1424 TREATMENT PATTERNS AND OUTCOMES BY MISMATCH REPAIR/MICROSATELLITE INSTABILITY (MMR/MSI) STATUS AMONG PATIENTS WITH PRIMARY ADVANCED OR RECURRENT ENDOMETRIAL CANCER (PA/REC) IN THE UNITED STATES

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Background Approximately 30% of ECs exhibit disruption of the MMR system.[1–3] Two randomized trials have demonstrated that the combination of chemotherapy with immunotherapy improves progression-free survival compared with chemotherapy alone in pA/rEC, with a stronger effect in patients with MMR-deficient/MSI-high (dMMR/MSI-H) disease.[4 5] To contextualize these outcomes, this study described real-world treatment patterns and clinical outcomes in pA/rEC according to MMR/MSI status.

Methods This study used the nationwide Flatiron Health electronic health record-derived deidentified database. Patients (≥18 years) had an initial diagnosis of stage III/IV EC or stage I/II EC with subsequent locoregional or distant recurrence on or after 01/01/2013, with ≥2 documented clinical encounters, and received ≥1 line of therapy between 01/01/2013 and 08/31/2022. Index date was date of initiation of 1L treatment. Patients with documented clinical study drug treatment, uterine sarcoma, or other active primary cancers were excluded. Patient characteristics, treatment patterns, and outcomes were described according to drug therapy class and the 5 most frequent drug regimens by MMR/MSI status: dMMR/MSI-H, MMR-proficient/microsatellite stable (MMRp/MSS), and unknown. Duration of therapy (DOT), time to next treatment (TTNT), and overall survival (OS) were estimated using Kaplan-Meier methods.

Results Of 2022 patients, 11.0% were dMMR/MSI-H, 27.8% were MMRp/MSS, and 61.2% had unknown MMR/MSI status at index (**table 1**). The most frequent 1L regimen class was platinum-based combination chemotherapy (dMMR/MSI-H, 49.3%; MMRp/MSS, 55.5%; unknown, 65.1%). The second most frequent 1L regimen class was PD-1/PD-L1 monotherapy in the dMMR/MSI-H subgroup (17.9%) and hormonal therapies in the MMRp/MSS (12.1%) and unknown status (13.5%) subgroups. Carboplatin-paclitaxel was the most frequent 1L regimen in all subgroups (dMMR/MSI-H, 45.7%; MMRp/MSS, 48.8%; unknown, 58.2%). The most frequent 2L regimen class was PD-1/PD-L1 monotherapy in the dMMR/MSI-H subgroup (35.2%) and hormonal therapies in the MMRp/MSS (22.9%) and unknown (23.2%) subgroups. Kaplan-Meier estimates of DOT, TTNT, and OS with platinum-based chemotherapy combinations, hormonal therapies, PD-1/PD-L1 combination therapies, and PD-1/PD-L1 monotherapy are summarized in table 2. OS with 1L carboplatin-paclitaxel is summarized in figure 1.

Conclusions Platinum-based chemotherapies, specifically carboplatin-paclitaxel, were the predominant 1L treatments irrespective of MMR/MSI status. Twenty-four-month OS in dMMR/MSI-H and MMRp/MSS subgroups was comparable to the placebo-plus-carboplatin-paclitaxel arm in RUBY (NCT03981796),[4] highlighting the unmet need of US real-world patients and the potential for combination platinum-based chemotherapy with immunotherapy to improve outcomes. Patients with dMMR/MSI-H pA/rEC have better long-term survival beyond 24 months, likely due to use of immunotherapies in later lines of therapy.

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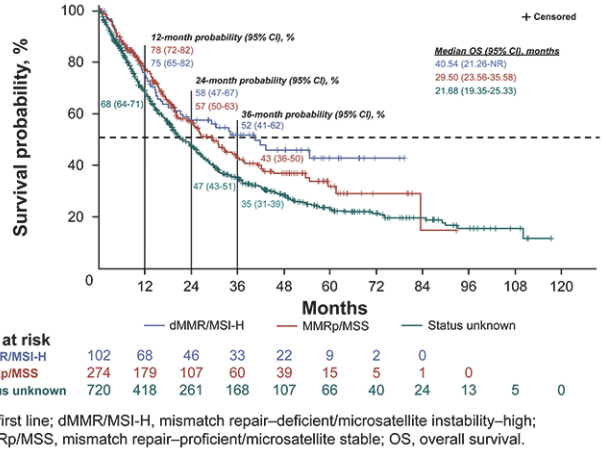
Ethics Approval This study used a deidentified database that was created for research purposes. This study complied with all applicable laws regarding patient privacy. No direct patient contact or primary collection of individual human patient data occurred. Study results are presented in tabular form and aggregate analyses that omit patient identification; therefore, no informed consent, ethics committee, or institutional review board approval was required by GSK.



1L, first line; dMMR/MSI-H, mismatch repair–deficient/microsatellite instability–high; MMRp/MSS, mismatch repair–proficient/microsatellite stable; OS, overall survival.

Abstract 1424 Figure 1 OS in patients with 1L carboplatin and paclitaxel according to MMR/MSI status

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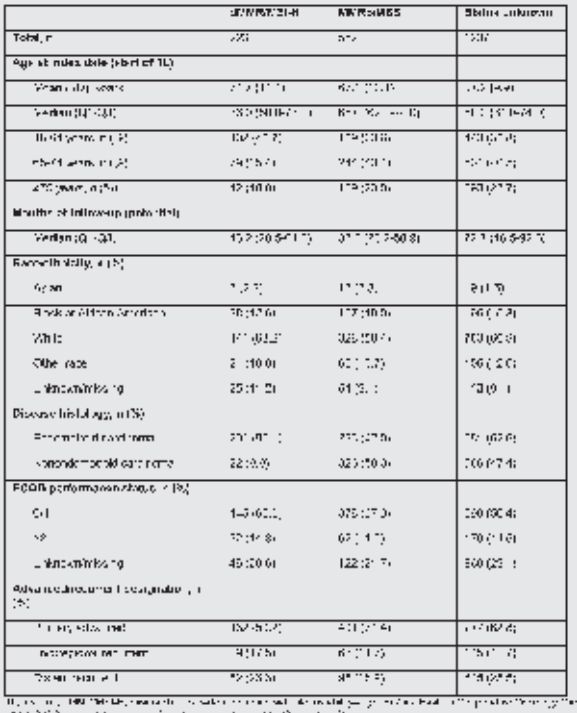
Abstract 1424 Table 1 Baseline Demographics and Clinical Characteristics



Abstract 1424 Table 2 DOT. TINT, and OS

	dMMR/MSI-H	MMRp/MSS	Status unknown
Total, n	223	562	1237
Platinum-based chemotherapy combinations, n (%)	110 (49.33)	312 (55.52)	805 (65.08)
DOT, median (95% CI), months	3.48 (3.06-3.58)	3.48 (3.48-3.52)	3.52 (3.48-3.71)
12-month probability	0.01 (0-0.05)	0.00 (0-0.02)	0.02 (0.01-0.03)
24-month probability	NA[a]	NA[a]	NA[a]
36-month probability	NA[a]	NA[a]	NA[a]
TTNT, median (95% CI), months	6.87 (5.55-10.64)	8.08 (7.06-8.90)	7.85 (7.16-8.38)
12-month probability	0.37 (0.28-0.46)	0.33 (0.27-0.38)	0.34 (0.30-0.37)
24-month probability	0.27 (0.18-0.35)	0.15 (0.11-0.19)	0.18 (0.15-0.21)
36-month probability	0.22 (0.14-0.30)	0.13 (0.09-0.17)	0.13 (0.11-0.16)
OS, median (95% CI), months	41.89 (21.65-NR)	26.18 (20.90-32.99)	21.62 (19.35-25.00)
12-month probability	0.76 (0.67-0.83)	0.77 (0.72-0.82)	0.68 (0.64-0.71)
24-month probability	0.58 (0.47-0.67)	0.54 (0.48-0.60)	0.47 (0.44-0.51)
36-month probability	0.52 (0.42-0.62)	0.41 (0.35-0.48)	0.35 (0.31-0.39)
Hormonal therapies, n (%)	34 (15.25)	68 (12.10)	167 (13.50)
DOT, median (95% CI), months	7.06 (3.71-26.05)	6.01 (3.22-8.84)	5.62 (4.24-9.36)
12-month probability	0.41 (0.24-0.57)	0.31 (0.20-0.43)	0.39 (0.31-0.47)
24-month probability	0.35 (0.19-0.50)	0.23 (0.13-0.35)	0.26 (0.19-0.34)
36-month probability	0.24 (0.11-0.40)	0.12 (0.04-0.25)	0.20 (0.14-0.27)
TTNT, median (95% CI), months	12.91 (6.28-NR)	8.84 (5.52-14.88)	14.42 (9.40-20.73)
12-month probability	0.52 (0.34-0.67)	0.42 (0.30-0.54)	0.54 (0.46-0.62)
24-month probability	0.42 (0.25-0.58)	0.30 (0.19-0.43)	0.38 (0.30-0.46)
36-month probability	0.37 (0.21-0.54)	0.22 (0.11-0.35)	0.30 (0.22-0.38)
OS, median (95% CI), months	NR (30.65-NR)	26.91 (14.72-51.25)	38.70 (25.40-62.03)
12-month probability	0.82 (0.63-0.91)	0.67 (0.53-0.77)	0.75 (0.67-0.81)
24-month probability	0.74 (0.55-0.86)	0.55 (0.41-0.67)	0.60 (0.51-0.68)
36-month probability	0.70 (0.49-0.83)	0.44 (0.29-0.57)	0.51 (0.42-0.59)
PD-1/PD-L1 combination therapies, n (%)	7 (3.14)	44 (7.83)	10 (0.81)
DOT, median (95% CI), months	NA[b]	9.46 (3.58-15.90)	NA[b]
12-month probability	NA[b]	0.41 (0.24-0.57)	NA[b]
24-month probability	NA[b]	0.20 (0.05-0.42)	NA[b]
36-month probability	NA[b]	NA[a]	NA[b]
TTNT, median (95% CI), months	NA[b]	12.85 (7.00-20.93)	NA[b]
12-month probability	NA[b]	0.52 (0.35-0.67)	NA[b]
24-month probability	NA[b]	0.23 (0.07-0.44)	NA[b]
36-month probability	NA[b]	NA[a]	NA[b]
OS, median (95% CI), months	NA[b]	20.93 (9.26-NR)	NA[b]
12-month probability	NA[b]	0.67 (0.50-0.79)	NA[b]
24-month probability	NA[b]	0.38 (0.17-0.58)	NA[b]
36-month probability	NA[b]	0.30 (0.11-0.52)	NA[b]
PD-1/PD-L1 monotherapy, n (%)	40 (17.94)	12 (2.14)	7 (0.57)
DOT, median (95% CI), months	9.69 (3.48-21.32)	NA[b]	NA[b]
12-month probability	0.49 (0.33-0.64)	NA[b]	NA[b]
24-month probability	0.25 (0.11-0.41)	NA[b]	NA[b]
36-month probability	0.20 (0.08-0.36)	NA[b]	NA[b]
TTNT, median (95% CI), months	15.90 (4.73-NR)	NA[b]	NA[b]
12-month probability	0.54 (0.38-0.68)	NA[b]	NA[b]
24-month probability	0.45 (0.29-0.60)	NA[b]	NA[b]
36-month probability	0.40 (0.24-0.56)	NA[b]	NA[b]
OS, median (95% CI), months	NR (13.63-NR)	NA[b]	NA[b]
12-month probability	0.73 (0.56-0.84)	NA[b]	NA[b]
24-month probability	0.57 (0.39-0.71)	NA[b]	NA[b]
36-month probability	0.57 (0.39-0.71)	NA[b]	NA[b]

1L, first line; dMMR/MSI-H, mismatch repair–deficient/microsatellite instability–high; DOT, duration of treatment; MMRp/MSS, mismatch repair–proficient/microsatellite stable; NA, not available; NR, not reached; OS, overall survival; PD-1, programmed death protein 1; PD-L1, programmed protein 1 ligand 1; TTNT, time to next treatment.

[a]Event numbers and/or follow-up were insufficient to obtain estimates.

[b]Estimates not reported because sample sizes are <30.

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