

Table SI. Clinicopathological characteristics of the patients.

Case	Age, years	Sex	Stage	Grade	LVI	Adjuvant 5-FU	Initial relapse site
1	80	M	T1NxM0	1	-	-	-
2	69	M	T1NxM0	1	-	-	-
3	74	M	T1NxM0	2	-	-	-
4	59	M	T3N0M0	3	+	-	RPLN
5	71	F	T3N0M0	3	+	-	RPLN
6	76	F	T4N0M0	3	+	-	Lumbar bone
7	51	M	T4N0M0	3	+	-	RPLN
8	74	F	T4N1M0	3	+	-	Local recurrence
9	69	M	T3N0M0	2	+	-	-
10	64	F	T4N0M0	3	+	-	RPLN
11	73	F	T1NxM0	2	-	-	Ureter
12	79	M	T3N0M0	3	+	-	Lung
13	74	F	T1NxM0	2	-	-	-
14	65	M	T3N0M0	2	+	+	-
15	75	F	T3NxM0	3	-	-	RPLN
16	71	M	T3N1M0	3	+	-	RPLN
17	64	M	T2NxM0	3	-	-	Urinary bladder
18	68	M	T1NxM0	2	+	+	Urinary bladder
19	73	F	T2NxM0	2	+	+	-
20	66	M	T3N0M0	2	+	+	-
21	76	F	T4N1M0	3	+	-	Liver
22	72	M	T3N1M0	3	+	-	Lung
23	54	M	T2NxM0	3	-	-	RPLN
24	68	M	T3N0M0	3	+	-	Lung
25	52	M	T3N0M0	3	+	+	RPLN
26	65	M	T4N0M0	3	+	+	Urinary bladder
27	71	M	T3N0M0	2	+	+	Urinary bladder
28	63	M	T2NxM0	3	+	+	-
29	65	M	T3N0M0	3	+	+	-
30	67	M	T3N1M0	3	+	+	RPLN
31	67	M	T3NxM0	2	+	+	RPLN
32	76	M	T1NxM0	2	-	-	-
33	82	M	T1NxM0	2	-	-	-
34	69	M	T2NxM0	2	-	-	Urinary bladder
35	45	M	T1NxM0	2	-	-	Urinary bladder
36	64	M	T1NxM0	2	-	-	-
37	74	M	T1NxM0	2	-	-	-
38	77	M	T3N0M0	2	+	-	Local recurrence
39	72	F	T2NxM0	3	-	-	Urinary bladder
40	76	M	T2NxM0	2	+	-	-
41	70	M	T1NxM0	2	-	-	-
42	82	F	T1NxM0	2	-	-	-
43	74	M	T3N0M0	2	-	-	Urinary bladder
44	75	M	T1NxM0	2	-	-	Urinary bladder
45	82	M	T2NxM0	3	+	+	-
46	64	M	T1NxM0	2	-	-	-
47	67	M	T1NxM0	2	-	-	-
48	85	F	T4N0M0	3	+	+	RPLN
49	72	F	T3N0M0	3	+	+	Urinary bladder
50	55	M	T2NxM0	2	+	-	-
51	85	M	T1NxM0	2	-	-	-
52	67	M	T4N0M0	3	+	+	RPLN

LVI, lymphovascular invasion; 5-FU, 5-fluorouracil; RPLN, retroperitoneal lymph node.

Figure S1. Association between the expression levels of 5-FU metabolism-related enzymes and clinical outcomes, excluding patients who received adjuvant 5-FU chemotherapy. Among the patients who did not receive adjuvant 5-FU chemotherapy, the overall survival rates (shown by Kaplan-Meier curves) for those with higher expression levels of (A) *DPD*, (B) *OPRT* and (C) *TS* in their primary tumors were compared with those showing lower expression. The progression-free survival rates (shown by Kaplan-Meier curves) for the patients with higher expression levels of (D) *DPD*, (E) *OPRT* and (F) *TS* were also compared. The patients with higher expression levels of *TS* and the patients with lower expression levels of *DPD* exhibited lower progression-free survival rates ($P < 0.05$ determined by log rank test). NS, not significant; 5-FU, 5-fluorouracil; *DPD*, dihydropyrimidine dehydrogenase; *OPRT*, orotatephosphoribosyltransferase; *TS*, thymidylate synthase.

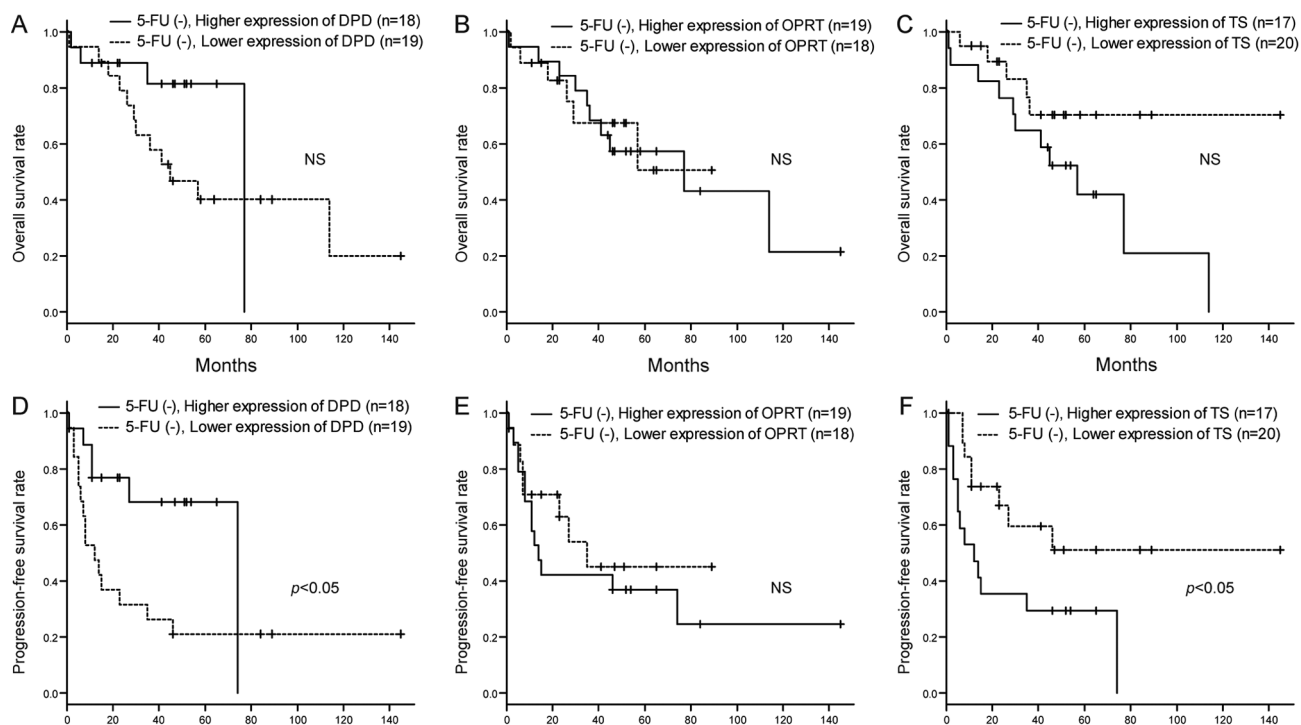


Figure S2. Association between the efficacy of adjuvant 5-FU chemotherapy and the expression of *OPRT*. (A) The overall survival rates (shown by Kaplan-Meier curves) of patients with lower expression levels of *OPRT* who received adjuvant 5-FU chemotherapy were compared with those of patients who did not. The UC-UUT patients who received 5-FU all had LVI, and among those who did not receive 5-FU, some had LVI and some did not. No significant differences were observed. (B) The overall survival rates (shown by Kaplan-Meier curves) of patients with higher expression levels of *OPRT* who received adjuvant 5-FU chemotherapy were compared with those of patients who did not. The UC-UUT patients who received 5-FU all had LVI, and among those who did not receive 5-FU, some had LVI and some did not. No significant differences were observed. (C) The overall survival rates (shown by Kaplan-Meier curves) of patients with lower expression levels of *OPRT* who received adjuvant 5-FU chemotherapy were compared with those of patients with higher expression levels of *OPRT* who also received the therapy. The two groups were comprised of UC-UUT patients with LVI. No significant differences were observed. (D-F) Progression-free survival rates were also investigated with the same 3 group comparisons, and no significant differences were observed. NS, not significant; LVI, lymphovascular invasion; 5-FU, 5-fluorouracil; UC-UUT, urothelial carcinoma of the upper urinary tract; *OPRT*, orotatephosphoribosyltransferase.

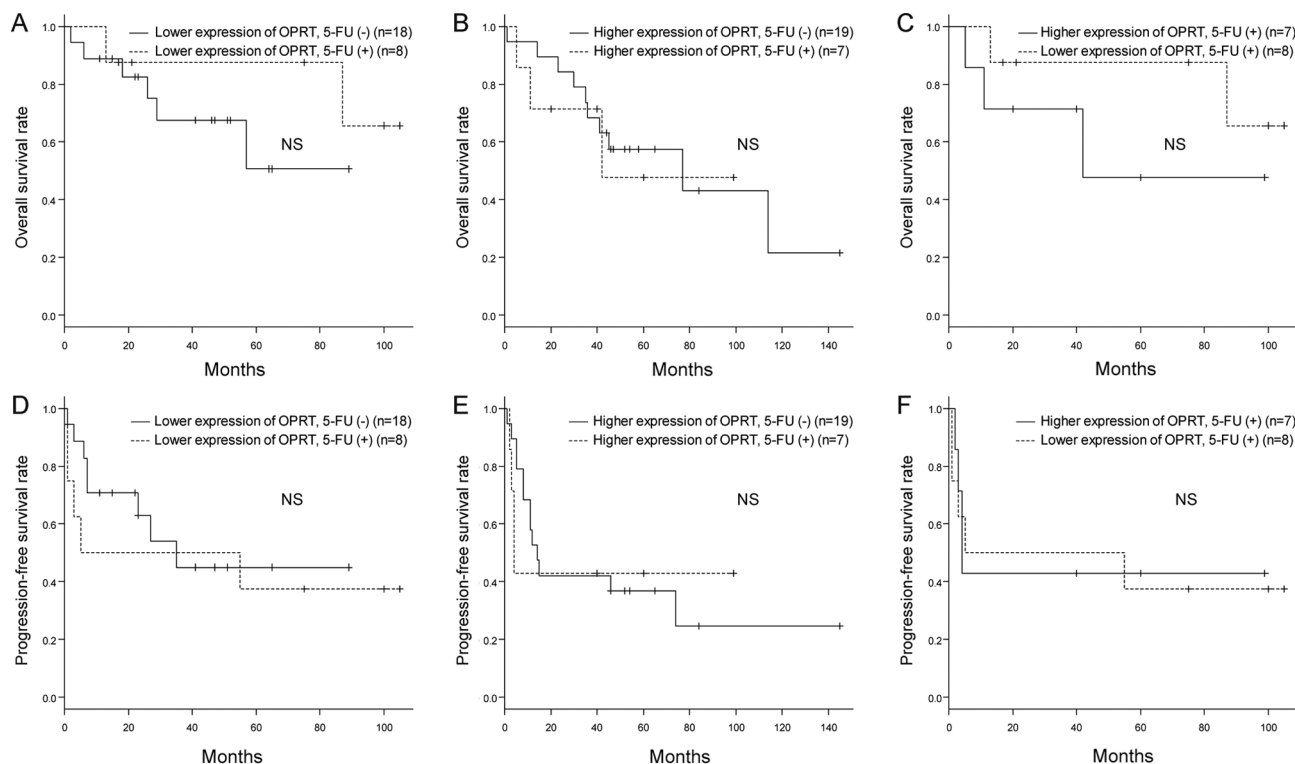


Figure S3. Association between the efficacy of adjuvant 5-FU chemotherapy and the expression of *TS*. (A) The overall survival rates (shown by Kaplan-Meier curves) of patients with lower expression levels of *TS* who received adjuvant 5-FU chemotherapy were compared with those of patients who did not. The UC-UUT patients who received 5-FU all had LVI, and among those who did not receive 5-FU, some had LVI and some did not. No significant differences were observed. (B) The overall survival rates (shown by Kaplan-Meier curves) of patients with higher expression levels of *TS* who received adjuvant 5-FU chemotherapy were compared with those of patients who did not. The UC-UUT patients who received 5-FU all had LVI, and among those who did not receive 5-FU, some had LVI and some did not. No significant differences were observed. (C) The overall survival rates (shown by Kaplan-Meier curves) of patients with lower expression levels of *TS* who received adjuvant 5-FU chemotherapy were compared with those of patients with higher expression of *TS* who also received the therapy. The two groups were comprised of UC-UUT patients with LVI. No significant differences were observed. (D-F) Progression-free survival rates were also investigated with the same 3 group comparisons, and no significant differences were observed. NS, not significant; LVI, lymphovascular invasion; 5-FU, 5-fluorouracil; UC-UUT, urothelial carcinoma of the upper urinary tract; *TS*, thymidylate synthase.

