Evaluation of the Optimal Sequence of Chemotherapy and Radiation Therapy in the Treatment of Advanced Endometrial Cancer

Jennifer McEachron[1], Nancy Zhou[1], Christina Spencer[2], Lisa Shanahan[2], Carolyn Chatterton[2], Saskia Naegele[1], Julie Katz[1], Pankaj Singhal[2], and Yi-Chun Lee[1]

Division of Gynecologic Oncology, SUNY Downstate Medical Center, Brooklyn, NY[1] & Division of Gynecologic Oncology, Good Samaritan Hospital Medical Center, West Islip, NY[2]

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Objectives:

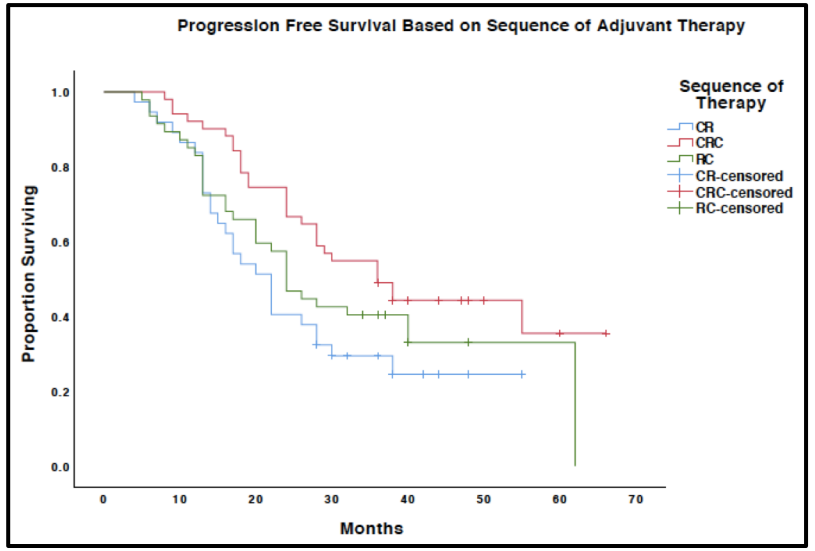
Evidence supports the use of multimodality therapy in the treatment of advanced endometrial carcinoma (EC). However, the optimal sequence of chemotherapy (CT) and radiation (RT) remains unclear. In the present study, we evaluated the outcomes of patients treated with multimodality therapy in sandwich fashion, defined as CT followed by RT then further CT (CRC), versus those treated in sequence with CT followed by RT (CR) or RT followed by CT (CR), to determine if there is a survival advantaged associated with a particular treatment sequence.

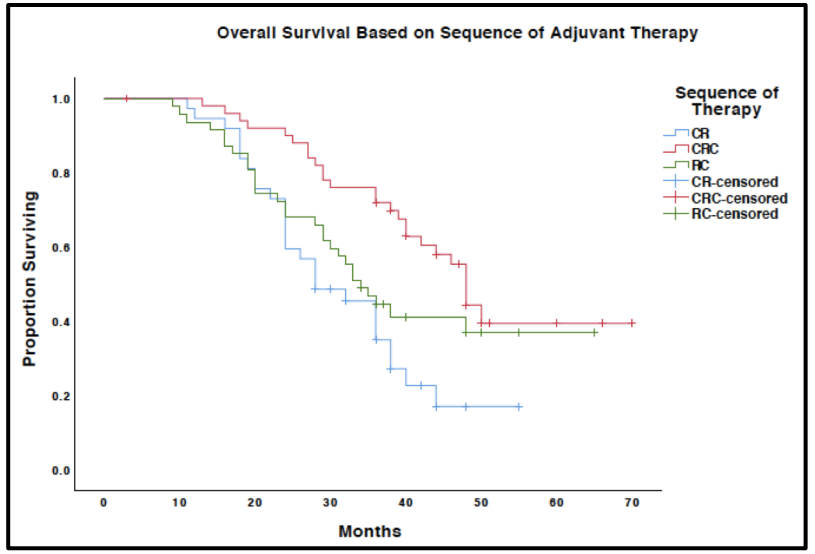
Methods:

A multicenter retrospective analysis of patients with stage III and IV EC from 2000 - 2016 was conducted. Inclusion criteria were patients with a diagnosis of EC who had undergone comprehensive surgical staging, followed by both adjuvant CT and RT. Differences in the frequencies of histology, stage, cytoreduction status, treatment delays and sites of disease recurrence were identified using Pearson's chi-square test. PFS and OS rates were calculated using Kaplan-Meier estimates.

	CRC N (%)	CR N (%)	RC N (%)
Total number of recurrences:	26	29	33
Recurrence Site:			
Abdominal	22 (56)	23 (62)	28 (64)
Pelvic	11 (28)	7 (19)	13 (30)
Retroperitoneum	3 (8)	7 (19)	3 (6)
Extra-abdominopelvic	3 (8)	0 (0)	0 (0)

Table 1: Location of recurrence based on therapy sequence





	CRC	CR	RC	*p*
Median PFS (months)	36	22	24	0.038
Median OS (months)	48	28	34	0.003

Table 2: Median survival time based on therapy sequence

Results:

Final analysis included 152 patients receiving dual modality postoperative adjuvant therapies; 36.8% (n=56) CRC, 28.9% (n=44) CR, and 34.2% (n=51) RC. The median age was 65 years (range 47-87); histology included 44.0% endometrioid, 47.5% serous and 8.5% clear cell tumors. 95% of patients underwent optimal cytoreduction. The median duration of follow up was 34.6 months. There was no difference in the frequency of different histologic subtypes (p=0.97), stage (p=0.14), cytoreduction status (p=0.93), or treatment delays (p=0.57) between the various adjuvant therapy sequences. The most frequent location of disease recurrence was abdomen, followed by pelvis, retroperitoneum and extra-peritoneal distant sites. The distribution of recurrence did not differ between treatment sequences (p=0.378). There was a significant improvement in both the PFS (long rank p=0.038) and OS (log rank p=0.003) in those patients receiving CRC which demonstrated superior 3-year PFS (54%) and OS (71%) compared to CR (34% and 50%) and RC (37% and 52%).

Conclusions:

Adjuvant therapy delivered in CRC sequence was associated with improvements in both PFS and OS in patients with advanced EC compared to alternant therapy sequencing.