Heterogeneity of Patients with High-Intermediate and High-Risk Endometrial Cancer Included in Prospective Trials

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Background

Objective: To assess the long-term survival of women with high-intermediate and high-risk endometrial cancer as classified by GOG 249 and PORTEC-3.

- Adjuvant therapy for endometrial cancer remains controversial
- Specific clinical and pathologic characteristics have been used to stratify women based on risk of recurrence
- GOG 99 and PORTEC-1 established the first risk stratifying methods for patients with early stage endometrial cancer, and used risk factors such as age, myometrial invasion, and grade to determine risk categorization
- Recently, several prospective trials have examined the use of various combinations of adjuvant chemotherapy and radiation for women with high-intermediate and high-risk endometrial cancers
- However, these prospective trials included a wide spectrum of tumor types and stages, which may ultimately impact long-term survival rates within specific risk stratification groups

Methods

- We used data from the National Cancer Database (NCDB) to identify women with endometrial cancer who underwent hysterectomy from 2004 to 2016
- The inclusion criteria for GOG 249 were determined (pelvic radiotherapy vs. vaginal brachytherapy)
- The inclusion criteria for PORTEC-3 were determined (pelvic radiation vs. pelvic radiation and chemotherapy)
- The reported entry criteria for GOG 249 and PORTEC-3 were then used to select the cohort (Table)
- We analyzed the five-year overall survival for the population of women who met the inclusion criteria for GOG 249 and PORTEC-3

	Clinical trial inclusion		NCDB survival estimate	
	GOG 249	PORTEC-3	N	Five-year survival (95% CI)
Endometrioid				
Stage I, >70yo with 1 risk factor	x		14,639	78.3% (77.5-79.1)
Stage I, 50-69yo with 2 risk factors	x		11,313	86.3% (85.5-87.0)
Stage I, 18-49yo with 3 risk factors	x		122	86.8% (77.6-92.4)
Stage IA, grade 3, with LVSI		x	843	76.1% (72.0-79.7)
Stage IB, grade 3		x	5,528	70.8% (69.4-72.2)
Stage II		x	14,107	80.1% (79.4-80.9)
Stage IIIA		x	3,685	71.2% (69.3-73.0)
Stage IIIB		x	1,337	55.2% (52.0-58.3)
Stage IIIC		x	12,807	66.2% (65.3-67.2)
Uterine Papillary Serous				
Stage IA	x		6,440	77.4% (76.1-78.6)
Stage IB	x	x	1,523	58.5% (55.4-61.4)
Stage II	x	x	1,553	56.7% (53.8-59.5)
Stage III		x	4,944	36.5% (34.9-38.1)
Clear Cell				
Stage IA	x		1,539	77.8% (75.3-80.1)
Stage IB	x	x	305	64.3% (57.6-70.2)
Stage II	x	x	477	66.2% (61.2-70.8)
Stage III		x	966	41.8% (38.2-45.3)
*Risk factors: grade 2 or 3, >50% myometrial invasion, LVSI				

Table. Five-year survival estimates for patients by inclusion criteria for GOG 249 and PORTEC-3 prospective trials.

Results

- A total of 81,128 patients were identified who fulfilled the entry criteria for GOG 249 or PORTEC-3
- Overall five-year survival ranged from 56.7% to 86.8% for various stage/grade groups for women included in GOG 249
- Overall five-year survival ranged from 36.5% to 80.1% for various stage/grade groups for women included in PORTEC-3
- The highest survival of 86.8% was noted for women ages 18-49years old with stage 1 tumors and 3 risk factors
- The lowest survival of 36.5% was noted for women with stage III serous cancers
- Survival for serous and clear cell tumors was significantly lower than that seen for endometrioid tumors

Conclusions

- Recent prospective trials of adjuvant therapy for high-intermediate and high-risk endometrial cancer have included heterogeneous groups of patients with widely varying prognoses
- The variable risk of included patients may result in insufficient power to detect clinical benefit, or alternatively, result in overestimation of benefit for lower risk patients

References

1. de Boer SM, Powell ME, Mileshkin L, et al. Adjuvant chemoradiotherapy versus radiotherapy alone in women with high-risk endometrial cancer (PORTEC-3): patterns of recurrence and post-hoc survival analysis of a randomised phase 3 trial. Lancet Oncol 2019;20:1273-85.
2. Randall ME, Filiaci V, McMeekin DS, et al. Phase III Trial: Adjuvant Pelvic Radiation Therapy Versus Vaginal Brachytherapy Plus Paclitaxel/Carboplatin in High-Intermediate and High-Risk Early Stage Endometrial Cancer. J Clin Oncol 2019;37:1810-8.