RESULTS FROM THE GERMAN REGISTRY PLATFORM SMARAGD

REAL-WORLD DATA ON SYSTEMIC TREATMENT AND BIOMARKER TESTING IN PATIENTS WITH ADVANCED OR METASTATIC ENDOMETRIAL CANCER

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INTRODUCTION

Endometrial carcinoma (EC) is the sixth most common cancer and the second most common gynecological malignancy in women worldwide. Chemotherapy (CT) is recommended for patients with metastatic or locally advanced and inoperable EC (a/m EC). Recently, various immune checkpoint inhibitors (ICIs) in combination with platinum-containing chemotherapy have been approved by the EMA in first palliative treatment line.

Molecular classification is encouraged in all EC patients by the ESGO/ESTRO/ESP guidelines and was incorporated in the FIGO (2023) EC staging. While new biomarker-dependent targeted therapies have expanded treatment options, data on implementation of biomarker testing and outcome in clinical routine are still scarce and limited data exist on how quickly new treatments are implemented in routine care.

METHODS

SMARAGD (NCT05129969) is a prospective, observational, multicenter and intersectoral clinical registry collecting data on 1975 patients with ovarian cancer or EC from over 140 sites in Germany (comprehensive cancer centers, clinics, and office-based medical oncologists). Since November 2021, patients with a/m EC (at initial diagnosis or at diagnosis of relapse) are recruited at start of first-line treatment. Detailed information on patients and tumor characteristics, biomarker testing, systemic treatment, and outcome data are documented over the whole course of disease. Follow-up continues up to 3 years or until death.

Here, we present data on first- and second-line treatment, on MMR/MSI biomarker test frequency and progression-free survival of patients with a/m EC in real-world in Germany.

RESULTS

At database cut (31Dec2024), 195 patients with a/m EC (at initial diagnosis or at diagnosis of relapse) had been recruited by 125 sites. Median age of patients was 65 years, for 80% at least one comorbidity was reported and 11% of patients had an ECOG ≥ 2 at start of first palliative systemic treatment line. 66% of patients presented with initial a/m disease (FIGO stage III/IV), 74% of patients had an endometrioid carcinoma (**Table 1**).

For first-line treatment, 59% (n=115) of all patients were tested for MMR and/or MSI (47% for MMR; 43% for MSI). Over time, the test rate has increased from 52% in 2022 to 62% in 2024. 30% of tested patients had a dMMR/MSI-high tumor (**Table 2**). P53 was tested in 51%, POLE in 19% of patients (**Table 3**).

First-line carboplatin-based CT was administered in most of the patients (88%), mainly in combination with paclitaxel. Since the approval of dostarlimab for patients with dMMR/MSI-high tumors, chemotherapy has been supplemented by dostarlimab in 3% of patients in 2023 and 20% of patients in 2024 (**Figure 1**). Of 17 patients with dMMR/MSI-high tumors and start of first-line treatment after approval of dostarlimab, seven (41%) received CAR+PAC in combination with dostarlimab.

55 patients (28%) had already received a subsequent second-line treatment, mostly an ICI-based treatment: 56% of patients received lenvatinib in combination with pembrolizumab, 20% received dostarlimab (**Figure 2**).

Median progression-free survival from start of first-line treatment for all patients was 9.1 months (95% confidence interval: 7.8-10.6 months, **Figure 3**).

CONCLUSION

In routine clinical practice, first-line platin-based CT is standard of care for patients with a/m EC in Germany. With implementation of molecular classification and availability of targeted treatments, the biomarker test frequency has increased since 2022, and in 2024 over 60% of the patients are tested for MSI and/or MMR for first-line treatment. Our data indicate that ICIs are increasingly supplementing chemotherapy in first-line and are treatment of choice in second-line treatment.

Future analyses of SMARAGD registry will provide insights into the impact of new treatment options on patients outcomes and quality of life in Germany.

Table 1 Patient characteristics of patients with advanced/metastatic EC

	Total
Number of patients	195
Median age at start of first-line	65.3
25 % / 75 % quantiles	59.4 - 72.1
ECOG Performance Status at start of first-line	
ECOG 0	73 (37.4 %)
ECOG 1	84 (43.1 %)
ECOG ≥2	21 (10.8 %)
Unknown / missing	17 (8.7 %)
Comorbidities at start of first-line	
Any comorbidity	156 (80.0 %)
Comorbidity according to CCI	
CCI 0	146 (74.9 %)
CCI ≥1	48 (24.6 %)
FIGO stage at diagnosis	
I	42 (21.5 %)
II	7 (3.6 %)
III	52 (26.7 %)
IVA	3 (1.5 %)
IVB	74 (37.9 %)
Unknown / missing	17 (8.7 %)
Histology of primary tumor	
Endometrioid carcinoma	144 (73.8 %)
Serous carcinoma	22 (11.3 %)
Mixed carcinoma	9 (4.6 %)

CCI: Charlson Comorbidity Index.
CCI: Comorbidities according to Charlson et al 1987 [1] current weighting according to Quan et al. 2011 [2]. Range 0-24.
Any comorbity: comorbidities according to CCI and other comorbidities combined.
ECOG: Eastern Cooperative Oncology Group performance status. ECOG according to Oken et al. 1982 [3].
FIGO: Tumor stage is calculated from documented values for T- and N-stage. If values are documented as "TX" or "NX" or if subcategories for the T-stage (such as T2a and T2b) are not documented, the exact stage cannot always be specified.

Table 2 Biomarker testing for 1-line treatment | Testing for MMR and/or MSI

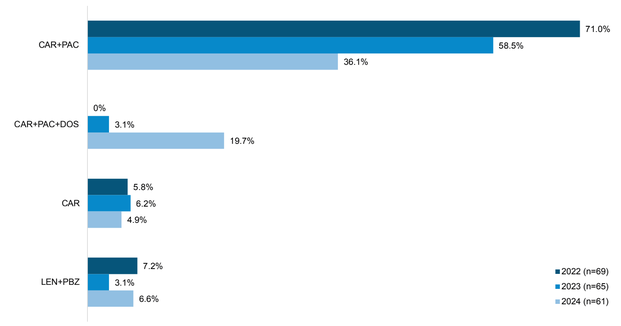
	2022	2023	2024	Total
Number of patients	69	65	61	195
Documented test				
Yes	36 (52.2 %)	41 (63.1 %)	38 (62.3 %)	115 (59.0 %)
MMR/MSI test result according to tested patients [a]				
dMMR and/or MSI-H	13 (36.1 %)	8 (19.5 %)	14 (36.8 %)	35 (30.4 %)
Not dMMR and/or MSI-H or unknown	23 (63.9 %)	33 (80.5 %)	24 (63.2 %)	80 (69.6 %)

a Displayed are all patients tested for MMR and/or MSI.

Table 3 Biomarker testing for 1-line treatment | Testing for p53 and POLE

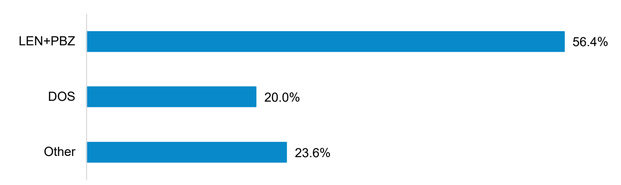
	2022	2023	2024	Total
Number of patients	69	65	61	195
Documented test for p53				
Yes	30 (43.5 %)	29 (44.6 %)	40 (65.6 %)	99 (50.8 %)
Documented test for POLE				
Yes	13 (18.8%)	12 (18.5%)	11 (18.0%)	36 (18.5%)

Figure 1 Most frequently used 1-line treatments over time



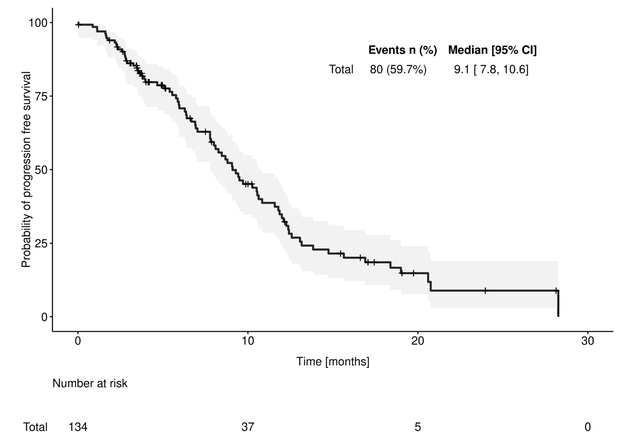
The percentage refers to all patients with 1-line treatments (n=195).
CAR: Carboplatin | DOS: Dostarlimab | LEN: Lenvatinib | PAC: Paclitaxel | PBZ: Pembrolizumab

Figure 2 Most frequently used 2-line treatments



The percentage refers to all patients with 2-line treatments (n=55).
DOS: Dostarlimab | LEN: Lenvatinib | PBZ: Pembrolizumab

Figure 3 Progression-free survival from first-line treatment



Patients who started their first-line of treatment at least twelve months before database cut (n=134).

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Conflicts of Interest

Gratzke K.: no conflicts of interest

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