REAL-WORLD PATIENT CHARACTERISTICS AND INITIAL MANAGEMENT STRATEGIES FOR EARLY AND LOCALLY ADVANCED OPERABLE ENDOMETRIAL CANCER IN GREECE: RESULTS OF THE RETROSPECTIVE 'LAVENDER' STUDY

Poster # AA022

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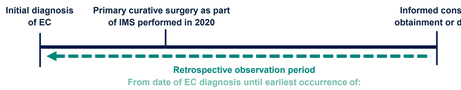
Background

- In view of the evolving treatment landscape of endometrial cancer (EC) and the shift to a molecular-based recurrence risk classification, real-world data are essential for characterizing patient profiles and enhancing the understanding of risk-stratification algorithms that guide initial management strategies (IMS).
- The aim of this study was to capture real-world treatment practice (IMS), utilization of systematic adjuvant therapy, patient characteristics and recurrence rate, in the overall study population and in the physician-determined risk groups, among patients diagnosed with **early stage or locally advanced (ES/LA) operable EC during 2020** in **Greece**.

Methods

- **LAVENDER** was a multicenter, retrospective, chart review study, based on secondary data collection.
- A total of **200** patients **newly diagnosed with ES/LA EC** who had undergone their **primary surgical** treatment between **01 January 2020** and **31 December 2020** (**index period**) were planned to be included.
- The study design, eligibility criteria, and objectives are shown in **Figure 1**.
- All alive patients provided **written informed consent**, while a **waiver of consent** was granted by the site Institutional Review Boards for deceased patients.

Figure 1. Study design.



Inclusion criteria

- **Adult** female patients **newly diagnosed with ES or LA histologically confirmed EC**, who underwent their **primary curative surgery between 01-Jan-2020 and 31-Dec-2020** (both dates inclusive), who were **disease-free postoperatively** (i.e., no evidence of locoregional disease or distant metastasis), and with sufficient available medical records for data abstraction to meet the study objectives.

Exclusion criteria

- Patients who had **stage IVB tumors** with **persistent/recurrent disease** at their first postoperative imaging, and patients who participated in any **investigational program/interventional clinical trial** for initial EC management.

Primary objectives presented herein

- To describe the **rate** and **patterns** of utilisation of **(neo)adjuvant therapy** (ST and/or RT), as part of IMS.
- To describe the **patient and disease characteristics**.

Secondary objectives presented herein

- To describe the **rate** and **patterns** of 1st disease recurrence after primary surgical treatment for EC.

- Study objectives were assessed in the **overall** study population and in the subpopulations by **physician-determined risk of disease recurrence***.

* It is noted that the guidelines that were available during the study-specific index period included the "*2016 ESMO/ESGO/ESTRO Consensus Conference on EC*"[1] and the "*2021 ESGO/ESTRO/ESP guidelines for the management of patients with EC*"[2].

- **Initial management strategy (IMS) refers to:**

the sequence of all different treatment modalities [primary curative surgery, systemic pharmacologic therapy (ST), and radiation therapy (RT)] administered (in any setting, including neoadjuvant and adjuvant) from the date of confirmation of initial EC diagnosis until the earliest date of 1st disease recurrence, IC obtainment, or death. Supportive treatments were excluded.

Statistical considerations

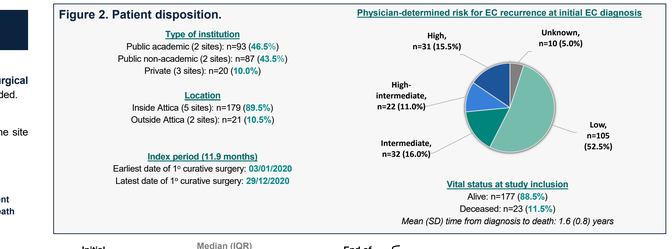
- The **normality of distribution** of continuous variables was examined with the Shapiro-Wilk test.
- **Summary statistics** of continuous variables are presented as mean and standard deviation (SD) when data follow a normal distribution; otherwise, the median and interquartile range (IQR) is presented. For variables not following a normal distribution in ≥1 of the study (sub)populations, a uniform presentation of median (IQR) was applied.
- **No imputation of missing data** was performed except for partially missing dates.
- Statistical analyses were performed using SAS® software (version 9.4).

Results

Patient disposition

- Between **29-Sep-2023** (First Patient In) and **23-Jul-2024** (Last Patient In), a total of **206 patients** were **consecutively** included by Medical Oncologists/Gynecologists practicing in **7 hospital clinics**.
- Six patients did not fulfill all study eligibility criteria. Thus, **200 eligible patients** comprised the Full Analysis Set population.
- The overall study population represented **97.1%** (200/206) **of all ES/LA EC cases undergoing primary curative surgery** at the participating study sites **during the entire index period** (01-Jan-2020 and 31-Dec-2020).

Figure 2. Patient disposition.



Patient profile

Table 1. Patient and disease characteristics at initial EC diagnosis*.

		Overall (N=200)	Physician-determined risk of EC recurrence at initial diagnosis			
			Low (N=105)	Intermediate (N=32)	High-Intermediate (N=22)	High (N=31)
Patient characteristics						
Age at initial EC diagnosis (years)	Mean (SD)	63.6 (10.7)	62.4 (10.6)	62.2 (9.2)	67.5 (13.1)	65.7 (9.6)
	≥65 years, % (n/N)	48.5 (97/206)	42.9 (45/105)	40.6 (13/32)	72.7 (16/22)	58.1 (18/31)
Employed, % (n/N)		22.5 (20/89)	33.3 (14/42)	27.8 (5/18)	7.1 (1/14)	.
Ever-smokers, % (n/N)		36.9 (52/141)	38.2 (26/68)	32.0 (8/25)	61.1 (11/18)	25.0 (6/24)
Health insurance coverage, % (n/N)		99.2 (131/132)	100.0 (64/64)	100.0 (21/21)	100.0 (16/16)	100.0 (22/22)
BMI (kg/m²)	Median (IQR)	30.4 (24.8-35.7)	31.2 (24.8-36.5)	31.3 (25.2-35.9)	29.4 (25.8-31.6)	29.4 (23.7-34.5)
	Obese (≥30kg/m²), % (n/N)	54.1 (72/133)	52.6 (30/57)	61.5 (16/26)	50.0 (9/18)	50.0 (13/26)
ECOG PS, % (n/N)	PS 0	83.6 (112/134)	90.7 (49/54)	85.2 (23/27)	70.6 (12/17)	73.1 (19/26)
	PS 1	10.4 (14/134)	9.3 (5/54)	3.7 (1/27)	23.5 (4/17)	15.4 (4/26)
	PS ≥2	6.0 (8/134)	.	11.1 (3/27)	5.9 (1/17)	11.5 (3/26)
Family history of cancer in first-degree relatives, % (n/N)		40.3 (58/144)	37.1 (26/70)	56.0 (14/25)	33.3 (6/18)	37.5 (9/24)
Clinically significant medical/surgical history comorbid conditions other than EC (past/active), % (n/N)		40.8 (69/169)	40.7 (35/86)	18.5 (5/27)	47.4 (9/19)	44.8 (13/29)
Most frequent (≥5.0%) conditions, % (n/N)	Hypertension	17.8 (30/169)	18.6 (16/86)	11.1 (3/27)	26.3 (5/19)	13.8 (4/29)
	Hypothyroidism	10.1 (17/169)	11.6 (10/86)	3.7 (1/27)	15.8 (3/19)	6.9 (2/29)
	Dyslipidaemia	10.1 (17/169)	14.0 (12/86)	3.7 (1/27)	15.8 (3/19)	3.4 (1/29)
	Diabetes mellitus	10.1 (17/169)	11.6 (10/86)	3.7 (1/27)	5.3 (1/19)	10.3 (3/29)
Disease characteristics						
Primary tumor histologic type, % (n/N)	Pure endometrioid	77.0 (154/200)	86.7 (91/105)	84.4 (27/32)	81.8 (18/22)	38.7 (12/31)
	Serous adenocarcinoma	15.5 (31/200)	7.6 (8/105)	9.4 (3/32)	13.6 (3/22)	45.2 (14/31)
	Other	7.5 (15/200)	5.7 (6/105)	6.3 (2/32)	4.5 (1/22)	16.1 (5/31)
Primary tumor size ≥2 cm, % (n/N)		75.7 (134/177)	62.1 (54/87)	93.3 (28/30)	85.7 (18/21)	86.2 (25/29)
Invasion or involvement of other organ/tissue (reported with frequency ≥10.0% in the overall or any of the subpopulations), % (n/N)	Any	94.2 (179/190)	89.5 (85/95)	100.0 (32/32)	100.0 (22/22)	96.8 (30/31)
	Myometrial invasion (MI)	89.4 (177/198)	80.6 (83/103)	100.0 (32/32)	100.0 (22/22)	96.8 (30/31)
	LVSI	22.5 (41/182)	7.6 (7/92)	25.8 (8/31)	38.1 (8/21)	41.4 (12/29)
	Cervical stroma involvement	20.7 (41/198)	2.9 (3/103)	9.4 (3/32)	68.2 (15/22)	51.6 (16/31)
	Pelvic lymph nodes	15.1 (30/199)	4.8 (5/105)	9.4 (3/32)	22.7 (5/22)	36.7 (11/30)
	Ovary	8.5 (17/200)	.	6.3 (2/32)	13.6 (3/22)	22.6 (7/31)
	Parametrium	7.0 (14/200)	1.9 (2/105)	6.3 (2/32)	.	19.4 (6/31)
	Uterine serosa involvement	6.1 (12/196)	1.0 (1/103)	.	14.3 (3/21)	22.6 (7/31)
	Vagina	6.0 (12/199)	2.9 (3/105)	6.3 (2/32)	4.5 (1/22)	16.7 (5/30)
	Fallopian tube	3.5 (7/200)	.	3.1 (1/32)	.	12.9 (4/31)
Intraoperative disease stage, % (n/N)	Assessed	99.0 (197/199)	99.0 (103/104)	100.0 (32/32)	100.0 (22/22)	100.0 (31/31)
	FIGO 2018 update	97.8 (176/180)	100.0 (95/95)	96.6 (28/29)	94.4 (17/18)	93.5 (29/31)

Key abbreviations: BMI, body mass index; ECOG PS, Eastern Cooperative Oncology Group Performance Status; FIGO, International Federation of Gynecology and Obstetrics (system); LVSI, Lymphovascular Space Invasion; n, number of patients with variable; N, number of patients with available data. *Within 3 months of initial EC diagnosis.

- Intraoperative stage and histologic grade per International Federation of Gynecology and Obstetrics (FIGO) system are shown in **Figure 3**.
  - ✓Staging was predominantly based on the 2018 FIGO staging system (**Table 1**).
- Of the patients, 42.5% (85/200) performed EC-related gene mutation/biomarker tests from the start of diagnostic evaluation of EC until the end of the study observation period.
  - ✓Testing frequency for biomarkers of interest was: 27.5% (55/200) for **p53 expression** [45.5% (25/55) abnormal], 5.5% (11/200) for **MMR proteins** and 1% (2/200) for **POLE mutation**.
- The criteria used for the assessment of risk for EC recurrence by physicians are shown in **Figure 4**.

Figure 3. (A) Intraoperative FIGO disease stage and (B) FIGO primary tumor histologic grade.

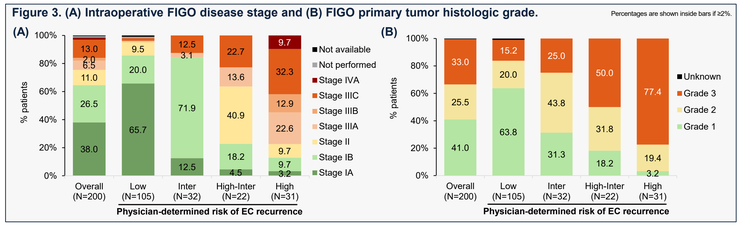
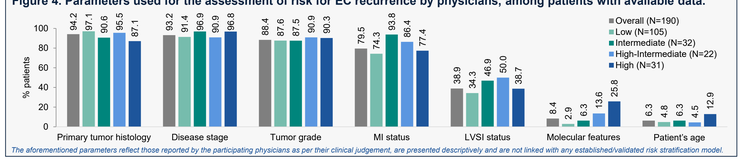


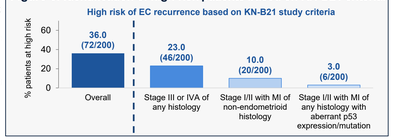
Figure 4. Parameters used for the assessment of risk for EC recurrence by physicians, among patients with available data.



The aforementioned parameters reflect those reported by the participating physicians as per their clinical judgement, are presented descriptively and are not linked with any established/validated risk stratification model.

- As per protocol, we proceeded to re-assessment of patients for confirming the percentage of patients that would be eligible for adjuvant systemic treatment based on KEYNOTE-B21 (KN-B21) study[3]. Criteria used were the following:
  - Without known presence of POLE mutation and at high risk for recurrence defined as FIGO surgical stage:
    - ✓ I/II with myometrial invasion of non-endometrioid histology;
    - ✓ I/II with myometrial invasion of any histology with known aberrant p53 expression or p53 mutation;
    - ✓ III or IVA of any histology [source: Lavender Study Protocol].
- The results are shown in **Figure 5**.

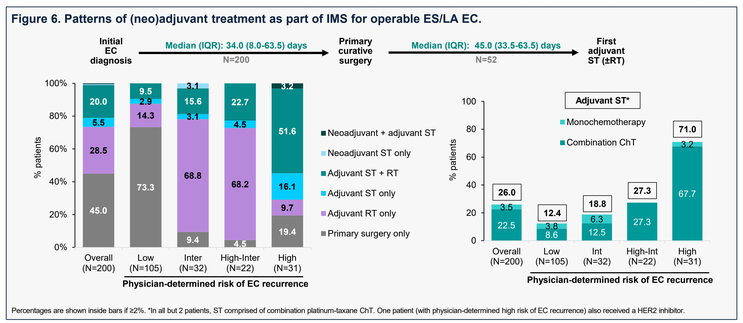
Figure 5. Identification of high-risk patients based on KN-B21 criteria.



Rate and patterns of utilisation of (neo)adjuvant therapy, as part of IMS

- **Total hysterectomy with bilateral salpingo-oophorectomy** was performed in **89.0%** (178/200) of patients overall; in 88.6% (93/105), 93.8% (30/32), 95.5% (21/22), and 87.1% (27/31) of patients with physician-determined low, intermediate, high-intermediate and high risk of EC recurrence, respectively.
- **Adjuvant treatment** was administered to **54.5%** (109/200) of patients; radiotherapy (RT) only in 28.5%, systemic therapy (ST) + RT in 20.0%, ST only in 6.0% (**Figure 6**).

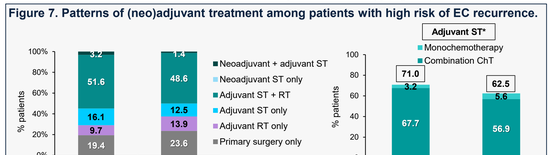
Figure 6. Patterns of (neo)adjuvant treatment as part of IMS for operable ES/LA EC.



Percentages are shown inside bars if ≥2%. *In all but 2 patients, ST comprised of combination platinum-taxane ChT. One patient (with physician-determined high risk of EC recurrence) also received a HER2 inhibitor.

- **29.0%** of patients determined by the physicians as being at high risk of recurrence and **37.5%** of those classified as high risk of recurrence based on KN-B21 criteria **did not receive adjuvant chemotherapy** (**Figure 7**).

Figure 7. Patterns of (neo)adjuvant treatment among patients with high risk of EC recurrence.



*One patient (who belonged in both groups of high risk) also received a HER2 inhibitor.

Rate and patterns of EC recurrence

- Over a median follow-up of 3.6 years, **14.0%** of patients experienced **recurrence** (**Table 2**), a median of 12.7 months post-surgery.
- Half (**50.0%**; 14/28) of patients who experienced EC recurrence, had received **adjuvant chemotherapy as part of IMS**.
- Among patients who experienced EC recurrence,
  - ❖ **46.4%** (13/28) had **physician-determined high risk** of EC at initial diagnosis.
  - ❖ **71.4%** (20/28) had **high risk** of EC at initial diagnosis **based on KN-B21 criteria**.

Table 2. Information on 1st disease recurrence after primary surgery for EC.

		Overall (N=200)	Risk of EC recurrence at initial diagnosis				
			Physician-determined				Based on KN-B21 criteria
			Low (N=105)	Intermediate (N=32)	High-Interm (N=22)	High (N=31)	High (N=72)
Recurrence (confirmed and/or unconfirmed), % (n/N)		14.0 (28/200)	3.8 (4/105)	9.4 (3/32)	22.7 (5/22)	41.9 (13/31)	27.8 (20/72)
Time from surgery to first recurrence, median (IQR), months		12.7 (9.5-22.4)	15.6 (8.5-31.5)	9.3 (7.8-15.0)	11.1 (9.9-23.7)	16.2 (9.7-28.0)	12.7 (9.8-27.0)
Type of recurrence, % (n/N)	Distant	69.2 (18/26)	25.0 (1/4)	66.7 (2/3)	75.0 (3/4)	75.0 (9/12)	77.8 (14/18)
	Local	15.4 (4/26)	50.0 (2/4)	.	.	16.7 (2/12)	11.1 (2/18)
	Regional	15.4 (4/26)	25.0 (1/4)	33.3 (1/3)	25.0 (1/4)	8.3 (1/12)	11.1 (2/18)

n, number of patients with variable; N, number of patients with available data.

Conclusions

- The LAVENDER study population is representative of patients with ES/LA operable EC in Greece.
- The variability between risk stratification and management strategies highlights the need for more standardized multidisciplinary team (MDT) approaches to risk assessment and treatment decision-making.
- The low molecular testing rate, particularly for dMMR, signals the urgency of advancing the integration of molecular profiling into clinical practice, as it is essential for guiding risk assessment and personalized treatment planning.
- The integration of biomarkers frequently modifies the classification of risk groups, prompting the need for adjustments in treatment strategies. This situation emphasizes the importance of proactive engagement from stakeholders.

❖ The findings of this study address knowledge gaps and provide insights to guide the future development of treatment strategies for EC, supporting informed healthcare decision-making.

Disclosures

- **Liontos M (Presenter):** Grants ASTELLAS, ASTRA ZENECA; Consulting fees MSD, JANSSEN, ASTRA ZENECA, GSK, NOVARTIS, PFIZER, ABBVIE; Honoraria ASTRA ZENECA, MSD, IPSEN, NOVARTIS, PFIZER, BMS
- This work was funded by Merck Sharp & Dohme LLC, a subsidiary of Merck & Co., Inc., Rahway, NJ, USA (MSD).

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3. https://clinicaltrials.gov/ct2/show/NCT04634877.

Acknowledgments

Optimapharm Greece S.A. provided medical writing and editorial support as part of the project work performed for MSD Greece.

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Presented at 31st Hellenic Conference of Clinical Oncology (HeSMO 2025), Athens; April 09 - 12, 2025.