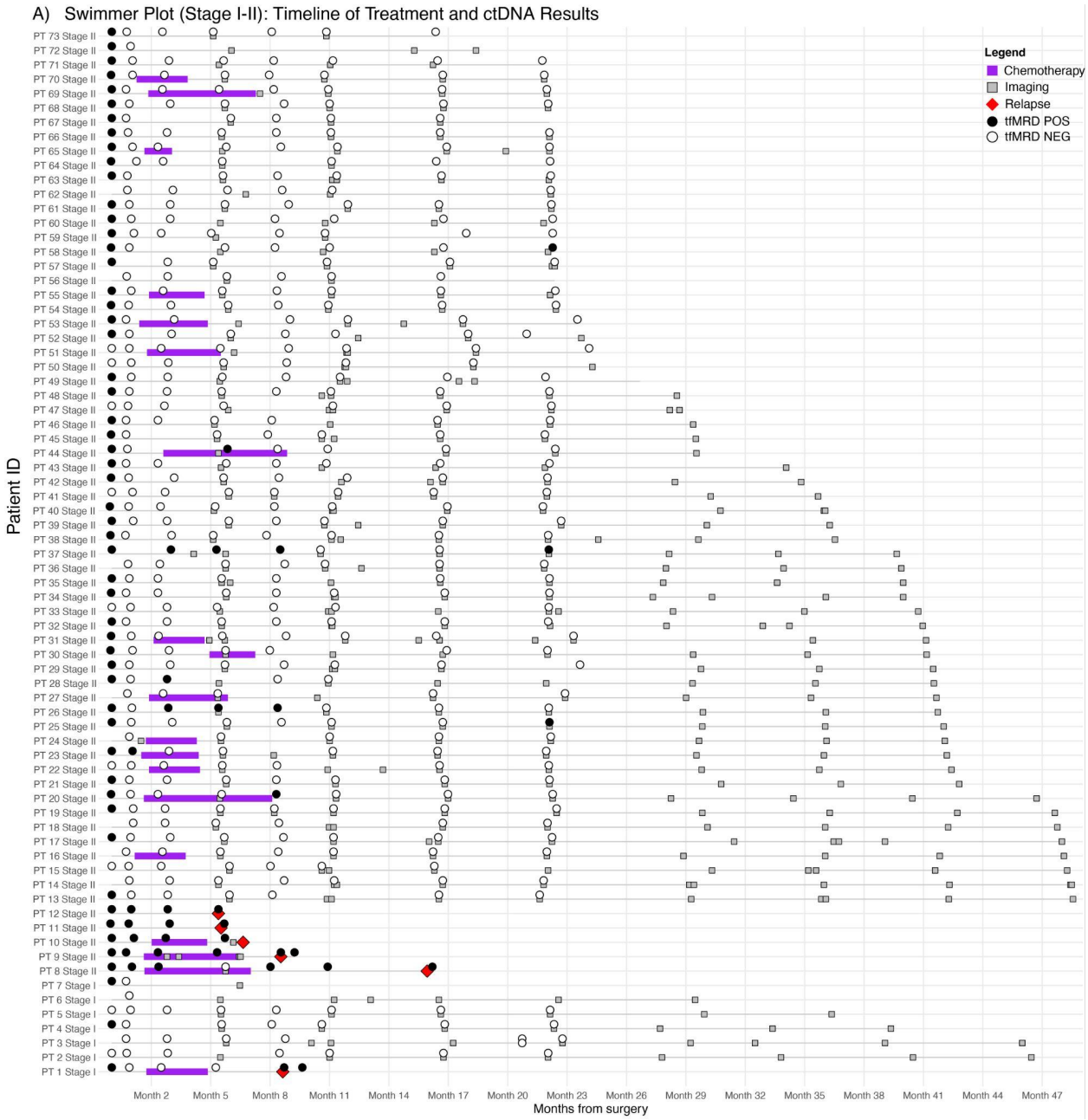
Supplementary Material

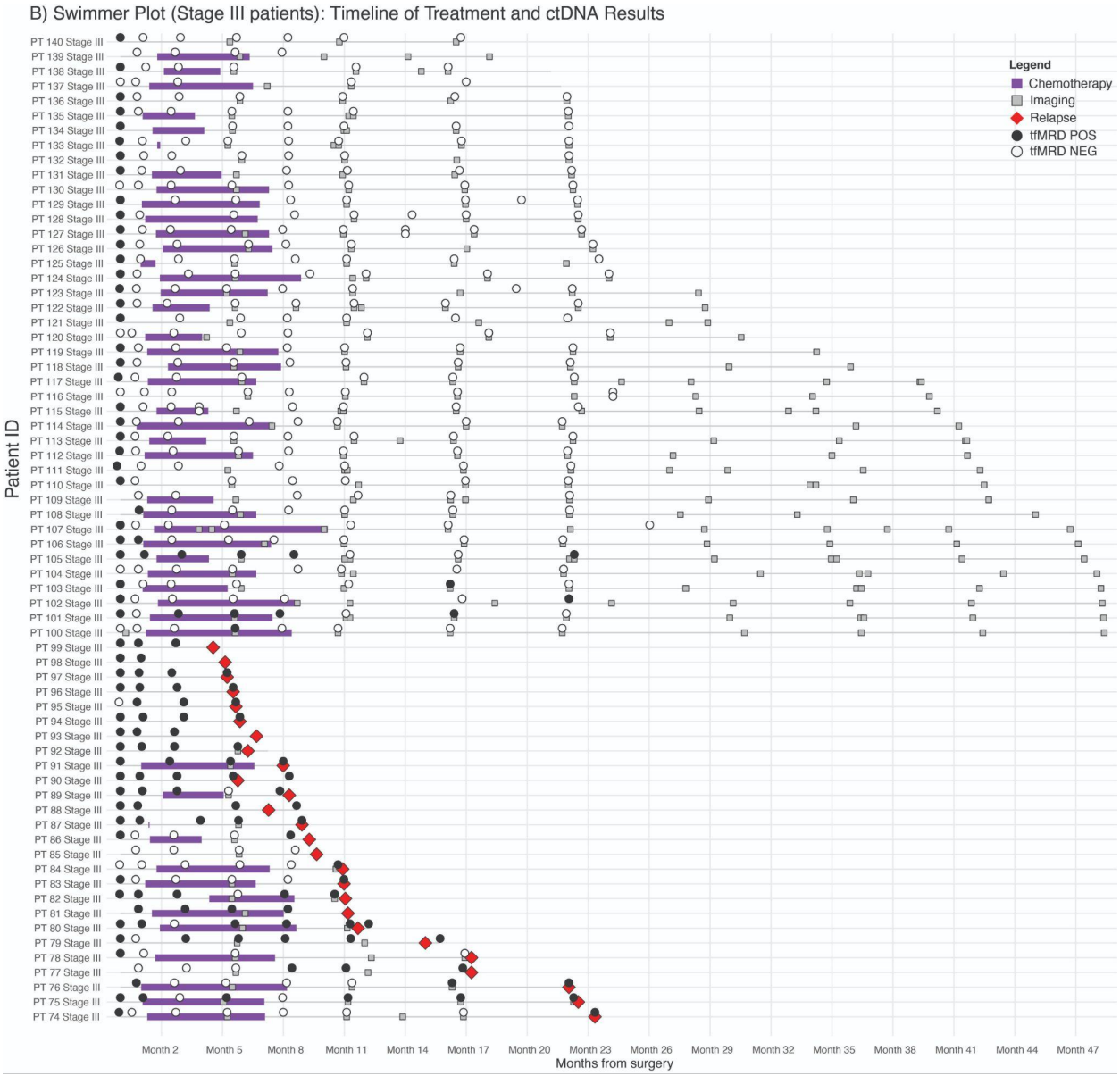
Supplementary Table 1. Comparison of clinicopathological factors: Latitude clinical validation cohort vs. full Galaxy cohort.

Characteristic		*N* = 195	Nakamura 2024	Statistics
Age, median (range)	Years	68 (29-88)	69 (28-95)	p=0.7884
Sex, n (%)	Female	91 (47)	1091 (49)	p=0.602
	Male	104 (53)	1149 (51)	
Pathological stage, n (%)	I	7 (3.6)	234 (10)	p=0.001[a]
	II	66 (34)	652 (29)	p=0.165
	III	67 (34)	936 (42)	p=0.050
	IV	55 (28)	418 (19)	p=0.002[a]
Primary site, n (%)[b]	Right-sided colon	64 (33)	863 (39)	p=0.1243
	Left-sided colon	131 (67)	1377 (61)	
ECOG score, n (%)	0	171 (88)	2046 (91)	p=0.090
	1	24 (12)	194 (9)	
Pathological T stage, n (%)	T1-T2	12 (7.7)	317 (14)	p=0.002[a]
	T3-T4	151 (93)	1630 (73)	
	Unknown	32	293 (13)	
Pathological N stage, n (%)	N0	77 (47)	922 (41)	p=0.422
	N1-2	86 (53)	1025 (46)	
	Unknown	32	293 (13)	
ACT, n (%)	Adjuvant chemotherapy	84 (43)	946 (42)	p=0.821
	Observation	111 (57)	1294 (58)	
BRAF V600E	BRAF wildtype	183 (94)	2062 (92)	p=0.485
	BRAF V600E	12 (6.2)	178 (8)	
RAS, n (%)	Wildtype	124 (64)	1303 (58)	p=0.150
	Mutated	71 (36)	937 (42)	
MSI status, n (%)	MSS	180 (92)	2052 (90)	p=0.521
	MSI-High	15 (7.7)	215 (10)	
Radiological recurrence, n (%)	Yes	68 (35)	500 (22)	p=0.001[a]
	No	127 (65)	1740 (78)	
Recurrence site, n (% of 68 for this study, % of 500 for Nakamura et al 2024)	Liver	26 (38)	144 (29)	p=0.121
	Liver+lung	4 (6)	24 (5)	p=0.763
	liver+bone	1(1)	1 (<1)	p=0.225
	Liver+lymph node	1(1)	6 (1)	p=0.593
	Local	4 (6)	5 (1)	p=0.015[c]
	Local+lymph	1 (1)	1 (<1)	p=0.225
	Lung	11 (16)	128 (26)	p=0.0992
	Lung+brain	2 (3)	2 (<1)	p=0.0723
	Lymph node	6 (9)	29 (6)	p=0.292
	Peritoneum	4 (6)	56 (11)	p=0.212
	Peritoneum + other	7 (10)	63 (13)	p=0.697
	Spleen	1 (1)	1 (<1)	p=0.225
	Other	0 (0)	40 (8%)	p=0.009[c]

The latitude subset cohort was selected following the inclusion and exclusions as outlined in the consort diagram, including availability of sufficient blood volume (>8mL of plasma samples) to run Latitude assay. [a]The cohort was enriched for recurrent cases to ensure statistical power for the estimation of clinical performance, resulting increase in stage IV, and decrease in stage I and T1-T2 tumors. [b]Rectal patients (N=24) were combined with left-sided colon in “Primary site” to match the comparison withthe larger GALAXY study. cMinor variations in relapse sites are attributed to the sampling design and do not reflect a bias in tumor fraction.

Supplementary Figure 1




B) Swimmer Plot (Stage III patients): Timeline of Treatment and ctDNA Results
Patient ID
PT 140 Stage III
PT 139 Stage III
PT 138 Stage III
PT 137 Stage III
PT 136 Stage III
PT 135 Stage III
PT 134 Stage III
PT 133 Stage III
PT 132 Stage III
PT 131 Stage III
PT 130 Stage III
PT 129 Stage III
PT 128 Stage III
PT 127 Stage III
PT 126 Stage III
PT 125 Stage III
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PT 120 Stage III
PT 119 Stage III
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PT 102 Stage III
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PT 95 Stage III
PT 94 Stage III
PT 93 Stage III
PT 92 Stage III
PT 91 Stage III
PT 90 Stage III
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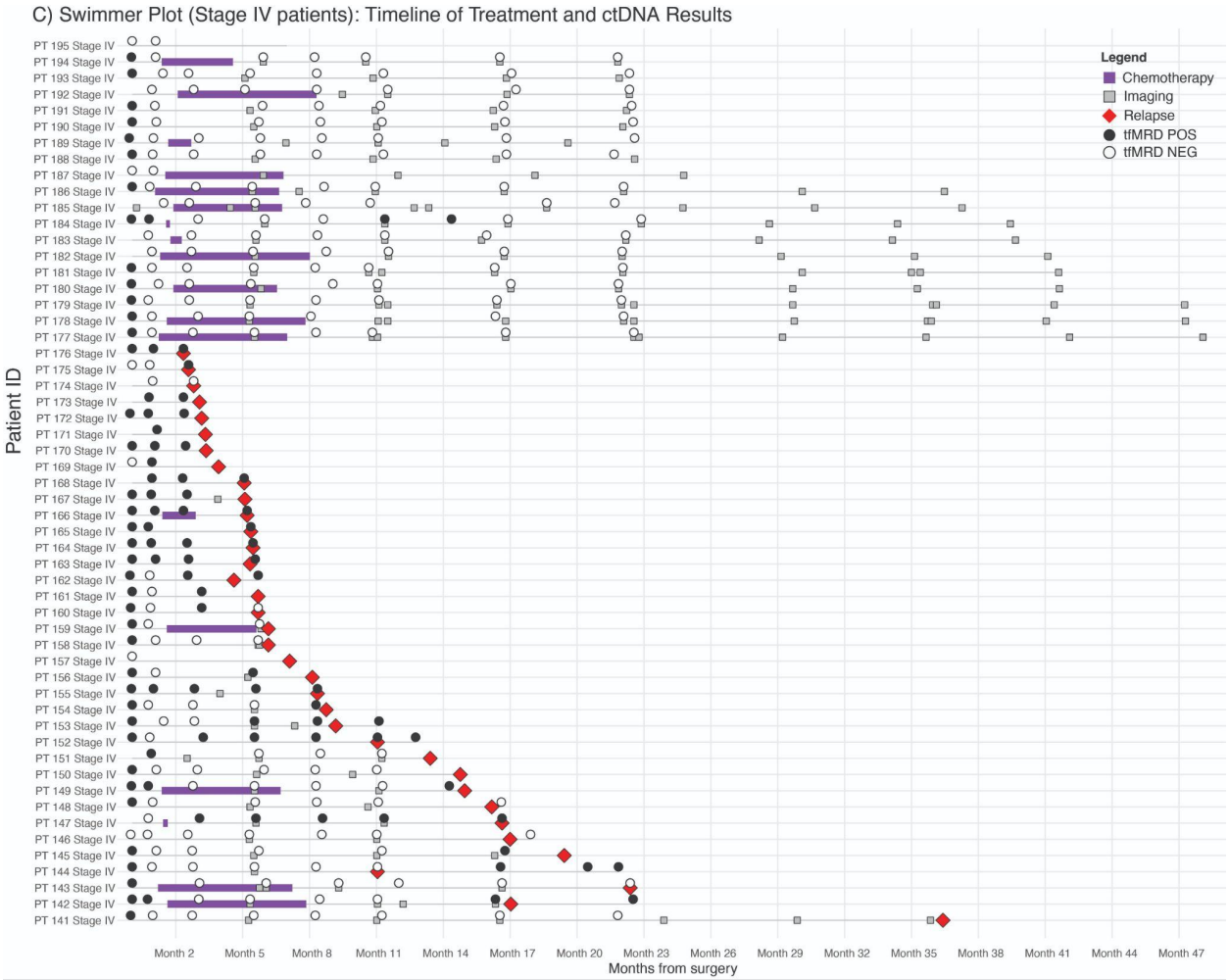
PT 85 Stage III
PT 84 Stage III
PT 83 Stage III
PT 82 Stage III
PT 81 Stage III
PT 80 Stage III
PT 79 Stage III
PT 78 Stage III
PT 77 Stage III
PT 76 Stage III
PT 75 Stage III
PT 74 Stage III
Month 2
Month 5
Month 8
Month 11
Month 14
Month 17
Month 20
Month 23
Month 26
Month 29
Month 32
Month 35
Month 38
Month 41
Month 44
Month 47
Months from surgery
Legend
Chemotherapy
Imaging
Relapse
tfMRD POS
tfMRD NEG



Supplementary Fig 1. Overview plots depicting the complete clinical course of all patients with (A) Stage I-II, (B) Stage III, and (C) Stage IV colorectal cancer, including results of longitudinal ctDNA analysis.