

Fig S1 Progression-free and overall survival in the per-protocol population.

Kaplan-Meier plots for (A) progression-free survival (PFS) and (B) overall survival (OS) in the intent-to-treat population by treatment group: Log-rank $P = 0.347$ for PFS; unadjusted HR, 0.699; 95% CI, 0.331 to 1.478; Log-rank $P = 0.190$ unadjusted HR, 0.542; 95% CI, 0.213 to 1.367. The HR for PFS excluding the predefined non-inferiority boundary of 1.9, demonstrating a significant noninferiority. Estimated overall survival were similarly as PFS. Numbers in parentheses represent the number of events (deaths or progressions) between the two time points.

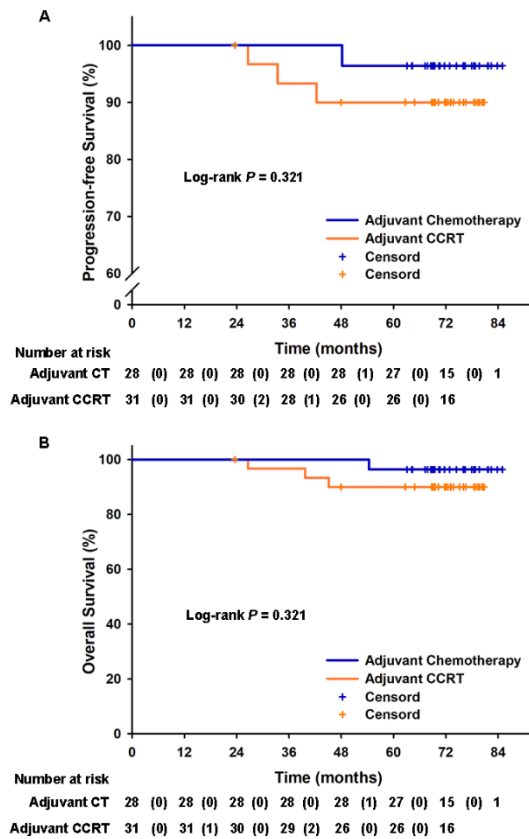


Fig S2 Progression-free and overall survival in low grade (G2-3) single-risk factor group.

Kaplan-Meier plots for (A) progression-free survival and (B) overall survival in the group with lymph node metastasis and / or positive parametrial invasion; no significant differences for PSF and OS between the two treatment groups, Log-rank $P = 0.321$ for PFS; Log-rank $P = 0.321$ for OS.

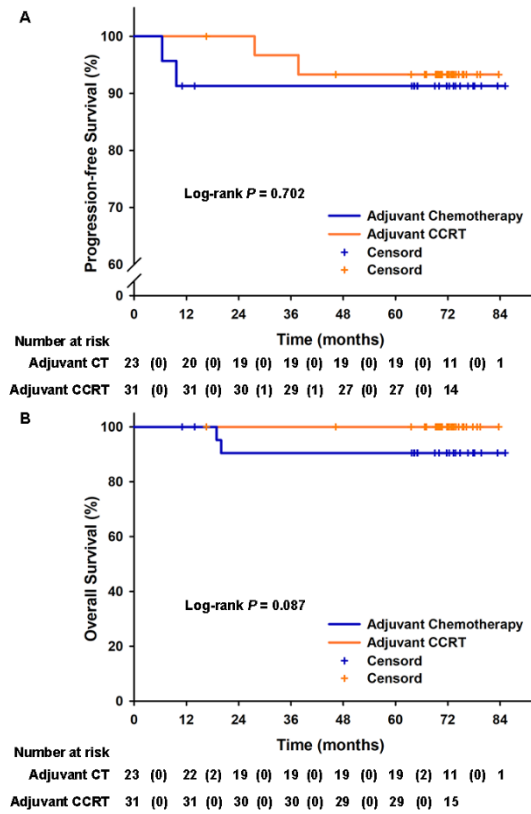


Fig S3 Progression-free and overall survival in deep stromal invasive (DSI) single-risk factor group.

Kaplan-Meier plots for (A) progression-free survival and (B) overall survival in the group with lymph node metastasis and / or positive parametrial invasion; no significant differences for PFS and OS between the two treatment groups, Log-rank $P = 0.702$ for PFS; Log-rank $P = 0.087$ for OS.

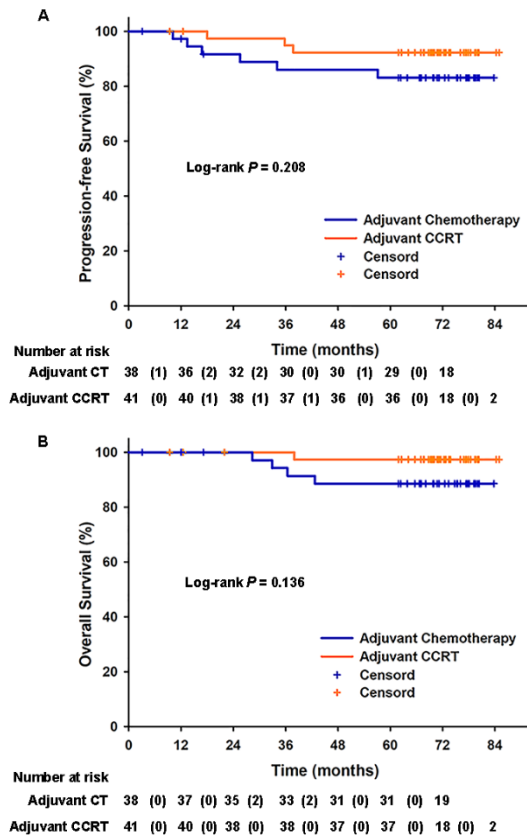


Fig S4 Progression-free and overall survival in Sedlis criteria group.

Kaplan-Meier plots for (A) progression-free survival and (B) overall survival in the group with lymph node metastasis and / or positive parametrial invasion; no significant differences for PSF and OS between the two treatment groups, Log-rank $P = 0.226$ for PFS; Log-rank $P = 0.145$ for OS.

Table S1. Baseline characteristics of intention-to-treat population (329 patients)

Various	Combination CT group (n = 165)	CCRT group (n = 164)
<i>Age at randomization (year)</i>		
Range	24-64	27-60
Average	45.8 ± 8.5	46.4 ± 7.5
≤ 40 (%)	44 (26.7)	40 (24.4)
41 – 50 (%)	69 (41.8)	65 (39.6)
> 50 (%)	52 (31.5)	59 (36.0)
<i>FIGO stage (%)</i>		
IB1	83 (50.3)	84 (51.2)
IB2	43 (26.1)	44 (26.8)
IIA1	27 (16.4)	25 (15.2)
IIA2	12 (7.3)	11 (6.7)
<i>Deep stromal invasion (%)</i>	90 (54.5)	97 (59.1)
<i>Histopathological grade G2-G3 (%)</i>	75 (45.5)	67 (40.9)
<i>Lymphatic vascular space involvement (%)</i>	41 (24.8)	34 (20.7)
<i>Diameter (mm, Average)</i>	26.4 ± 11.9	26.9 ± 12.5
<i>Lymph node metastasis (%)</i>	30 (18.2)	34 (20.7)
Single positive node	17	18
Multiple positive nodes (≥ 2)	13	16
<i>Positive parametrial invasion (%)</i>	5 (3.0)	4 (2.4)
<i>Single risk factor w/o LNM or PMI (%)</i>	78 (47.3)	74 (45.1)
<i>Multiple risk factors or LNM or PMI (%)</i>	87 (52.7)	90 (54.9)
<i>Ovarian conservation (%)</i>	66 (40.0)	61 (37.2)
<i>Initial SCCA (ng/mL, Median)</i>	1.50	1.76
<i>Per-protocol population (%)</i>	152 (92.1)	144 (87.8)

Abbreviations: CT, chemotherapy; CCRT, concurrent chemoradiotherapy; FIGO, International Federation of Gynecology and Obstetrics; SCCA, squamous cell carcinoma antigen.

Table S2. Progression-free and overall survival in ITT and PP population

Comparison	3-year survival rate (%)	5-year survival rate (%)	Log-rank P value	Unadjusted HR (95% CI)
Progression-free Survival (Combination CT group vs CCRT group)				
Intention-to-treat population	91.9% vs 91.9%	90.6% vs 90.0%	.846	0.933 (0.461 to 1.887)
Per-protocol population	93.2% vs 90.8%	91.9% vs 88.6%	.347	0.699 (0.331 to 1.478)
Overall Survival (Combination CT group vs CCRT group)				
Intention-to-treat population	95.6% vs 95.6%	93.7% vs 92.4%	.654	0.826 (0.357 to 1.911)
Per-protocol population	96.6% vs 95.0%	95.2% vs 91.4%	.190	0.542 (0.213 to 1.376)

Abbreviation: ITT, intention-to-treat; PP, per-protocol; CT, chemotherapy; CCRT, concurrent chemoradiotherapy; HR, hazard ratio; CI, confidence interval.

HR < 1 indicates benefit with adjuvant chemotherapy.

Table S3. Univariable and multivariable cox regression analysis for progression-free survival and overall survival

Progression-free survival				
Variable	Univariable		Multivariable	
	HR (95% CI)	P	HR (95% CI)	P
<i>Treatment (Combination CT vs CCRT)</i>	0.933 (0.461 to 1.887)	0.846	0.854 (0.415 to 1.757)	0.667
<i>Age</i>	1.054 (1.006 to 1.105)	0.027	1.049 (1.002 to 1.099)	0.042
<i>Stage</i>		0.147		
<i>IB1</i>	reference	/		
<i>IB2</i>	2.033 (0.846 to 4.885)	0.113		
<i>IIA1</i>	2.487 (0.946 to 6.535)	0.065		
<i>IIA2</i>	2.999 (0.940 to 9.562)	0.063		
<i>Deep stromal invasion</i>	1.943 (0.894 to 4.219)	0.093		
<i>Histopathological grade G2-G3</i>	1.213 (0.600 to 2.453)	0.592		
<i>Tumor diameter</i>	1.013 (0.988 to 1.038)	0.312		
<i>Lymphatic vascular space involvement</i>	1.194 (0.534 to 2.670)	0.665		
<i>Lymph node metastasis</i>	2.943 (1.428 to 6.065)	0.003	2.996 (1.427 to 6.293)	.004
<i>Positive parametrial invasion</i>	7.424 (2.594 to 21.247)	0.000	4.613 (1.480 to 14.378)	.008
Overall survival				
Variable	Univariable		Multivariable	
	HR (95% CI)	P	HR (95% CI)	P
<i>Treatment (Combination CT vs CCRT)</i>	0.826 (0.357 to 1.911)	0.655	0.673 (0.277 to 1.640)	0.384
<i>Age</i>	1.081 (1.021 to 1.146)	0.008	1.068 (1.010 to 1.130)	0.022
<i>Stage</i>		0.198		
<i>IB1</i>	reference	/		
<i>IB2</i>	1.500 (0.521 to 4.324)	0.453		
<i>IIA1</i>	1.798 (0.541 to 5.972)	0.338		
<i>IIA2</i>	3.706 (1.116 to 12.310)	0.032		
<i>Deep stromal invasion</i>	1.383 (0.580 to 3.297)	0.465		
<i>Histopathological grade G2-G3</i>	1.877 (0.802 to 4.391)	0.147		
<i>Tumor diameter</i>	1.451 (0.535 to 3.934)	0.464		
<i>Lymphatic vascular space involvement</i>	1.290 (0.505 to 3.297)	0.594		
<i>Lymph node metastasis</i>	2.611 (1.095 to 6.227)	0.030	2.645 (1.077 to 6.497)	0.034
<i>Positive parametrial invasion</i>	11.293 (3.815 to 33.427)	0.000	6.943 (2.059 to 23.413)	0.002

Abbreviations: CT, chemotherapy; CCRT, concurrent chemoradiotherapy; HR, hazard ratio.

Table S4. Cases met Sedlis criteria in subgroups

Subgroup	Sedlis criteria	
	Yes	No
<i>Single risk factor w/o LNM or PMI group (%)</i>	10 (6.6)	142 (93.4)
<i>Deep stromal invasion (%)</i>	4 (7.4)	50 (92.6)
<i>Histopathological grade G2-G3 (%)</i>	0 (0)	59 (100)
<i>Lymphatic vascular space involvement (%)</i>	2 (8.0)	23 (92.0)
<i>Bulky Tumor (tumor diameter > 4 cm)</i>	4 (28.6)	10 (71.4)
<i>Multiple risk factors group (%)</i>	69 (63.9)	39 (36.1)

Abbreviation: LNM, lymph node metastasis; PMI, positive parametrial invasion.

Table S5. Progression-free and overall survival in subgroups

Subgroup	Combination CT group	CCRT group	3-yr PFS, <i>P</i> value	Unadjusted HR for PFS (95% CI)	5-yr OS, <i>P</i> value	Unadjusted HR for OS (95% CI)
<i>Single risk factor w/o LNM or PMI (%)</i>	78 (47.3)	74 (45.1)	96.1% vs 95.8%, 0.685	0.762 (0.205 to 2.840)	96.1% vs 95.8%, 0.953	0.954 (0.192 to 4.721)
<i>Deep stromal invasion (%)</i>	23 (42.6)	31 (57.4)	91.3% vs 96.7%, 0.702	1.463 (0.206 to 10.394)	90.5% vs 100 %, 0.087	/
<i>Histopathological grade G2-G3 (%)</i>	28 (47.5)	31 (52.5)	100% vs 93.3%, 0.321	0.336 (0.035 to 3.228)	96.4% vs 90.0%, 0.321	0.336 (0.035 to 3.228)
<i>Lymphatic vascular space involvement (%)</i>	18 (72.0)	7 (28.0)	94.4% vs 100%, 0.533	/	100% vs 100%	/
<i>Bulky tumor (tumor diameter > 4 cm)(%)</i>	9 (64.3)	5 (35.7)	100% vs 100%	/	/	/
<i>Multiple risk factors w/o LNM or PMI (%)</i>	54 (50%)	54 (50%)	90.3% vs 96.2%, 0.278	2.117 (0.529 to 8.467)	90.2% vs 96.1%, 0.230	2.628 (0.510 to 13.546)
<i>Sedlis Criteria (%)</i>	38 (48.1)	41 (51.9)	86.0% vs 94.9%, 0.208	2.370 (0.593 to 9.481)	88.6% vs 97.4%, 0.136	4.558 (0.509 to 40.787)
<i>LNM or PMI (%)</i>	33 (47.8)	36 (52.2)	84.4% vs 77.8%, 0.390	0.615 (0.201 to 1.881)	93.6% vs 80.0%, 0.103	0.292 (0.061 to 1.407)

Abbreviation: CT, chemotherapy; CCRT, concurrent chemoradiotherapy; PFS, progression-free survival; OS, overall survival; LNM, lymph node metastasis; PMI, positive parametrial invasion, CI, confidence interval.

Constipation	44	56	81	0.016*				0.003*																
	(56.4%)	(75.7%)	(56.3%)	0.982#	0	8 (10.8%)	14 (9.7%)	0.004#	16	18	23 (16.5%)	0.333	0	3 (4.2%)	5 (3.6%)	0.217	0	7 (10.0%)	12	0.807‡	0	3 (4.3%)	4	0.232
				0.005‡					(20.8%)	(25.0%)									(9.0%)				(3.0%)	
Diarrhea	10	13	39	0.414*																				
	(12.8%)	(17.6%)	(27.1%)	0.014#	0	3 (4.1%)	7 (4.9%)	0.150	0	0	6	/	0	0	2 (1.4%)	/	0	0	10	/	0	1 (1.4%)	5	0.185
				0.119‡							(4.3%)								(7.5%)			(3.7%)		
Urinary tract infection	12	14	21	0.235*																				
	(15.4%)	(18.9%)	(14.6%)	0.702	0	2 (2.7%)	12 (8.3%)	0.009#	0	6 (8.3%)	16 (11.5%)	0.474‡	0	3 (4.2%)	8 (5.8%)	0.105	0	3 (4.3%)	12	0.225‡	0	3 (4.3%)	6	0.185
				0.108‡															(9.0%)			(4.5%)		
Skin	5	11	33	0.090*																				
	(6.4%)	(14.9%)	(22.9%)	0.002#	0	0	0	/	0	0	3	/	0	0	0	/	0	0	0	/	0	0	0	/
				0.161‡							(2.2%)													
Creatinine	6	14	31	0.041*																				
	(7.7%)	(18.9%)	(21.5%)	0.008#	0	4 (5.4%)	6 (4.2%)	0.140	0	2 (2.8%)	9	0.051	0	2 (2.8%)	3 (2.2%)	0.375	0	0	0	/	0	0	0	/
				0.652‡							(6.5%)													
ALT / AST	15	28	49	0.011*																				
	(20.3%)	(37.3%)	(34.3%)	0.020#	0	0	0	/	0	0	0	/	0	0	0	/	0	0	0	/	0	0	0	/
				0.577‡																				

Abbreviations: CT-3, Three-cycle adjuvant chemotherapy group; CT-6, Six-cycle adjuvant chemotherapy group; CCRT, adjuvant CCRT group; ALT, alanine transaminase; AST, aspartate transaminase;

**P*, CT-3 vs. CT-6; #*P*, CT-3 vs. CCRT; ‡*P*, CT-6 vs. CCRT.

Table S7. Quality of life symptoms using the EORTC QLQ-C30 and CX24 over the treatment and two-year follow-up

	<i>Time point</i>										Difference between groups over time		
	Baseline		After treatment		Six-month follow-up		One-year follow-up		Two-year follow-up			Time	Treatment
	(n=296)		(n=296)		(n=288)		(n=278)		(n=272)				
Score	<i>P</i> value	Score	<i>P</i> value	Score	<i>P</i> value	Score	<i>P</i> value	Score	<i>P</i> value	<i>P</i> value	<i>P</i> value	<i>P</i> value	
<i>Q30 functioning scales</i>													
Global health status		0.375		0.455		0.604		0.600		0.738	<0.001	0.802	0.822
Chemotherapy	49.1 ± 15.2		59.0 ± 20.3		77.9 ± 13.4		84.4 ± 9.5		72.5 ± 22.2				
CCRT	47.5 ± 14.9		57.3 ± 24.6		77.8 ± 10.5		83.8 ± 9.6		75.8 ± 13.0				
Physical functioning		0.154		0.250		0.122		<0.001		<0.001	<0.001	0.119	0.120
Chemotherapy	99.9 ± 0.5		66.2 ± 14.8		85.3 ± 10.8		93.3 ± 5.5		95.7 ± 4.9				
CCRT	99.5 ± 2.8		64.1 ± 16.9		87.7 ± 7.2		90.8 ± 4.5		92.1 ± 5.6				
Role functioning		0.840		0.136		0.011		0.208		0.635	<0.001	0.021	0.018
Chemotherapy	90.8 ± 16.9		61.3 ± 34.1		85.6 ± 19.8		91.1 ± 11.3		93.1 ± 9.6				
CCRT	91.2 ± 18.4		67.1 ± 33.1		90.8 ± 7.2		92.8 ± 11.1		94.1 ± 8.0				
Emotional functioning		0.073		0.760		0.288		0.177		0.120	<0.001	0.053	0.019
Chemotherapy	79.9 ± 13.6		77.3 ± 15.1		91.3 ± 10.0		91.3 ± 9.9		94.6 ± 6.2				
CCRT	77.2 ± 12.5		76.7 ± 16.8		90.0 ± 10.5		89.7 ± 9.5		93.4 ± 6.4				
Cognitive functioning		0.815		0.630		0.346		0.155		0.355	<0.001	0.373	0.375
Chemotherapy	97.9 ± 7.3		81.0 ± 21.2		88.6 ± 16.6		93.6 ± 11.6		93.0 ± 12.6				
CCRT	96.7 ± 11.5		77.7 ± 26.3		90.5 ± 18.3		90.9 ± 14.4		94.4 ± 12.6				
Social functioning		0.286		0.338		0.125		0.558		0.797	<0.001	0.373	0.327
Chemotherapy	80.8 ± 22.8		63.5 ± 31.6		83.6 ± 20.1		90.4 ± 15.0		95.1 ± 9.2				
CCRT	77.9 ± 24.2		67.2 ± 35.7		87.5 ± 23.7		91.4 ± 14.1		95.5 ± 10.1				
<i>Q30 symptom scales</i>													
Fatigue		0.488		0.025		0.222		0.884		0.199	<0.001	0.148	0.142
Chemotherapy	1.5 ± 4.1		44.9 ± 18.3		6.5 ± 8.8		4.9 ± 7.4		2.4 ± 5.5				
CCRT	1.9 ± 5.6		49.8 ± 19.0		7.8 ± 9.9		4.8 ± 7.3		3.3 ± 6.3				

Nausea and vomiting		0.146		0.035	/	/	/		0.214	0.206
Chemotherapy	0		33.8 ± 21.3	0.1 ± 1.4	0	0				
CCRT	0.2 ± 1.9		38.9 ± 20.3	0	0	0				
Pain		0.603		0.003	0.093	0.333	0.639	<0.001	0.168	0.164
Chemotherapy	2.2 ± 5.7		8.3 ± 11.0	2.5 ± 7.1	0.9 ± 4.3	0.4 ± 2.4				
CCRT	2.5 ± 6.0		12.2 ± 11.0	1.1 ± 4.1	0.5 ± 2.8	0.5 ± 2.9				
Dyspnoea		0.610		0.814	0.203	0.712	/		0.495	0.500
Chemotherapy	0.4 ± 3.8		5.0 ± 12.0	0.9 ± 5.4	0.7 ± 4.8	0				
CCRT	0.7 ± 4.8		6.9 ± 17.6	0.3 ± 2.8	0.5 ± 4.1	0				
Insomnia		0.850		0.638	0.543	0.271	0.543	<0.001	0.566	0.572
Chemotherapy	5.7 ± 13.7		21.3 ± 23.2	13.9 ± 19.8	4.6 ± 12.2	6.6 ± 13.9				
CCRT	6.0 ± 15.1		21.5 ± 27.4	15.3 ± 21.3	6.5 ± 14.4	5.6 ± 14.9				
Appetite loss		0.938		0.018	0.739	/	/		0.328	0.320
Chemotherapy	1.3 ± 8.5		46.7 ± 18.5	2.2 ± 8.4	0	0				
CCRT	1.4 ± 7.8		52.1 ± 21.5	1.9 ± 7.8	0	0				
Constipation		0.119		0.089	0.256	0.117	0.071	<0.001	0.200	0.202
Chemotherapy	2.2 ± 8.3		11.4 ± 21.0	4.3 ± 11.2	5.1 ± 14.4	3.1 ± 9.7				
CCRT	3.9 ± 10.8		16.2 ± 24.6	6.4 ± 15.0	2.7 ± 10.1	1.3 ± 6.4				
Diarrhea		/		<0.001	/	0.152	/	<0.001	<0.001	<0.001
Chemotherapy	0		0	0	0.2 ± 2.8	0				
CCRT	0		3.5 ± 10.2	0	1.0 ± 5.7	0				
Financial difficulties		0.371		0.058	<0.001	0.578	0.089	<0.001	0.058	0.048
Chemotherapy	28.1 ± 29.5		50.4 ± 41.3	28.4 ± 31.3	18.1 ± 23.0	14.9 ± 18.9				
CCRT	31.3 ± 31.6		41.2 ± 42.3	15.8 ± 29.3	16.4 ± 26.1	18.9 ± 20.3				
<i>CX24 functioning scales</i>										
Body image		0.420		0.364	0.006	0.050	0.874	<0.001	0.049	0.042
Chemotherapy	78.9 ± 23.1		67.5 ± 29.1	83.2 ± 18.9	86.5 ± 14.9	93.2 ± 11.7				
CCRT	76.7 ± 24.8		70.6 ± 27.1	89.3 ± 18.6	90.0 ± 14.3	93.4 ± 10.1				

Sexual activity		0.510		0.279		<0.001		0.160		0.344		<0.001		0.193		0.192
Chemotherapy	63.3 ± 36.2		100		76.1 ± 31.4		86.5 ± 14.9		79.0 ± 26.6							
CCRT	62.5 ± 29.5		99.5 ± 5.9		90.6 ± 21.3		90.0 ± 14.3		82.1 ± 25.3							
<i>CX24 symptom scales</i>																
Symptom experience		0.639		<0.001		0.628		0.595		0.003		<0.001		<0.001		<0.001
Chemotherapy	8.2 ± 9.0		7.6 ± 7.8		5.0 ± 7.9		2.6 ± 4.3		1.3 ± 2.0							
CCRT	8.6 ± 9.2		15.3 ± 8.1		5.4 ± 7.7		3.4 ± 5.6		2.9 ± 4.6							
Lymphoedema		0.158		0.861		0.505		0.948		0.471		<0.001		0.849		0.847
Chemotherapy	0.2 ± 2.7		17.5 ± 25.1		11.6 ± 23.2		8.6 ± 20.7		3.1 ± 11.2							
CCRT	0.9 ± 5.5		18.1 ± 24.9		8.4 ± 16.1		8.7 ± 14.7		4.0 ± 10.9							
Peripheral neuropathy		0.255		0.381		0.091		0.579		0.075		<0.001		0.808		0.815
Chemotherapy	2.9 ± 10.8		15.8 ± 28.4		11.6 ± 24.5		5.1 ± 14.9		2.6 ± 9.0							
CCRT	4.4 ± 13.2		15.2 ± 22.9		6.7 ± 18.5		7.5 ± 19.9		5.6 ± 14.4							
Menopausal symptoms		0.273		0.019		0.001		0.010		0.035		<0.001		<0.001		<0.001
Chemotherapy	0.7 ± 4.7		3.1 ± 11.7		3.8 ± 12.6		1.4 ± 6.7		0.7 ± 4.8							
CCRT	1.4 ± 6.7		7.2 ± 17.9		11.5 ± 22.2		4.2 ± 11.1		2.5 ± 8.9							
Sexual worry		0.247		0.029		0.702		0.056		0.351		0.017		0.002		0.002
Chemotherapy	2.7 ± 9.9		10.7 ± 23.7		14.8 ± 18.8		8.3 ± 17.8		11.0 ± 16.7							.
CCRT	4.6 ± 14.0		22.7 ± 64.6		18.4 ± 26.1		11.9 ± 19.3		13.3 ± 18.8							

Abbreviations: CCRT, adjuvant CCRT group.

Table S8. Serum concentration of FSH and E2 and symptoms of patients with ovarian conservation

Treatment group	Combination CT group (n=48)	CCRT group (n=34)	P value
<i>Age (Median, year)</i>	39.0	39.0	0.158
<i>Serum FSH (mIU/mL)</i>			
Range	5.54 - 102.8	5.81-128.6	
Median	7.9	28.5	0.002
<i>Serum E2 (pg/mL)</i>			
Range	25 - 120.3	14.0 - 92.0	
Average	61.6 ± 21.1	48.1 ± 19.6	0.004
<i>Symptoms</i>			
Hot-flash	11	16	0.022
Vaginal atrophy	10	23	<0.001
<i>POI (> 25 mIU/mL)</i>	5	10	0.028
<i>Menopause (> 45 mIU/mL)</i>	4	9	0.027

Abbreviation: CT, chemotherapy; CCRT, concurrent chemoradiotherapy; POI, premature ovarian insufficiency.