TREATMENT PATTERNS, REAL-WORLD OUTCOMES, AND RESOURCE USE IN PATIENTS WITH NON-MSI-HIGH OR MISMATCH REPAIR PROFICIENT ADVANCED ENDOMETRIAL CANCER: THE ENDOMETRIAL CANCER HEALTH OUTCOMES (ECHO) STUDY

Sneha S. Kelkar, MSc, MPH[1]; Shelby Corman, PharmD, MS, BCPS[1]; Cynthia Macahilig, MA[2]; Vimalanand S. Prabhu, BE, MMgmt, PhD[3]; Jingchuan Zhang, PhD[4]; Nifasha Rusibamayila, MPH[1]; M. Shardul Odak, Pharm, MS[2]; Linda Duska, MD, MPH[5]

[1]OPEN Health, Bethesda, MD, USA; [2]RTI Health Solutions, Research Triangle Park, NC, USA; [3]Merck & Co., Inc., Kenilworth, NJ, USA; [4]Eisai Inc., Woodcliff Lake, NJ, USA; [5]Gynecologic Oncology Division, Department of Obstetrics and Gynecology, University of Virginia Health System, Charlottesville, VA, USA

INTRODUCTION

- Treatment for endometrial cancer (EC) has traditionally been based on disease stage and histology, with platinum-based systemic chemotherapy as the standard of care for advanced EC (aEC) in the first line[1,2]
- Research has established that microsatellite instability (MSI) tumor status plays a role in determining the treatment path and prognosis in aEC patients. Prior trials evaluating chemotherapy regimens in aEC were all in patients without known MSI status[3,4]
- The FDA approval in the United States (US) of pembrolizumab plus lenvatinib combination therapy has changed the treatment landscape for aEC patients with non-MSI-high or DNA mismatch repair proficient (pMMR) tumors[5]
- There is no data on real-world clinical outcomes in aEC patients with non-MSI-high/pMMR tumor status treated with standard of care systemic therapies prior to pembrolizumab plus lenvatinib approval

OBJECTIVE

- The objective of the ECHO study was to assess real-world treatment patterns, clinical outcomes, and health care resource utilization in women in the US diagnosed with non-MSI-high/pMMR aEC previously treated with systemic therapy

METHODS

- The ECHO study is a multicenter retrospective chart review study in women diagnosed with non-MSI-high/pMMR aEC treated at oncology practices across the US
- The ECHO study was approved by IRB, which granted the study a waiver for obtaining informed consent from patients
- Physicians who consented to participate in the study were selected from the Definitive Healthcare National Database representing a geographically dispersed sample of EC-treating oncologists (medical oncologist or gynecologic oncologist) in the US
- Data provided by physicians were obtained from medical records of adult women (≥18 years) in the US diagnosed with non-MSI-high/pMMR aEC between July 1, 2016 and December 31, 2018, who had disease progression between July 1, 2016 and June 30, 2019 after failing a systemic therapy and initiated a second-line treatment. Patients were excluded if they had any prior malignancy active within the previous 3 years of diagnosis, except for locally curable cancers that had been cured
- De-identified patient chart data were extracted by physicians using pilot-tested electronic case report forms via a secure online portal. Data collected included patient demographics and clinical characteristics, treatment patterns, time to therapy discontinuation, and resource utilization
- Clinical outcomes assessed included overall survival (OS) and real-world progression-free survival (rwPFS)
- Descriptive analysis of baseline characteristics was performed. We reported mean, standard deviation (SD), median, interquartile range (IQR), and range for continuous variables and counts and frequencies for categorical or ordinal variables
- Time to event outcomes (time to therapy discontinuation, OS, and rwPFS) were analyzed using Kaplan-Meier analysis, stratified by drug class
- Analyses were conducted in the overall patient cohort that received chemotherapy ± vascular endothelial growth factor (VEGF) inhibitor or hormonal therapy in the second line and reported for the overall cohort as well as separately for each of the two drug groups
- All analyses were conducted using SAS version 9.4 (SAS Institute, Inc., Cary, NC)

RESULTS

Physician characteristics

Among the 48 oncologists who participated and provided patient data to the study:

- 77.1% were medical oncologists, 47.9% had 15+ years of practice experience, 89.6% practiced in an urban setting, 66.7% had a group-based practice, and 95.8% were affiliated with an academic hospital cancer center
- The average caseload of aEC patients per physician in the past 12 months was 57, and 83.3% followed an established aEC treatment protocol or guideline

Patient characteristics (Table 1)

- A total of 165 non-MSI-high/pMMR aEC patients who had progressed following a prior systemic therapy and initiated a second-line treatment were included in this analysis
- Patients' mean age at aEC diagnosis was 64.8 years. Patients were predominantly White/Caucasian
- Endometrioid carcinoma was the most common tumor histology (52.7%)
- The majority exhibited a metastasis at diagnosis
- ECOG status at the start of second-line therapy was ≥2 in 40.0% of patients indicating poor performance status
- All patients had insurance coverage; 57.0% were insured with Medicare

Treatment patterns (Figure 1)

- After progression following a prior systemic therapy, 140 (84.8%) of patients received chemotherapy ± VEGF inhibitor and 25 (15.2%) received hormonal therapy
- Median time to treatment discontinuation was 4.0 months (95% confidence interval [CI]: 3.0-5.0) for chemotherapy ± VEGF group and 6.0 months (95% CI: 4.0-30.0) for hormonal therapy group
- The most common reasons for treatment discontinuation across both groups were disease progression (n=95; 66.4%), followed by completion of planned regimen (n=22; 15.4%), patient refusal (n=14; 9.8%), and death (n=14; 9.8%)

Clinical outcomes

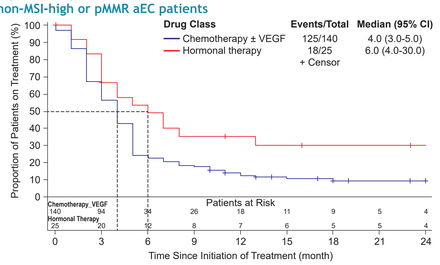
- Overall survival (Figure 2)
  - Median OS was 10 months (95% CI: 8.0-12.0) in the overall cohort
    - Chemotherapy ± VEGF: 10.0 months (95% CI: 8.0-13.0)
    - Hormonal therapy: 9.0 months (95% CI: 6.0-NA)
  - Estimated probability of survival at 6, 12, and 24 months since initiation of second-line therapy
    - Chemotherapy ± VEGF: 61.9%, 41.0%, and 21.8%, respectively
    - Hormonal therapy: 61.4%, 43.9%, and 32.9%, respectively

Table 1. Characteristics of non-MSI-high/pMMR aEC patients (overall and stratified by treatment category)

Characteristics	All (N = 165)	Chemotherapy ± VEGF (N = 140)	Hormonal therapy (N = 25)
Age at aEC diagnosis, years			
Mean (SD)	64.8 (9.4)	63.9 (9.2)	69.4 (9.2)
Median (IQR)	66 (59.0-70.0)	65 (58.0-70.0)	69 (66.0-74.0)
BMI at aEC diagnosis, kg/m²			
Mean (SD)	28.5 (5.6)	28.4 (5.8)	28.9 (4.9)
Median (IQR)	27.9 (24.4-30.9)	27.9 (24.3-31.2)	28.4 (25.5-30.6)
Race, N (%)			
White	106 (64.2)	86 (61.4)	20 (80.0)
Black	46 (27.9)	41 (29.3)	5 (20.0)
Other	13 (7.9)	13 (9.3)	0 (0.0)
Ethnicity, N (%)			
Hispanic or Latino	28 (17)	22 (15.7)	6 (24.0)
Not Hispanic or Latino	137 (83)	118 (84.3)	19 (76.0)
Charlson Comorbidity Index at aEC diagnosis			
Mean (SD)	1.6 (2.0)	1.5 (1.7)	2.5 (3.1)
Median (IQR)	1 (0.0-2.0)	1 (0.0-2.0)	1 (0.0-4.0)
ECOG-PS at start of second-line therapy, N (%)			
0	8 (4.8)	7 (5.0)	1 (4.0)
1	86 (52.1)	76 (54.3)	10 (40.0)
2	63 (38.2)	49 (35.0)	14 (56.0)
3	3 (1.8)	3 (2.1)	0 (0.0)
Not assessed/unknown	5 (3.0)	5 (3.6)	0 (0.0)
Disease stage at diagnosis, N (%)			
IA	4 (2.4)	3 (2.1)	1 (4.0)
IB	12 (7.3)	10 (7.1)	2 (8.0)
II	30 (18.2)	27 (19.3)	3 (12.0)
IIIA	3 (1.8)	3 (2.1)	0 (0.0)
IIIB	1 (0.6)	1 (0.7)	0 (0.0)
IIIC	5 (3.0)	4 (2.9)	1 (4.0)
IVA-T4, any N, M0	7 (4.2)	6 (4.3)	1 (4.0)
IVB-any T, any N, M1	103 (62.4)	86 (61.4)	17 (68.0)
Histology at diagnosis, N (%)			
Carcinosarcoma	4 (2.4)	4 (2.9)	0 (0.0)
Clear cell carcinoma	22 (13.3)	17 (12.1)	5 (20.0)
Endometrioid carcinoma	87 (52.7)	75 (53.6)	12 (48.0)
Mucinous carcinoma	14 (8.5)	13 (9.3)	1 (4.0)
Serous carcinoma	30 (18.2)	24 (17.1)	6 (24.0)
Undifferentiated carcinoma/ mixed cell tumors	7 (4.2)	6 (4.3)	1 (4.0)
Uterine carcinosarcoma	1 (0.6)	1 (0.7)	0 (0.0)
Metastatic site at aEC diagnosis, N (%)			
Bone	24 (14.5)	22 (15.7)	2 (8.0)
Distant lymph nodes	58 (35.2)	51 (36.4)	7 (28.0)
Kidney	4 (2.4)	4 (2.9)	0 (0.0)
Liver	51 (30.9)	41 (29.3)	10 (40.0)
Lung	90 (54.5)	75 (53.6)	15 (60.0)
Pancreas	1 (0.6)	1 (0.7)	0 (0.0)
Other	17 (10.3)	13 (9.3)	4 (16.0)

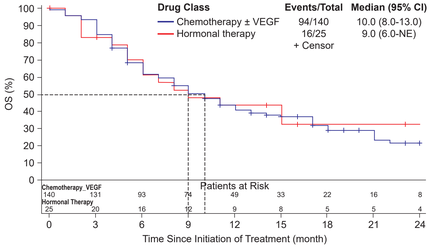
IQR, interquartile range; SD, standard deviation; VEGF, vascular endothelial growth factor inhibitor; aEC, advanced endometrial cancer; BMI, body mass index; ECOG-PS, Eastern Cooperative Oncology Group-performance status.

Figure 1. Kaplan-Meier plot of time to treatment discontinuation in non-MSI-high or pMMR aEC patients



Abbreviations: CI, confidence interval; VEGF, vascular endothelial growth factor.

Figure 2. Kaplan-Meier plot of overall survival (OS) in non-MSI-high or pMMR aEC patients



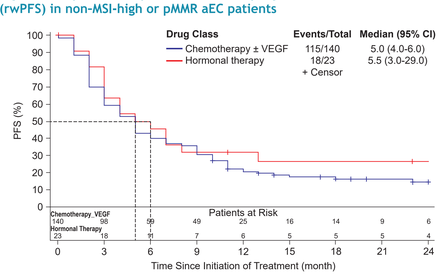
Abbreviations: CI, confidence interval; NE, not estimable; OS, overall survival; VEGF, vascular endothelial growth factor.

- Real-world progression-free survival (Figure 3)
  - Median rwPFS was 5 months (95% CI: 4.0-6.0) in the overall cohort
    - Chemotherapy ± VEGF: 5 months (95% CI: 4.0-6.0)
    - Hormonal therapy: 5.5 months (95% CI: 3.0-29.0)
  - Estimated probabilities of rwPFS at 6, 12, and 24 months since the initiation of second-line therapy
    - Chemotherapy ± VEGF: 40.0%, 20.5%, and 14.4%, respectively
    - Hormonal therapy: 45.5%, 31.8%, and 26.5%, respectively

Healthcare resource utilization

- A total of 31 (18.8%) patients had at least one hospitalization; 77.4% of these were admissions from the emergency room. The mean length of hospital stay per admission was approximately 8 days
  - 19.3% of patients treated with chemotherapy ± VEGF and 16.0% of those treated with hormonal therapy had at least one hospitalization
  - The mean length of hospital stay was 8 and 6 days for those who received chemotherapy ± VEGF and hormonal therapy, respectively

Figure 3. Kaplan-Meier plot of real-world progression-free survival (rwPFS) in non-MSI-high or pMMR aEC patients



Abbreviations: CI, confidence interval; PFS, progression-free survival; VEGF, vascular endothelial growth factor.

Limitations

- Our study had limitations inherent to the retrospective nature of the study design such as physicians or patient selection bias, data collection limited to the information available and as extracted from patients' medical charts
- In addition, lack of standard assessment schedule or stringent guidelines implemented in clinical practice to define outcomes such as disease progression needs to be considered when interpreting the results

CONCLUSIONS

- **To our knowledge, this is the first retrospective chart review study assessing real-world treatment patterns, clinical outcomes, and healthcare resource utilization in patients with non-MSI-high/pMMR aEC in the US who initiated treatment with a chemotherapy ± VEGF or with a hormonal therapy following failure of a prior systemic therapy in the mid-2016 to mid-2019 timeframe**
- **Poor clinical outcomes and high hospitalization rates demonstrate a significant unmet clinical need in aEC patients with non-MSI-high/pMMR tumors, indicating the need for novel therapies that delay progression and/or improve overall survival**

References

1. Surveillance, Epidemiology, and End Results Program (SEER). Cancer Stat Facts: Uterine Cancer. Accessed August 17, 2021. https://seer.cancer.gov/statfacts/html/corp.html
2. National Comprehensive Cancer Network. NCCN Guidelines® for Uterine Neoplasms Version 3.2021. NCCN. Accessed August 17, 2021. https://www.nccn.org/guidelines/guidelines-detail
3. Miller DS, Filiaci VL, Mannel RS, et al. Carboplatin and Paclitaxel for Advanced Endometrial Cancer: Final Overall Survival and Adverse Event Analysis of a Phase III Trial (NRG Oncology/GOG0209). *J Clin Oncol*. 2020;38(33):3841-3850. doi:10.1200/JCO.20.01076
4. Kurnit KC, Westin SN, Coleman RL. Microsatellite instability in endometrial cancer: New purpose for an old test. *Cancer*. 2019;125(13):2154-2163. doi:10.1002/cncr.32058
5. Eisai, INC. LENVIMA® (lenvatinib). Accessed August 17, 2021. https://www.accessdata.fda.gov/drugsatfda_docs/label/2019/206947s011lbl.pdf

Disclosure

This study was funded by Merck Sharpe and Dohme Corp., a subsidiary of Merck & Co., Inc., Kenilworth, NJ, USA and Eisai Inc., Woodcliff Lake, NJ, USA.

Presented at the HOPA Annual Conference; Boston, MA, USA; March 30-April 1, 2022.