ESGO
European Society of Gynaecological Oncology
25th European Congress on Gynaecological Oncology
March 7-10, 2024 | Barcelona, Spain

New FIGO Staging for Endometrial Cancer

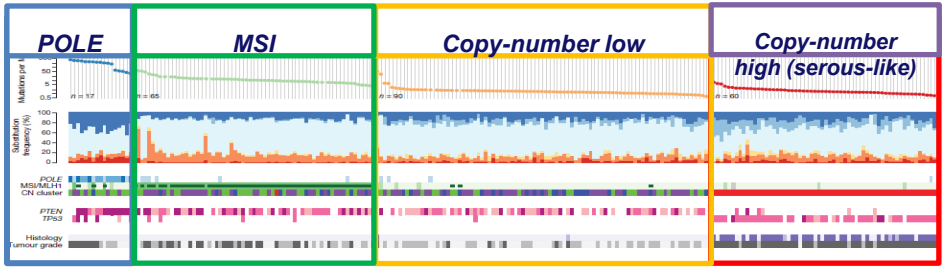
"The Evolution of the Revolution"

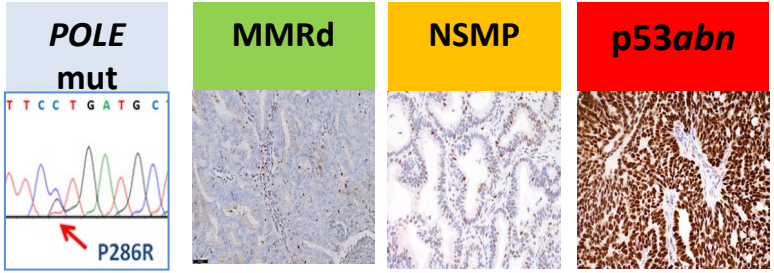
Nicole Concin
Dept. Gynaecology & Gynaecological Oncology
Medical University of Vienna
Austria

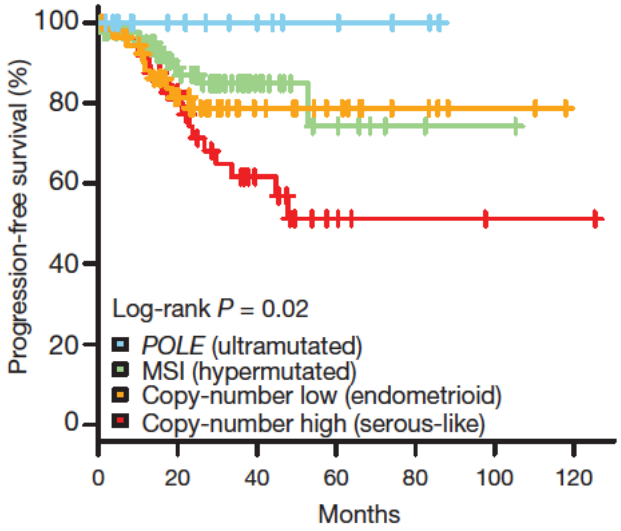
Declaration of Interest

Consulting/Advisory:	MSD, ImmunoGen, Seagen, Akesobio, EISAI, GSK, AstraZeneca, Mersana, Seattle Genetics, KARTOS, eTheRNA immunotherapies NV
Travel Expenses:	Roche, Genmab, Amgen
Educational fees:	Kartos, MSD, Medscape Oncology, TouchIME
Functions in societies:	President of ESGO Chair of ENGOT Early Drug Development Network FIGO committee for women`s cancer

What The Cancer Genome Atlas (TCGA) has taught us……



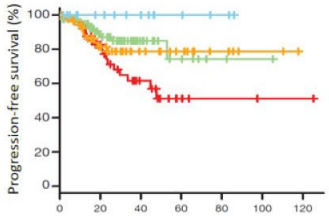




- **Immunohistochemistry** for **p53** & **mismatch repair proteins**
- **DNA sequencing** for ***POLE*** exonuclease domain mutations

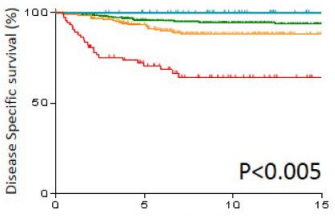
Kandoth et al, Nature 2013; Stelloo et al, Clin Cancer Research 2016 ; Talhouk et al, Cancer 2017

Prognostic significance of molecular subgroups



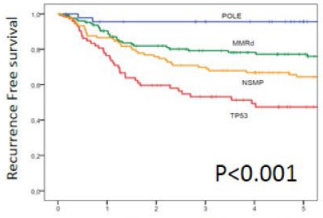
TCGA (n=373)

Kandoth et al., Nature 2013



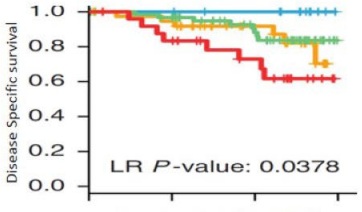
PORTEC-1/-2 (n=834)

Stelloo et al., CCR 2016



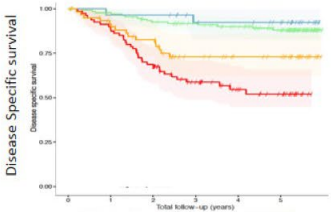
Grade 3 EEC (n=376)

Bosse et al., Am J Surg Path 2018



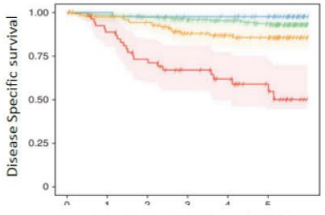
Unselected (n=142)

Talhouk et al, BJC 2015



Unselected (n=319)

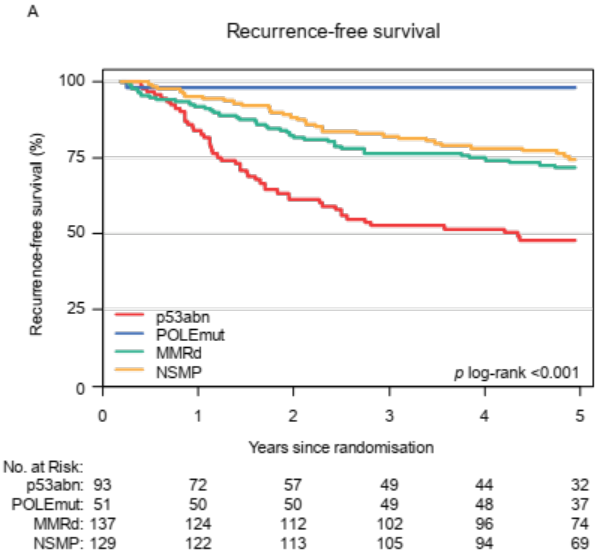
Talhouk et al, Cancer 2017



Unselected (n=415)

Kommoss et al, Ann of Onc 2018

PORTEC-3 translational results

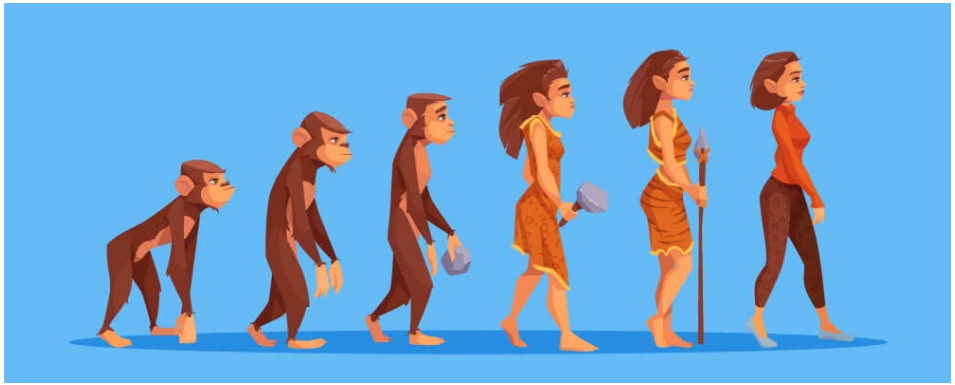


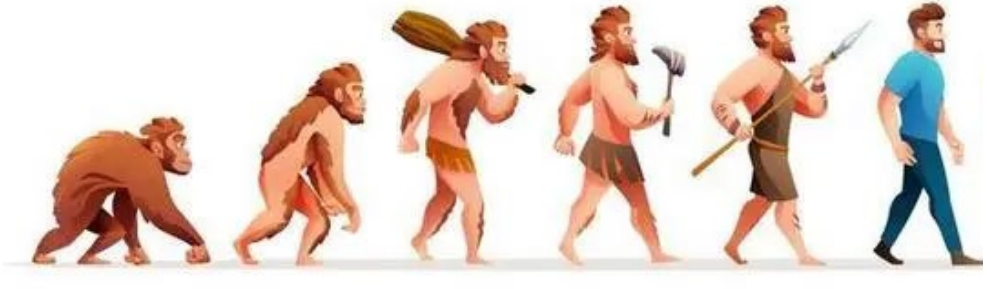
No. at Risk:						
p53abn:	93	72	57	49	44	32
POLEmut:	51	50	50	49	48	37
MMRd:	137	124	112	102	96	74
NSMP:	129	122	113	105	94	69

----- POLEmut **------ MMRd** **------ NSMP** **------ p53abn**

Leon del Castillo et al, JCO 2020

Evolution of the Revolution …





Integration of
TUMOR BIOLOGY
into prognostic risk group stratification of patients with Endometrial Cancer

in International Guidelines

ESGO-ESTRO-ESP Endometrial Cancer Guidelines

Nicole Concin

Carien Creutzberg

Xavier Matias-Guiu

Multidisciplinary, international working group

Concin et al, Int J Gynecol Cancer Dec 2020; Radiother Oncol 2021; Virchows Arch 2021

OPEN ACCESS: https://ijgc.bmj.com/content/ijgc/31/1/12.full.pdf.

ESGO-ESTRO-ESP Endometrial Cancer Guidelines: PROGNOSTIC RISK GROUPS

ESMO-ESGO-ESTRO
Consensus Conference **2015**

TABLE 2. New risk groups to guide adjuvant therapy use

Risk group	Description	LOE
Low	Stage I endometrioid, grade 1–2, <50% myometrial invasion, LVSI negative	I
Intermediate	Stage I endometrioid, grade 1–2, ≥50% myometrial invasion, LVSI negative	I
High-intermediate	Stage I endometrioid, grade 3, <50% myometrial invasion, regardless of LVSI status	I
	Stage I endometrioid, 1–2, LVSI unequivocally positive, regardless of depth of invasion	II
High	Stage I endometrioid, grade 3, ≥50% myometrial invasion, regardless of LVSI status	I
	Stage II	I
	Stage III endometrioid, no residual disease	I
	Non endometrioid (serous or clear cell or undifferentiated carcinoma, or carcinosarcoma)	I
Advanced	Stage III residual disease and stage IVA	I
Metastatic	Stage IVB	I

FIGO 2009 staging used; molecular factors were considered but not included; tumour size was considered but not included; nodal status may be considered for treatment recommendations.
LOE, level of evidence; LVSI, lymphovascular space invasion.

Colombo et al,
Ann Oncol 2016;
Int J Gynecol Cancer 2016;
Radiother Oncol 2015

2020/21
Integration of molecular markers

Risk group	Molecular classification unknown	Molecular classification known*†
Low	▶ Stage IA endometrioid + low-grade‡ + LVSI negative or focal	▶ Stage I–II ***POLEmut*** endometrial carcinoma, [illegible] residual disease ▶ Stage IA **MMRd/NSMP** endometrioid carcinoma + low-grade‡ + LVSI negative or focal
Intermediate	▶ Stage IB endometrioid + low-grade‡ + LVSI negative or focal ▶ Stage IA endometrioid + high-grade‡ + LVSI negative or focal ▶ Stage IA non-endometrioid (serous, clear cell, undifferentiared carcinoma, carcinosarcoma, mixed) without myometrial invasion	▶ Stage IB **MMRd/NSMP** endometrioid carcinoma + low-grade‡ + LVSI negative or focal ▶ Stage IA **MMRd/NSMP** endometrioid carcinoma + high-grade‡ + LVSI negative or focal ▶ Stage IA **p53abn** and/or non-endometrioid (serous, clear cell, undifferentiated carcinoma, carcinosarcoma, mixed) without myometrial invasion
High–intermediate	▶ Stage I endometrioid + substantial LVSI regardless of grade and depth of invasion ▶ Stage IB endometrioid high-grade‡ regardless of LVSI status ▶ Stage II	▶ Stage I **MMRd/NSMP** endometrioid carcinoma + substantial LVSI regardless of grade and depth of invasion ▶ Stage IB **MMRd/NSMP** endometrioid carcinoma high-grade‡ regardless of LVSI status ▶ Stage II **MMRd/NSMP** endometrioid carcinoma
High	▶ Stage III–IVA with no residual disease ▶ Stage I–IVA non-endometrioid (serous, clear cell, undifferentiated carcinoma, carcinosarcoma, mixed) with myometrial invasion, and with no residual disease	▶ Stage III–IVA **MMRd/NSMP** endometrioid carcinoma [illegible] residual disease ▶ Stage I–IVA **p53abn** endometrial carcinoma with myometrial [illegible], with no residual disease ▶ Stage I–IVA **NSMP/MMRd** serous, undifferentiated carcinoma, carcinosarcoma with myometrial invasion, with no residual disease
Advanced metastatic	▶ Stage III–IVA with residual disease ▶ Stage IVB	▶ Stage III–IVA with residual disease of any molecular type ▶ Stage IVB of any molecular type

ESGO European Society of Gynaecological Oncology
ESTRO European Society for RADIOTHERAPY & ONCOLOGY
European Society of Pathology

Concin et al,
Int J Gynecol Cancer 2021;
Radiother Oncol 2021;
Virchows Arch 2021

Molecular classification in European Guidelines

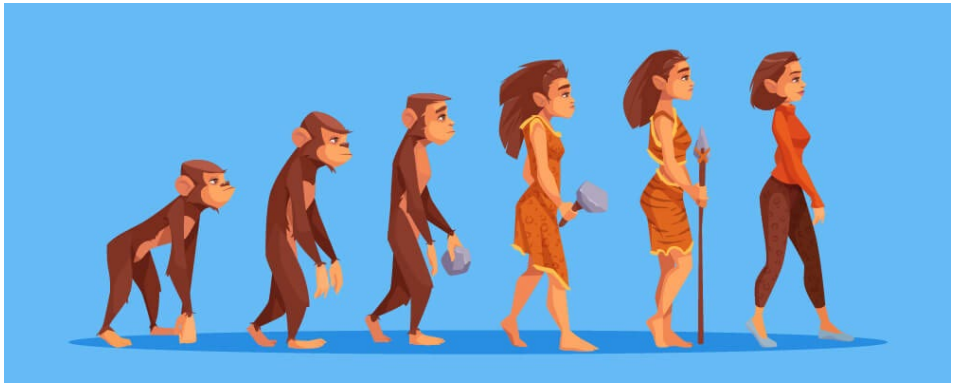
Molecular classification
is encouraged in ALL
endometrial carcinomas,
especially high-grade tumours
[IV, B].

Concin N et al, Int J Gynecol Cancer **Dec 2020**
Radiother Oncol **Jan 2021**
Virchows Arch **Feb 2021**

Molecular classification ……
should be carried
out for ALL EC pathology
specimens regardless of
histological type [IV, A].

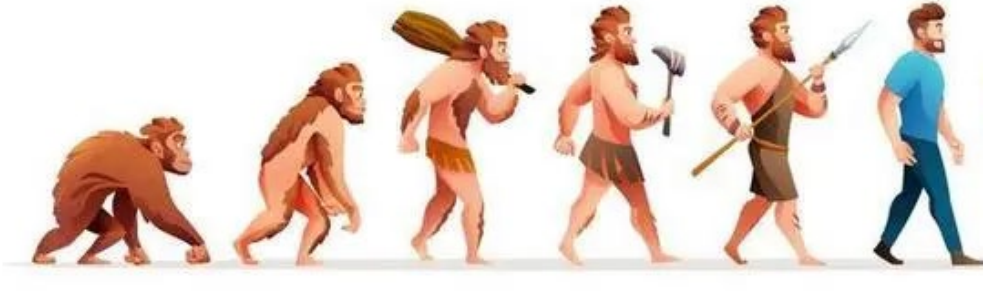
Oaknin A et al, Annals Oncol **June 2022**

Evolution of the Revolution …



Integration of
TUMOR BIOLOGY
into

FIGO staging system



Int J Gynecol Obstet. 2023;00:1–12.

DOI: 10.1002/ijgo.14923

SPECIAL ARTICLE

FIGO staging of endometrial cancer: 2023

Jonathan S. Berek[1] | Xavier Matias-Guiu[2] | Carien Creutzberg[3] | Christina Fotopoulou[4] | David Gaffney[5] | Sean Kehoe[6] | Kristina Lindemann[7] | David Mutch[8] | Nicole Concin[9,10] | Endometrial Cancer Staging Subcommittee, FIGO Women's Cancer Committee

= PROGNOSTIC SYSTEM

FIGO staging of endometrial cancer: 2023

Jonathan S. Berek[1] | Xavier Matias-Guiu[2] | Carien Creutzberg[3] | Christina Fotopoulou[4] | David Gaffney[5] | Sean Kehoe[6] | Kristina Lindemann[7] | David Mutch[8] | Nicole Concin[9,10] | Endometrial Cancer Staging Subcommittee, FIGO Women's Cancer Committee

Int J Gynecol Obstet, **Sept 2023**

FIGO International Federation of Gynecology and Obstetrics
the Global Voice for Women's Health

Challenges

- **14 years of evidence** between ”old” 2009 FIGO staging system and now **“Cinderella disease”**
- FIGO being traditionally a surgical-anatomical-pathological staging system -> **Integration of tumor biology/ parameters**

Opportunities

HAVE AN UP-TO-DATE staging system
integrating the current level of evidence

- **HIGHER PROGNOSTIC PRECISION**
- Identification of **TREATMENT RELEVANT SUBGROUPS**
- **DATA COLLECTION** on clinically relevant subgroups

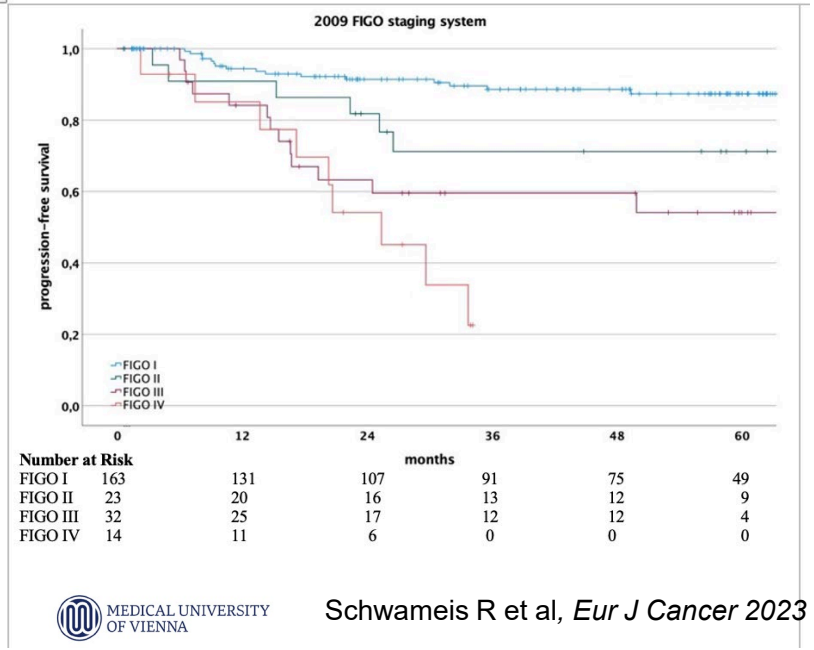
KEY CHANGES

- Incorporation of **histological subtypes** (low-grade endometroid *vs* aggressive histological types)
- Incorporation of the degree of **LVSI** (no/focal *vs* substantial)
- Integration of **molecular classification** *if available*
- Distinction of **low-grade endometrioid carcinoma involving the endometrium and the ovary** from (other) metastatic spread to the ovary
- More differentiated **anatomical spread** (adnexal *vs* (sub)serosa, pelvic *vs* extrapelvic peritoneum, discrimination peritoneal carcinomatosis and distant metastases)
- Refined description of **lymph node involvement** *(micro- vs macrometastasis)*

„Old“ FIGO staging system 2009

based on anatomical spread of disease only

Stage I	Tumour confined to the corpus uteri
I A	NO or less than half myometrial invasion
I B	Invasion equal to or more than half of the myometrium
Stage II	Tumour invades cervical stroma, but does not extend beyond the uterus
Stage III	Local and/or regional spread of the tumour
III A	Tumour invades the serosa of the corpus uteri and/or adnexae
III B	Vaginal and/or parametrial involvement
III C	Metastasis to pelvic and/or para-aortic lymph nodes
III C1	Positive pelvic nodes
III C2	Positive para-aortic lymph nodes with or without positive pelvic lymph nodes
Stage IV	Tumour invades bladder and/or bowel mucosa, and/or distant metastases
IV A	Tumour invasion of bladder and/or bowel mucosa
IV B	Distant metastases, including intra-abdominal metastases and/or inguinal lymph nodes



Schwameis R et al, *Eur J Cancer 2023*

2023 FIGO staging system: a PROGNOSTIC classification

FIGO International Federation of Gynecology and Obstetrics

2023 FIGO stages are based on surgical/anatomical and histological findings

Stage	Description
Stage I	Confined to the uterine corpus and ovary[c]
IA	Disease limited to the endometrium OR non-aggressive histological type, i.e. low-grade endometroid, with invasion of less than half of myometrium with no or focal lymphovascular space involvement (LVSI) OR good prognosis disease
	IA1 Non-aggressive histological type limited to an endometrial polyp OR confined to the endometrium
	IA2 Non-aggressive histological types involving less than half of the myometrium with no or focal LVSI
	IA3 Low-grade endometrioid carcinomas limited to the uterus and ovary[c]
IB	Non-aggressive histological types with invasion of half or more of the myometrium, and with no or focal LVSI[d]
IC	Aggressive histological types[e] limited to a polyp or confined to the endometrium
Stage II	Invasion of cervical stroma without extrauterine extension OR with substantial LVSI OR aggressive histological types with myometrial invasion
IIA	Invasion of the cervical stroma of non-aggressive histological types
IIB	Substantial LVSI[d] of non-aggressive histological types
IIC	Aggressive histological types[e] with any myometrial involvement
Stage III	Local and/or regional spread of the tumor of any histological subtype
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)[c] IIIA2 Involvement of uterine subserosa or spread through the uterine serosa
IIIB	Metastasis or direct spread to the vagina and/or to the parametria or pelvic peritoneum
	IIIB1 Metastasis or direct spread to the vagina and/or the parametria IIIB2 Metastasis to the pelvic peritoneum
IIIC	Metastasis to the pelvic or para-aortic lymph nodes or both[f]
	IIIC1 Metastasis to the pelvic lymph nodes IIIC1i Micrometastasis IIIC1ii Macrometastasis IIIC2 Metastasis to para-aortic lymph nodes up to the renal vessels, with or without metastasis to the pelvic lymph nodes IIIC2i Micrometastasis IIIC2ii Macrometastasis
Stage IV	Spread to the bladder mucosa and/or intestinal mucosa and/or distance metastasis
IVA	Invasion of the bladder mucosa and/or the intestinal/bowel mucosa
IVB	Abdominal peritoneal metastasis beyond the pelvis
IVC	Distant metastasis, including metastasis to any extra- or intra-abdominal lymph nodes above the renal vessels, lungs, liver, brain, or bone

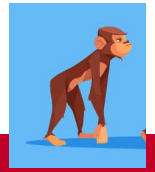
OPTION:
Integration of molecular markers
when known

-> to further
increase
prognostic PRECISION

Evolution of FIGO Endometrial Cancer Staging System

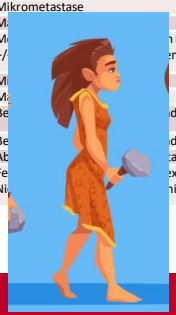
FIGO 2009 anatomy- based only

Stage I	Tumour confined to the corpus uteri
I A	NO or less than half myometrial invasion
I B	Invasion equal to or more than half of the myometrium
Stage II	Tumour invades cervical stroma, but does not extend beyond the uterus
Stage III	Local and/or regional spread of the tumour
III A	Tumour invades the serosa of the corpus uteri and/or adnexae
III B	Vaginal and/or parametrial involvement
III C	Metastasis to pelvic and/or para-aortic lymph nodes
III C1	Positive pelvic nodes
III C2	Positive para-aortic lymph nodes with or without positive pelvic lymph nodes
Stage IV	Tumour invades bladder and/or bowel mucosa, and/or distant metastases
IV A	Tumour invasion of bladder and/or bowel mucosa
IV B	Distant metastases, including intra-abdominal metastases and/or inguinal lymph nodes



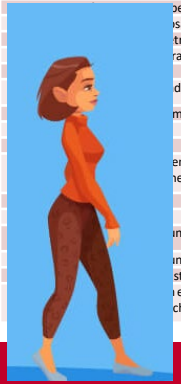
FIGO 2023 tumorbiology + anatomy *without* molecular subgroups

FIGO	
I	Begrenzt auf Corpus uteri und Ovarien
IA1	Low-grade endometrioides Karzinom begrenzt auf Endometriumpolypen ODER auf das Endometrium
IA2	Low-grade endometrioides Karzinom Befall von <50% des Myometriums, ohne substantielle LVSI
IA3	Low-grade endometrioides Karzinom begrenzt auf Corpus uteri und Ovarien *
IB	Low-grade endometrioides Karzinom mit Befall von ≥ 50% des Myometriums, ohne substantielle LVSI
IC	Aggressiver histologischer Typ, begrenzt auf Endometriumpolypen ODER auf das Endometrium
II	Zervixstromabefall ohne extrauterine Ausdehnung ODER mit substantieller LVSI ODER aggressiver histologischer Typ mit Invasion des Myometriums
IIA	Low-grade endometrioides Karzinom mit Zervixstromabefall
IIB	Low-grade endometrioides Karzinom mit substantieller LVSI
IIC	Aggressiver histologischer Typ mit Beteiligung des Myometriums
III	Jeder histologische Typ mit lokaler und/oder regionaler Ausbreitung
IIIA	Befall von Uterusserosa und/oder der Adnexe
IIIA1	Ausbreitung auf Ovari oder Tube (außer bei Stadium IA3)
IIIA2	Befall von Subserosa oder Serosa des Uterus
IIIB	Befall von Vagina oder Parametrien oder Beckenperitoneum
IIIB1	Befall von Vagina und/oder Parametrien
IIIB2	Befall von Beckenperitoneum
IIIC	Metastasen in den pelvinen und/oder para-aortalen Lymphknoten
IIIC1	Metastasen in den pelvinen Lymphknoten
IIIC1i	Mikrometastase
IIIC1ii	Ma
IIIC2	Me n Lymphknoten bis zu den Nierengefäßen, +/ en Lymphknoten
IIIC2i	M
IIIC2ii	Ma
IV	Be d/oder Darmschleimhaut +/- Fernmetastasen
IVA	Be d/oder Darmschleimhaut
IVB	Ab asen jenseits des Beckens
IVC	Fe xtra- oder intraabdominneller LK-Metastasen oberhalb der Ni irn oder Knochen

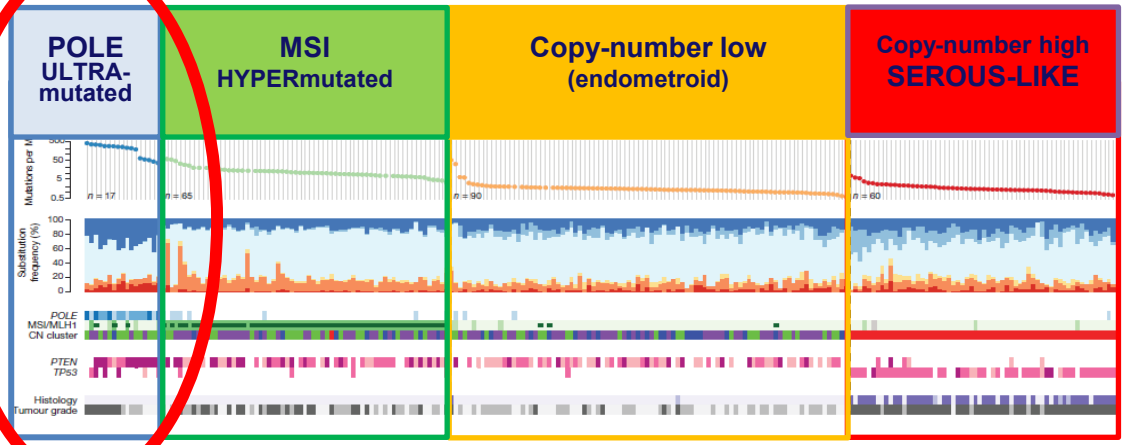


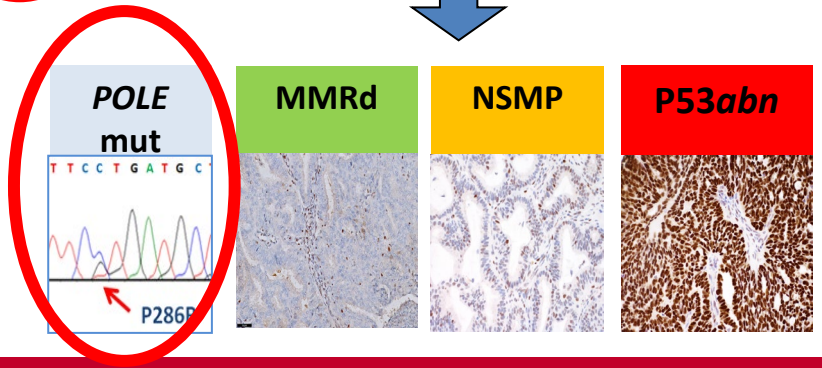
FIGO 2023 tumorbiology + anatomy *WITH* molecular subtypes

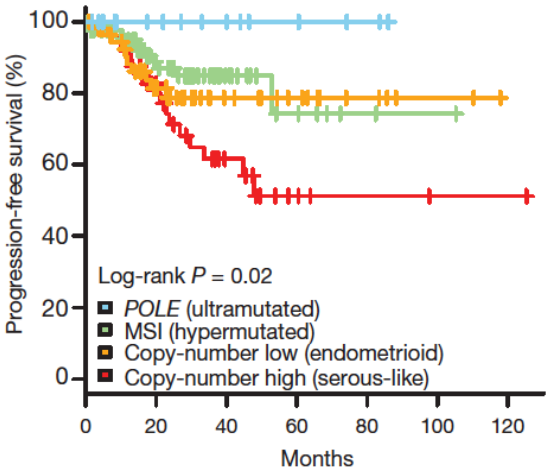
FIGO	
I	Begrenzt auf Corpus uteri und Ovarien
$IAm_{POLEmut}$	POLEmut Tumoren begrenzt auf den Uterus +/- Zervixinvasion (unabhängig von LVSI oder histologischem Subtyp)
IA1	Low-grade endometrioides Karzinom begrenzt auf Endometriumpolypen ODER auf das Endometrium
IA2	Low-grade endometrioides Karzinom Befall von <50% des Myometriums, ohne substantielle LVSI
IA3	Low-grade endometrioides Karzinom begrenzt auf Corpus uteri und Ovarien *
IB	Low-grade endometrioides Karzinom mit Befall von ≥ 50% des Myometriums, ohne substantielle LVSI
IC	Aggressiver histologischer Typ, begrenzt auf Endometriumpolypen ODER auf das Endometrium
II	Zervixstromabefall ohne extrauterine Ausdehnung ODER mit substantieller LVSI ODER aggressiver histologischer Typ mit Invasion des Myometriums
IIA	Low-grade endometrioides Karzinom mit Zervixstromabefall
IIB	Low-grade endometrioides Karzinom mit substantieller LVSI
IIC	Aggressiver histologischer Typ mit Beteiligung des Myometriums
$IICm_{p53abn}$	p53abn beschränkt auf Uterus +/- Zervixinvasion mit myometran histologischem Subtyp)
III	Jeder histologische Typ mit lokaler und/oder regionaler Ausbreitu
IIIA	Befall von Uterusserosa und/oder der Adnexe
IIIA1	pe (außer bei Stadium IA3)
IIIA2	sa des Uterus
IIIB	trien oder Beckenperitoneum
IIIB1	rametrien
IIIB2	
IIIC	d/oder para-aortalen Lymphknote
IIIC1	mphknoten
IIIC1i	
IIIC1ii	
IIIC2	en Lymphknoten bis zu den Nieren hen Lymphknoten
IIIC2i	
IIIC2ii	
IV	nd/oder Darmschleimhaut +/- Fer
IVA	nd/oder Darmschleimhaut
IVB	stasen jenseits des Beckens
IVC	extra- oder intraabdominneller LK- chen



What the TCGA has taught us?





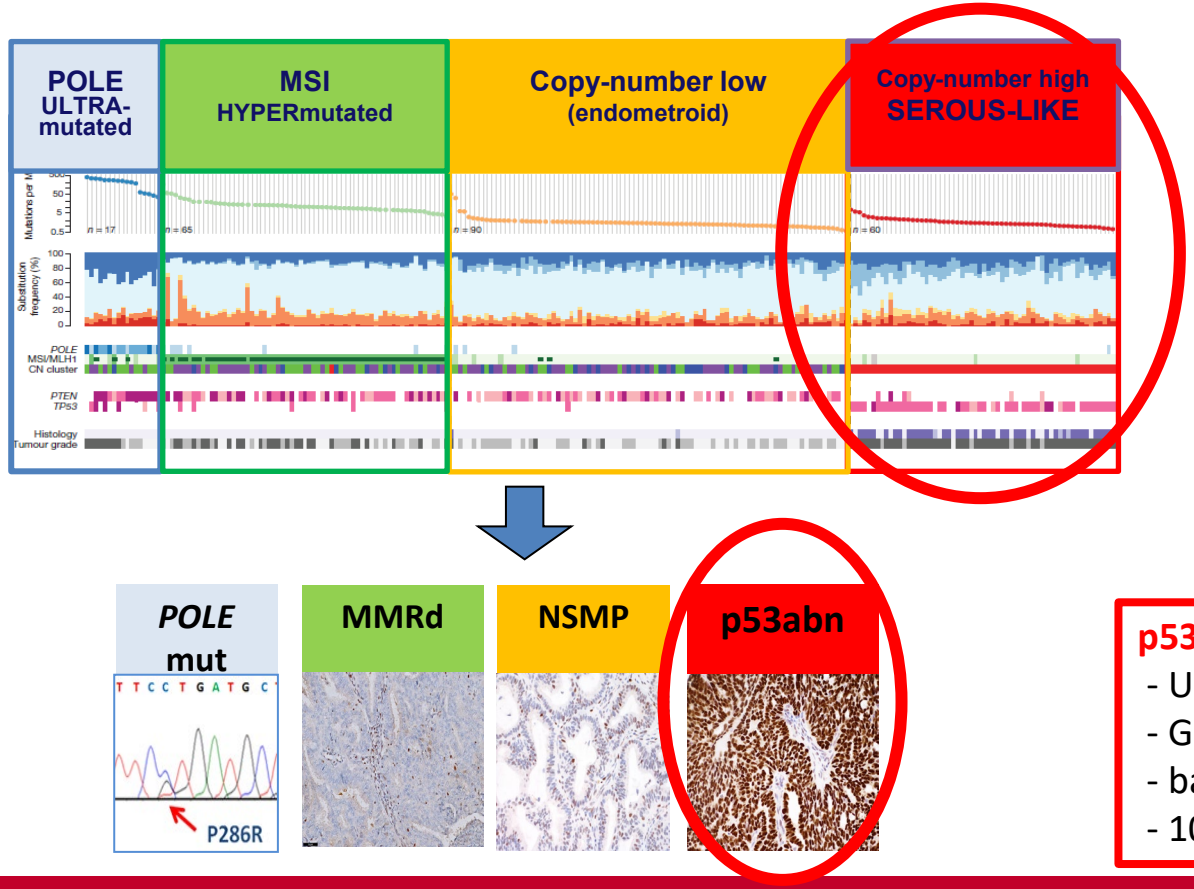


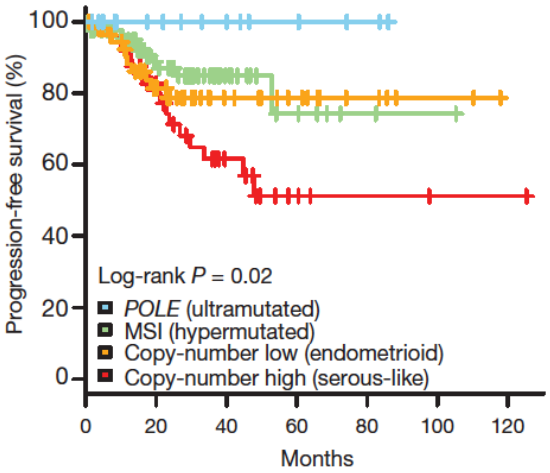
POLE mutated EC:

- Rare, 5-10% of ECs
- Excellent prognosis
- ULTRA-mutated

Kandoth et al, Nature 2013; Stelloo et al, Clin Cancer Research 2016 ; Talhouk et al, Cancer 2017

What the TCGA has taught us?





p53 abnormal
- Universal *TP53* mutations
- Genomic instability
- bad prognosis
- 10-20%

Kandoth et al, Nature 2013; Stelloo et al, Clin Cancer Research 2016 ; Talhouk et al, Cancer 2017

Prognostic relevance of the molecular classification in high-grade endometrial cancer for patients staged by lymphadenectomy and without adjuvant treatment

Gynecol Oncol 2022

Alicia Leon-Castillo [a], Nanda Horeweg [b], Elke E.M. Peters [a,c], Tessa Rutten [a], Natalja ter Haar [a], Vincent T.H.B.M. Smit [a], Cor D. Kroon [d], Marie Boennelycke [e], Estrid Hogdall [e], Claus Hogdall [f], Remi R.A. Nout [b], Carien L. Creutzberg [b], Gitte Ortoft [f], Tjalling Bosse [a,*]

[a] *Leiden University Medical Center, Department of Pathology, P.O. Box 9600, 2300, RC, Leiden, the Netherlands*
[b] *Leiden University Medical Center, Department of Radiation Oncology, P.O. Box 9600, 2300, RC, Leiden, the Netherlands*
[c] *Haaglanden Medical Center, P.O. Box 432, 2501, CK, The Hague, the Netherlands*
[d] *Leiden University Medical Center, Department of Gynaecology, P.O. Box 9600, 2300, RC, Leiden, the Netherlands*
[e] *Department of Pathology, Copenhagen University Hospital, Herlev and Gentofte Hospital, Borgmester Ib Juuls Vej 73, 2730 Herlev, Denmark*
[f] *Copenhagen University Hospital, Rigshospitalet, Department of Gynaecology, Juliane Maries Vej 8, 2100 Copenhagen, OE, Denmark*

Danish Gynaec. Cancer Database: molecularly profiled **high grade EC, stage I-III** (n=367)

Aim:
Evaluate prognostic relevance of the molecular subgroups
in patients with high-grade EC
staged by lymphadenectomy and in **those without adjuvant treatment**

PROGNOSTIC significance of molecular subgroups in patients who underwent lymphadenectomy

Danish Gynaec. Cancer Database

molecularly profiled **high grade EC, stage I-III** (n=367), **subgroup (n=251) lymph node staged**

Multivariate analysis of molecular subgroups and clinco-pathological features

	Recurrence			Overall survival			Disease specific survival		
	n events = 64			n events = 78			n events = 53		
Parameter	HR	95%CI	*p*-value	HR	95%CI	*p*-value	HR	95%CI	*p*-value
Age									
<70	1			1			1		
>70	0.896	0.516–1.553	0.695	1.779	1.081–2.926	0.023	1.073	0.581–1.984	0.821
Molecular subgroups									
MMRd	1			1			1		
p53abn	3.938	1.924–8.058	<0.001	1.875	1.064–3.304	0.030	3.244	1.510–6.969	0.003
*POLE*mut	–	–	–	0.622	0.180–2.156	0.454	–	–	–
NSMP	4.685	2.083–10.537	<0.001	2.031	1.007–4.096	0.048	3.954	1.648–9.486	0.002
Stage									
I-II	1			1			1		
III	0.379	0.122–1.176	0.093	0.498	0.167–1.485	0.395	0.448	0.123–1.625	0.222
LVSI									
Absent or focal	1			1			1		
Substantial	2.495	1.336–4.658	0.004	2.377	1.366–4.133	0.002	2.93	1.508–5.692	0.002
Adjuvant treatment									
No	1			1			1		
Yes	0.671	0.351–1.281	0.226	0.684	0.362–1.293	0.243	0.654	0.323–1.325	0.238
ASA score									
1–2	1			1			1		
3–5	1.440	0.466–4.455	0.526	2.248	0.980–5.158	0.056	1.314	0.362–4.770	0.678

LVSI, lymphovascular-space invasion; ASA, American Society of Anesthesiologist Physical Status Classification System.
Results are corrected for confounding by indication by a propensity score.

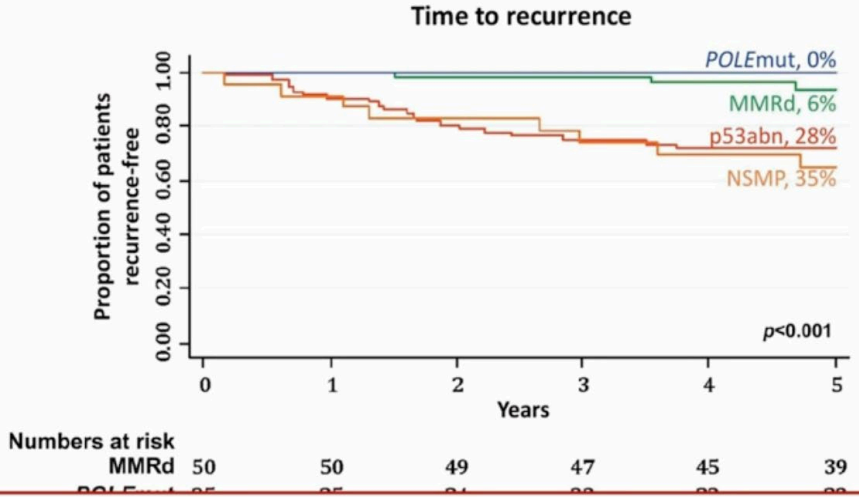
In **multivariable analysis** molecular subgroups remain a strong prognostic factor for **Recurrence, Overall Survival & Disease Specific Survival INDEPENDENT OF STAGE**

ESGO European Society of Gynaecological Oncology
25th European Congress on Gynaecological Oncology
March 7-10, 2024 | Barcelona, Spain

PROGNOSTIC significance of molecular subgroups in stage I patients who underwent lymphadenectomy

Clinical outcome: Stage I patients (staged by lymphadenectomy)

N=172

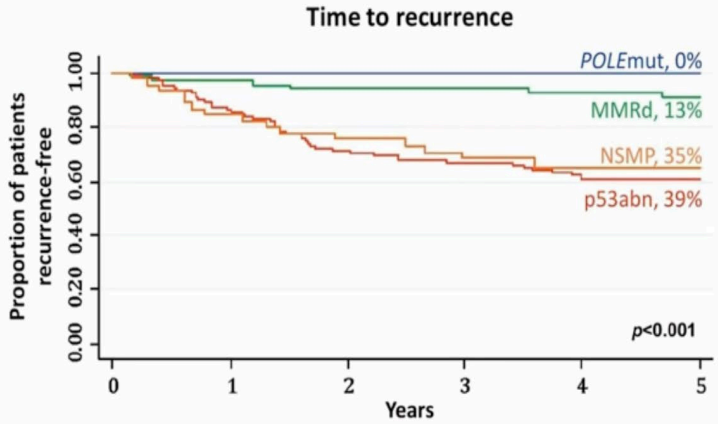


P53abn ECs have a poor clinical outcome, also when staged by lymphadenectomy as stage I.

PROGNOSTIC significance of *POLEmut*

Clinical outcome: Patients not receiving adjuvant treatment

N=264



Patients with *POLE*mut EC have an excellent clinical outcome even when not receiving adjuvant treatment.

Leon Castillo et al, Gynecol Oncol 2022 & ESGO Prague Congress 2021

2023 FIGO staging system: Integrating molecular markers (when known)

TWO specific situations when molecular profile CHANGES the FIGO stage

Stage designation	Molecular findings in patients with early endometrial cancer (Stages I and II after surgical staging)
Stage IAm POLEmut	*POLEmut* endometrial carcinoma, confined to the uterine corpus or with cervical extension, regardless of the degree of LVSI or histological type
Stage IICm p53abn	p53abn endometrial carcinoma confined to the uterine corpus with any myometrial invasion, with or without cervical invasion, and regardless of the degree of LVSI or histological type

Abbreviation: LVSI, lymphovascular space involvement.

m....for „molecular“

For ALL other situation molecular classification is recorded (but does not change FIGO stage)
goal: data collection, therapeutic implication

FIGO stage
according to **surgical/anatomical** and **histological findings**

+

m molecular classification

examples:
FIGO IBm$_{MMRd}$
FIGO IIIC2m$_{p53abn}$
FIGO IIIA1m$_{NSMP}$

Validation Studies of new FIGO Endometrial Cancer

1) Verification of the prognostic precision of the new 2023 FIGO staging system in endometrial cancer patients – *an international pooled analysis of three ESGO accredited centers*

Richard Schwameis, Francesco Fanfani, Christoph Ebner, Naomi Zimmerman, Inge Peters, Camilla Nero, Christian Marth, Robin Ristl, Katharina Leitner, Christoph Grimm, Felicitas Oberndorfer, Ilaria Capasso, Alain G. Zeimet, Stephan Polterauer, Giovanni Scambia, Anna Fagotti and Nicole Concin.

Eur J Cancer, 2023

2) Validation of the 2023 FIGO staging schema for advanced endometrial cancer

Koji Matsuo, Maximilian Klar, Bonnie B Song, Lynda D Roman, Jason D Wright

Eur J Cancer, 2023

Editorial: ***New FIGO 2023 endometrial cancer staging validation. Welcome to the first molecular classifiers and new pathological variables!***

Vergote I & Matias-Guiu X.

Eur J Cancer 2023

3) The right time for change: A report on the heterogeneity of IVB endometrial cancer and improved risk-stratification provided by new 2023 FIGO staging criteria.

Haight PJ, Riedlinger CJ, Backes FJ, O'Malley DM, Cosgrove CM.

Gynecol Oncol 2023

4) Utility of the revised FIGO 2023 staging with molecular classification in endometrial cancer.

Kobayashi-Kato M, Fujii E, Asami Y, Ahiko Y, Hiranuma K, Terao Y, et al

Gynecol Oncol 2023

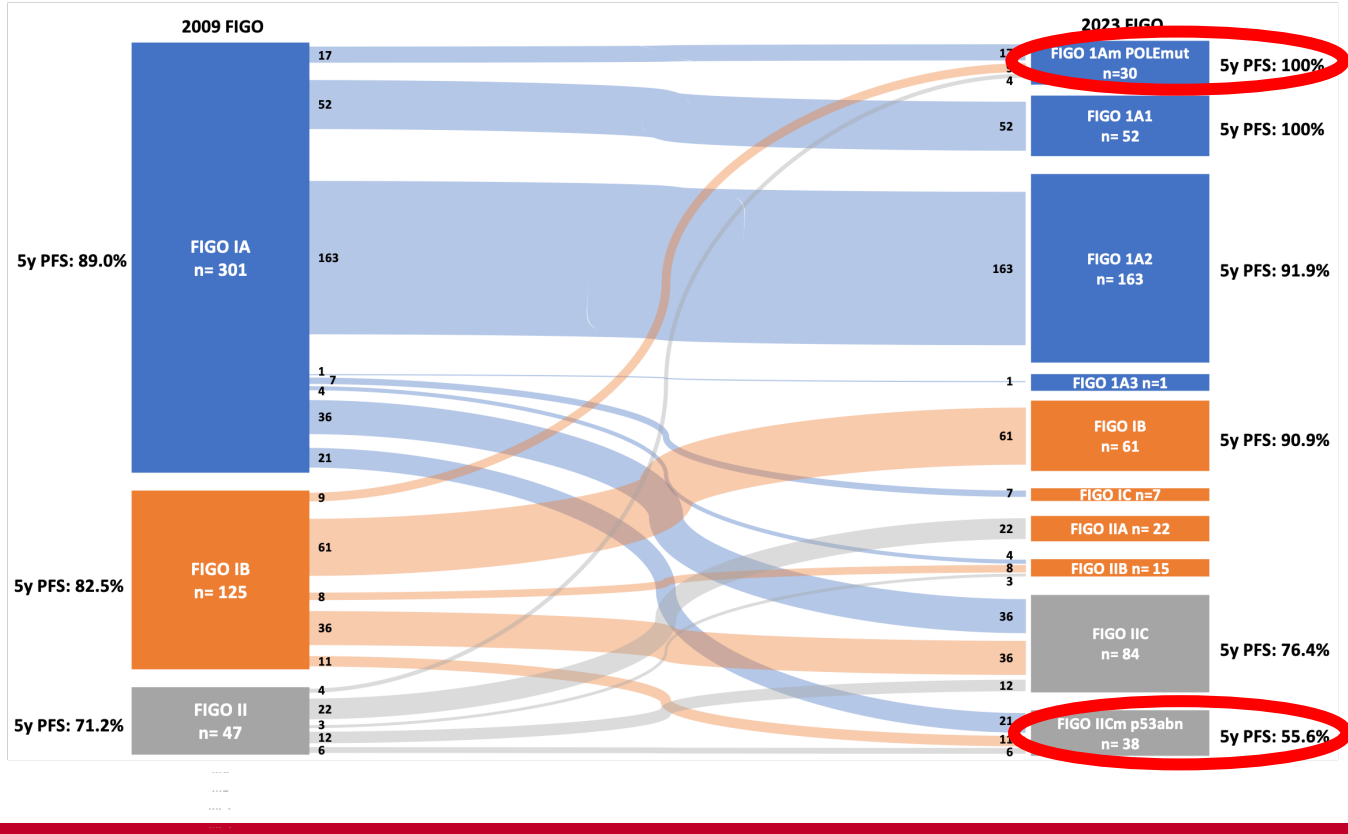
5) Differentiation of survival outcomes by anatomic involvement and histology with the revised 2023 International Federation of Gynecology and Obstetrics staging system for endometrial cancer.

Gravbrot N, Weil Ch R, DeCesaris CM, Gaffney DK, Suneja G, Burt LM

Eur J Cancer, 2024

Verification of the prognostic precision of the new 2023 FIGO staging system in endometrial cancer patients – *an international pooled analysis of three ESGO accredited centers*

Stage shifts between 2009 and 2023 FIGO in **early stage endometrial carcinoma** (stages I/II N= 473)



$IAm_{POLEmut}$

IIC_{p53abn}

Verification of the prognostic precision of the new 2023 FIGO staging system in endometrial cancer patients –
an international pooled analysis of three ESGO accredited centers

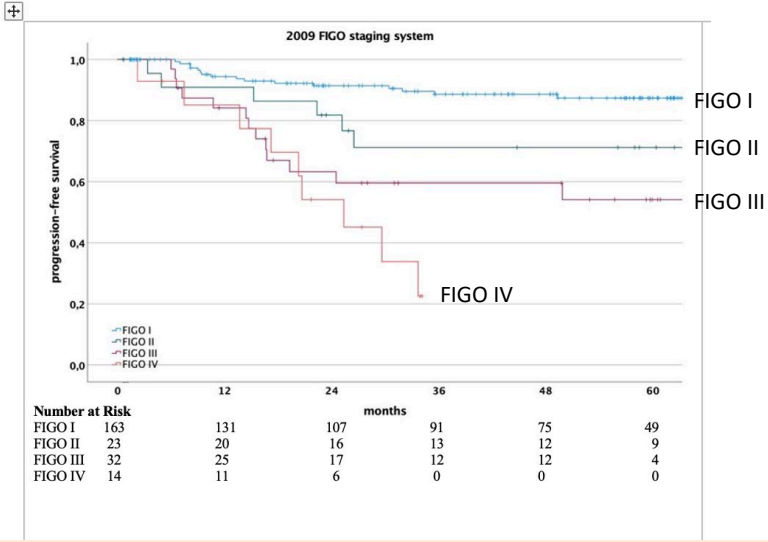
MEDICAL UNIVERSITY OF VIENNA

Gemelli
Fondazione Policlinico Universitario A. Gemelli
Università Cattolica del Sacro Cuore

MEDIZINISCHE UNIVERSITÄT
INNSBRUCK

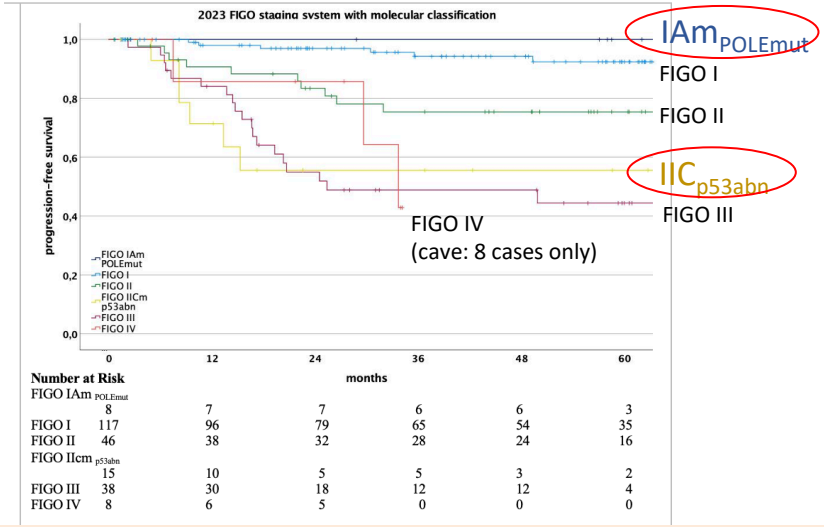
Progression-free survival in a study cohort of 232 endometrial cancer patients *according to*

2009 FIGO



Number at Risk						
FIGO I	163	131	107	91	75	49
FIGO II	23	20	16	13	12	9
FIGO III	32	25	17	12	12	4
FIGO IV	14	11	6	0	0	0

2023 FIGO



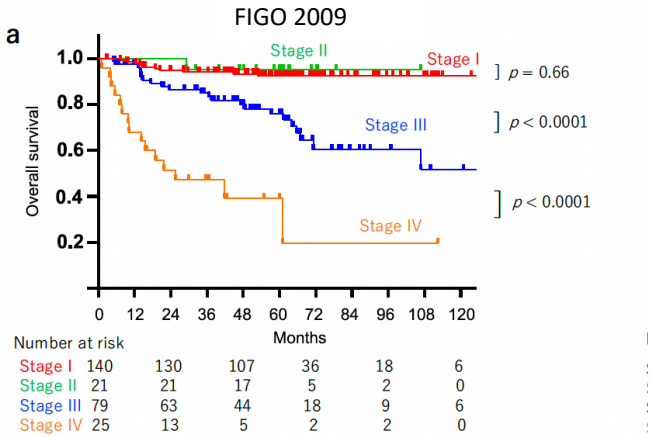
$IAm_{POLEmut}$
FIGO I
FIGO II
IIC_{p53abn}
FIGO III
FIGO IV
(cave: 8 cases only)

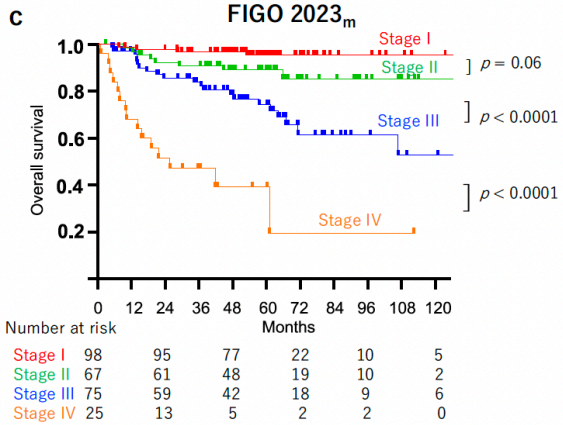
Number at Risk						
FIGO IAm POLEmut	8	7	7	6	6	3
FIGO I	117	96	79	65	54	35
FIGO II	46	38	32	28	24	16
FIGO IIcm p53abn	15	10	5	5	3	2
FIGO III	38	30	18	12	12	4
FIGO IV	8	6	5	0	0	0

Statistical tests demonstrated superiority of 2023 FIGO staging system compared to 2009 to predict PFS and OS

Schwameis R et al, Eur J Cancer 2023; ESGO congress Istanbul best oral session Oct 2023

Utility of the revised FIGO2023 staging with molecular classification in endometrial cancer





National Cancer Center Hospital, Tokyo, n=265 patients

- **FIGO 2023m** had the **best discriminatory ability** compared to FIGO 2009 and FIGO203
- Adding molecular subtype to staging can **improve prognosis prediction especially for Stage I and II**
- Even in **advanced stages**, **p53 status** was a poor prognostic factor

When feasible, molecular subtypes can be added to the staging criteria to allow better prognosis prediction in all stages

ESGO European Society of Gynaecological Oncology
25th European Congress on Gynaecological Oncology
March 7-10, 2024 | Barcelona, Spain

Kobayashi-Kato et al, Gynecol Oncol 2023

Molecular FIGO substages:

Beyond prognosis…
identification of treatment-relevant subgroups

ESGO-ESTRO-ESP Endometrial Cancer Guidelines: LOW RISK

Risk Group	Molecular Classification Unknown	Molecular Classification Known[Δ],*
Low	• Stage IA endometrioid + low-grade** + LVSI negative or focal	• Stage I-II ***POLE*mut** endometrial carcinoma, no residual disease • Stage IA **MMRd/NSMP** endometrioid carcinoma + low-grade** + LVSI negative or focal

[Δ] For **stage III-IVA *POLE*mut** endometrial carcinoma **insufficient data are available to allocate these patients to a prognostic risk-group** in the molecular classification. Prospective registries are recommended

- For patients with **low-risk** endometrial carcinoma, **no adjuvant treatment is recommended** [I, A].

When molecular classification is known:

- For patients with **endometrial carcinoma stage I-II**, low-risk based on **pathogenic *POLE*-mutation**, **omission of adjuvant treatment should be considered** [**III, A**].

ESGO-ESTRO-ESP Endometrial Cancer Guidelines: HIGH RISK

Risk Group	Molecular Classification Unknown	Molecular Classification Known[Δ],*
High	□Stage III-IVA with no residual disease □Stage I-IVA non-endometrioid (serous, clear cell, undifferentiated carcinoma, carcinosarcoma, mixed) with myometrial invasion, and with no residual disease	□Stage III-IVA **MMRd/NSMP** endometrioid carcinoma with no residual disease □Stage I-IVA **p53abn** endometrial carcinoma with myometrial invasion, with no residual disease □Stage I-IVA **NSMP/MMRd** serous, undifferentiated carcinoma, carcinosarcoma with myometrial invasion, with no residual disease

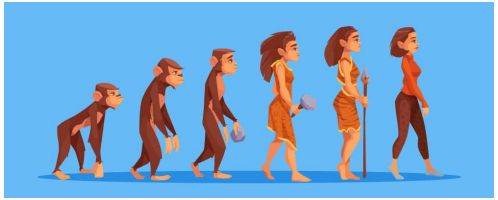
[Δ] For stage I-IVA MMRd or NSMP clear cell endometrial carcinoma with myometrial invasion, insufficient data are available to allocate these patients to a prognostic risk-group in the molecular classification.

- **EBRT with concurrent and adjuvant chemotherapy** [I, A],
  or alternatively **sequential** chemotherapy and radiotherapy is recommended [I, B].
- **Chemotherapy alone** is an alternative option [I, B].

Key takeaways

- New 2023 FIGO staging system critically **integrates tumour biology - paradigm shift**
- Molecular characterisation is **encouraged** in the new 2023 FIGO, it is **OPTIONAL** and integrated, if known.
- If known, molecular subtype **changes FIGO stage in 2 distinct situations in early stage disease** and should be **recorded** in all other cirucumstances
- **Higher prognostic precision** demonstrated in to date 5 validation studies
- 2023 FIGO **identifies treatment-relevant groups**
- Integration of molecular classification into **international Guidelines & FIGO leverages** this approach for the benfits of our patients with endometrial cancer

Evolution of the Revolution …



GCIG consensus conference in Seoul 2023 on CLINICAL TRIALS in endometrial cancer patients

ESGO
European Society of Gynaecological Oncology

25th European Congress on Gynaecological Oncology

March 7-10, 2024 | Barcelona, Spain

Thank you !

congress.esgo.org