**A Phase 3 Trial of Pelvic Radiation Therapy Versus Vaginal Cuff Brachytherapy Followed by Paclitaxel/Carboplatin Chemotherapy in Patients with High-Risk, Early-Stage Endometrial Cancer: A Gynecology Oncology Group Study**

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**Purpose/Objective(s):** To determine if vaginal cuff brachytherapy and chemotherapy (VCB/C) could increase recurrence-free survival (RFS) compared to pelvic external beam radiation therapy (PXRT). Secondary objectives included comparisons of overall survival (OS), patterns of failure, and frequency/severity of adverse events between the treatment arms.

**Materials/Methods:** A randomized phase 3 trial was performed in endometrial cancer patients meeting eligibility criteria. All patients were required to undergo hysterectomy. Eligible patients had stage I endometrioid histology with GOG 99-based high intermediate risk criteria (based on age, tumor grade, depth of invasion, and presence of lymphovascular space invasion), stage II, or stage I-II serous (S) or clear cell (CC) tumors. Central pathology review was performed. Patients assigned to PXRT were treated with standard 4-field or Intensity-Modulated Radiation Therapy (IMRT) techniques to a mean dose of 45 Gy over 5 weeks. Additional VCB was optional for patients with S/CC tumors or stage II disease. Patients assigned to VCB/C received HDR or LDR brachytherapy followed by paclitaxel 175 mg/m2 (3 hour) + carboplatin AUC 6 q 21 days for a total of 3 cycles.

**Results:** A total of 601 pts were accrued; PXRT was assigned to 301 (18 did not receive study treatment) and VCB/C to 300 (9 did not receive study treatment). The median age was 63 years, 74% had stage I disease, and 89% underwent lymphadenectomy. Histology included 71% with endometrioid type, 15% S, and 5% CC. Nearly all pts completed the prescribed therapy (91% PXRT, 87% VCB/C). In the PXRT arm, IMRT was used in 36%, and vaginal cuff brachytherapy boost was added in approximately 35%. Acute toxicity was more common and more severe with VCB/C. Grade 3 or higher adverse events were reported in 32 patients on the PXRT arm versus 187 patients on the VCB/C arm. Grade 3 or higher late effects were seen in 37 and 35 patients on the PXRT and VCB/C arms, respectively. With a median follow-up of 53 months, the 36 month RFS was 82% for both PXRT and VCB/C. The 36-month OS was 91% versus 88% for PXRT and VCB/C, respectively. No significant differences were noted between the two arms in terms of vaginal or distant failure. However, pelvic or para-aortic nodal recurrences were significantly more common in the VCB/C arm (25 vs 12), largely driven by the difference in pelvic nodal failure (20 vs 6 patients). There was no statistically significant treatment effect heterogeneity with respect to RFS among clinical-pathologic variables evaluated.

**Conclusion:** This study did not demonstrate a superiority of VCB/C to PXRT in women with HR endometrial cancer. Acute and late toxicity and pelvic and para-aortic nodal failure were more frequent in the VCB/C arm. Both arms appeared to be well tolerated with high completion rates. PXRT remains an effective, well-tolerated, and acceptable adjuvant treatment in patients with high risk, early-stage endometrial carcinoma.