Article

Not peer-reviewed version

Analysis of Differences in the Classification of Endometrial Cancer Patients in Poland

Wiktor Szatkowski *, Tomasz Kluz, Małgorzata Cieślak-Steć, Magdalena Śliwińska, Małgorzata Nowak-Jastrząb *, Izabela Winkler, Jacek Tomaszewski, Paweł Blecharz

Posted Date: 23 December 2024

doi: 10.20944/preprints202412.1970.v1

Keywords: cancer; DNA polymerase epsilon; MSI; p53; molecular classification; FIGO 2023

Article

Analysis of Differences in the Classification of Endometrial Cancer Patients in Poland

Wiktor Szatkowski [1,*], Tomasz Kluz [2], Małgorzata Cieślak-Steć [2], Magdalena Śliwińska [3], Małgorzata Nowak-Jastrząb [1,*], Iza Winkler [4], Jacek Tomaszewski [4] and Paweł Blecharz [1]

[1] Department of Gynaecologic Oncology Maria Sklodowska-Curie National Research Institute of Oncology Krakow Branch, Poland
[2] Department of Gynecology and Obstetrics, Institute of Medical Sciences, Medical College of Rzeszow University, Rzeszów, Poland
[3] Department of III Clinic of Radiotherapy and Chemotherapy Maria Sklodowska-Curie National Research Institute of Oncology Gliwice Branch, Poland
[4] Second Department of Gynecological Oncology, St. John's Center of Oncology of the Lublin Region, Lublin, Poland
* Correspondence: wiktor.szatkowski@krakow.nio.gov.pl (W.S.); malgorzata.nowak@krakow.nio.gov.pl (M.N.-J.); Tel.: +48-123067331 (M.N.-J.)

Simple Summary: Endometrial cancer is the most common gynecological malignancy in developed countries, with increasing incidence and mortality rates. The introduction of new molecular technologies and the updated 2023 FIGO staging system have revolutionized diagnostics and enabled personalized treatment approaches. In this study, we analyzed clinical and molecular data from patients treated in southeastern Poland to understand the impact of the new FIGO classification on clinical practice. The results demonstrated significant differences in stage assignment and molecular profiles across medical centers, suggesting variations in diagnostic strategies and access to advanced testing methods. These findings emphasize the importance of standardized diagnostic practices and equitable access to molecular testing to ensure consistent implementation of the new FIGO staging system and to improve treatment outcomes for patients with endometrial cancer.

Abstract: Background: Endometrial cancer (EC) incidence and mortality have been steadily rising globally over recent decades. The introduction of advanced molecular technologies, such as next-generation sequencing (NGS), alongside the FIGO 2023 classification, presents opportunities for refined diagnostics and risk stratification. This study aimed to analyze differences in EC classification among oncology centers in southeastern Poland. **Methods:** Data were collected from 461 consecutive patients newly diagnosed with EC between 2022 and 2024 at four major oncology centers in southeastern Poland. Molecular and immunohistochemical (IHC) analyses were conducted on formalin-fixed paraffin-embedded (FFPE) tissues to identify key markers, including POLE mutations, MSI-H, and p53 status. **Results:** The application of the FIGO 2023 staging system revealed statistically significant inter-center differences, with Centers 1 and 4 diagnosing a higher proportion of early-stage cases. The most prevalent subtype was NSMP, observed in 51% of cases. MSI-H occurred in 13%-36% of patients, depending on the center. p53 mutations ranged from 9% to 26%. POLE mutations were identified in 4% overall. Significant variations in molecular subtype distribution across centers highlight potential differences in diagnostic access or tumor biology. **Conclusions:** The findings demonstrate regional differences in EC staging and molecular profiles in Poland, potentially reflecting disparities in diagnostic resources, methodologies, or tumor characteristics. Addressing these variations through standardized diagnostic protocols and equitable access to molecular tools is critical for optimizing patient outcomes. Future research should focus on evaluating the impact of molecular markers on therapy response and prognosis to guide personalized treatment strategies.

 doi:10.20944/preprints202412.1970.v1

Keywords: endometrial cancer; DNA polymerase epsilon; MSI; p53; molecular classification; FIGO 2023

1. Introduction

Endometrial cancer (EC) is the most common gynecological malignancy in developed countries, with both incidence and mortality rates rising in recent years. This trend highlights the critical need for advancements in diagnostic and therapeutic strategies. The updated 2023 FIGO classification represents a significant milestone by incorporating molecular markers into traditional anatomical staging. These markers, including DNA polymerase epsilon (POLE) mutations, p53 status, and microsatellite instability (MSI-H), are now recognized as key predictive and prognostic factors in EC [1].

Modern EC diagnostics leverage a combination of next-generation sequencing (NGS), Sanger sequencing (PCR), and traditional immunohistochemistry (IHC). The gold standard integrates molecular diagnostics for POLE mutations, mismatch repair (MMR) proteins, and p53 into a comprehensive approach such as the PROMISE algorithm [2]. While some oncology centers exclusively use molecular techniques like NGS and PCR, this approach is supported by international guidelines [3]. These technological advancements are pivotal for achieving more precise diagnostic insights and facilitating personalized treatment.

This study represents the first comprehensive analysis of the prevalence of key molecular features of EC in Poland. It evaluates the implementation of the FIGO 2023 classification in oncology centers across southeastern Poland. Specifically, the study aims to:

1. Identify differences in staging and molecular subtype classification among centers.
2. Highlight regional disparities in the use of advanced molecular diagnostics.

The findings contribute to the growing body of evidence regarding FIGO 2023's clinical utility and underscore the importance of diagnostic standardization for optimizing treatment outcomes. By addressing gaps in molecular and clinical practices, this research offers valuable insights for improving patient care both regionally and globally.

2. Materials and Methods

2.1. Study Design and Population

This study included consecutive patients newly diagnosed with endometrial cancer (EC) between April 2022 and April 2024. The patients were treated at four major gynecologic oncology centers in southeastern Poland, located in the Silesian, Lesser Poland, Subcarpathian, and Lublin Voivodeships. Cases without complete medical records or treated prior to the implementation of the FIGO 2023 classification were excluded. Molecular and immunohistochemical (IHC) analyses were performed on surgical specimens obtained during hysterectomy procedures.

2.2. Immunohistochemistry (IHC) Analysis

IHC analyses of MLH, MSH, PMS, and p53 proteins were performed using OptiView and UltraView kits (Ventana) on the BenchMark Ultra system.

2.3. DNA Extraction

DNA was extracted from formalin-fixed paraffin-embedded (FFPE) tissue samples. Pathologists pre-assessed the tissue blocks to select the most suitable samples for molecular analysis and to evaluate the percentage of tumor cells. The following kits were used for DNA isolation:

QIAamp DSP DNA FFPE Tissue Kit (Qiagen)

Maxwell® RSC DNA FFPE Kit and Maxwell® RSC Instrument (Promega)

 doi:10.20944/preprints202412.1970.v1

2.4. Molecular Analysis

POLE Sequencing: Sanger sequencing was conducted on exons 9, 11, 13, and 14 of the POLEgene.

NGS Analysis: Next-generation sequencing (NGS) was performed on the IonTorrent platform using a custom-designed panel (Thermo Fisher Scientific Ion AmpliSeq Designer). The panel targeted key genes, including MLH1, MSH2, MSH6, PMS2, POLE, and TP53. Sequencing was carried out on CHEF and S5 instruments with Ion 510™, Ion 520™, and Ion 530™ kits (Thermo Fisher Scientific).

2.5. Variant Classification

Detected genetic variants were categorized into five classes:

Pathogenic, Likely pathogenic, Variants of unknown significance (VUS), Likely benign, Benign

Bioinformatics tools and databases, including Cancer Genome Interpreter, Varsome, ClinVar, OncoKB, and Franklin, were utilized for variant classification. Polymorphisms, benign, likely benign, and VUS variants were excluded from the final analysis.

2.6. Ethical Considerations

All data were anonymized before analysis to ensure compliance with data protection regulations.

3. Results

Clinical, microscopic, and molecular data were collected for 461 patients diagnosed with endometrial cancer (EC) across four oncology centers in southeastern Poland. The mean age of the patients was 65.8 years, with no statistically significant differences observed in mean age between the centers. The histological subtypes of EC were distributed as presented in Table 1, showing significant inter-center variability.

Molecular analyses revealed that the most common molecular subtype was NSMP, representing 51% of cases. Microsatellite instability (MSI-H) was identified in 13%–36% of patients depending on the center, while p53 mutations ranged from 9% to 26%. POLE mutations were observed in 4% of all cases. Differences in molecular subtype distributions were statistically significant across the centers, indicating variability in the prevalence of key molecular features.

Additionally, staging according to the FIGO 2023 classification showed significant inter-center differences. Centers 1 and 4 had a higher proportion of early-stage cases, while Centers 2 and 3 reported more advanced-stage cases.

Table 1. Analysis of histological types in individual centers.

	Center 1		**Center2**		**Center 3**		**Center 4**		**Total**		**statistical significance p**
	n	**%**	**N**	**%**	n	%	N	%	n	%	
Non-aggressive types											
Endometrioid carcinoma G1/G2	69	74,2	79	62,7	53	76,8	156	90,2	357	77,4	p<0,001
Aggressive types											
Endometrioid carcinoma G3	11	11,8	35	27,9	9	13,0	7	4,0	62	13,4	
Serous carcinoma	7	7,6	7	5,5	4	5,9	3	1,8	21	4,5	
other	6	6,4	5	3,9	3	4,3	7	4,0	22	4,7	

 doi:10.20944/preprints202412.1970.v1

Table 2. Analysis of Myometrial and Cervical Stroma Invasion by Individual Centers.

	Center 1		Center 2		Center 3		Center 4		Total		statistical significance p
	n	**%**	**n**	**%**	n	%	n	%	n	%	
Myometrial invasion											
limited to the endometrium	4	4,3	3	2,3	6	8,7	6	3,5	19	4,1	
invasion of less than half	46	49,5	60	47,6	33	47,8	92	53,2	231	50,0	p=0,151
invasion of half or more	40	43,0	63	50,0	27	39,1	67	38,7	197	42,7	
Invasion of uterine serosa	3	3,2	0	0	3	4,3	8	4,6	14	3,0	
Invasion of cervical stroma	14	15,1	24	19,1	7	10,1	33	19,1	68	14,7	p=0,326

Table 3. Analysis of LVSI and Lymph Node Involvement by Individual Centers.

	Center 1		Center 2		Center 3		Center 4		Total		statistical significance p
	n	**%**	**N**	**%**	n	%	N	%	n	%	
LVSI											
substantial LVSI	28	30,1	34	26,9	16	23,2	61	35,3	139	30,1	p=0,008
focal LVSI	10	10,7	13	10,3	4	5,8	2	1,2	29	6,3	
Metastasis to the pelvic lymph nodes											p=0,413
makroprzerzuty	8	8,6	7	5,6	4	5,8	14	8,1	33	7,2	
mikroprzerzuty	2	2,2	1	0,8	0	0	0	0	2	0,4	
Metastasis to para-aortic lymph nodes											
Macrometastasis	5	5,4	2	1,6	1	1,5	0	0	8	1,7	p=0,016
Micrometastasis	0	0	0	0	0	0	0	0	0	0	

Table 4. Distribution of FIGO 2023 Staging Across Individual Centers.

	Center 1		Center 2		Center 3		Center 4		Total		statistical significance p
	N	**%**	**n**	**%**	**n**	**%**	**n**	**%**	n	%	
I	57	61	68	55	33	48	81	47	239	52	
IA	40	44	46	35	19	27	68	40			
IB	17	18	21	17	12	17	12	6			p=0,019
IC	0	0	1	1	2	3	1	0,5			
II	13	14	39	30	28	40	62	36	142	31	
IIA	4	4	4	3	3	4	13	7			
IIB	1	1	12	10	7	10	26	15			
IIC	8	9	23	20	18	26	23	13			

 doi:10.20944/preprints202412.1970.v1

III	21	22	17	13	7	10	28	16	73	16
IIIA	5	6	3	2	2	3	4	2		
IIIB	1	1	4	3	2	3	9	5		
IIIC	15	16	10	8	3	4	15	8		
IV	2	3	2	2	1	2	2	1	7	1
IVA	2	2	0	0	0	0	0	0		
IVB	0	0	2	2	1	1	2	1		
Total	93	100	126	100	69	100	173	100	461	100

Table 5. Analysis of Molecular Features by Individual Centers.

	Center 1		**Center 2**		**Center 3**		**Center 4**		**Total**		**p**
NGS/Sanger/IHC	**n**	**%**	**N**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	
POLE	7	7	4	3	3	4	7	4	21	4	
MSI-H	23	24	45	36	9	13	49	28	126	27	
p53	18	19	11	9	17	26	31	18	77	18	p=0,018
NSMP	45	50	66	52	40	57	86	50	227	51	
	93	100	126	100	69	100	173	100	461	100	

4. Discussion

The 2023 FIGO classification for endometrial cancer (EC) represents a significant advance in personalized medicine by integrating traditional anatomical criteria with critical pathological parameters, such as histological subtype, histopathological grade, the presence of lymphovascular space invasion (LVSI), and molecular alterations including POLE mutations, p53 status, and MSI-H [2]. This approach enhances prognostic precision by differentiating aggressive subtypes—serous, clear cell, poorly differentiated endometrioid, mucinous, mesonephric, gastrointestinal type, undifferentiated carcinomas, and carcinosarcomas—from less aggressive subtypes such as G1/G2 endometrioid carcinoma. Moreover, incorporating aggressive features like LVSI in staging has shifted treatment paradigms, particularly in tailoring adjuvant therapies to improve patient outcomes [4,5].

Our study revealed significant inter-center variability in the application of the FIGO 2023 classification, highlighting regional disparities in Poland. Centers 1 and 4 had a higher proportion of early-stage diagnoses, which could reflect better access to advanced diagnostic tools and greater patient awareness of early symptoms. In contrast, Centers 2 and 3 reported a higher percentage of advanced cases, potentially due to limited access to specialized care or delays in diagnosis. These findings emphasize how infrastructure and healthcare access can influence the clinical stage at diagnosis and subsequent management.

4.1. Molecular Profiles

Significant differences in molecular subtype distributions were also observed. For instance, p53 mutations were detected in 27% of cases in Center 3 compared to only 9% in Center 2. Variability in the detection of molecular markers such as MSI-H (13%-36%) and POLE mutations (4%) highlights the lack of standardized diagnostic protocols across centers. This variability likely stems from the use of different diagnostic tools—ranging from next-generation sequencing (NGS) to immunohistochemistry (IHC)—and local differences in testing practices, which aligns with findings in other studies [8,9,12].

 doi:10.20944/preprints202412.1970.v1

4.2. Comparison with International Data:

When comparing these results with international benchmarks, similarities and discrepancies are evident. For example, POLE mutations in our study (4%) are slightly lower than the 7% reported in TCGA [10] but align with findings in ProMisE studies, where POLE mutations are observed in 5–12% of cases [11]. Similarly, the MSI-H subtype (13%-36%) reflects variability consistent with TCGA findings, which report a prevalence of 28% [10].

For p53 mutations, our study shows rates of 9%-26%, aligning with TCGA data, where p53 abnormalities are predominantly found in the copy-number high (CNH) subtype, which comprises 26% of all endometrial carcinoma cases and is strongly associated with serous carcinoma and poor prognosis [10]. Similarly, the NSMP subtype, representing 51% of cases in our cohort, is consistent with findings from ProMisE studies, where NSMP accounts for approximately 40%-50% of cases [18]. This molecular subtype typically exhibits low levels of genomic instability and an intermediate prognosis. These comparisons underscore the congruence of molecular patterns between Polish and international data while highlighting the necessity of standardizing molecular diagnostic practices to reduce inter-center variability and ensure robust classification.

4.3. Challenges in Pathological Evaluation:

Our findings echo previous studies that identified significant challenges in histopathological evaluation. Retrospective analyses, such as PORTEC-3, demonstrated reclassification rates as high as 43% after central review, while Grevenkamp et al. reported critical discrepancies in 9.7% of cases, which directly influenced therapeutic decisions [14,15]. These observations underscore the need for centralized reviews and stricter adherence to standardized guidelines.

4.4. Standardization Issues in LVSI Assessment:

Defining significant LVSI remains inconsistent across international guidelines. While FIGO 2023, WHO 2020, and ESGO/ESTRO/ESP guidelines define LVSI involvement as five or more lymphovascular spaces, the NCCN recommends a threshold of four spaces on a single H&E slide. This lack of uniformity introduces the risk of "stage drift," complicating comparisons of treatment outcomes and prognostic evaluations between institutions [16].

4.5. Future Directions:

Our study highlights the urgent need for the standardization of diagnostic protocols and equitable access to advanced molecular tools across all centers. Centralized pathology reviews and the adoption of uniform criteria for molecular diagnostics, such as the PROMISE algorithm, could significantly improve consistency in EC classification and management. Future research should focus on evaluating how molecular markers such as **p53, MSI-H, and POLE mutations** influence treatment responses and outcomes. This could guide the development of more tailored therapeutic strategies and improve outcomes for EC patients globally.

4.6. Strengths and Limitations:

This study is the first in the literature to examine EC molecular profiles within the Polish population. The geographically coherent data and the inclusion of consecutive cases strengthen its reliability. However, variability in genetic testing methods and the combination of molecular and immunohistochemical approaches across centers may have influenced the results. While this reflects real-world clinical practice, it underscores the need for greater methodological standardization in future studies.

5. Conclusions

Our study highlights significant variability in the application of the FIGO 2023 classification for endometrial cancer, particularly in staging and molecular profiling, across different oncology centers

in southeastern Poland. These differences underscore the urgent need for diagnostic standardization and equitable access to advanced molecular tools. By adopting uniform protocols and ensuring consistency in diagnostic approaches, the clinical utility of the FIGO 2023 classification can be fully realized. Future research should focus on evaluating the influence of molecular markers on treatment response and prognosis, thereby supporting the development of more personalized therapeutic strategies for endometrial cancer patients both in Poland and globally.

Author Contributions: For research articles with several authors, a short paragraph specifying their individual contributions must be provided. The following statements should be used "Conceptualization, W.Sz. M.N-J., P.B. ; methodology, W.Sz, T.K., P.B.; software,W.Sz, M.N.-J.; validation, W.Sz. P.B. formal analysis W.Sz. M.N.-J. P.B.; investigation W.Sz.,T.K., M.Ś. M.C.-S, M.N-J., I.W. J.T., P.B.; resources W.Sz, M.C-S. M.Ś, I.W. J.T.; data curation W.Sz.,T.K., M.Ś. M.C.-S, M.N-J., I.W. J.T., P.B, X.X.; writing—original draft preparation W.Sz. M.N-J, P.B.; writing—review and editing W.Sz. M.N-J, P.B.;.; visualization, W.Sz. M.N-J, P.B.; X.X.; supervision,P.B.; project administration, W.Sz, M.N-J..; All authors have read and agreed to the published version of the manuscript.

Funding: "This research received no external funding".

Institutional Review Board Statement: The study did not require ethical approval.

Informed Consent Statement: "Not applicable.".\

Informed Consent Statement: Any research article describing a study involving humans should contain this statement. Please add "Informed consent was obtained from all subjects involved in the study." OR "Patient consent was waived due to REASON (please provide a detailed justification)." OR "Not applicable." for studies not involving humans. You might also choose to exclude this statement if the study did not involve humans.

Data Availability Statement: The original contributions presented in this study are included in the article. Further inquiries can be directed to the corresponding author(s).

Conflicts of Interest: "The authors declare no conflicts of interest.

References

1. Berek JS, Matias-Guiu X, Endometrial Cancer Staging Subcommittee, FIGO Women's Cancer Committee. FIGO staging of endometrial cancer: 2023. Int J Gynaecol Obstet. 2023 Aug;162(2):383-394. doi: 10.1002/ijgo.14923. Epub 2023 Jun 20. Erratum in: Int J Gynaecol Obstet. 2024 Sep;166(3):1374. doi: 10.1002/ijgo.15193. PMID: 37337978.
2. León-Castillo A, Gilvazquez E, Clinicopathological and molecular characterisation of 'multiple-classifier' endometrial carcinomas. J Pathol. 2020 Mar;250(3):312-322. doi: 10.1002/path.5373. Epub 2020 Jan 12. PMID: 31829447; PMCID: PMC7065184.
3. Talhouk A, McConechy MK, Confirmation of ProMisE: A simple, genomics-based clinical classifier for endometrial cancer. Cancer. 2017 Mar 1;123(5):802-813. doi: 10.1002/cncr.30496. Epub 2017 Jan 6. PMID: 28061006.
4. Tortorella L, Restaino S, Substantial lymph-vascular space invasion (LVSI) as predictor of distant relapse and poor prognosis in low-risk early-stage endometrial cancer. J Gynecol Oncol. 2021 Mar;32(2):e11. doi: 10.3802/jgo.2021.32.e11. Epub 2021 Jan 11. PMID: 33470061; PMCID: PMC7930448.
5. Koskas M, Bassot K, Impact of lymphovascular space invasion on a nomogram for predicting lymph node metastasis in endometrial cancer. Gynecol Oncol. 2013 May;129(2):292-7. doi: 10.1016/j.ygyno.2013.02.027. Epub 2013 Feb 26. PMID: 23480871.
6. Li H, Zhang R, Prognostic value of different metastatic sites for patients with FIGO stage IVB endometrial cancer after surgery: A SEER database analysis. J Surg Oncol. 2020 Oct;122(5):941-948. doi: 10.1002/jso.26102. Epub 2020 Jul 18. PMID: 32682330.
7. Kobayashi-Kato M, Fujii E, Utility of the revised FIGO2023 staging with molecular classification in endometrial cancer. Gynecol Oncol. 2023 Nov;178:36-43. doi: 10.1016/j.ygyno.2023.09.011. Epub 2023 Sep 23. PMID: 37748269.
8. Matsuo K, Klar M, Validation of the 2023 FIGO staging schema for advanced endometrial cancer. Eur J Cancer. 2023 Nov;193:113316. doi: 10.1016/j.ejca.2023.113316. Epub 2023 Sep 21. PMID: 37741790.
9. Schwameis R, Fanfani F., Verification of the prognostic precision of the new 2023 FIGO staging system in endometrial cancer patients - An international pooled analysis of three ESGO accredited centres. Eur J Cancer. 2023 Nov;193:113317. doi: 10.1016/j.ejca.2023.113317. Epub 2023 Sep 1. PMID: 37748967.
10. Cancer Genome Atlas Research Network; Kandoth C. Integrated genomic characterization of endometrial carcinoma. Nature. 2013 May 2;497(7447):67-73. doi: 10.1038/nature12113. Erratum in: Nature. 2013 Aug 8;500(7461):242. PMID: 23636398; PMCID: PMC3704730.

11. Espinosa I, D'Angelo E, Endometrial carcinoma: 10 years of TCGA (the cancer genome atlas): A critical reappraisal with comments on FIGO 2023 staging. Gynecol Oncol. 2024 Jul;186:94-103. doi: 10.1016/j.ygyno.2024.04.008. Epub 2024 Apr 13. PMID: 38615479.
12. Stasenko M, Tunnage I, Clinical outcomes of patients with POLE mutated endometrioid endometrial cancer. Gynecol Oncol. 2020 Jan;156(1):194-202. doi: 10.1016/j.ygyno.2019.10.028. Epub 2019 Nov 19. PMID: 31757464; PMCID: PMC6980651.
13. Corr B, Cosgrove C. Endometrial cancer: molecular classification and future treatments. BMJ Med. 2022 Oct 31;1(1):e000152. doi: 10.1136/bmjmed-2022-000152. PMID: 36936577; PMCID: PMC9978763.\
14. de Boer SM, Wortman BG. Clinical consequences of upfront pathology review in the randomised PORTEC-3 trial for high-risk endometrial cancer. Ann Oncol. 2018 Feb 1;29(2):424-430. doi: 10.1093/annonc/mdx753. PMID: 29190319; PMCID: PMC5834053.
15. Grevenkamp F, Kommoss F. Second Opinion Expert Pathology in Endometrial Cancer: Potential Clinical Implications. Int J Gynecol Cancer. 2017 Feb;27(2):289-296. doi: 10.1097/IGC.0000000000000870. PMID: 27922981.
16. McCluggage WG, Bosse T,. FIGO 2023 endometrial cancer staging: too much, too soon? Int J Gynecol Cancer. 2024 Jan 5;34(1):138-143. doi: 10.1136/ijgc-2023-004981. PMID: 37935523.
17. Spoor E, Cross P. Audit of Endometrial Cancer Pathology for a Regional Gynecological Oncology Multidisciplinary Meeting. Int J Gynecol Pathol. 2019 Nov;38(6):514-519. doi: 10.1097/PGP.0000000000000547. PMID: 30252729.
18. Talhouk, A., McConechy. Molecular Subtype Classification of Endometrial Cancer Using a Proactive Molecular Risk Classifier. Cancer, 121(24), 4008–4017