

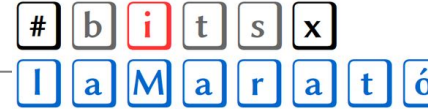
Hack the Uterus !:
el repte NEST



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NSMP Endometrial Stratification Tool

Grup de Recerca en Patologies Ginecològiques i de la Mama

Alba Farrés, Ramon Rovira, Silvia Martorell, Andrea Amadeo, Miguel Ángel Rios,
Nicolás Martínez, Elisa Llurba, Silvia Cabrera.

#BitsxlaMarató
12 Desembre 2024



Endometrial cancer: the molecular era

Most common gynecologic **cancer** in developed countries; incidence **rising**

Typical age: 60–65 years

Key symptom: postmenopausal **abnormal** uterine **bleeding**

Risk factors: **obesity, nulliparity, metabolic syndrome/diabetes**

Histology: mainly **endometrioid**; **serous/clear cell** less common but more aggressive

Primary treatment: **surgery**; adjuvant therapy per **risk stratification**

Prognosis: ~**75%** diagnosed at **stage I–II**; **5-year OS** in stage I >**80–90%**

Endometrial cancer: the molecular era

Two Pathogenetic Types of Endometrial Carcinoma

JAN V. BOKHMAN, M.D.

Department of Gynecology, N. N. Petrov Research Institute of Oncology, USSR Ministry of Health, Leningrad, USSR

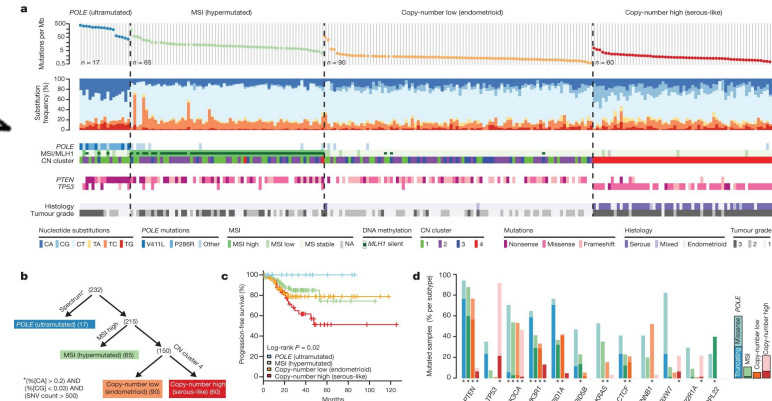
Received May 6, 1981

TABLE 2
INFLUENCE OF PATHOGENETIC TYPE OF THE DISEASE ON TUMOR PECULIARITIES

Tumor peculiarity	Pathogenetic type	
	I	II
Duration of symptoms	Usually long duration	Usually short duration
Degree of tumor differentiation	Highly or moderately differentiated (more frequent G ₁ or G ₂)	Poorly differentiated (more frequent G ₃)
Depth of invasion in the myometrium	Frequent prevalence of superficial invasion	Frequent prevalence of deep invasion
Potentiality for lymphogenic metastatic spread	Not high	High
Sensitivity to progestogens	High	Not high
Primary multiple tumors	Ovaries, breast, colon	Not characteristic
Prognosis	Favorable	Doubtful

Integrated genomic characterization of endometrial carcinoma

The Cancer Genome Atlas Research Network*



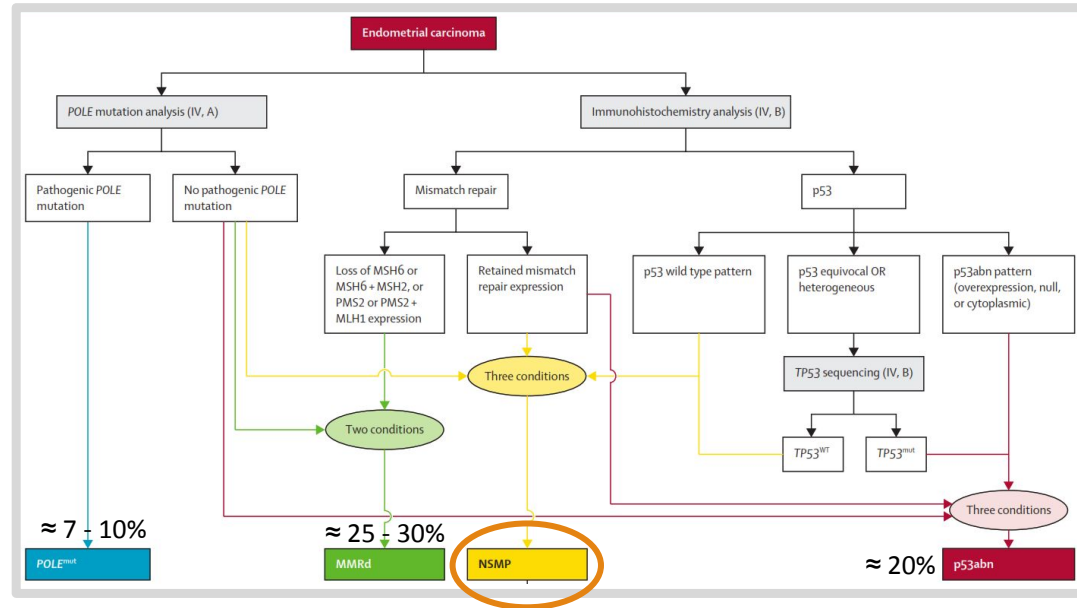
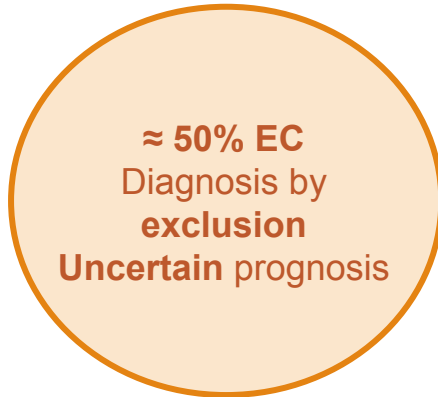
Gynecol Oncol. 1983 Feb;15(1):10-7. doi: 10.1016/0090-8258(83)90111-7

Nature 497, 67–73 (2013). <https://doi.org/10.1038/nature12113>

Endometrial cancer: the molecular era

ESGO-ESTRO-ESP guidelines for the management of patients with endometrial carcinoma: update 2025

Nicole Concin, Xavier Matias-Guiu, David Cibula, Nicoletta Colombo, Carlen I. Creutzberg, Jonathan Ledermann, Mansoor Raza Mirza, Ignace Vergote, Nadeem R Abu-Rustum, Tjalling Bosse, Cyrus Chargari, Sophie Espenel, Anna Fagotti, Christina Fotopoulou, Sonia Gattus, Antonio González-Martín, Sigurd Lax, Bar Levy, Domenica Lorusso, Gabriella Macchia, Christian Marth, Philippe Morice, Ana Oaknin, Maria Rosaria Raspollini, Richard Schwameis, Jalid Sehouli, Alina Sturdza, Alexandra Taylor, Anneke Westermann, Pauline Wimberger, François Planchamp, Remi A Nout

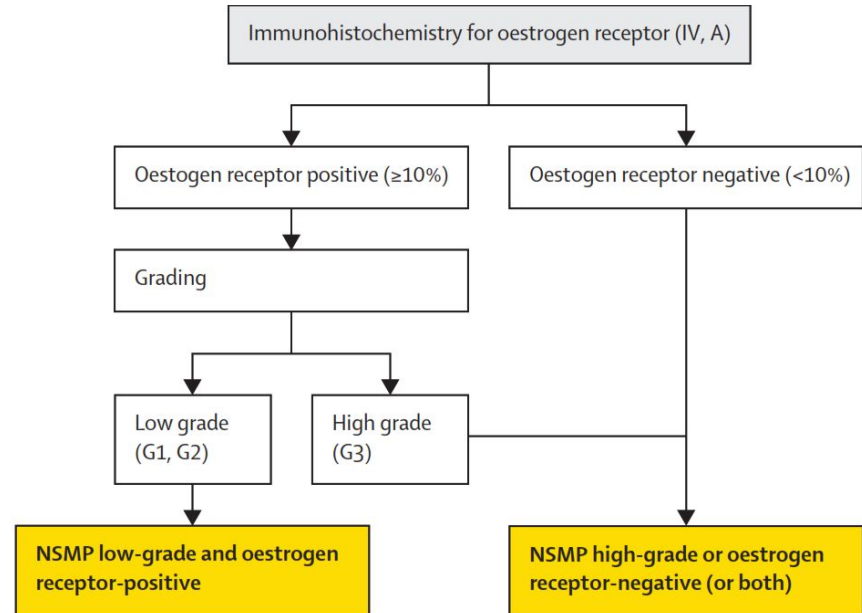


Algorithm for assessment of molecular classification of endometrial carcinoma

Endometrial cancer: the molecular era

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Algorithm for assessment of molecular classification of endometrial carcinoma

Endometrial cancer: the molecular era

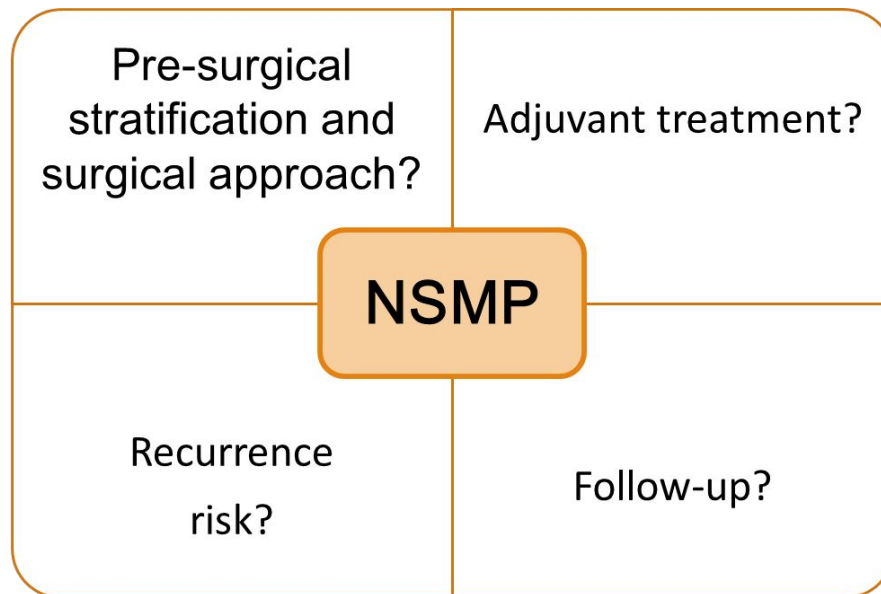
FIGO staging of endometrial cancer: 2023

Jonathan S. Berek¹ | Xavier Matias-Guiu² | Carien Creutzberg³ | Christina Fotopoulou⁴ | David Gaffney⁵ | Sean Kehoe⁶ | Kristina Lindemann⁷ | David Mutch⁸ | Nicole Concin^{9,10} | Endometrial Cancer Staging Subcommittee, FIGO Women's Cancer Committee

2023 FIGO staging*			Molecular classification†		NSMP		p53abn
			POLE***	MMRd	Low-grade ade Rc Es +	High-grade ade Rc Es -	
I	Confined to the uterine corpus						
IA	IA1	Low-grade endometrioid, confined to polyp or endometrium (no myoinvasion)	IAm POLE***			†	IIcm p53abn
	IA2	Low-grade endometrioid, myoinvasion <50%, no or focal lymphovascular space invasion	IAm POLE***			†	IIcm p53abn
	IA3	Low-grade endometrioid carcinoma of the endometrium and ovary§				†	
IB		Low-grade endometrioid, myoinvasion ≥50%, no or focal lymphovascular space invasion	IAm POLE***			†	IIcm p53abn
IC		High-grade histologies¶, limited to polyp or endometrium	IAm POLE***		NA		
II	Confined to the uterus						
IIA		Low-grade endometrioid, invasion of the cervical stroma	IAm POLE***			†	IIcm p53abn
IIB		Low-grade endometrioid, substantial lymphovascular space invasion	IAm POLE***			†	IIcm p53abn
IIC		High-grade histologies¶, myoinvasion	IAm POLE***	Myoinvasion <50%, no or focal lymphovascular space invasion	NA		IIcm p53abn
			IAm POLE***	Myoinvasion ≥50%, no or focal lymphovascular space invasion			
			IAm POLE***	Cervical stromal invasion, no or focal lymphovascular space invasion			
			IAm POLE***	Substantial lymphovascular space invasion			
III	Local spread, regional spread, or both						
IIIA	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	IIIB1	Metastasis or direct spread to the vagina, parametria, or both					
	IIIB2	Metastasis to the pelvic peritoneum					
IIIC	IIIC1	Pelvic lymph node metastasis					
	IIIC1i	Micrometastasis					
	IIIC1ii	Macrometastasis					
	IIIC2	Para-aortic lymph node metastasis (up to renal vessels)					
	IIIC2i	Micrometastasis					
	IIIC2ii	Micrometastasis					



Why We Need a Prognostic Tool for NSMP





Our Proposal: Developing a Prognostic Model

We aim to improve risk stratification for NSMP endometrial cancer
through a robust and validated prognostic model

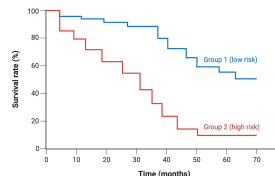


Developing a Prognostic Model:

Clinico – pathological and Molecular Tool

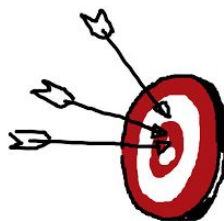
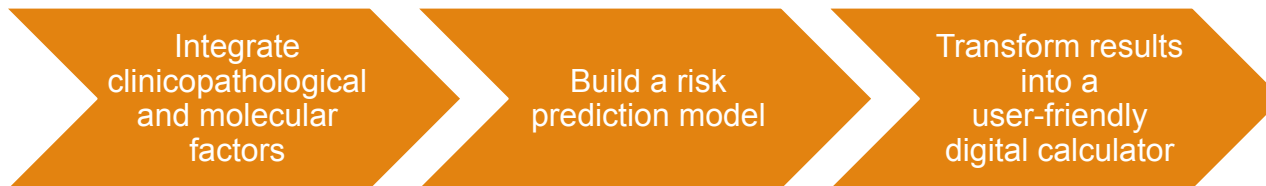


Kaplan-Meier Survival Curve



Developing a Prognostic Model:

Clinico – pathological and Molecular Tool



- Support personalized treatment decisions
- Improve accuracy of risk stratification
- Provide a practical tool for clinicians



Study Design and Potential Digital Health Integration

Study design

- Retrospective observational cohort study
- Development cohort: N≈150
- Validation: internal (testing the model) + external (multicenter cohort)
- Outcomes: recurrence-free survival, overall survival

Digital Health

- Goal: translate the model into a practical tool
- Potential forms: web-based calculator, Mobile interface, Integration into clinical workflow

Variables of interest

- **Fecha nacimiento**
- **Edad**
- **INC**
- **Fecha diagnóstico (AP)**
- **Tipo histológico**
- **Grado**
- **Infiltración miometrial**
- **Metástasis a distancia**
- **Riesgo preIQ ?? Estadíaje preIQ ??**
- **Tratamiento neoadyuvante**
- **Tratamiento 1º quirúrgico**
- **RSR**
- **Tipo histológico definitivo**
- **Grado histológico**
- **Tamaño tumoral**
- **Afectación linfvascular**
- **AP centinela pélvico**
- **AP ganglios pélvicos**
- **AP ganglios paraórticos**
- **Receptores Estrogenos**
- **Receptores Progesterona**
- **Estudio genético**
- **Estadio quirúrgico FIGO 2018 / 2023**
- **Grupo de riesgo definitivo (???)**
- **Tributaria a radioterapia / braquiterapia / sistémico**
- **Fecha última visita**
- **Recidiva**
- **Estado actual paciente**
- **Causa muerte**
- **Fecha muerte**
- **Libre enfermedad**
- **Numero recidiva**
- **Fecha recidiva**
- **Diagnóstico, numero, lugar**
- **Tratamiento recibido para la recidiva**
- **Tratamiento quirúrgico recidiva**
- **Resección macroscópica completa**
- **Tratamiento RT / sistémico**

Expected Impact: Towards Personalized Care

More personalized
treatment decisions



Clinical
impact

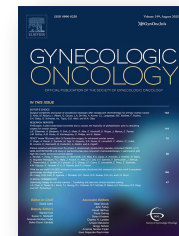
Scientific
impact

Technologic
al impact

Digital tool
ready for clinical
use



First NSMP-specific prognostic
model externally validated





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Thank you for your attention
