

# Molecular Classification in Endometrial Cancer: A Real-World Approach to Staging and Treatment

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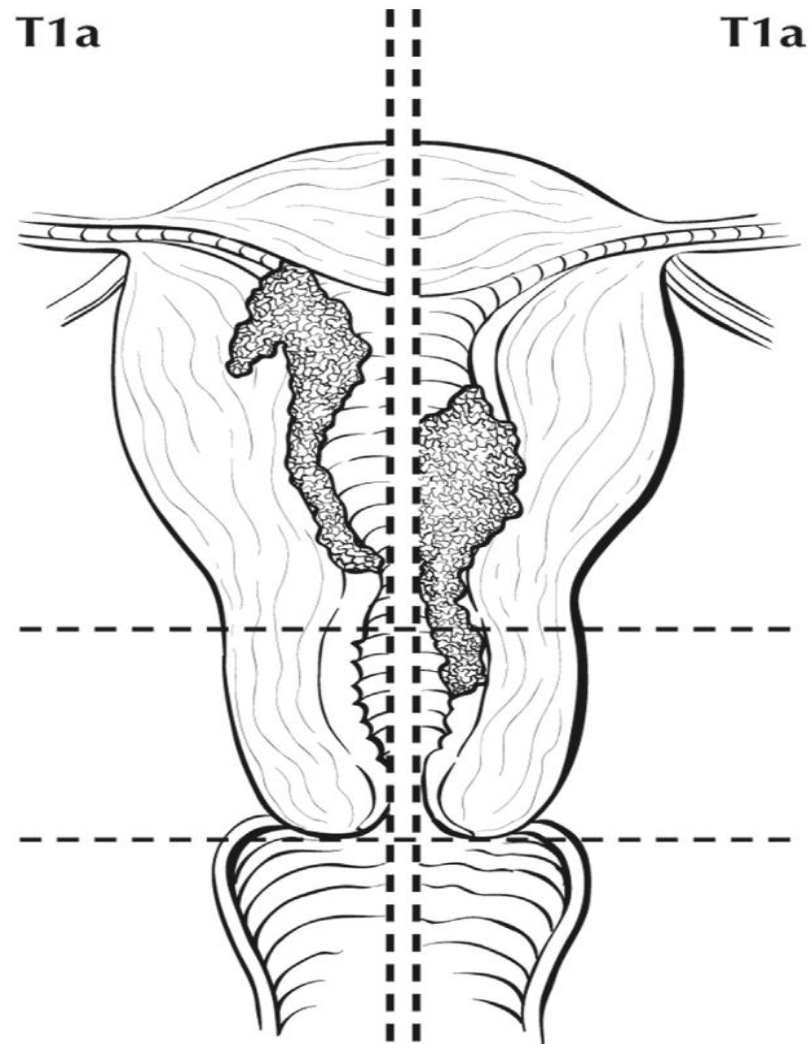


# Purpose of staging

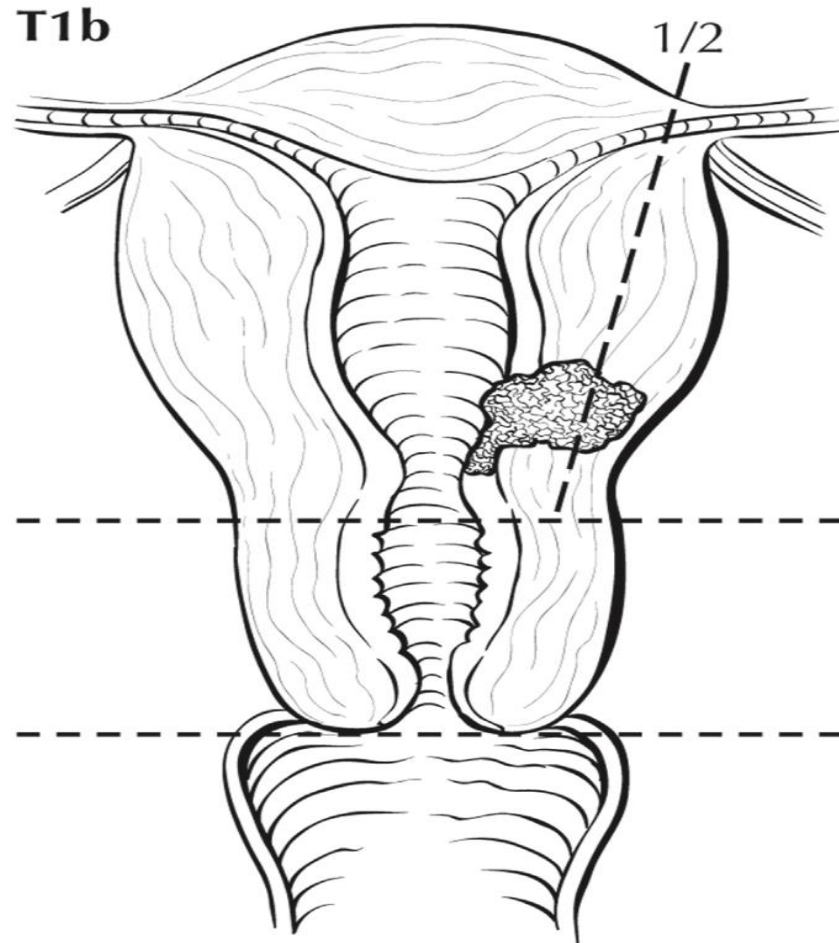
- ❖ **Define disease extent**
- ❖ **Prognostication**
- ❖ **Guide treatment decisions**
- ❖ **Compare treatment options**
- ❖ **Communication across treatment scenarios**
- ❖ **Research**



# AJCC 8<sup>th</sup> Edition Staging Manual, T1a

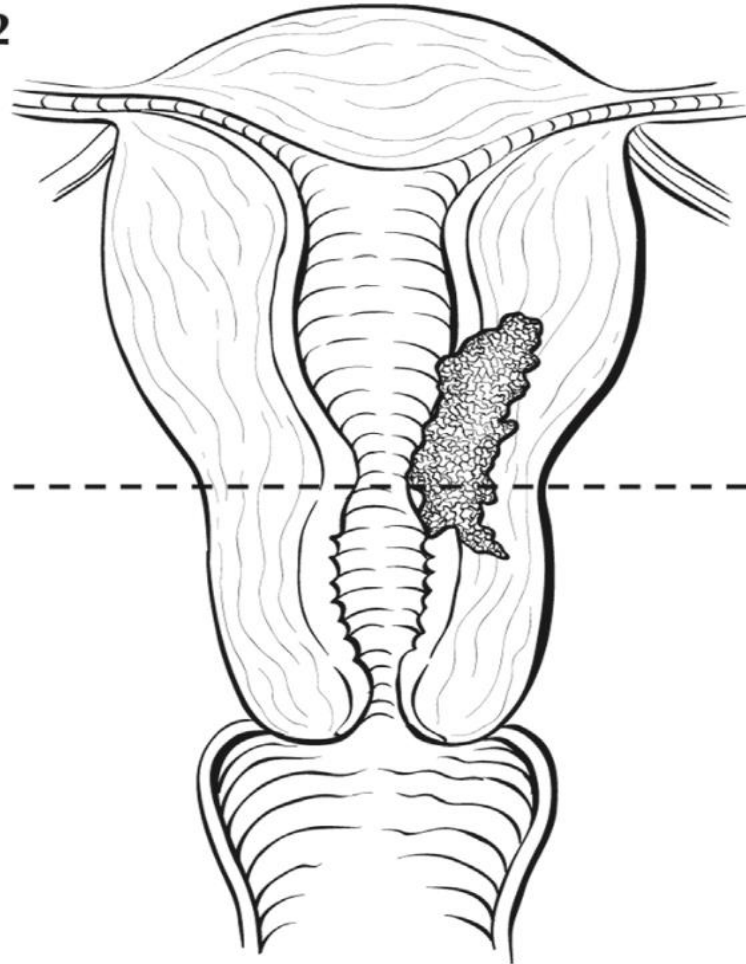


# AJCC 8<sup>th</sup> Edition Staging Manual, T1b

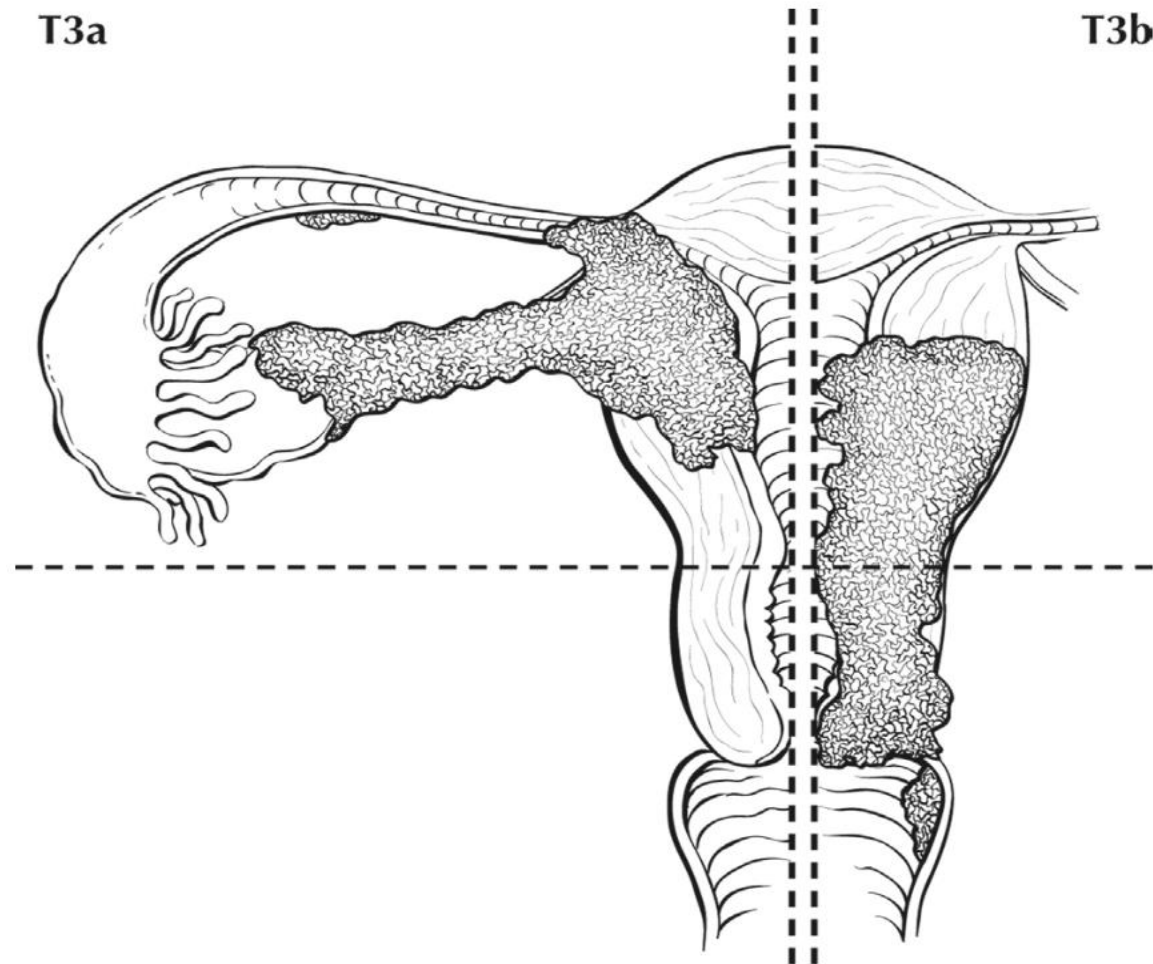


# AJCC 8<sup>th</sup> Edition Staging Manual, T2

T2

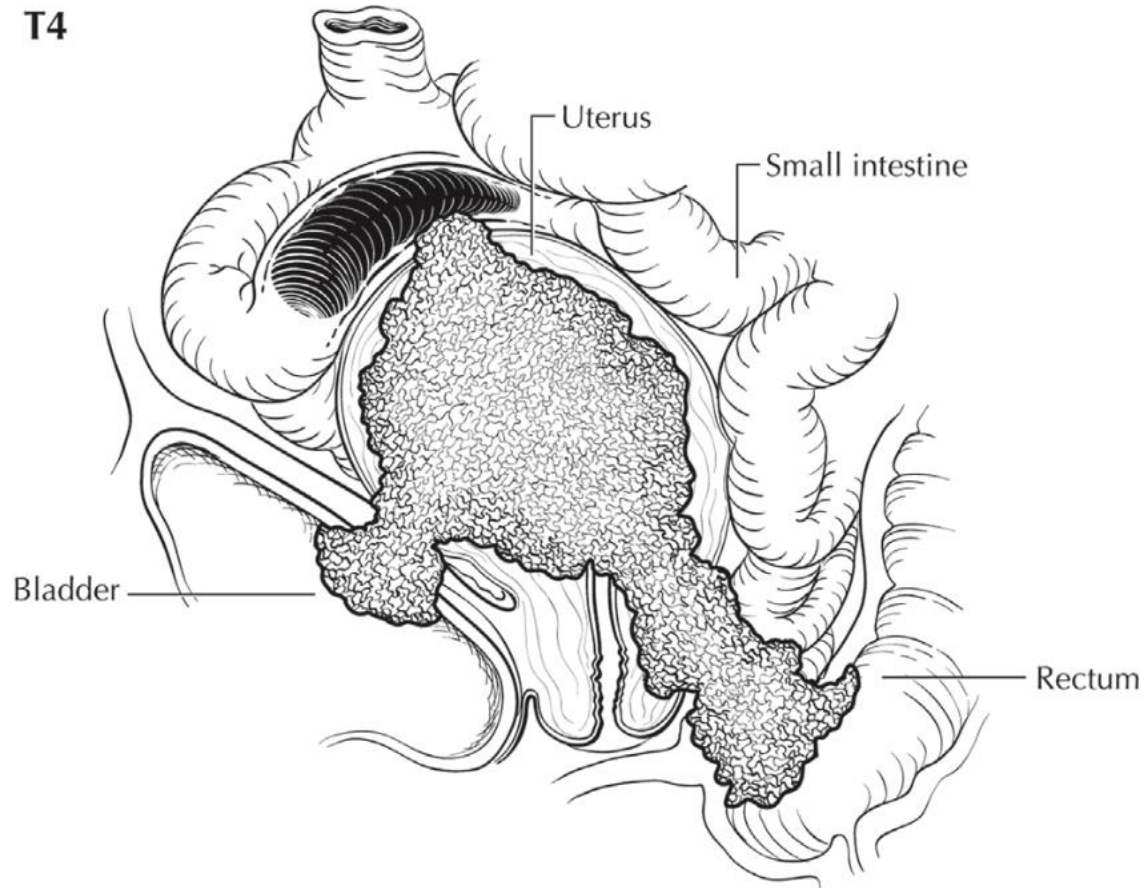


# AJCC 8<sup>th</sup> Edition Staging Manual, T3



# AJCC 8<sup>th</sup> Edition Staging Manual, T4

T4



# Genomic Characterization of EC

Nature

Nature Publishing Group

**THIS ARTICLE HAS BEEN CORRECTED.**

See the correction in volume 500 on page 242.

## Integrated genomic characterization of endometrial carcinoma

Douglas A. Levine and The Cancer Genome Atlas Research Network





# Genomic Characterization of EC

Using a combination of;

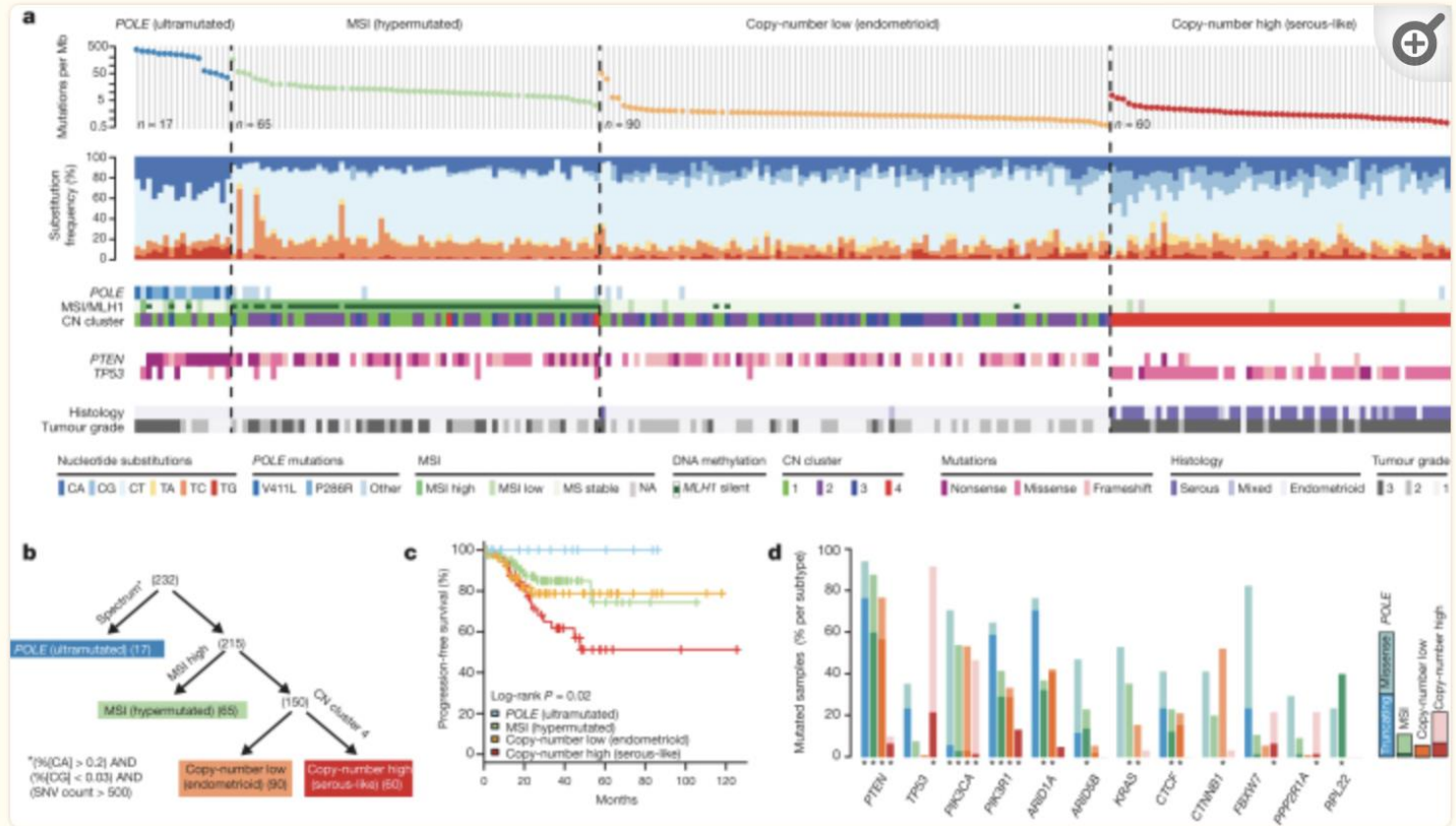
- ❖ nucleotide substitutions
- ❖ MSI
- ❖ SCNAs

Endometrial carcinomas were characterized into 4 groups;

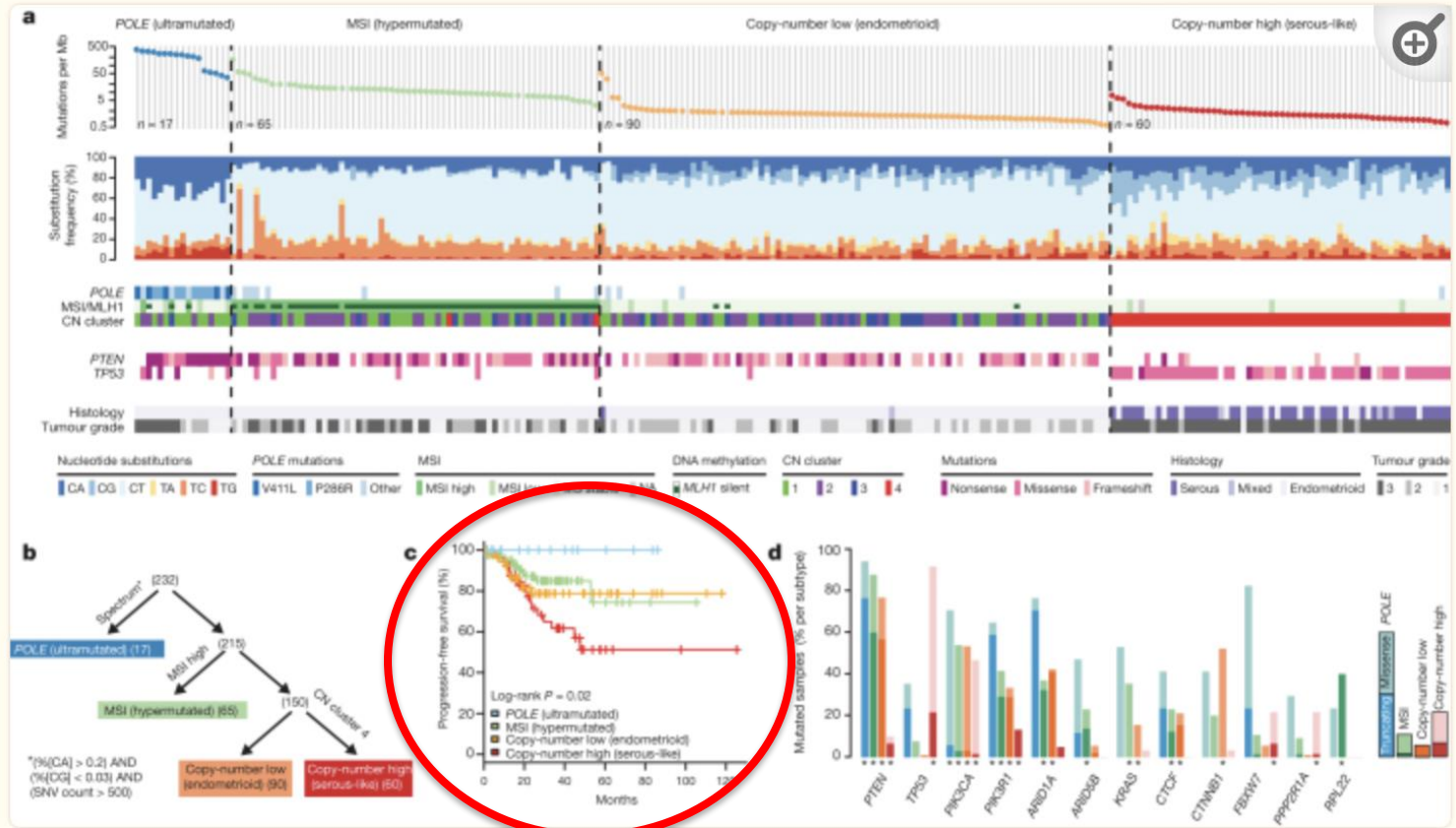
1. Ultramutated group (*POLE*-EDM)
2. Hypermuted group (MSH)
3. Copy number low (MSS)
4. Copy number high (Serous-like)



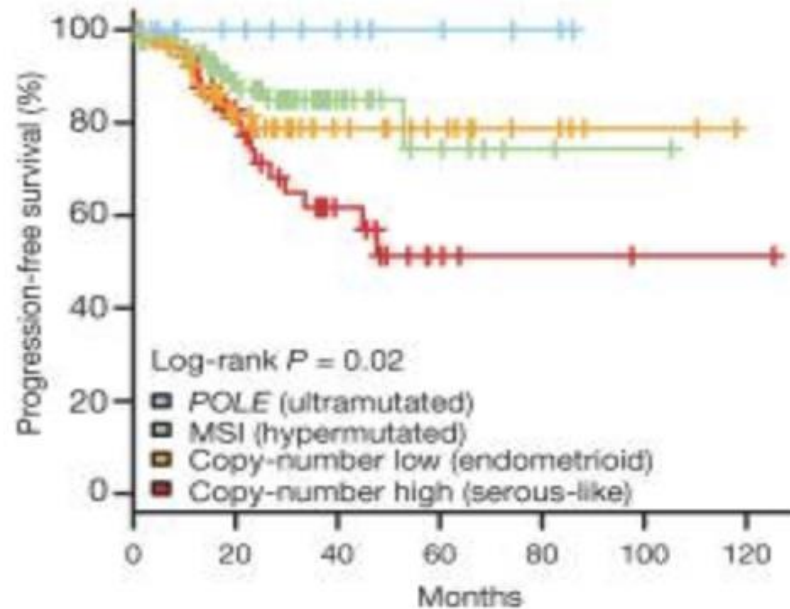
# Genomic Characterization of EC



# Genomic Characterization of EC



# Genomic Characterization of EC



# Key Research Finding

**Approximately 25% of endometrial tumors classified as endometrioid by pathologists have a molecular phenotype similar to uterine serous carcinomas.**



# 2023 Endometrial Cancer staging by FIGO



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# STAGE I

## Stage I

## Confined to the uterine corpus & good prognosis

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- **IA**      **Disease limited to the endometrium, OR non-aggressive histotype with invasion of less than half of myometrium with no or focal lymphovascular space involvement (LVSI), OR good prognosis disease**
- 

*IA1 Disease limited to an endometrial polyp, OR confined to the endometrium*

*IA2 Non-aggressive histotype involving less than half of the myometrium with no or focal LVSI*

*IA3 Low-grade endometrioid carcinomas limited to the uterus and ovary \**

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- **IB**      **Non-aggressive histotypes with invasion of half or more of the myometrium, and with no or focal lymphovascular space involvement (LVSI)\*\***
- 



# STAGE II

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**Stage II**

**Invasion of cervical stroma without extrauterine extension, OR substantial LVSI, OR aggressive histological types with myometrial invasion**

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• **IIA**      **Invasion of the cervical stroma**

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• **IIB**      **Substantial LVSI \*\***

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• **IIC**      **Aggressive histologic types with myometrial involvement, i.e., high-grade histologies\*\*\***





# STAGE III

## Stage III

## Local and/or regional spread of the tumor

- **IIIA**

**Invasion of uterine serosa, adnexa, or both by direct extension or metastasis**

*IIIA1 Spread to ovary or fallopian tube*

- *Except when meeting stage IA3 criteria \**

*IIIA2 Involvement of uterine subserosa or spread through the uterine serosa*

- **IIIB**

**Metastasis or direct spread to the vagina, and/or to parametria, or to pelvic peritoneum**

*IIIB1 Metastasis or direct spread to the vagina, and/or to parametria*

*IIIB2 Metastasis to pelvic peritoneum*

- **IIIC**

**Metastasis to pelvic or para-aortic lymph nodes or both \*\*\*\***

*IIIC1 Metastasis to pelvic lymph nodes*

*IIIC1i Micrometastasis*

*IIIC1ii Macrometastasis*

*IIIC2 Metastasis to para-aortic lymph nodes, with or without metastasis to pelvic lymph nodes*

*IIIC2i Micrometastasis*

*IIIC2ii Macrometastasis*



# STAGE IV

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**Stage IV**      **Spread to the bladder and/or intestinal mucosa and/or distant metastasis**

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• **IVA**      **Invasion of the bladder, intestinal mucosa, or both**

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• **IVB**      **Abdominal peritoneal metastasis/intraperitoneal carcinomatosis beyond the pelvis**

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• **IVC**      **Distant metastasis, including metastasis to the inguinal lymph nodes, lungs, liver, or bone**

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# 2023 FIGO Staging of Endometrial Cancer, The Good

**Incorporates molecular profile into endometrial cancer staging with the potential for improved prognostication and better treatment guidance**



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# 2023 FIGO Staging of Endometrial Cancer, The Bad

**Incorporation of molecular profile into endometrial cancer staging  
does not follow the fundamental principle of cancer staging**



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## 2023 FIGO Staging of Endometrial Cancer, The Ugly

**The new endometrial cancer staging has too many substages  
that are not driven by strong evidence therefore unlikely to  
separate prognostically**



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## ***SAME PATIENT – DIFFERENT STAGE***

***Institution A***

***G2 endometrioid, 3/15 mm DOI, no LVSI, node negative***

***STAGE IA2***

***Institution B***

***CLEAR CELL, 3/15 mm DOI, no LVSI, node negative***

***STAGE IIC***

***Institution C***

***CLEAR CELL, 3/15 mm DOI, no LVSI, node negative, POLE mut***

***STAGE IA<sub>m</sub>POLE<sub>mut</sub>***



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## ***ALL Stage IIC\****

***Clear cell, 1mm DOI, no LVSI***

***Serous carcinoma, 14/15 mm DOI, ext LVSI***

***G3 endometrioid, 1/18mm DOI, no LVSI***

***Carcinosarcoma, 14/15 mm DOI, LVSI $\geq$ 5, cervix stroma invasion***

***\*unless you have resources to do POLE  
MMRd, CN-L/NSMP, other emerging classifiers ignored if POLE wt and p53 wt***



## In conclusion

- ❖ **The attempt by FIGO to incorporate molecular profile into endometrial cancer staging is bold, great and commendable**
- ❖ **It is premature**
- ❖ **It could have been done better**
- ❖ **The new endometrial cancer staging is confusing and difficult to use clinically**



*Thank you*

