EE408

Healthcare resource utilization and costs following disease progression with first-line systemic therapy in patients with advanced endometrial cancer in the US

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Supplemental data

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Introduction

- Endometrial cancer (EC) is the most common gynecological malignancy worldwide, with incidence rates rising by 0.6% per year and death rates an average of 1.8% per year in the last decade; stage IV EC has a 5-year survival rate of only 19%[1-3]
- Until recently, platinum-based chemotherapy (carboplatin-paclitaxel) was the established standard-of-care first-line systemic therapy in patients with advanced or recurrent EC; however, long-term outcomes remained poor, with most patients experiencing disease progression or recurrence requiring subsequent therapy[4,5]
  - A longer treatment-free interval (TFI) following first-line systemic therapy has been associated with better overall survival (OS) and may predict response to rechallenge with platinum-based chemotherapy[6]
- In 2021, the US Food and Drug Administration granted accelerated approval to the anti–programmed cell death 1 protein (PD-1) monoclonal antibody dostarlimab for patients with mismatch repair–deficient recurrent or advanced endometrial cancer after a platinum-containing regimen; approval of the anti–PD-1 monoclonal antibody pembrolizumab for use after systemic therapy in this patient population followed in 2022[5,7-9]
  - Since 2023, immunotherapy with anti–PD-1 antibodies has moved into the first-line setting, with both dostarlimab and pembrolizumab now approved in combination with carboplatin-paclitaxel followed by single-agent immunotherapy maintenance in patients with primary advanced or recurrent EC[5,7-9]
- EC is associated with a significant economic burden, with estimated mean per-patient-per-month (PPPM) costs ranging from $11,363 to $14,645, with outpatient costs accounting for the highest percentage of total costs across all treatments at roughly 73%[10]
  - However, the relative impact of recurrence and subsequent lines of therapy (LOTs) on healthcare resource utilization (HCRU) and costs in EC has not been well characterized
- This retrospective claims-based analysis was conducted to estimate HCRU and direct medical costs among patients with advanced EC who reached at least a second LOT (LOT2) and to explore the association of TFI with these measures

Methods

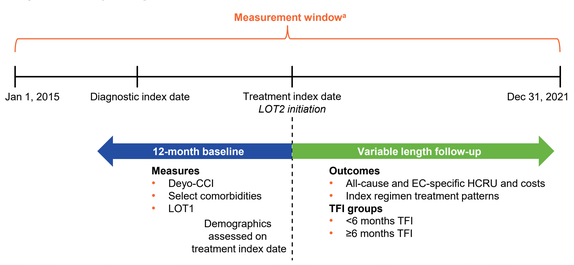
Data Sources

- Data were derived from:
  - The **Medicare Fee-for-Service (FFS) database**, which includes all Part A/B medical encounters and Part D Prescription Drug Events
  - The **MORE² Registry** of closed claims, which includes medical, retail, and mail-order pharmacy claims sourced from over 140 health plans and statistically deidentified

Study Design and Patient Selection

- The **measurement period** was from January 1, 2015, to December 31, 2021 (**Figure 1**)
- Patients were required to have either ≥1 inpatient claim with a primary diagnosis code for EC or ≥2 outpatient claims (on separate dates within 1 year) with a diagnosis code for EC in any position between January 1, 2016, and June 30, 2021
  - Earliest appearance of an EC diagnosis was set as the **diagnostic index date**, which was preceded by a 6-month washout period of continuous enrollment to ensure identification of incident patients
- LOTs were identified on or following the diagnostic index date, and the date of initiation of LOT2 was set as the **treatment index date**
  - The analysis was restricted to patients with a qualifying LOT2 and ≥12 months of continuous enrollment before and ≥30 days after treatment index
- Patients were ineligible if they had any claims with a diagnosis code for EC during the 6-month period preceding the diagnostic index date, diagnosis of another primary cancer other than basal or squamous cell skin carcinoma during the pretreatment index period, or evidence of clinical trial participation during the entire study

Figure 1: **Study Design**



CCI, Charlson Comorbidity Index; EC, endometrial cancer; HCRU, healthcare resource utilization; LOT1, first line of therapy; LOT2, second line of therapy; TFI, treatment-free interval.
[a] Within the measurement window, the indexing window ran from January 1, 2016, to December 1, 2021, ensuring ≥12 months of continuous enrollment before diagnostic index to capture incident patients and ≥30 days of follow-up after treatment index for the last eligible patient.

LOT Identification and Cohorts

- LOT identification was adapted from a previously published claims-based algorithm in conjunction with clinical guidance,[11] with qualifying treatments including surgery, radiotherapy, systemic therapy (chemotherapy and immunotherapy), and hormonal therapy (**see QR code**)
- The first systemic treatment on or following the diagnostic index date was designated as LOT1; subsequent LOTs were initiated if any new systemic therapy, radiotherapy, or surgical procedure claim occurred ≥28 days after initiation of the previous LOT (excluding a switch between 2 platinum therapies)
  - LOT end was defined by any of the following: discontinuation (>90-day gap in all components of that LOT); switch/augmentation (a claim for a new EC treatment that did not appear during the LOT initiation period); or end of study (December 31, 2021), end of health plan enrollment, or death
    - The official LOT end date was set to the last administration claim (for injectable medications) or the date of the last prescription claim plus the days' supply (for oral medications)
- LOT2 initiators were divided into TFI cohorts defined by the time between LOT1 termination and LOT2 initiation as:
  - TFI duration of <6 months
  - TFI duration of ≥6 months

Treatment Patterns

- The following were derived for all identified LOTs (mean/median/SD):
  - Time between diagnostic and treatment index dates: number of days from diagnostic index date to LOT initiation
  - Duration of therapy: number of days from LOT initiation to the earliest of either switch, discontinuation, death (Medicare FFS only), end of health plan enrollment, or end of study (December 31, 2021)
  - Time to next treatment: number of days from prior LOT initiation to subsequent LOT initiation
  - TFI: number of days from prior LOT termination to subsequent LOT initiation

HCRU and Costs

- All-cause and EC-specific HCRU and costs were reported PPPM over the variable-length follow-up, derived as "Costs observed during window / Total days in window * 30"
  - EC-related HCRU and costs were based on inpatient admissions with a primary diagnosis for EC, outpatient medical claims with a diagnosis for EC in any position, and outpatient pharmacy claims for treatments indicated for EC

HCRU

- For each HCRU service category, a binary measure indicating any use of the service and continuous measures indicating the number of services incurred were created
- HCRU services included physician (oncologist and hematologist) office visits, emergency department (ED) visits, hospitalizations, post–acute care visits (eg, hospice/home health), and Part D drug prescriptions

Costs

- Medicare FFS costs were based on the Medicare payment amount reported on the claim plus beneficiary cost sharing; for the MORE² Registry, standardized costs were derived by imputing the amount a plan would reimburse a provider for services rendered using a standardized set of algorithms based on Medicare fee schedules[12]
  - All costs were adjusted for inflation using the medical care component of the Consumer Price Index and standardized to 2022 US dollars
- Costs included total healthcare costs, total medical costs, inpatient hospital costs, physician office costs, ED and other outpatient costs, and pharmacy costs

Statistical Analysis

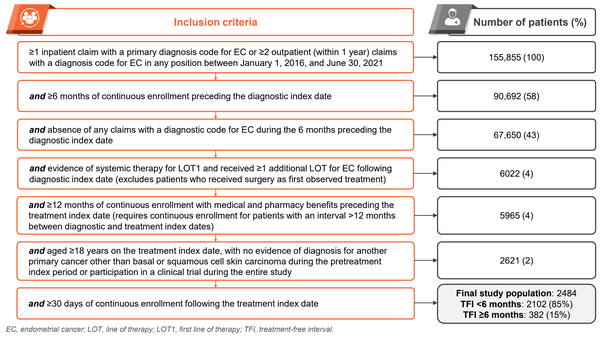
- The following were described overall and by TFI cohort:
  - Demographic and clinical characteristics at treatment index date, summarized descriptively as mean (SD) and/or median for continuous variables and number (%) for categorical variables
  - All-cause and EC-specific HCRU PPPM, summarized as number (%) of patients and mean (SD) number of visits
  - All-cause and EC-specific costs PPPM, summarized as mean (SD)
  - Generalized linear models (GLMs) with log-link and gamma distribution were estimated to assess the association between TFI and costs, adjusting for patient characteristics

Results

Patients and Treatment Patterns

- Patient selection is shown in **Figure 2**; of 2484 patients included in the study, 2102 (85%) had a TFI of <6 months and 382 (15%) had a TFI of ≥6 months
- Baseline characteristics are summarized in **Table 1**; patients with a TFI of ≥6 months were numerically older than patients with a TFI of <6 months (mean, 70.1 vs 67.0 years), and follow-up was longer (mean, 12.6 vs 9.7 months)

Figure 2: **Patient Attrition and Selection**



EC, endometrial cancer; LOT, line of therapy; LOT1, first line of therapy; TFI, treatment-free interval.

Table 1: **Baseline Characteristics[a]**

	LOT2 initiators (N=2484)	TFI <6 months (n=2102)	TFI ≥6 months (n=382)
Age, mean (SD), years	67.5 (10.9)	67.0 (10.7)	70.1 (11.7)
Median	68.0	68.0	70.0
Race and ethnicity, n (%)			
White	1465 (59)	1218 (58)	247 (65)
Black	332 (13)	281 (13)	51 (13)
Asian, Pacific Islander, American Indian/Alaskan Native	53 (2)	45 (2)	<11
Hispanic or Latino	93 (4)	78 (4)	<30
Unknown	541 (22)	480 (23)	61 (16)
Census region, n (%)			
Northeast	561 (23)	457 (22)	104 (27)
Midwest	622 (25)	541 (26)	81 (21)
South	802 (32)	689 (33)	113 (30)
West	459 (18)	381 (18)	<90
US territory/unknown	40 (2)	34 (2)	<11
Length of follow-up, mean (SD), months	10.2 (11.1)	9.7 (10.4)	12.6 (14.1)
Median	6.6	6.7	6.4
Deyo-CCI, mean (SD)	6.0 (3.5)	6.1 (3.4)	5.7 (3.6)

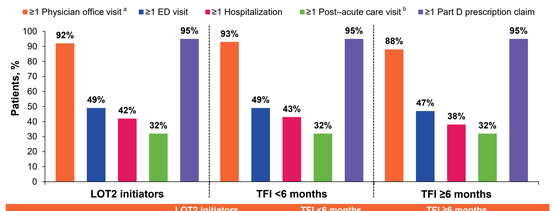
CCI, Charlson Comorbidity Index; LOT2, second line of therapy; TFI, treatment-free interval.
[a] Exact values for certain cohorts were masked to prevent patient identification per Medicare requirements.

- During LOT2, 1338 patients (54%) received systemic therapy, 777 (31%) received radiotherapy, 266 (11%) received surgery, and 103 (4%) received combination therapy
- Mean time from diagnosis to treatment index (LOT2 initiation) was 208.2 (SD, 185.6) days, mean time to next treatment (LOT1 initiation to LOT2 initiation) was 154.1 (SD, 155.3) days, and mean TFI (LOT1 termination to LOT2 initiation) was 110.5 (SD, 154.8) days
- Mean duration of LOT2 was 104.8 (156.1) days; the most common reasons for LOT2 termination were a treatment switch in 1514 patients (61%) and discontinuation in 923 patients (37%)

All-Cause HCRU and Costs

- All-cause HCRU (physician office visits, ED visits, and inpatient hospitalizations) and total healthcare costs PPPM were numerically higher among patients with a TFI of <6 months (**Figures 3** and **4**)
  - For patients with a TFI of <6 months, more than half of total costs were driven by outpatient services (55%), followed by inpatient hospitalization (33%)
  - Retail and mail-order pharmacy costs were more than twice as high in patients with a TFI of ≥6 months ($2631 [SD, $9359] vs $1221 [SD, $5612])

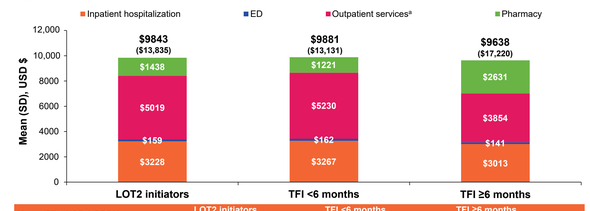
Figure 3: **All-Cause HCRU**



Mean (SD), PPPM	LOT2 initiators (N=2484)	TFI <6 months (n=2102)	TFI ≥6 months (n=382)
Physician office visits	1.42 (1.39)	1.45 (1.42)	1.29 (1.26)
Oncologist	0.12 (0.50)	0.12 (0.50)	0.08 (0.51)
Hematologist	0.16 (0.63)	0.18 (0.66)	0.10 (0.36)
ED visits	0.26 (0.48)	0.26 (0.49)	0.22 (0.47)
Hospitalizations	0.21 (0.48)	0.21 (0.49)	0.16 (0.42)
Post–acute care visits	0.14 (0.30)	0.14 (0.31)	0.12 (0.25)
Part D prescription claims	3.86 (4.03)	3.76 (3.85)	4.43 (4.85)

ED, emergency department; HCRU, healthcare resource utilization; LOT2, second line of therapy; PPPM, per patient per month; TFI, treatment-free interval.
[a] Includes oncologist and hematologist visits. [b] Includes hospice, home health, skilled nursing facility, inpatient rehabilitation facility, and long-term acute care hospital.

Figure 4: **All-Cause Healthcare Costs**



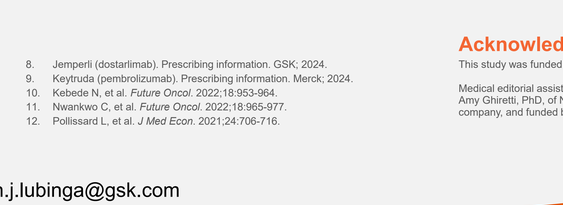
Mean (SD), USD $ PPPM	LOT2 initiators (N=2484)	TFI <6 months (n=2102)	TFI ≥6 months (n=382)
Medical	8406 (11,393)	8660 (11,073)	7008 (12,945)
Inpatient hospitalizations	3228 (8879)	3267 (8605)	3013 (10,264)
ED visits	159 (437)	162 (444)	141 (399)
Outpatient services[a]	5019 (NR)	5230 (NR)	3854 (NR)
Outpatient visits	3031 (3646)	3189 (3555)	2161 (4006)
Physician services/testing	1240 (2398)	1301 (2453)	903 (2037)
Post-acute care	709 (1973)	708 (2027)	715 (1648)
Durable medical equipment	39 (334)	32 (241)	75 (639)
Pharmacy	1438 (6352)	1221 (5612)	2631 (9359)
Total	9843 (13,835)	9881 (13,131)	9638 (17,220)

ED, emergency department; LOT2, second line of therapy; NR, not reported; PPPM, per patient per month; TFI, treatment-free interval; USD, US dollar.
[a] Includes all outpatient services other than ED visits, comprising outpatient visits, physician services and tests (including office visits), post-acute care (hospice, home health, skilled nursing facility, inpatient rehabilitation facility, and long-term acute care hospital), and durable medical equipment.

EC-Specific HCRU and Costs

- EC-specific HCRU (physician office visits, ED visits, inpatient hospitalizations, and post–acute care visits) and total EC-specific costs PPPM were also numerically higher among patients with a TFI of <6 months (**Figures 5** and **6**)
  - Overall, EC-specific costs contributed to 61% and 55% of total all-cause costs for the TFI <6 months and ≥6 months cohorts, respectively; EC-specific outpatient costs were 63% higher in the shorter TFI cohort

Figure 5: **EC-Specific HCRU**



Mean (SD), PPPM	LOT2 initiators (N=2484)	TFI <6 months (n=2102)	TFI ≥6 months (n=382)
Physician office visits	0.81 (1.09)	0.85 (1.11)	0.56 (0.95)
Oncologist	0.09 (0.46)	0.10 (0.46)	0.06 (0.43)
Hematologist	0.16 (0.62)	0.17 (0.66)	0.09 (0.35)
ED visits	0.06 (0.19)	0.07 (0.19)	0.04 (0.14)
Hospitalizations	0.05 (0.20)	0.06 (0.19)	0.04 (0.26)
Post–acute care visits	0.10 (0.26)	0.11 (0.27)	0.07 (0.19)
Part D prescription claims	0.16 (0.41)	0.14 (0.39)	0.29 (0.50)

EC, endometrial cancer; ED, emergency department; HCRU, healthcare resource utilization; LOT2, second line of therapy; PPPM, per patient per month; TFI, treatment-free interval.
[a] Includes oncologist and hematologist visits. [b] Includes hospice, home health, skilled nursing facility, inpatient rehabilitation facility, and long-term acute care hospital.

Figure 6: **EC-Specific Healthcare Costs**

Mean (SD), USD $ PPPM	LOT2 initiators (N=2484)	TFI <6 months (n=2102)	TFI ≥6 months (n=382)
Medical	4980 (6072)	5282 (6000)	3318 (6200)
Inpatient hospitalizations	909 (3695)	964 (3710)	604 (3601)
ED visits	59 (260)	63 (270)	36 (188)
Outpatient services[a]	4012 (NR)	4254 (NR)	2677 (NR)
Outpatient visits	2566 (3512)	2738 (3458)	1620 (3662)
Physician services/testing	969 (2256)	1031 (2329)	622 (1770)
Post-acute care	475 (1464)	483 (1483)	433 (1355)
Durable medical equipment	2 (14)	2 (14)	2 (12)
Pharmacy	901 (5513)	711 (4652)	1945 (8802)
Total	5880 (8567)	5993 (7958)	5263 (11,341)

EC, endometrial cancer; ED, emergency department; LOT2, second line of therapy; NR, not reported; PPPM, per patient per month; TFI, treatment-free interval; USD, US dollar.
[a] Includes all outpatient services other than ED visits, comprising outpatient visits, physician services and tests (including office visits), post-acute care (hospice, home health, skilled nursing facility, inpatient rehabilitation facility, and long-term acute care hospital), and durable medical equipment.

GLMs for Total Healthcare Costs

- After adjusting for baseline characteristics, the difference in all-cause total costs PPPM based on TFI was not statistically significant (cost ratio, 0.961; *P*=.4854); however, EC-specific total costs among patients with a TFI of <6 months remained significantly higher compared with patients with a TFI of ≥6 months (cost ratio, 0.747; *P*<.0001) (**Table 2**)

Table 2: **Adjusted GLM Results for Total Healthcare Costs**

Covariate	Level	All-cause costs Cost ratio (95% CI)	*P* value	EC-specific costs Cost ratio (95% CI)	*P* value
TFI	**<6 months (reference)**				
	≥6 months	0.961 (0.858-1.076)	.4854	0.747 (0.649-0.860)	**<.0001**
Age at index	Per 10-year increase	0.940 (0.901-0.981)	**.0048**	0.975 (0.926-1.027)	.3411
Race and ethnicity	**White (reference)**				
	Black	1.602 (1.414-1.815)	**<.0001**	1.471 (1.262-1.716)	**<.0001**
	Asian, Pacific Islander, American Indian/Alaskan Native, Hispanic or Latino	0.996 (0.832-1.191)	.9606	0.954 (0.765-1.189)	.674
	Unknown	0.939 (0.840-1.049)	.266	1.031 (0.898-1.184)	.667
Region	**South/US territory/unknown (reference)**				
	Northeast	1.059 (0.949-1.183)	.3059	1.029 (0.898-1.179)	.682
	Midwest	1.055 (0.946-1.176)	.3387	1.028 (0.898-1.176)	.6915
	West	0.920 (0.817-1.037)	.172	0.986 (0.851-1.142)	.8461
Baseline Deyo-CCI comorbidity score	Per 1 score unit increase	1.074 (1.061-1.086)	**<.0001**	1.065 (1.049-1.080)	**<.0001**
LOT1	**Systemic treatment ± any other treatment (reference)**				
	Radiotherapy only	0.626 (0.534-0.733)	**<.0001**	0.542 (0.446-0.659)	**<.0001**
	Hormonal treatment only	0.542 (0.490-0.600)	**<.0001**	0.423 (0.373-0.480)	**<.0001**
Index year	**2016 (reference)**				
	2017	1.008 (0.828-1.227)	.9391	0.908 (0.711-1.160)	.4393
	2018	0.988 (0.818-1.195)	.9042	0.966 (0.764-1.222)	.7737
	2019	1.104 (0.913-1.334)	.3074	1.201 (0.948-1.520)	.1291
	2020	0.944 (0.784-1.138)	.5474	1.024 (0.813-1.291)	.8379
	2021	1.023 (0.862-1.215)	.7947	1.305 (1.054-1.615)	.0145

CCI, Charlson Comorbidity Index; EC, endometrial cancer; GLM, generalized linear model; LOT1, first line of therapy; TFI, treatment-free interval.

Limitations

- This study may only be generalizable to insured patients with EC who received first-line systemic therapy followed by a subsequent LOT in the US, and it focused specifically on patients with ≥12 months of continuous enrollment prior to and ≥30 days following diagnosis
- Cause and effect cannot be definitively determined from administrative claims data, and measures such as TFI may vary when derived from claims vs clinical data; although patients may have been misclassified due to miscoding or misdiagnosis, errors are thought to be minimal as accurate information is required for adjudication and payment
- Medication usage for this study was based on filled outpatient prescriptions and medical claims for physician-administered medications only, and confirmation that medications were taken as prescribed was not possible

Conclusions

- To our knowledge, this is the first study based on a large database using nationally representative data from medical and pharmacy claims in the US to assess the association between TFI and HCRU in an EC population
- In this study, which examined the period before immunotherapy was incorporated in standard first-line treatment, the majority of patients had a TFI of <6 months, indicating faster disease progression and correlating with numerically higher HCRU and significantly increased EC-specific costs
- Regardless of TFI, initiation of subsequent LOTs in patients with advanced EC was associated with considerable HCRU and costs
- These analyses underscore the high medical need in patients with advanced EC requiring subsequent LOTs, and suggest that delaying disease progression with more effective and tolerable up-front treatments could help to alleviate this downstream economic burden of disease

Abbreviations

CCI, Charlson Comorbidity Index; EC, endometrial cancer; ED, emergency department; FFS, Fee-for-Service; GLM, generalized linear model; HCRU, healthcare resource utilization; LOT, line of therapy; LOT1, first line of therapy; LOT2, second line of therapy; NR, not reported; PD-1, programmed cell death 1 protein; PPPM, per patient per month; TFI, treatment-free interval; USD, US dollar.

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Disclosures

LMS and **JT** report employment with Inovalon, which performed the current analysis with support from GSK. **SJL** reports employment with and stock/stock options in GSK.

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