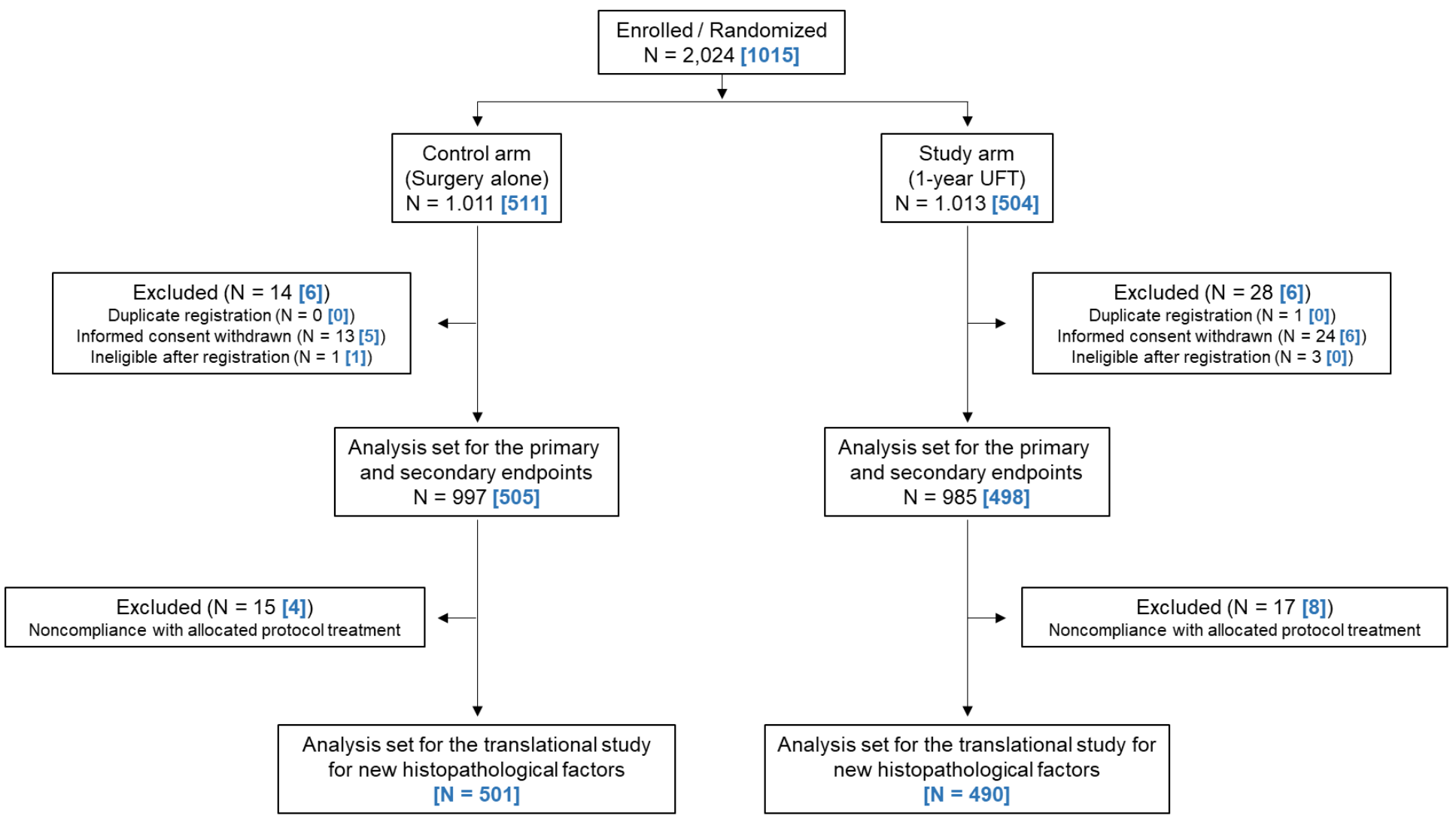
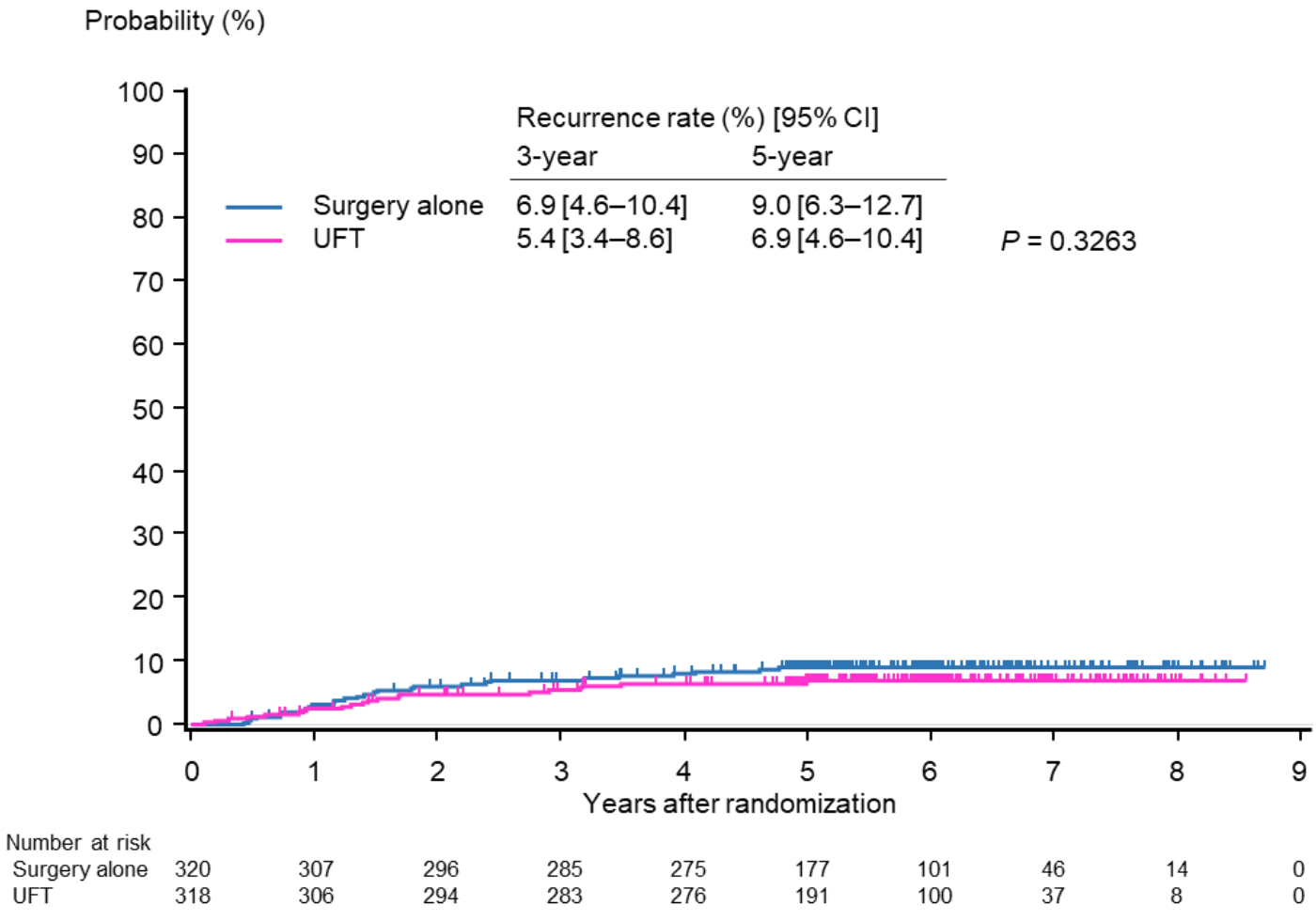


Supplemental Figure 1. CONSORT diagram



Supplemental Figure 2. Comparison of time to recurrence between the surgery-alone group and the chemotherapy group in A) patients with tumors classified as Mature pattern and B) those with tumors classified as non-Mature pattern.

The 5-year recurrence rates (95% CI) for surgery-alone and the UFT groups were 9.0% (6.3%–12.7%) and 6.9% (4.6%–10.4%) in the Mature group and 26.2% (20.4%–33.3%) and 20.9% (15.5%–27.9%) in the non-Mature group, respectively. UFT, tegafur–uracil

Supplemental Table 1.

A list of institutions that participated in the translational study for new histopathological prognostic factors in the SACURA trial

1. Osaka General Medical Center	42. Osaka City General Hospital	83. Gunma University Graduate School of Medicine
2. National Defense Medical College	43. Higashi Takarazuka Satoh Hospital	84. Nagahama City Hospital
3. Kobe City Hospital Organization Kobe City Medical Center West Hospital	44. Tokyo Yamate Medical Center	85. Shinshu University Hospital
4. Koseiren Takaoka Hospital	45. Takarazuka City Hospital	86. Japanese Red Cross Society Nagano Hospital
5. Hamamatsu University School of Medicine	46. Kurashiki Central Hospital	87. Tottori University Hospital
6. Saiseikai Yokohamashi Tobu Hospital	47. kurume university school of medicine	88. Kyoritsu General hospital
7. Tokyo Medical and Dental University	48. Hakodate Municipal Hospital	89. Saitama Medical University International Medical Center
8. JCHO Osaka Hospital	49. Tochigi Cancer Center	90. Numazu City Hospital
9. Suita Municipal Hospital	50. Kitakyushu Municipal Medical Center	91. Nishijin Hospital
10. Japanese Red Cross Kyoto Daini Hospital	51. Hashima City Hospital	92. Shizuoka City Shizuoka Hospital
11. Nippon Medical School Chiba Hokusoh Hospital	52. Kure Medical Center and Chugoku Cancer Center	93. Fujita Health University Banbuntane Hotokukai Hospital
12. Shizuoka City Shimizu Hospital	53. Hokushin General Hospital	94. Hokkaido chuo rosai hospital
13. Sano Hospital	54. Miyagi Cancer Center	95. Heisei Yokohama Hospital
14. Saiseikai Tondabayashi Hospital	55. Yamagata University Hospital	96. Iida Municipal Hospital
15. Fukui-ken Saiseikai Hospital	56. Yamaguchi University Graduate School of Medicine	97. Gifu City Hospital
16. National Hospital Organization Kyoto Medical Center	57. Oita University Graduate School of Medicine	98. Hiraka General Hospital
17. St. Mary's Hospital	58. Nagano Municipal Hospital	99. Tokyo Women's Medical University Hospital
18. Sakai City Medical Center	59. Shimonoseki Medical Center	100. University of Fukui Hospital
19. Ogaki Municipal Hospital	60. Himeji St. Mary's Hospital	101. Midori Municipal Hospital
20. Tokyo Metropolitan Tama Medical Center	61. Nagoya Ekisaikai Hospital	102. Kawakita General Hospital
21. Social Insurance Tagawa Hospital	62. Tokushima University Hospital	103. Chigasaki Municipal Hospital
22. Chugoku Central Hospital	63. Anan Kyoei Hospital	104. Minamiosaka Hospital
23. Teikyo University School of Medicine	64. Kumamoto University	105. Saiseikai Hiroshima Hospital
24. National Hospital Organization Kobe Medical Center	65. National Hospital Organization Shikoku Cancer Center	106. Kobe City Nishi-Kobe Medical Center
25. Hakodate Goryoukaku Hospital	66. Kanagawa Cancer Center	107. Nanpuh Hospital
26. Gunma Prefectural Cancer Center	67. Matsunami General Hospital	108. Noshiro Kousei Medical Center
27. Hyogo College of Medicine	68. Otemae Hospital	109. Niigata University Medical & Dental Hospital
28. Kagawa Prefectural Central Hospital	69. Japanese Red Cross Osaka Hospital	110. Hoshigaoka Medical Center
29. International Goodwill Hospital	70. Hyogo Cancer Center	111. Almeida Memorial Hospital
30. Kobe University Graduate School of Medicine	71. Aichi Cancer Center Aichi Hospital	112. Kagawa Rosai Hospital
31. Rinku General Medical Center	72. University of Yamanashi Hospital	113. Japanese Red Cross Wakayama Medical Center
32. Kyorin University	73. Jichi Medical University Hospital	114. Kansai Medical University Medical Center
33. Niigata Cancer Center Hospital	74. Otsu City Hospital	115. Saitama Medical Center
34. Osaka Police Hospital	75. Oita Red Cross Hospital	116. Himeji Central Hospital
35. Kansai Rosai Hospital	76. Teikyo University Chiba Medical Center	117. Katsushika Edogawa Hospital
36. National Center for Global Health and Medicine	77. Tohoku Rosai Hospital	118. Matsuda Hospital
37. Fukushima Medical University	78. Kitasato University East Hospital	119. International University of Health and Welfare, Mita Hospital
38. Osaka Rosai Hospital	79. Minoh City Hospital	120. National Hospital Organization Kumamoto Minami Hospital
39. Sapporo Medical University	80. Asahikawa Medical University	121. Saitama Medical Center
40. Miyoshi Central Hospital	81. Kyushu University Graduate School of Medical Sciences	122. Ishikawa Prefectural Central Hospital
41. Nagoya University Hospital	82. Nissay Hospital	123. Saiseikai Nara Hospital

Supplemental Table 2.

The incidence of postoperative oncological events according to the DR pattern

Oncological event	Organ of recurrence	DR pattern			*P* value
		Mature (N=638)	Intermed. (N=294)	Immature (N=59)	
Recurrence	Overall	49 (7.7)	63 (21.4)	19 (32.2)	<0.0001
	Liver	*27 (4.2)*	*29 (9.9)*	*4 (6.8)*	*0.0035*
	Lung	*13 (2.0)*	*14 (4.8)*	*10 (16.9)*	*<0.0001*
	Non-regional lymph node	*4 (0.6)*	*8 (2.7)*	*5 (8.5)*	*0.0002*
	Peritoneum	*4 (0.6)*	*10 (3.4)*	*5 (8.5)*	*<0.0001*
	Local	*3 (0.5)*	*7 (2.4)*	*1 (1.7)*	*0.0271*
Second cancer		64 (10.0)	21 (7.1)	2 (3.4)	0.1310

DR, desmoplastic reaction

Supplemental Table 3. Multivariate analyses for RFS as sensitivity analysis

Parameter	Category	Selected prognostic factors (N = 991)		Full prognostic factors** (N = 916)	
		HR (95% CI)	*P* value	HR (95% CI)	*P* value
Sex	Female			1	
	Male			1.21 [0.85–1.72]	0.2912
Age (average; years)	≤70			1	
	71–80			1.41 [1.00–2.00]	0.0488
Tumor location	Right-sided colon			1	
	Left-sided colon			1.02 [0.70–1.48]	0.9300
	Rectosigmoid			1.07 [0.67–1.71]	0.7694
Extent of LN dissection*	D3			1	
	D1, D2			1.51 [1.02–2.24]	0.0380
No. of LN examined	≥12	1		1	
	<12	1.27 [0.90–1.80]	0.1715	1.11 [0.76–1.63]	0.5995
Tumor differentiation	G1	1		1	
	G2	1.15 [0.83–1.60]	0.3914	1.08 [0.76–1.52]	0.6762
	G3	0.39 [0.12–1.26]	0.1162	0.70 [0.21–2.38]	0.5650
T-stage	T3	1		1	
	T4	2.14 [1.51–3.04]	<.0001	2.19 [1.52–3.16]	<.0001
Lymphatic invasion	Negative	1		1	
	Positive	0.92 [0.66–1.27]	0.5980	0.97 [0.68–1.37]	0.8391
Venous invasion	Negative	1		1	
	Positive	1.15 [0.82–1.62]	0.4210	1.04 [0.72–1.49]	0.8499
Preoperative CEA (ng/ml)	≤5.0			1	
	>5.0			1.38 [0.98–1.96]	0.0672
MSI	MSI-Low, MSS			1	
	MSI-High			0.34 [0.10–1.14]	0.0801
Treatment arm	Surgery-alone	1		1	
	UFT	0.84 [0.62–1.16]	0.2872	0.91 [0.65–1.27]	0.5821
Tumor budding	BD1	1		1	
	BD2	1.27 [0.82–1.97]	0.2884	1.34 [0.84–2.13]	0.2195
	BD3	1.81 [1.15–2.85]	0.0102	1.98 [1.23–3.19]	0.0049
DR pattern	Mature	1		1	
	Intermediate	1.85 [1.28–2.67]	0.0011	1.76 [1.19–2.59]	0.0046
	Immature	2.21 [1.25–3.89]	0.0063	2.15 [1.20–3.84]	0.0096

RFS, relapse-free survival; LN, lymph node; CEA, carcinoembryonic antigen; MSI, microsatellite instability; MSS, microsatellite stable; UFT, tegafur–uracil; DR, desmoplastic reaction; HR, hazard ratio; CI, confidence interval; *Japanese Classification of Colorectal Carcinoma (Second English Edition); **Patients with CEA and MSI values were analyzed.