Patient Characteristics and Treatment Patterns in Post-Immune Checkpoint Inhibitor and Post-Platinum-Based Chemotherapy among Patients with Endometrial Cancer in the US

Kathleen M. McClain[1]; Vimalanand S. Prabhu[1]; Srujitha Marupuru[1]; Ke Meng[1]; Vy Tran[1]; Robert Orlowski[1]; Robin Meng[1]; Angela K. Green[2,3]; Christian Marth[4]; Vicky Makker [2,3]

[1]Merck & Co., Inc., Rahway, NJ, USA; [2]Gynecologic Medical Oncology Service, Department of Medicine, Memorial Sloan Kettering Cancer Center, New York, NY, USA; [3]Weill Cornell Medical College, New York, NY, USA; [4]Department of Obstetrics and Gynecology, Medical University Innsbruck, Innsbruck, Austria

Introduction

- Endometrial cancer (EC) is the most common gynecological cancer in the US and one of the few cancers with growing incidence[1]
- Immune checkpoint inhibitors (ICIs) have transformed the treatment paradigm for patients with EC. KEYNOTE-775,[2] KEYNOTE-158,[3] and GARNET[4] demonstrated benefit of ICI among patients treated following prior systemic therapy. Recent trials (NRG-GY018/KEYNOTE-868,[5] RUBY,[6] DUO-E[7]) have demonstrated evidence supporting ICI + chemotherapy in the first-line (1L) primary advanced and recurrent EC
- Together, these clinical trials established the integration of ICI into National Comprehensive Cancer Network (NCCN) guidelines across different settings. With increasing use in 1L,[8] ICI + chemotherapy is becoming standard of care in 1L
- However, there are no established guidelines to inform treatment decisions for patients who already have received ICI and platinum (PT) regimens. With the expanding post-ICI and post-PT population, especially following 1L therapy critical need to describe how these patients are managed in real-world practice

Objectives

- To describe patient demographics, clinical characteristics, and treatment patterns of advanced and recurrent EC in the post–ICI and post–PT therapy setting.

Methods

Design

- Study design: retrospective observational cohort study between January 1, 2013, and June 30, 2025
- Data source: Flatiron Health, a nationwide database of longitudinal electronic health records, comprising deidentified structured and unstructured data from ~280 US cancer care entities and 800 clinical care sites, including both community and academic oncology practices[9]
- Study population: women aged ≥18 years with recurrent EC with a history of prior ICI and prior PT, administered either simultaneously or in separate lines of therapy (LOTs), and initiated at least 1 subsequent LOT (see **Figure 1** for study cohort attrition)

Measures

Sociodemographic characteristics: age, race, ethnicity, geographical region of the US, socioeconomic status (SES), practice setting, and insurance type

Clinical characteristics: body mass index (BMI), Eastern Cooperative Oncology Group (ECOG) performance score, Charlson comorbidity index (CCI), stage at diagnosis, histology, 1L initiation before/after 2023 NCCN guidelines update, and tumor mismatch repair (MMR) and/or microsatellite instability (MSI) status

Treatment patterns: index LOTs (first LOT in the post-ICI+post-PT setting, e.g., patient received PT in 1L and ICI in 2L, index LOT is 3L) as defined by Flatiron's LOT algorithm (except in the instance of those who initiated pembrolizumab monotherapy and within 90 days initiated pembrolizumab + lenvatinib, those two LOTs were collapsed into one)

Index date: date of initiation of first LOT in the post-ICI + post-PT setting

Analyses

All analyses were descriptive. Categorical variables were summarized using frequencies and percentages, while continuous variables were summarized using medians and interquartile ranges (IQRs)

Results were presented overall, as well as stratified by MMR/MSI status (deficient mismatch repair [dMMR] and/or microsatellite instability-high [MSI-H] vs. proficient mismatch repair [pMMR] and/or microsatellite stable [MSS]) and index LOT

Results

A total of 241 women with recurrent EC had prior exposure to both ICI and PT in any treatment setting prior to the index date, and subsequently received at least 1 additional systemic therapy (**Figure 1**)

Figure 1. Study cohort attrition

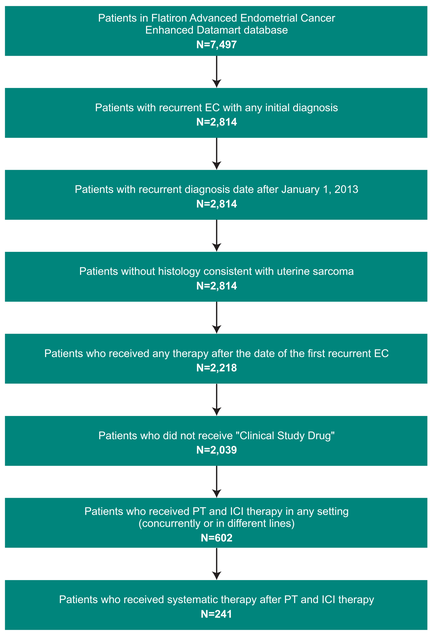


Table 1. Sociodemographic and clinical characteristics of recurrent EC in the post-ICI + post-PT setting

Baseline characteristics	Overall (N = 241)	dMMR and/or MSI-H[a] (N = 54)	pMMR and/or MSS[a] (N = 153)
Sociodemographics			
Age at recurrent EC diagnosis, yrs			
Median (Q1, Q3)	69.0 (63.0, 74.0)	67.5 (61.0, 74.0)	69.0 (63.0, 74.0)
Race, N (%)			
White	138 (57.3)	32 (59.3)	88 (57.5)
Other races	79 (32.8)	14 (25.9)	54 (35.3)
Unknown	24 (10.0)	8 (14.8)	11 (7.2)
Ethnicity, N (%)			
Hispanic or Latino	23 (9.5)	6 (11.1)	13 (8.5)
Not Hispanic or Latino	175 (72.6)	37 (68.5)	112 (73.2)
Unknown	43 (17.8)	11 (20.4)	28 (18.3)
Geographic region, N (%)			
Midwest	31 (12.9)	8 (14.8)	18 (11.8)
Northeast	27 (11.2)	5 (9.3)	18 (11.8)
South	86 (35.7)	18 (33.3)	61 (39.9)
West	28 (11.6)	7 (13.0)	16 (10.5)
Unknown	69 (28.6)	16 (29.6)	40 (26.1)
Practice type, N (%)			
Academic	54 (22.4)	13 (24.1)	31 (20.3)
Community	182 (75.5)	41 (75.9)	119 (77.8)
Both	≤5	0 (0)	≤5
SES index, N (%)			
1 – lowest SES	46 (20.5)	≤10	30 (21.6)
2	43 (19.2)	≤10	30 (21.6)
3	40 (17.9)	≤10	21 (15.1)
4	50 (22.3)	17 (32.1)	31 (22.3)
5 – highest SES	45 (20.1)	≤10	27 (19.4)
Unknown	17 (NA)	≤5	14 (NA)
Clinical characteristics			
BMI at recurrence diagnosis, kg/m²			
Median (Q1, Q3)	29.4 (24.5, 35.3)	30.7 (24.9, 36.2)	29.19 (23.9, 35.2)
EC diagnosis			
Histology at recurrence diagnosis, N (%)			
Carcinosarcoma/MMT	25 (10.4)	0 (0)	23 (15.0)
Clear cell carcinoma	13 (5.4)	0 (0)	12 (7.8)
EC, NOS	13 (5.4)	0 (0)	10 (6.5)
Endometrioid carcinoma	122 (50.6)	54 (100.0)	50 (32.7)
Serous carcinoma	68 (28.2)	0 (0)	58 (37.9)
Stage at initial diagnosis, N (%)			
I	72 (29.9)	16 (29.6)	38 (24.8)
II	13 (5.4)	≤5	8 (5.2)
III	140 (58.1)	32 (59.3)	96 (62.7)
IV	≤5	0 (0)	≤5
IVA	≤5	≤5	≤5
Unknown/not documented	11 (4.6)	≤5	7 (4.6)
ECOG at index date, N (%)			
0	59 (24.5)	13 (24.1)	36 (23.5)
1	75 (31.1)	16 (29.6)	50 (32.7)
2	25 (10.4)	6 (11.1)	17 (11.1)
3	≤5	0 (0)	≤5
4	≤5	0 (0)	≤5
Missing	76 (31.5)	19 (35.2)	45 (29.4)
MMR and/or MSI at any time before index date, N (%)			
Discordant	≤15	0 (0)	0 (0)
Missing	19 (7.9)	0 (0)	0 (0)
Other	≤5	0 (0)	0 (0)
dMMR and/or MSI-H	54 (22.4)	54 (100.0)	0 (0)
pMMR and/or MSS	153 (63.5)	0 (0)	153 (100.0)
Index LOT, N (%)			
1L	19 (7.8)	≤5	15 (9.8)
2L	72 (29.9)	19 (35.2)	46 (30.1)
3L	73 (30.3)	17 (31.5)	41 (26.8)
4L+	77 (32.0)	≤15	51 (33.3)

[a]Test results at any time before the index date.

2L, second-line; 3L, third line; 4L+, fourth-line or later; MMT, mixed Müllerian tumor; NOS, not otherwise specified.

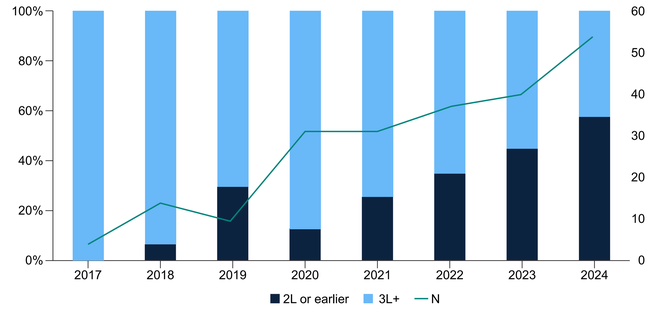
Cohort characteristics

- The median age of the cohort at the index therapy initiation was 69 years (**Table 1**; IQR, 63-74). Most patients were White (57.3%), followed by other races (32.8%), and unknown (10.0%); 72.6% were non-Hispanic
- The MMR and/or MSI biomarker status was: dMMR and/or MSI-H in 22.4%, pMMR and/or MSS in 63.5%, and other/unknown in 14.2%
- The most frequent histologic subtype was endometrioid (50.6%), followed by serous (28.2%), carcinosarcoma/mixed Müllerian tumor (10.4%), and clear cell (5.4%)
- The number and proportion of patients initiating therapy in the post-ICI + post-PT setting were 19 (7.9%) in 1L, 72 (29.9%) in second-line (2L), 73 (30.3%) in third-line (3L), and 77 (32.0%) in fourth-line (4L) or later LOTs

Increase in population over time

- The population of patients reaching both post-ICI and post-PT status expanded substantially over time. From 2017 to 2024, the total number of patients in the post-ICI + post-PT setting increased from ≤5 patients in 2017 to 54 patients in 2024 (**Figure 2**)

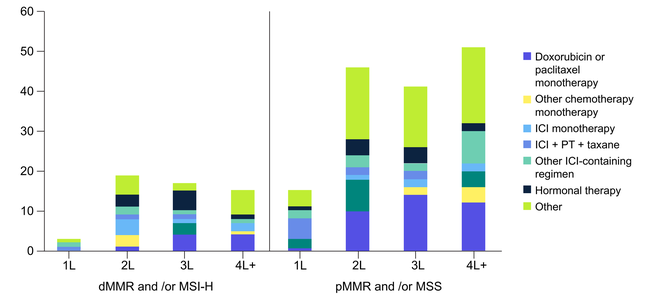
Figure 2. Proportion of EC patients initiating treatment in the post-ICI + post-PT setting by index LOT



Index LOTs

- Treatment patterns in the post-ICI + post-PT population varied, with no dominant regimen emerging (**Figure 3**)
- In this cohort, 77 patients (32.0%) received some form of ICI therapy, while 62 patients (25.7%) received chemotherapy monotherapy
- Treatment patterns did differ by MMR and/or MSI status
  - dMMR and/or MSI-H tumors: ICI-based regimens more frequently used
  - pMMR and/or MSS tumors: doxorubicin or paclitaxel monotherapy and ICI + TKI regimens more common
- Among those who received chemotherapy monotherapy in the index LOT:
  - 40 (64.5%) had doxorubicin monotherapy, 8 (61.5%) in dMMR and/or MSI-H and 29 (67.4%) in pMMR and/or MSS
  - 10 (16.1%) had a taxane monotherapy, 1 (7.7%) in dMMR and/or MSI-H and 8 (18.6%) in pMMR and/or MSS, all of which were paclitaxel monotherapy
  - 6 (9.7%) had a platinum monotherapy, 2 (15.4%) in dMMR and/or MSI-H and 3 (7.0%) in pMMR and/or MSS
- Among those who received ICI in the index LOT:
  - 17 (22.1%) had ICI monotherapy, 7 (46.7%) in dMMR and/or MSI-H and 5 (17.9%) in pMMR and/or MSS
  - 14 (18.2%) had ICI + chemotherapy, 3 (20.0%) in dMMR and/or MSI-H and 9 (32.1%) in pMMR and/or MSS
  - 25 (32.5%) had pembrolizumab + lenvatinib, 5 (33.3%) in dMMR and/or MSI-H and 14 (50.0%) in pMMR and/or MSS
- When considering index treatments by LOT, it varied substantially across LOTs, with greater diversity in later lines (e.g., 3L, 4L+)

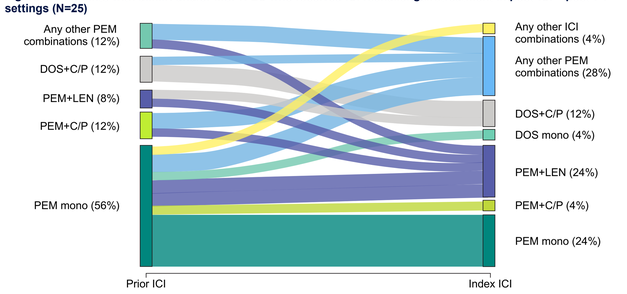
Figure 3. Treatment patterns in the post-ICI + post-PT setting, by index LOT and MMR and/or MSI status



ICI therapy in post-ICI + post-PT settings

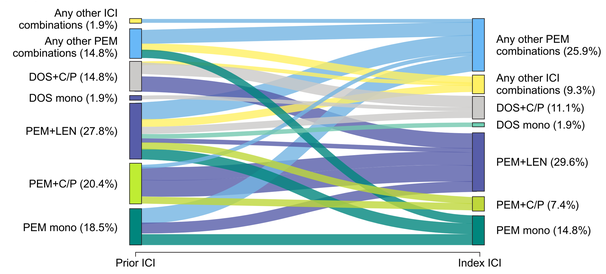
- The ICI-ICI sequence is shown by MMR/MSS status in **Figure 4A and 4B**. Among dMMR and/or MSI-H patients, 3 (5.6%), 19 (35.2%), 17 (31.5%), and 15 (27.8%) entered the post-ICI + post-PT setting in 1L, 2L, 3L, and ≥4L+, respectively; the corresponding proportions for pMMR patients were 15 (9.8%), 46 (30.1%), 41 (26.8%), and 51 (33.3%), respectively
- Among those who had ICI after ICI, the majority of patients received pembrolizumab in the prior setting (80.2%). In the post-ICI + post-PT settings (55.2%), pembrolizumab-based treatments were given either as monotherapy or combined with lenvatinib or carboplatin/paclitaxel. Despite this, no single ICI-to-ICI sequence predominated. Overall, there were 14 distinct ICI-to-ICI sequence combinations among dMMR and/or MSI-H patients, and 21 combinations among pMMR and/or MSS patients
- Mean and median ICI-free interval, an important predictor of rechallenge effectiveness, varied by LOT and MMR and/or MSI status (**Figure 5**). Similar trends were seen in a proportion of patients with IO-free interval >6 months, however most patients had ICI-free intervals ≤6 months; however, (data not shown)

Figure 4A. Patients with dMMR and/or MSI-H EC who received ICI rechallenge/retreatment in post-ICI + post-PT settings (N=25)



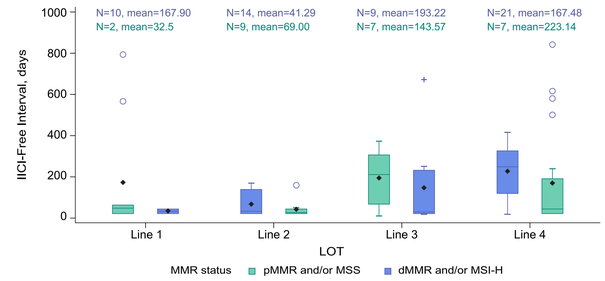
C/P, carboplatin + paclitaxel; DOS, dostarlimab; LEN, lenvatinib; mono, monotherapy; PEM, pembrolizumab.

4B. Patients with pMMR and/or MSS EC who received ICI rechallenge/retreatment in post-ICI + post-PT settings (N=54)



C/P, carboplatin + paclitaxel; DOS, dostarlimab; LEN, lenvatinib; mono, monotherapy; PEM, pembrolizumab.

Figure 5. ICI-free interval by LOT and MMR status



Discussion

- This study provides one of the first real-world descriptions of the post-ICI + post-PT treatment patterns among patients with recurrent EC
- Chemotherapy monotherapy (mainly doxorubicin) and ICI-based regimens (as monotherapy or in combination with lenvatinib or carboplatin/paclitaxel) were the most frequently used treatments in the post-ICI + post-PT setting. Few patients (<5%) had PT monotherapy in this setting
- Pembrolizumab was the most commonly used ICI agent across both first ICI exposure and post-ICI + post-PT settings, reflecting its widespread adoption in current practice
- Because ICI-free interval and LOT are confounders, and there is a wide variety of ICI-to-ICI combinations with ICI-free intervals that also differ by LOT and MMR status, estimating the effectiveness of ICI-to-ICI rechallenge with this small sample size is a challenge

Limitations

- The analysis was descriptive; no survival or clinical outcome endpoints were evaluated
- The sample size of certain subgroups (e.g., post-ICI rechallenge, rare histologies) was small, limiting precision in estimating treatment proportions
- Adequate stratification (e.g., by treatment type, by LOT, and by tumor molecular profile) was also limited by sample size

Conclusions

- The incidence of post-ICI + post-PT EC is increasing, with the most rapid rise observed in 2L and earlier treatment settings
- Common treatment strategies include ICI (either as monotherapy or combined with carboplatin/paclitaxel or lenvatinib) and chemotherapy monotherapy (predominantly doxorubicin; PT therapies were infrequently used in these settings).
- Among patients treated with ICI in post-ICI + post-PT settings, pembrolizumab-based regimens were the most frequently used in current and prior lines of therapy. Variation in ICI-ICD sequencing and ICI-free interval length across MMR and/or MSI status and LOTs may confound estimates of ICI-ICD effectiveness, a problem compounded by small subgroup sizes within specific LOTs and MMR and/or MSI intersections
- Overall, real-world practice shows no clear consensus on management in the post-ICI + post-PT setting
- In the absence of approved therapies for this population, these treatment patterns underscore a substantial unmet medical need and the necessity for novel therapeutic options in the post-ICI + post-PT setting

References

1. American Cancer Society. Key statistics for endometrial cancer. 2025. Accessed May 15, 2025. https://www.cancer.org/cancer/types/endometrial-cancer/about/key-statistics.html
2. Makker V, et al. *N Engl J Med.* 2022;386(5):437-448.
3. O'Malley DM, et al. *J Clin Oncol.* 2022;40(7):752-761.
4. Oaknin A, et al. *J Immunother Cancer.* 2022;10(1):e003777.
5. Eskander RN, et al. *N Engl J Med.* 2023;388(23):2159-2170.
6. Mirza MR, et al. *Ann Oncol.* 2024;35(suppl 2):S556.
7. Westin SN, et al. *J Clin Oncol.* 2024;42(3):283-299.
8. Marupuru S, et al. *Int J Gynecol Cancer.* 2025;35(11 suppl 1):102247.
9. Whiteley A, et al. *Curr Oncol.* 2025;32(5):268.

Disclosures

- Funding for this research was provided by Merck Sharp & Dohme LLC, a subsidiary of Merck & Co., Inc., Rahway, NJ, USA
- VT was a contractor working under contract with Atlas on behalf of Merck Sharp & Dohme LLC, a subsidiary of Merck & Co., Inc., Rahway, NJ, USA, at the time the study was conducted
- SM, VSP, KMM, KM, and RM are employees of Merck Sharp & Dohme LLC, a subsidiary of Merck & Co., Inc., Rahway, NJ, USA, who may own stock and/or hold stock options in Merck & Co., Inc., Rahway, NJ, USA
- RO is an employee of Merck Sharp & Dohme LLC, a subsidiary of Merck & Co., Inc., Rahway, NJ, USA, who may own stock and/or hold stock options in Merck & Co., Inc., Rahway, NJ, USA and owns stock in Nektar Pharmaceuticals
- CM has received consulting fees, administrative support, article publishing charges support, statistical analysis support, and writing assistance from Merck Sharp & Dohme LLC, a subsidiary of Merck & Co., Inc., Rahway, NJ, USA; reports relationships with Eisai Inc and GSK that includes: consulting or advisory, speaking and lecture fees, and travel reimbursement; and reports a relationship with AstraZeneca UK Limited that includes: consulting or advisory and speaking and lecture fees
- AKG has received consulting fees from Merck Sharp & Dohme LLC, a subsidiary of Merck & Co., Inc., Rahway, NJ, USA; has served as a consultant or advisory and received funding grants from Menarini Stemline Italia SrL, and has received funding grants from Aadi Biosciences and the American Society of Clinical Oncology
- VMM has received travel support from Merck Sharp & Dohme LLC, a subsidiary of Merck & Co., Inc., Rahway, NJ, USA; AstraZeneca; and Karyopharm; is an unpaid consultant for Merck Sharp & Dohme LLC, a subsidiary of Merck & Co., Inc., Rahway, NJ, USA; Antares Therapeutics; Clovis Oncology; Cullinan Oncology; DualityBio; Eisai; Faeth Therapeutics; GlaxoSmithKline; Genmab; Immunocore; iTeos Therapeutics; Karyopharm Therapeutics; Jazz Pharmaceuticals; Lilly; Mereo BioPharma; MorphoSys; MSD (UK) Limited, London, UK; Novartis; Ottimo; Regeneron; Scorpion Therapeutics; Stemline Therapeutics; Sutro Biopharma; and Zymeworks; and has received institutional grants or contracts from Merck Sharp & Dohme LLC, a subsidiary of Merck & Co., Inc., Rahway, NJ, USA; AstraZeneca; Bristol Myers Squibb; Cullinan Oncology; DualityBio; Eisai; Faeth Therapeutics; Jazz; Karyopharm Therapeutics; Takeda; and Zymeworks

Presented at the International Society for Pharmacoeconomics and Outcomes Research (ISPOR); May 17-20, 2026; Philadelphia, PA, USA.