (100)	0.44 (0.28-0.69, p<0.001)	0.50 (0.30-0.82, p=0.006)
	Doxorubicin single agent	90 (100)	0.43 (0.29-0.63, p<0.001)	0.38 (0.24-0.59, p<0.001)
	Sorafenib	51 (100)	0.37 (0.21-0.65, p=0.001)	0.33 (0.17-0.61, p=0.001)
	MTX/Vinca	62 (100)	0.68 (0.46-1.0, p=0.050)	0.73 (0.46-1.2, p=0.178)
	Other	130 (100)	0.85 (0.63-1.1, p=0.278)	1.01 (0.70-1.5, p=0.943)

Table S10. Kaplan Meier and Cox proportional hazard analysis for RECIST PFS, all treatment episodes by treatment type.

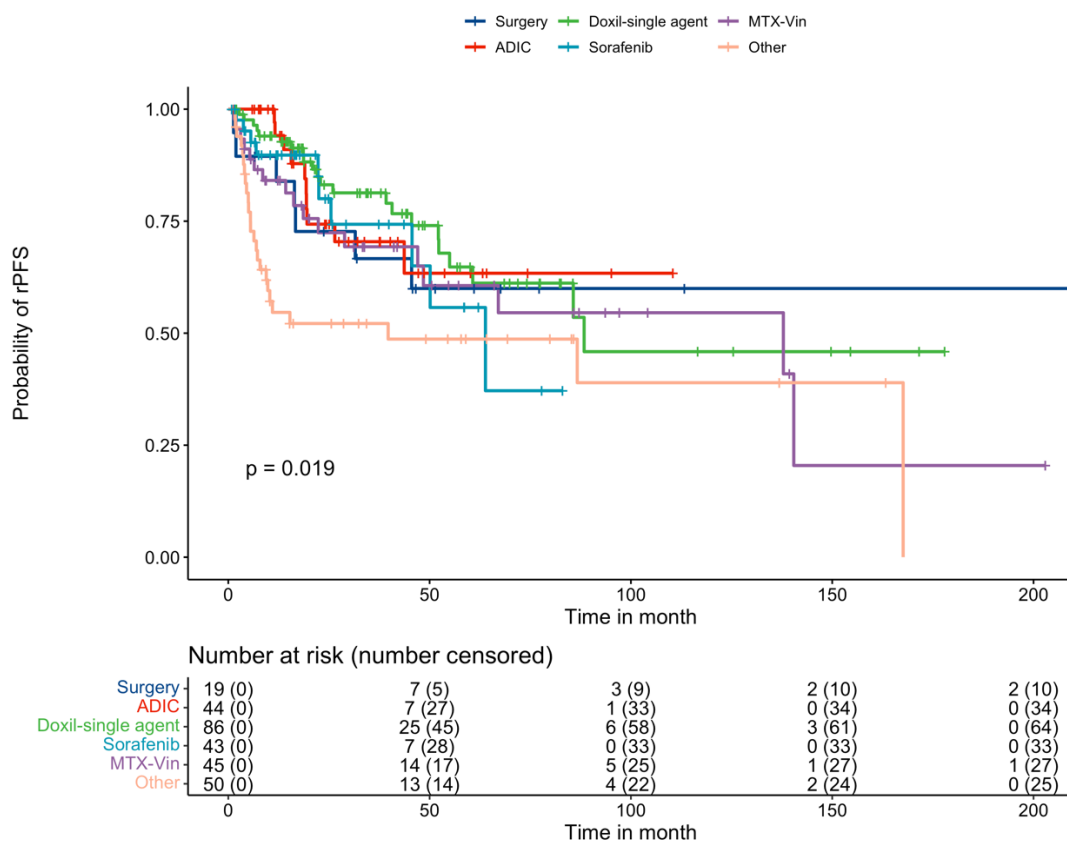
A. Kaplan-Meier – Median rPFS time by treatment type

	N	events	median	95% CI Lower Limit	95% CI Upper Limit
Surgery	19	7	Not Reached	32	Not Reached
ADIC	44	10	Not Reached	44	Not Reached
Doxil-single agent	86	22	88	61	Not Reached
Sorafenib	43	10	64	46	Not Reached
MTX-Vin	45	17	138	48	Not Reached
Other	50	25	40	9.4	Not Reached

B. Kaplan-Meier 1-year rPFS rate by treatment type

	N at risk	events	1-year survival	95% CI Lower Limit	95% CI Upper Limit
Surgery	15	3	0.84	0.69	1.0
ADIC	32	2	0.94	0.87	1.0
Doxil-single agent	74	5	0.94	0.89	0.99
Sorafenib	27	4	0.90	0.81	1.0
MTX-Vin	32	7	0.84	0.74	0.96
Other	22	21	0.55	0.42	0.71

The log-rank test suggests that rPFS is significantly different by treatment type (Chi-squared statistic = 14, df = 5, p-value = 0.019).



C. Cox proportional hazard analysis

Variable		All	HR (univariable) (95% CI, p value)	HR (multivariable) (95% CI, p value)
Sex	Female	192 (100)	-	-
	Male	96 (100)	1.1 (0.69-1.7, p=0.76)	1.0 (0.56-1.8, p=0.98)
Race	Caucasian	179 (100)	-	-
	Hispanic/Latino	35 (100)	0.65 (0.30-1.4, p=0.28)	0.68 (0.27-1.8, p=0.42)
	African-American	25 (100)	0.76 (0.35-1.66, p=0.49)	0.67 (0.24-1.8, p=0.43)
	Asian	8 (100)	0.00 (0.00-Inf, p=0.99)	NA (NA-NA, p=NA)
	Other/Unknown	16 (100)	1.4 (0.61-3.3, p=0.41)	1.0 (0.35-3.0, p=0.97)
Age	Mean (SD)	36 (14)	0.99 (0.98-1.0, p=0.29)	0.99 (0.97-1.0, p=0.27)
Frailty (ID)			-	-
History FAP	No	205 (100)	-	-
	Yes	68 (100)	2.0 (1.3-3.1, p=0.001)	2.0 (1.0-3.6, p=0.031)
# of Treatment Lines	1	99 (100)	-	-
	2	78 (100)	0.86 (0.48-1.6, p=0.62)	0.96 (0.49-1.9, p=0.91)
	3+	111 (100)	1.3 (0.80-2.1, p=0.30)	1.00 (0.53-1.9, p=0.99)
First-line treatment	Surgery	19 (100)	-	-
	ADIC	44 (100)	0.86 (0.32-2.3, p=0.76)	1.1 (0.34-3.3, p=0.92)
	Doxorubicin single agent	86 (100)	0.80 (0.34-1.9, p=0.60)	0.72 (0.26-2.0, p=0.53)
	Sorafenib	43 (100)	1.04 (0.39-2.8, p=0.95)	1.1 (0.35-3.6, p=0.83)
	MTX/Vinca	45 (100)	1.2 (0.50-2.9, p=0.68)	1.4 (0.45-4.1, p=0.58)
	Other	51 (100)	2.1 (0.90-4.9, p=0.086)	3.4 (1.2-9.9, p=0.024)

Table S11. Kaplan Meier and Cox proportional hazard analysis for Time to Next Treatment, all treatment episodes by treatment type.

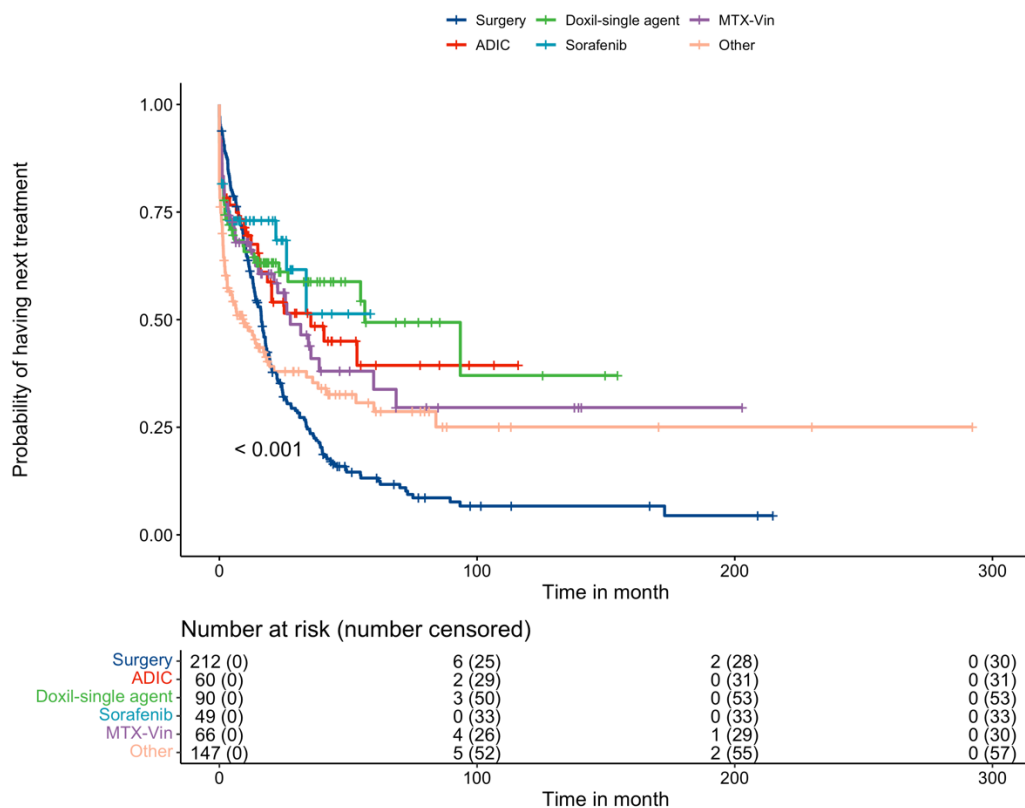
A. Kaplan-Meier – Median TTNT time by treatment type

	N	events	median	95% CI Lower Limit	95% CI Upper Limit
Surgery	212	182	16	14	18
ADIC	60	29	36	16	Not Reached
Doxil-single agent	90	37	56	27	Not Reached
Sorafenib	49	16	Not Reached	26	Not Reached
MTX-Vin	66	36	28	15	69
Other	147	90	9.3	3.1	18

B. Kaplan-Meier 1-year TTNT rate by treatment type

	N at risk	events	1-year survival	95% CI Lower Limit	95% CI Upper Limit
Surgery	124	82	0.61	0.55	0.68
ADIC	34	18	0.70	0.59	0.82
Doxil-single agent	52	30	0.66	0.57	0.77
Sorafenib	22	13	0.73	0.62	0.87
MTX-Vin	38	21	0.68	0.58	0.80
Other	50	74	0.47	0.40	0.57

The log-rank test suggests that TTNT is significantly different by treatment type (Chi-squared statistic = 32, df = 5, p-value < 0.001).



C. Cox proportional hazard analysis

Variable		All	HR (univariable) (95% CI, p value)	HR (multivariable) (95% CI, p value)
Sex	Female	429 (100)	-	-
	Male	195 (100)	1.0 (0.81-1.2, p=1)	1.0 (0.80-1.3, p=0.88)
Race	Caucasian	371 (100)	-	-
	Hispanic/Latino	92 (100)	1.1 (0.85-1.5, p=0.43)	1.0 (0.76-1.4, p=0.86)
	African-American	50 (100)	0.92 (0.64-1.3, p=0.68)	0.97 (0.66-1.4, p=0.87)
	Asian	20 (100)	1.1 (0.59-1.9, p=0.84)	1.2 (0.64-2.1, p=0.65)
	Other/Unknown	24 (100)	1.2 (0.68-1.9, p=0.60)	1.1 (0.66-1.9, p=0.67)
Age	Mean (SD)	34 (15)	0.99 (0.98-1.0, p=0.001)	0.99 (0.98-0.99, p<0.001)
Frailty (ID)		-	-	-
History FAP	No	466 (100)	-	-
	Yes	126 (100)	1.1 (0.87-1.4, p=0.41)	1.1 (0.81-1.4, p=0.64)
# of Treatment Lines	1	233 (100)	-	-
	2	163 (100)	0.87 (0.67-1.1, p=0.29)	0.84 (0.64-1.1, p=0.22)
	3+	228 (100)	0.98 (0.78-1.2, p=0.86)	0.91 (0.71-1.2, p=0.48)
First-line treatment	Surgery	212 (100)	-	-
	ADIC	60 (100)	0.55 (0.37-0.82, p=0.003)	0.69 (0.46-1.0, p=0.075)
	Doxorubicin single agent	90 (100)	0.50 (0.35-0.71, p<0.001)	0.56 (0.38-0.81, p=0.002)
	Sorafenib	49 (100)	0.47 (0.28-0.79, p=0.004)	0.49 (0.29-0.85, p=0.010)
	MTX/Vinca	66 (100)	0.63 (0.44-0.90, p=0.010)	0.78 (0.53-1.15, p=0.209)
	Other	147 (100)	0.97 (0.75-1.3, p=0.814)	1.2 (0.90-1.6, p=0.227)

Table S12: Best overall response rate and disease control rate for various treatment regimens, all lines of therapy, by mutation status.

Regimen	Outcomes	All patients	T41A	S45F	APC	Negative/ Other
ADIC	N (%) Best ORR ¹ DCR ¹	50 17 (34) 48 (96)	18 7 (39) 18 (100)	12 3 (25) 12 (100)	4 3 (75) 4 (100)	7 2 (29) 6 (86)
Single agent doxorubicin ²	N (%) Best ORR DCR	76 18 (24) 70 (92)	14 4 (29) 14 (100)	11 5 (45) 9 (81)	6 0 (0) 6 (100)	20 5 (25) 19 (95)
MTX/vinca alkaloids	N (%) Best ORR DCR	39 12 (31) 34 (87)	7 3 (43) 5 (71)	5 1 (20) 5 (100)	3 1 (33) 3 (100)	9 2 (22) 7 (78)
Sorafenib	N (%) Best ORR DCR	36 10 (28) 32 (89)	9 4 (44) 8 (89)	4 0 (0) 4 (100)	3 1 (33) 2 (67)	3 0 (0) 2 (67)
Other ³	N (%) Best ORR DCR	47 5 (11) 34 (72)	5 1 (20) 4 (80)	9 0 (0) 7 (78)	3 0 (0) 0 (0)	6 0 (0) 4 (67)

1. Overall response rate (ORR) includes proportion of patients achieving complete (CR) or partial response (PR), disease control rate (DCR) includes CR and PR as well as stable disease. 2. Includes liposomal doxorubicin and single agent traditional doxorubicin. 3. Other treatments include tamoxifen and other estrogen suppressive therapies, imatinib, other TKIs, and other chemotherapies (see Figure S1 for complete details). Abbreviations: MTX (methotrexate).