Quantifying the Therapeutic Benefit of External Beam Radiotherapy in Uterine Serous Carcinoma: A Real-World Study

CO198

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Background

- Approximately 10% of all endometrial cancers (ECs) are uterine serous (USC).[1]
- Distribution of stage at diagnosis is predominantly stage I (40%), followed by stage II (30%), stage III (20%), and stage IV (10%).[2]
- However, due to its aggressive nature, USC EC is associated with high recurrence and poor prognosis, and it accounts for 40% of EC-related deaths.[2]
- Treatment of EC may consist of multiple components:
  - Adjuvant chemotherapy (C) with carboplatin + paclitaxel is always recommended.
  - Surgery recommendations depend on diagnosis (e.g., total hysterectomy, bilateral salpingo-oophorectomy, pelvic and para-aortic lymph node dissection, omental biopsy and pelvic washings for staging and detection of cancer spread).
  - The benefit of adjuvant radiotherapy (vaginal brachytherapy or external beam radiotherapy [EBRT]) is currently unclear.
- Since the potential benefit and optimal timing of adjuvant radiotherapy is unclear, understanding its effectiveness and identifying patients who would benefit from EBRT would optimize the utility of this treatment.

Objective

- **The objective was to develop and evaluate an empirical algorithm aimed at identifying patients with USC EC who would benefit from adjuvant radiotherapy.**

Methods

- Retrospective observational cohort study
- Patients with USC receiving:
  - C
  - C + adjuvant EBRT
- All patients were treated at the McGill University Health Center (MUHC) between 2008 and 2023.
- Patient treatment characteristics and outcomes were ascertained from the MUHC Electronic Health Records and the MUHC Gyno-Oncology Database.
- Multi-variate logistic regression was used to identify predictors of progression or recurrence among those treated with EBRT.
- A receiver operating curve analysis was used to identify three groups with high, moderate, and low potential benefit from EBRT.

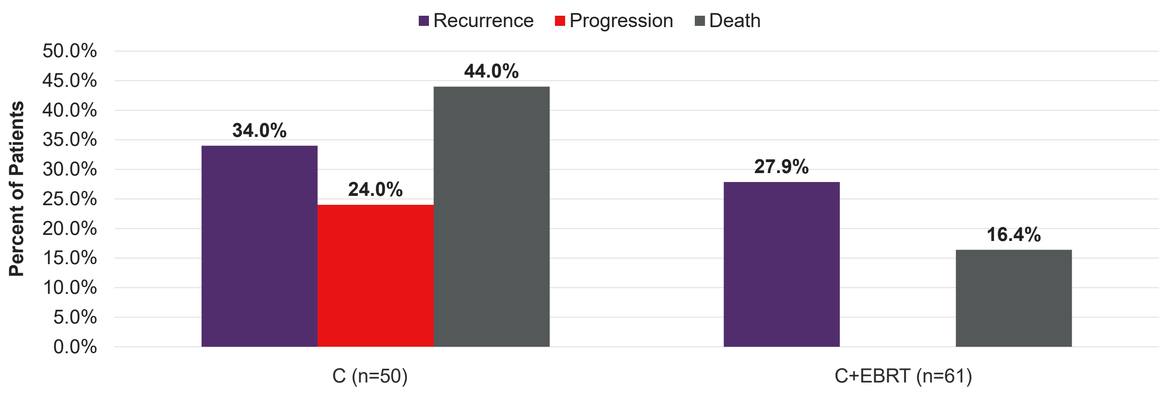
Results

Table 1. Patient characteristics

		Treatment Group				*P*-value
		C (n=50)		C+EBRT (n=61)		
Mean (SD) age, years		67.30	(9.07)	69.40	(8.11)	0.219
Stage I		13	26.0%	31	50.1%	<0.001
Stage II		0	0.0%	13	21.3%	
Stage III		13	26.0%	16	26.2%	
Stage IV		24	48.0%	1	1.6%	
PR+		27	54.0%	40	65.6%	0.028
Cytology	**Malignant**	23	46.0%	9	14.8%	<0.001

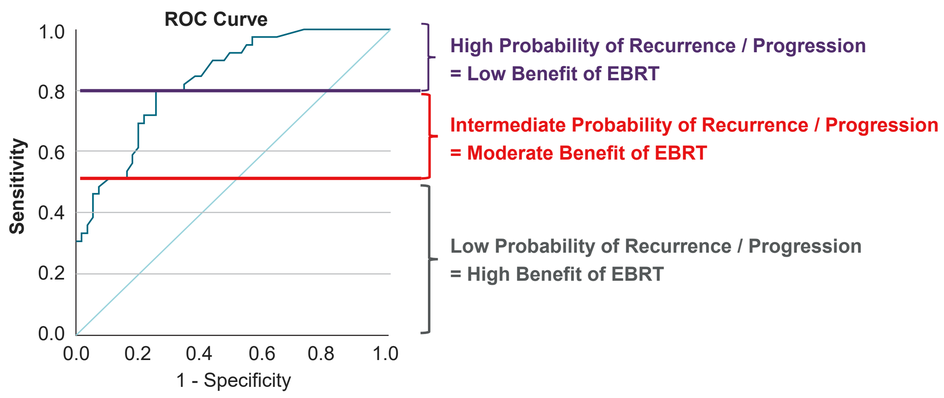
Abbreviations: C = chemotherapy; EBRT = external beam radiotherapy; PR = progesterone receptor

Figure 1. Proportion of patients with outcomes, stratified by treatment[a]



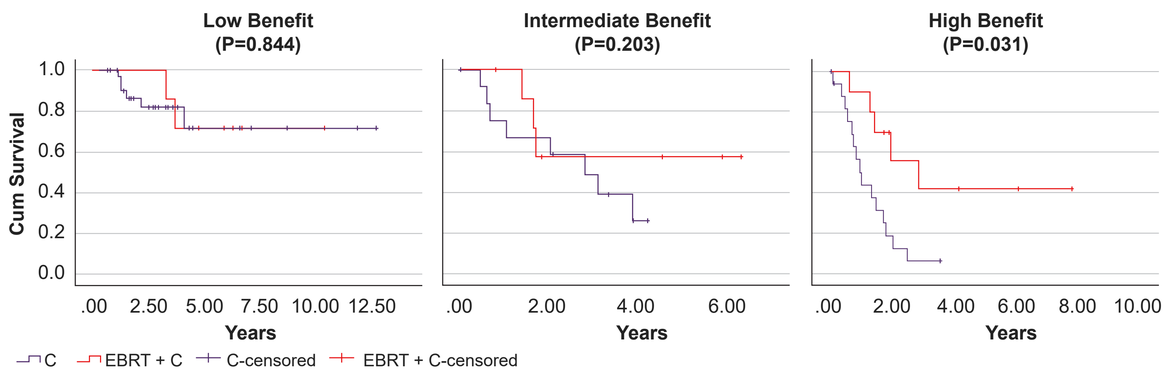
Abbreviations: C = chemotherapy; EBRT = external beam radiotherapy;
[a] It is possible for patients to be in more than one category of 'recurrence', 'progression' or 'death.' as these are not mutually exclusive.

Figure 2. Classification of EBRT benefit categories (*P*<0.001)



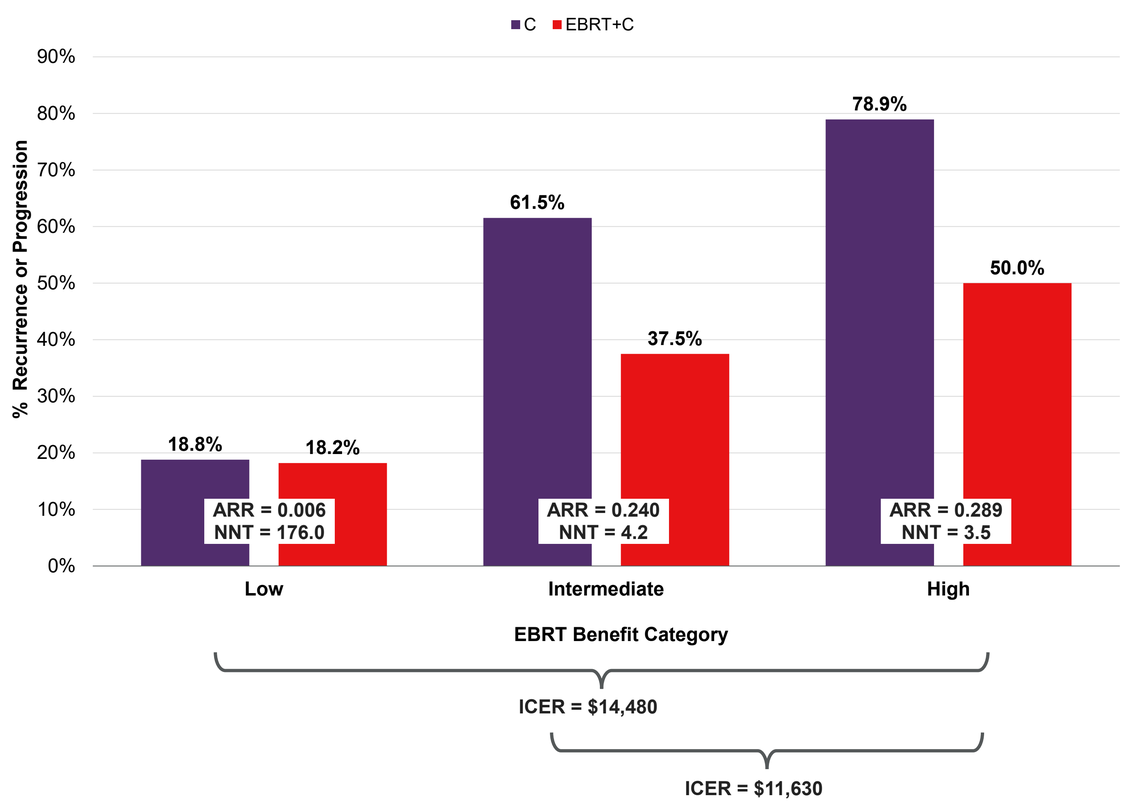
Abbreviations: EBRT = external beam radiotherapy; ROC = receiver operating characteristic

Figure 3. Progression-free survival by benefit categories



Abbreviations: C = chemotherapy; EBRT = external beam radiotherapy

Figure 4. Recurrence or progression by EBRT benefit category



Abbreviations: ARR = absolute risk reduction; C = chemotherapy; EBRT = external beam radiotherapy; ICER = incremental cost effectiveness ratio / progression-free survival year gained; NNT = number needed to treat

Discussion

- The real-world-derived algorithm for the selection of patients with USC ECs to be treated with EBRT has the potential to:
  - Improve the number needed to treat (NNT)
  - Reduce overall costs and improve cost-effectiveness
  - Prevent potentially non-beneficial EBRT in 33/61 (54.1%) patients.
    - With associated impact on quality of life and treatment-related adverse events

Limitations

- This was a single-site study conducted in a tertiary center that is highly specialized in the treatment of gynecological cancers.
  - Therefore, the study population may not be representative of the general patient population with USC EC.
- This study was conducted in Canada, where a universal, publicly funded healthcare system is in effect.
  - Results may be different in non-public/universal healthcare systems, where access to care may be a barrier to receiving radiation therapy.
- The study was conducted prior to increased use of targeted therapy and immunotherapy.
  - Thus, results may vary among inpatients treated with advanced therapies.

Conclusions

- **Adjuvant radiation therapy (EBRT) may be beneficial and cost-effective in a universal healthcare system.**
- **Using a real-word-derived algorithm to select patients who are most likely to benefit from EBRT may reduce overall costs.**

References

1. Bogani G, et al. *Gynecol Oncol.* 2021 Jul;162(1):226-234.
2. Ball A, et al. *J Obstet Gynaecol Can*. 2014 Dec;36(12):1085-1092.

Disclosures

NRB, MB, and **JS** are employees of PPD™ Observational Studies, Thermo Fisher Scientific. Funding for this poster was provided by Thermo Fisher Scientific.

Editorial and graphic design support were provided by Caroline Cole and Richard Leason of Thermo Fisher Scientific.

Presented at ISPOR —The Professional Society for Health Economics and Outcomes Research—Europe | 9–12 November 2025 | Glasgow, Scotland, UK