www.sgo.or.kr

부인암 분자진단 실무와 유전상담의 실제

Hyung Joon Yoon, MD
Pusan National University Hospital

Molecular Testing Is Not a Single Decision

PATIENT JOURNEY

ONE PATIENT'S TREATMENT

A FAMILY'S PREVENTION

1 Diagnosis — What?

2 Initial treatment — When?

3 Recurrence — Re-test?

4 Germline result

5 Family — Who else?

A growing biomarkers : BRCA · HRD · MMR · PD-L1 · HER2 · FRα · p53 · ...

The right test, on the right specimen, at the right time.

Overview

GUIDELINES

Ovarian cancer

BRCA + HRD at diagnosis

MMR / PD-L1 / HER2 / FRα

Germline test → Family counseling

Endometrial cancer

Molecular classification for all EC

MMR → Lynch screening

Cervical cancer

Selective, treatment-directed testing

PD-L1/MMR/HER2 at recurrent / metastatic disease

Guideline → **Test** → **Result** → **Action** — **Family**

Where care is often lost !

ESMO 2023 · ESGO–ESTRO–ESP 2025 (Concin N, et al. Lancet Oncol 2025) · ASCO (Konstantinopoulos PA, et al. J Clin Oncol 2020)

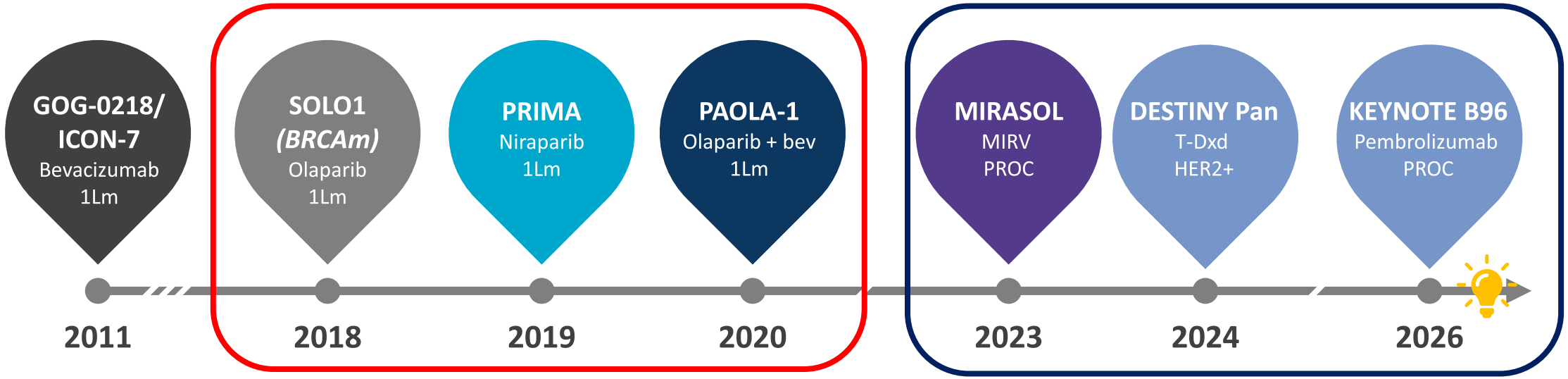
Five Questions for Everyday Practice

01	02	03	04	05
WHO?	WHEN?	WHAT?	RE-TEST?	FAMILY?

Ovarian → Endometrial → Cervical → Genetic counseling

PART 1. Ovarian cancer

Ovarian Cancer: What Should Be Tested at Diagnosis?



BRCA / HRD

A growing biomarkers : PD-L1 · HER2 · FRα

PARP inhibitor era

Biomarkers Change First-Line Maintenance

PART I · OVARIAN CANCER — PARP inhibitors

BRCA-mutated

SOLO-1

HR

0.30

HRD-positive

PAOLA-1

HR

0.33

HRD-positive

PRIMA

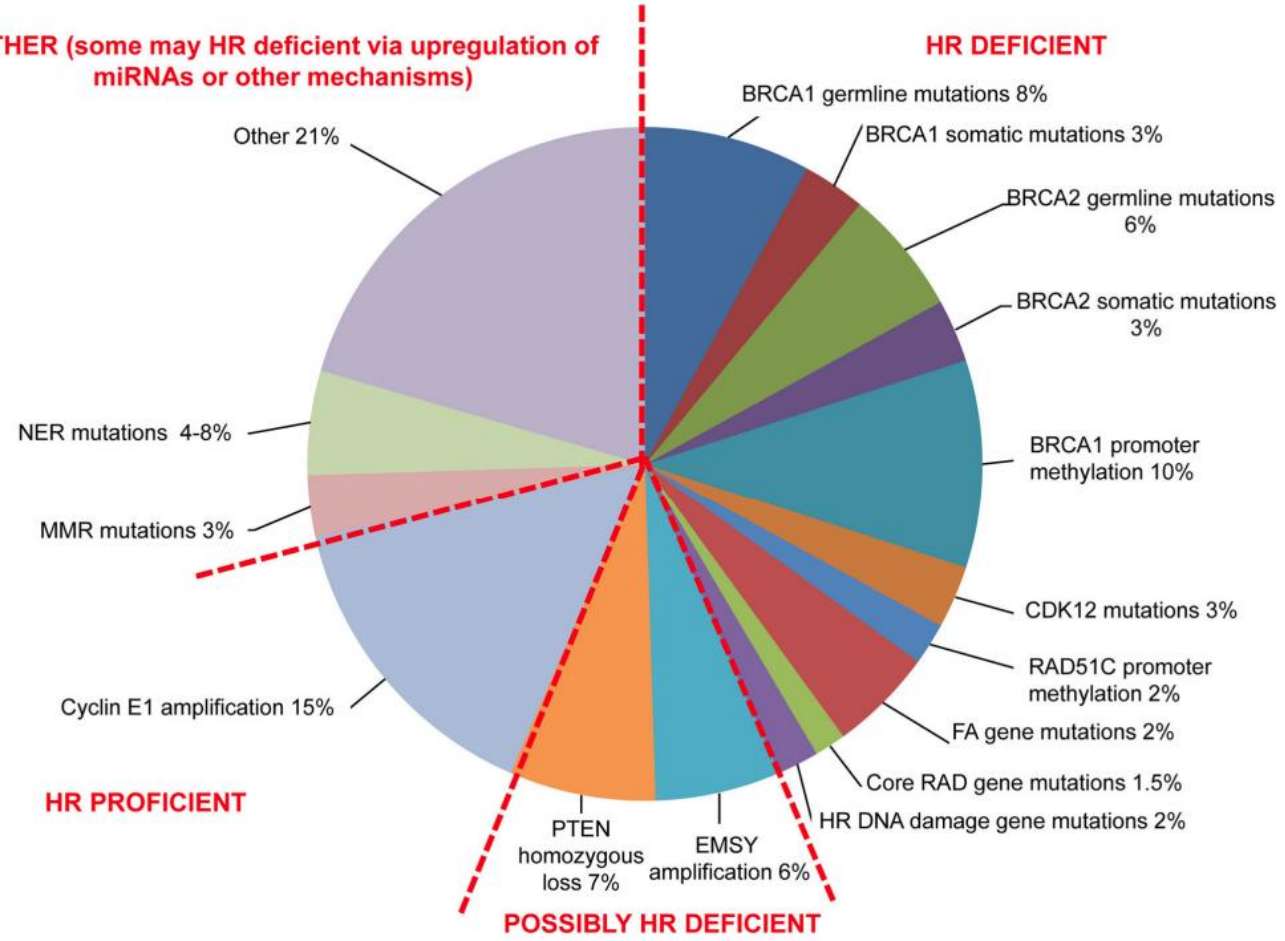
HR

0.43

The purpose of testing is not classification — it is a treatment decision.

Biomarkers Change First-Line Maintenance

PART I · OVARIAN CANCER — HRR state



- **Germline BRCA 1/2 mutation : 14%**
- **Somatic BRCA 1/2 mutation : 6%**
- **HRD : Approximate 50%**

1. Panagiotis A Konstantinopoulos et al. Cancer Discov. 2015 Nov;5(11):1137-54

Ovarian Ca

PART I · OVARIAN

PLEASE NOTE that use of this NCCN Content is governed by the Fr
Print

NCCN National Comprehensive Cancer Network®

NCC
Ovar
Perit

General

- The complete histologic classification fr
  NCCN Guidelines (WHO Histologic Clas
  pathology manual is also a useful resou
- Most ovarian cancers, including the LC
  analysis of a biopsy or surgical specime
  (FNA) should be avoided for diagnosis
  with presumed early-stage disease to p
  spilling malignant cells into the peritone
  be necessary in patients with bulky dise
  primary debulking.[2,3]
- Both primary peritoneal and fallopian tul
  postoperatively (if there is no major invc
  preoperatively (if there is a biopsy and t
  bilateral salpingo-oophorectomy). Prima
  cancers are treated in the same manne
- The College of American Pathologists (
  pathology reports.[4]
- Pathologic assessment should include:
  - Elements from CAP protocol[4]:
    - Tumor site(s) (eg, ovary, fallopian tu
    - Tumor size(s)
    - Other tissue/organ involvement
    - Ovarian/fallopian tumors: surface in
      determine), specimen integrity (cap
      fragmented)
    - Histologic type and grade
    - Extension and/or implants (if sampl
    - Cytology: peritoneal or ascitic fluid
    - Lymph nodes: number and location
      largest metastatic deposits
    - STIC, endometriosis (particularly if
      clear cell carcinoma), and/or endos
    - Staging information (FIGO and TNM

STAGE II, III, IV[w]
POST PRIMARY THERAPY

CR[v]/PR

- **Germline or somatic *BRCA1/2* pathogenic/likely pathogenic (P/LP) variants**
- ***BRCA1/2* wild-type or unknown and HR Deficient**
- ***BRCA1/2* wild-type or unknown and HR Proficient or HR unknown**

MAINTENANCE THERAPY[e,k,x]

Germline or somatic *BRCA1/2* pathogenic/likely pathogenic (P/LP) variants

If bevacizumab not used during primary chemotherapy:
- **Olaparib (category 1) or Niraparib (category 1) or Rucaparib**

or
- **Observe for select stage II disease with CR[x]**

If bevacizumab used during primary chemotherapy:
- **Olaparib + Bevacizumab (category 1)**

or
- **Niraparib + Bevacizumab (if unable to tolerate Olaparib)**

or
- **Olaparib[y] or Niraparib[y] or Rucaparib[y]**

***BRCA1/2* wild-type or unknown and HR Deficient**

If bevacizumab not used during primary chemotherapy:
- **Olaparib or Niraparib or Rucaparib**

or
- **Observe (if CR)**

If bevacizumab used during primary chemotherapy:
- **Olaparib + Bevacizumab (category 1)**

or
- **Niraparib + Bevacizumab (if unable to tolerate Olaparib)**

or
- **Bevacizumab**

or
- **Olaparib**

***BRCA1/2* wild-type or unknown and HR Proficient or HR unknown**

If bevacizumab not used during primary chemotherapy:
- **Observe (if CR)**

or
- **Therapy for Persistent Disease or Recurrence (OV-7)**

If bevacizumab used during primary chemotherapy:
- **Bevacizumab**

…on of molecular
…nform use of
…**ve demonstrated**

NCCN guideline 2026 ver.4

Ovarian Cancer: What Should Be Tested at Diagnosis?

PART I · OVARIAN CANCER — ASCO 2020 · ESGO–ESMO–ESP 2023 · NCCN Guideline

Clinical setting	Test	Why?
All epithelial OC	Germline BRCA1/2 + other OC genes	Patient + Family
EOC without germline BRCA1/2 PV	Somatic tumor BRCA1/2	PARPi eligibility
Clear cell / endometrioid / mucinous	**Tumor dMMR**	Lynch / tumor-agnostic therapy
Newly diagnosed HG non-mucinous†	HRD / genomic instability test	1L maintenance

Germline BRCA 1/2 + **Somatic tumor BRCA 1/2** + HRD (+ MMR)

Konstantinopoulos PA, et al. J Clin Oncol. 2020;38:1222–1245 · Ledermann JA, et al. Ann Oncol. 2024 (ESGO–ESMO–ESP consensus)

Germline-First or Tumor-First?

PART I · OVARIAN CANCER — TESTING SEQUENCE

Germline-first

Patient + family immediately

↓

Tumor testing if germline negative

or

Tumor-first

Captures somatic + germline candidates

↓

Reflex germline confirmation

The best pathway is the one that minimizes missed testing.

HRD Test on Diagnosis

FUTURE ONCOLOGY
2025, VOL. 21, NO. 3, 341–347
https://doi.org/10.1080/14796694.2024.2433412

Taylor & Francis
Taylor & Francis Group

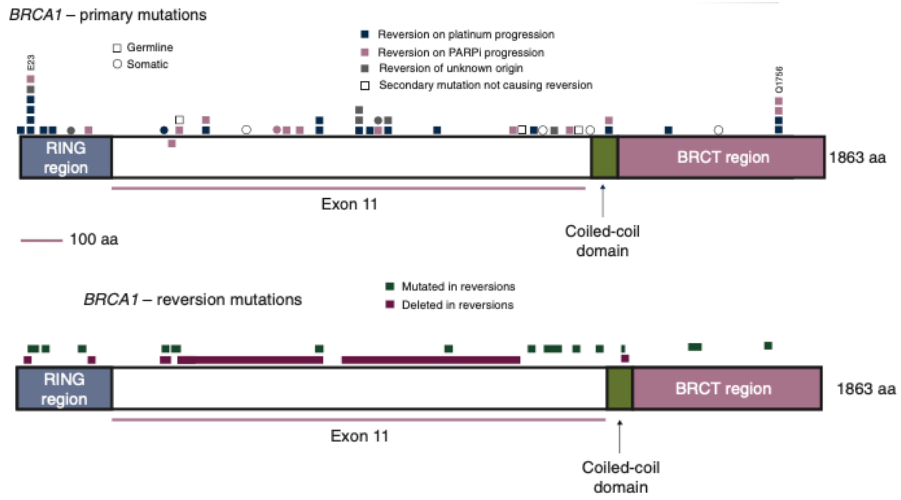
RESEARCH ARTICLE

OPEN ACCESS Check for updates

Homologous recombination deficiency testing in patients with high grade ovarian cancer: factors influencing test success

Ashton Hunt [a*], Daria Ditri [a,b*], Ankit Chadha[a*], Georgina Keogh[a], Jack Thompson[a], Will Loughborough[c], Iain McNeish[a,b], Jonathan Krell[a,b], Jacqueline McDermott[a,b], Laura Tookman[a] and Sadaf Ghaem-Maghami [a,b]

[a]Department of Gynaecological Oncology, Imperial College Healthcare NHS Trust, London, UK; [b]Department of Surgery and Cancer, Imperial College London, London, UK; [c]Department of Radiology, Royal Hospitals Bath, Bath, UK



Ashton et.al. FUTURE ONCOLOGY 2025, VOL. 21, NO. 3, 341–347

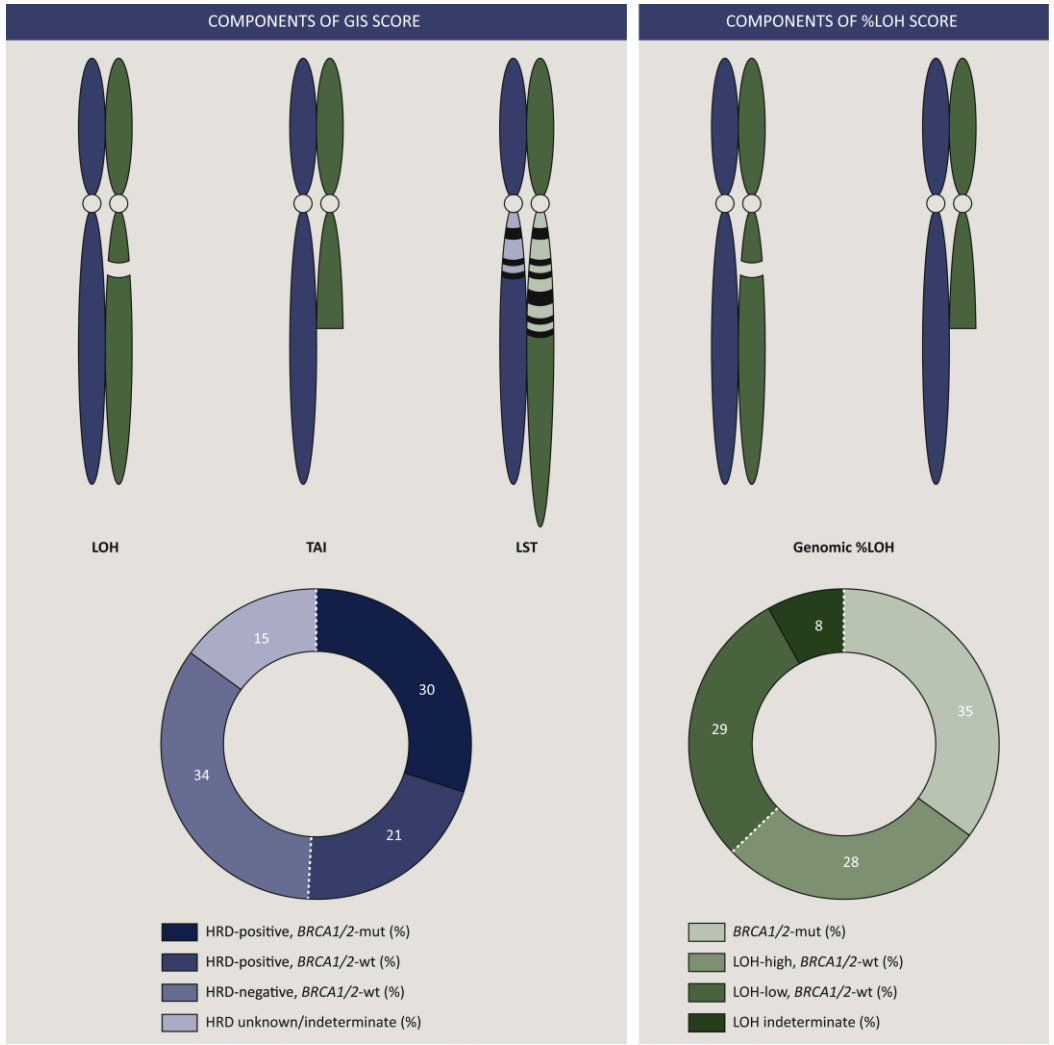
Tobalina et.al. ANNALS OF ONCOLOGY 2020

Article highlights

- Maintenance treatment with poly ADP-ribose polymerase (PARP) inhibitors alone or in combination with bevacizumab following first-line chemotherapy is now the standard of care for patients with advanced ovarian cancer.
- Access to a combination of PARP inhibitors and bevacizumab, and assessing the magnitude of benefit from PARP inhibitors, is guided by genomic testing for *BRCA* alterations and homologous recombination deficiency (HRD).
- In this paper, we assess the factors that influence a successful HRD test result using real-world data.
- We show that only 76.8% of samples taken receive a successful result from HRD testing.
- Factors associated with a successful HRD test include taking a sample prior to chemotherapy rather than after and, if the sample is obtained by biopsy, using a larger 16-gauge needle.
- Biopsy taken at surgery prior to chemotherapy carried the highest chance of success.
- We showed that there can be significant delays in getting results from HRD testing: only 27% of the tests returned results within 21 days.
- We conclude that pathways to obtaining timely genomic results need to be developed and existing pathways audited.
- As genomic testing is embedded into the care of all patients with advanced ovarian cancer, our results have direct implications for clinical care.

HRD Test on Diagnosis

PART I · OVARIAN CANCER — HRD test

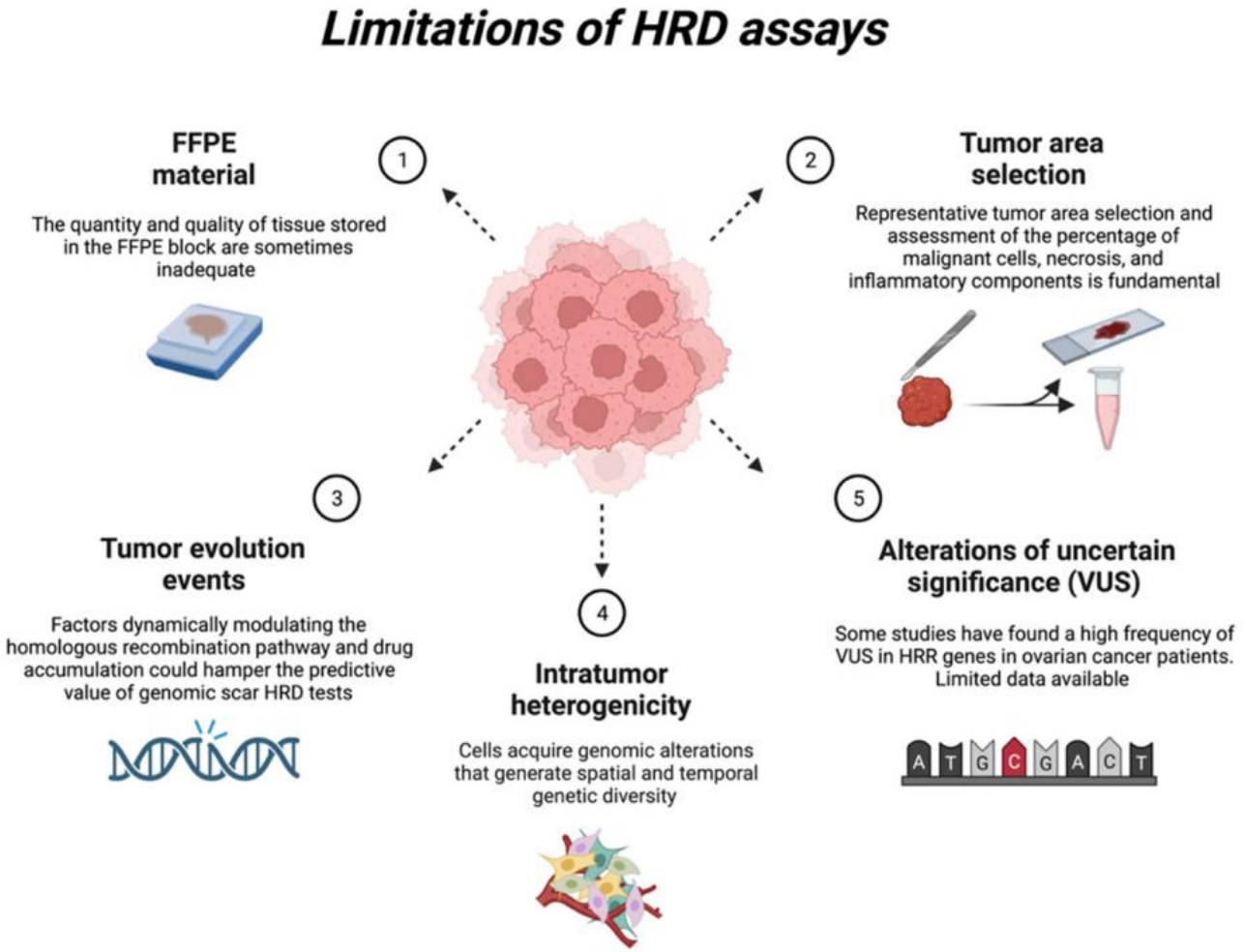


'Genomic scars' serve as an indirect measure of HRD as they represent a permanent historical footprint of genomic changes induced by DNA repair deficiency, irrespective of the underlying etiology

N. Y. L. Ngoi and D. S. P. Tan. ESMO OPEN science for optimal cancer care. 2021 Jun;6(3);100144 DOI:https://doi.org/10.1016/j.esmoop.2021.100144

HRD Test on Diagnosis

PART I · OVARIAN CANCER — HRD test



Tobalina et.al. ANNALS OF ONCOLOGY 2020

HRD Test on Diagnosis : Time and Tissue Are Both Lost

PART I · OVARIAN CANCER — REAL-WORLD HRD TESTING

37 days

Median HRD turnaround time

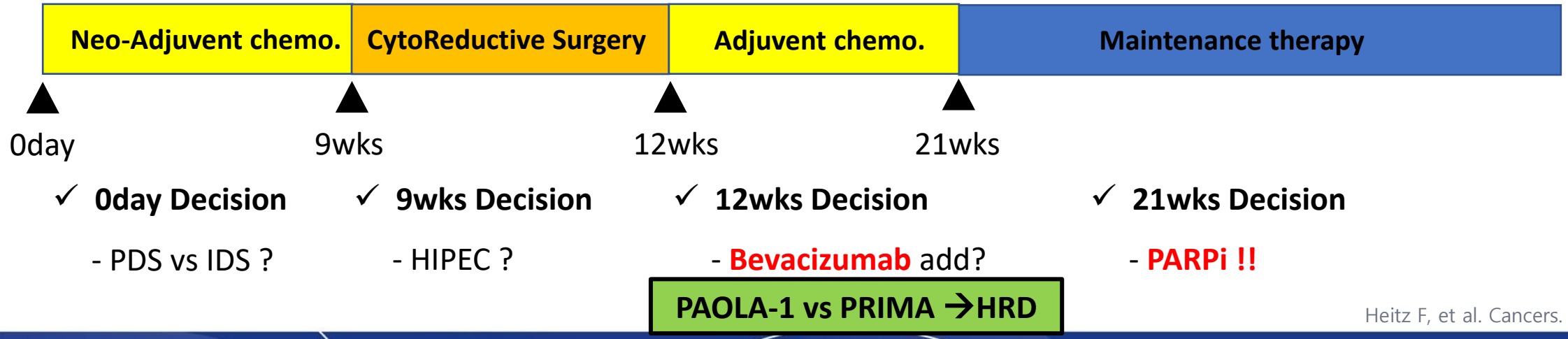
Range 8–97 days

27 / 190

tests failed (~14%)

because of insufficient tumor yield

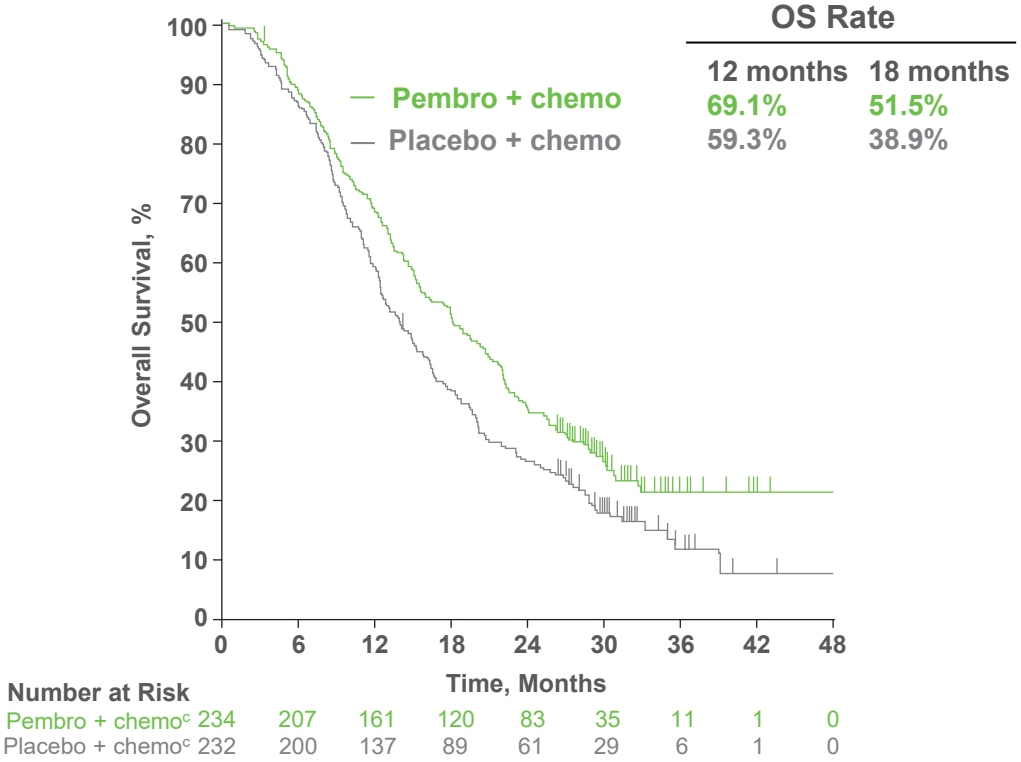
IDS setting



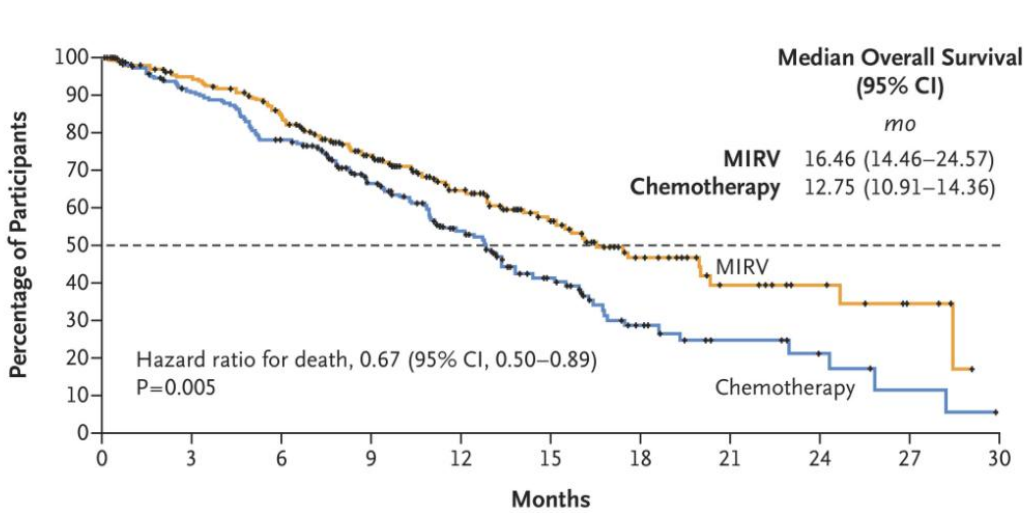
Heitz F, et al. Cancers. 2023;15:818.

Biomarker on Diagnosis : Growing biomarker

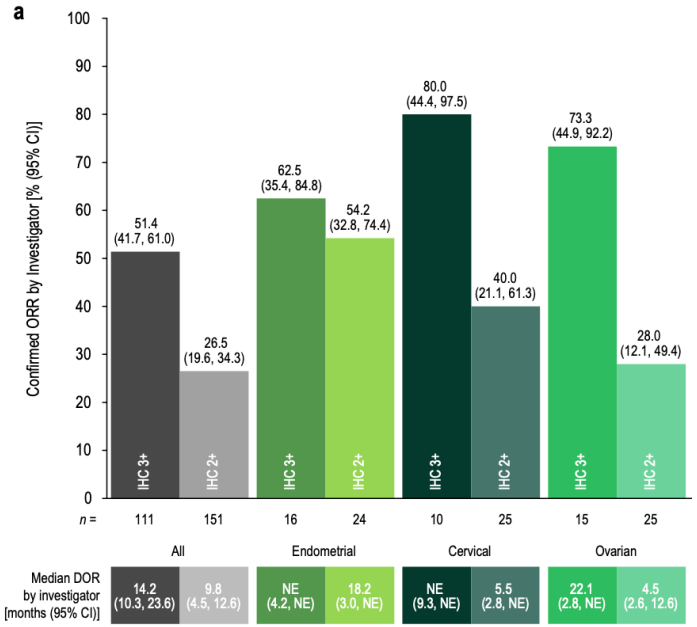
PART I · OVARIAN CANCER — PD-L1 / FRα / HER2



KEYNOTE-B96



MIRASOL



DESTINY Pan Tumor 02

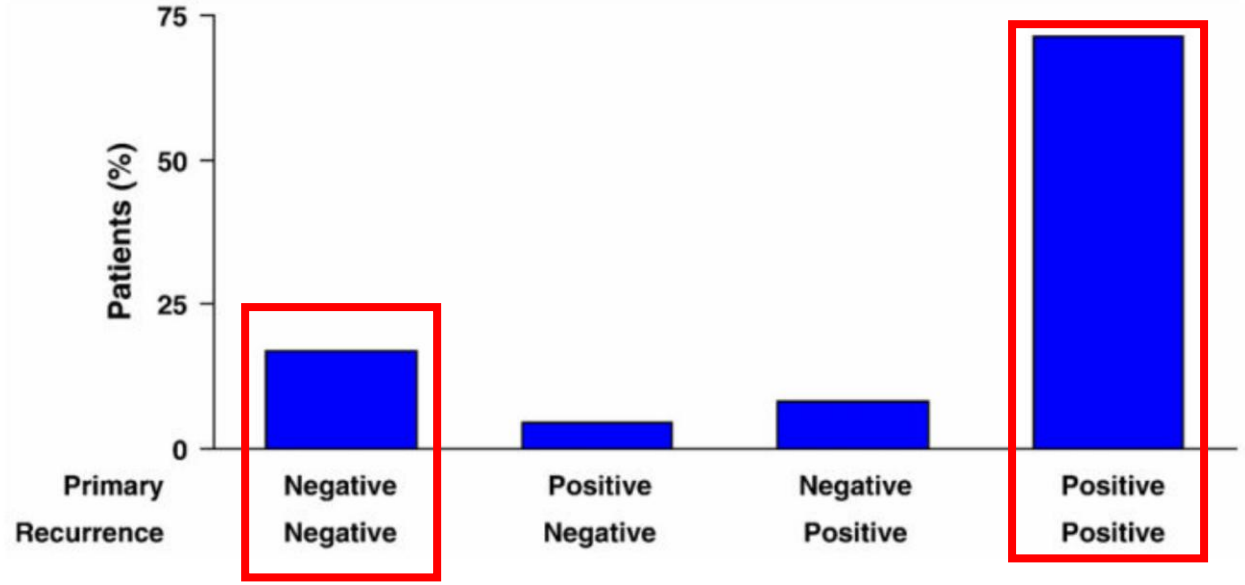
Biomarker on Diagnosis : Growing biomarker

PART I · OVARIAN CANCER — Folate Receptor alpha

Published in final edited form as:
Gynecol Oncol. 2008 March ; 108(3): 619–626. doi:10.1016/j.ygyno.2007.11.020.

Folate receptor alpha as a tumor target in epithelial ovarian cancer

Kimberly R. Kalli[a,*], **Ann L. Oberg**[b], **Gary L. Keeney**[c], **Teresa J.H. Christianson**[b], **Philip S. Low**[d], **Keith L. Knutson**[e], and **Lynn C. Hartmann**[a]



Validated IHC assay

≥75% viable tumor cells with moderate/strong (≥2+) membrane staining

MIRV

MIRASOL · OS
HR 0.67

Primary–recurrent concordance
87.5% (21/24)

→ **Routine serial retesting not established**

Moore KN, et al. N Engl J Med. 2023 (MIRASOL) · Kalli KR, et al. Gynecol Oncol. 2008

New Targets, Different Retesting Logic

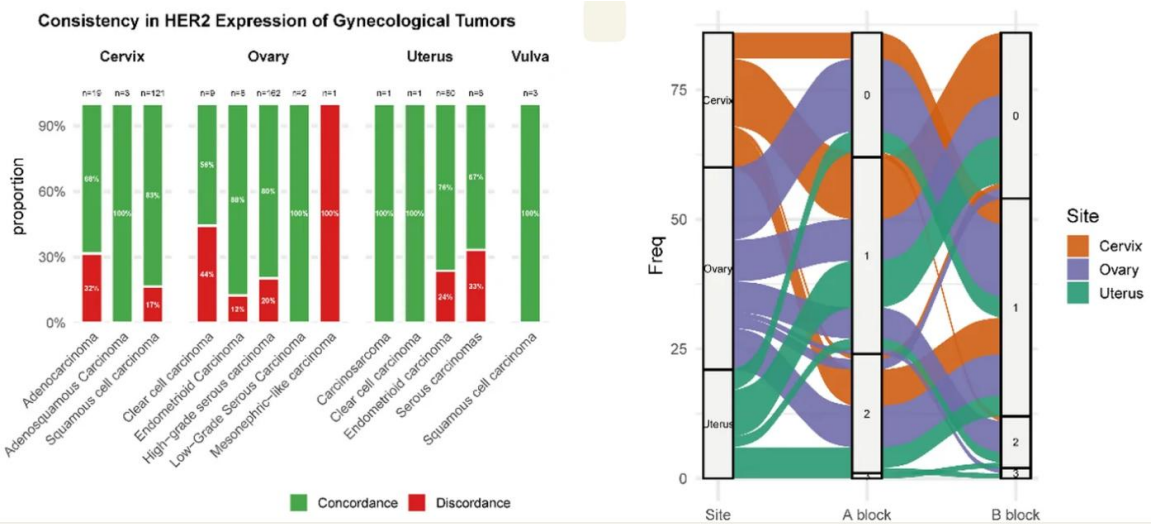
PART I · OVARIAN CANCER — HER2

Journal of Translational Medicine BMC

J Transl Med. 2026 Jul 3;24:1219. doi: 10.1186/s12967-026-08546-8

Dual-block HER2 assessment reveals clinically relevant intratumoral heterogeneity in gynecologic cancers: a single-center landscape analysis

Xiaonan Zhou [1,#], Jing Gao [1,2,#], Ling Cui [1], Hui Li [1], Huijuan Ge [1], Lin Yu [1], Jiaojie Lv [1], Ke Zuo [1], Tian Tian [1], Yue Wang [1], Hui Sun [1], Yufan Cheng [1], Rui Bi [1,✉]



Does Specimen Type Have an Impact on HER2 Status in Endometrial Serous Carcinoma? Discordant HER2 Status of Paired Endometrial Biopsy and Hysterectomy Specimens in the Presence of Frequent Intratumoral Heterogeneity

Douglas Rottmann, Hisham Assem, Nana Matsumoto, Serena Wong, Pei Hui, Natalia Buza

Authors and Affiliations >

International Journal of Gynecological Pathology 40(3):p 263-271, May 2021. | ***DOI:*** 10.1097/PGP.0000000000000690

EM Bx vs. Uterus

- Concordance : 84% (31/37)
- HER2 identical status : 65% (26/40)
- False negative rate : 15.4% - 26.7%

Heterogenous / Dynamic biomarker!
→ Dual-block & Retest needed !

Biomarker on Diagnosis : Growing biomarker

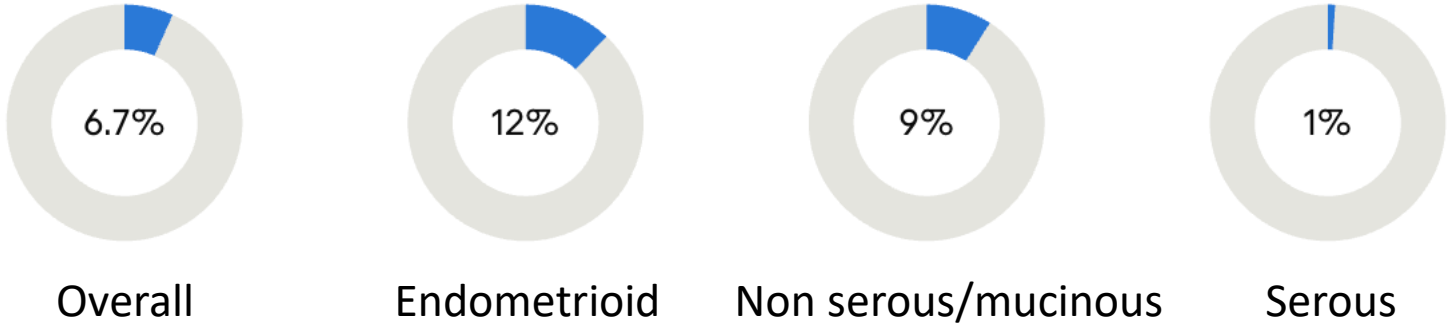
PART I · OVARIAN CANCER — PD-L1, MMR

KN-158 : ORR 33.3% (5/15) → **CR 3**

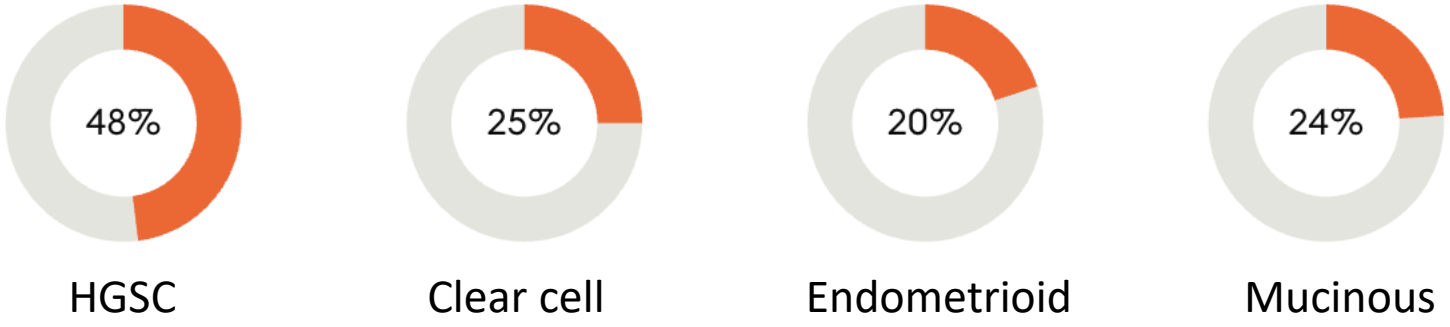
KN-028 : ORR 11.5% (3/26) → **CR 1**

	2L	3L
Ovarian cancer	**KN-B96** Pem+Paclitaxel± BEV **(CPS≥1)**	**KN-028** Pem mono **(CPS≥1)**
	KN-158 -Pem mono **(dMMR / MSI-H)**	

dMMR ratio in OC [1,2]



PD-L1 (CPS≥1)ratio in OC [3]



Primary vs. recur/Meta concordance:

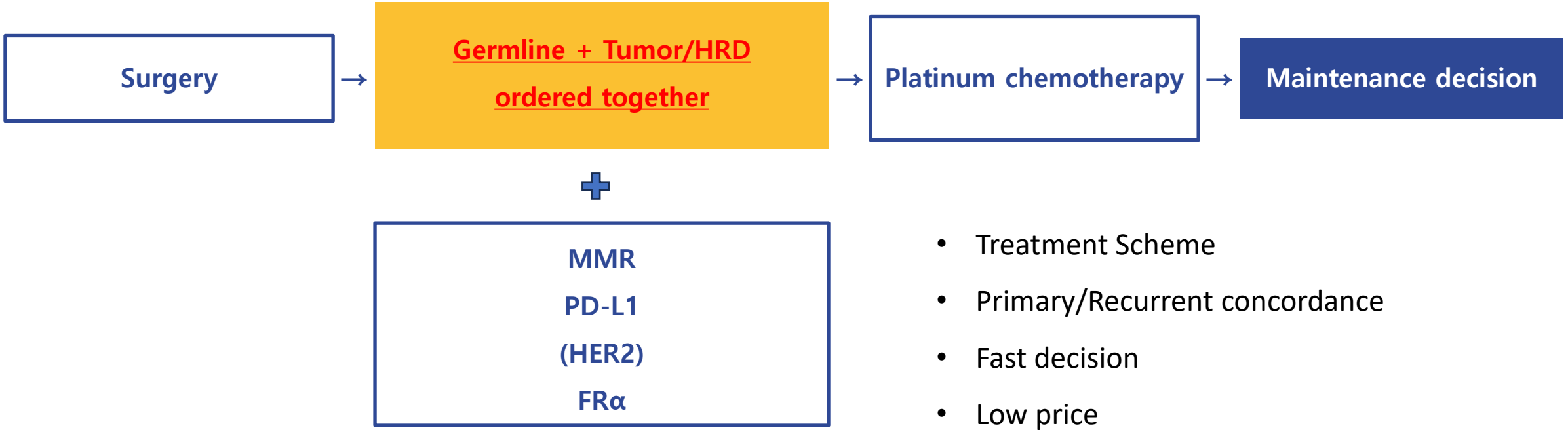
MMR IHC 74–96%, PD-L1 40–67%

1. *Atwal A et al. Int. J. Cancer. 2022; 151(9): 1626-1639.*
2. *Mitric et al. Gynecology oncol. Volume 170, March 2023, Pages 133-142*
3. *American Journal of Surgical Pathology 44(8):p 1050-1060, August 2020.*

Biomarker on Diagnosis

PART I · OVARIAN CANCER — RECOMMENDATION

Sequential testing creates avoidable delay.



- Treatment Scheme
- Primary/Recurrent concordance
- Fast decision
- Low price

Ovarian Cancer: When Should I Test Again?

PART I · OVARIAN CANCER — RE-TESTING AT RECURRENCE

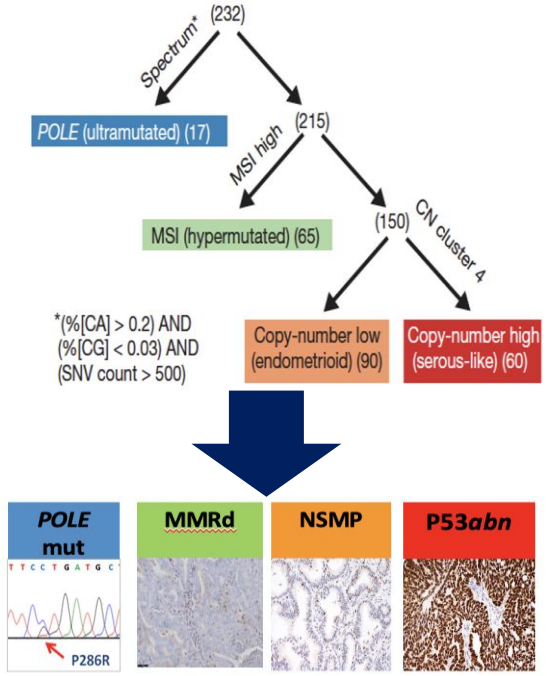
Biomarker	Repeat at recurrence?	Why? / evidence
HRD (genomic scar)	**Usually, no**	gLOH stable in paired samples (r^2 = 0.79)
Somatic NGS	**Selected cases**	BRCA / HRR reversion after Platinum based chemo.
FRα	**Yes**	Archival result usable; retest if prior negative / borderline
HER2	**Consider if treatment-relevant**	Heterogenous / Dynamic biomarker → T-DXd
MMR	**If not done at diagnosis**	ASCO Rec 1.2–1.3 · dMMR → ICI option
PD-L1 (CPS)	**Yes**	CPS ≥1 → pembrolizumab + paclitaxel ± bev
TMB	**Selected CGP only**	TMB-H ≥10 mut/Mb → pembrolizumab

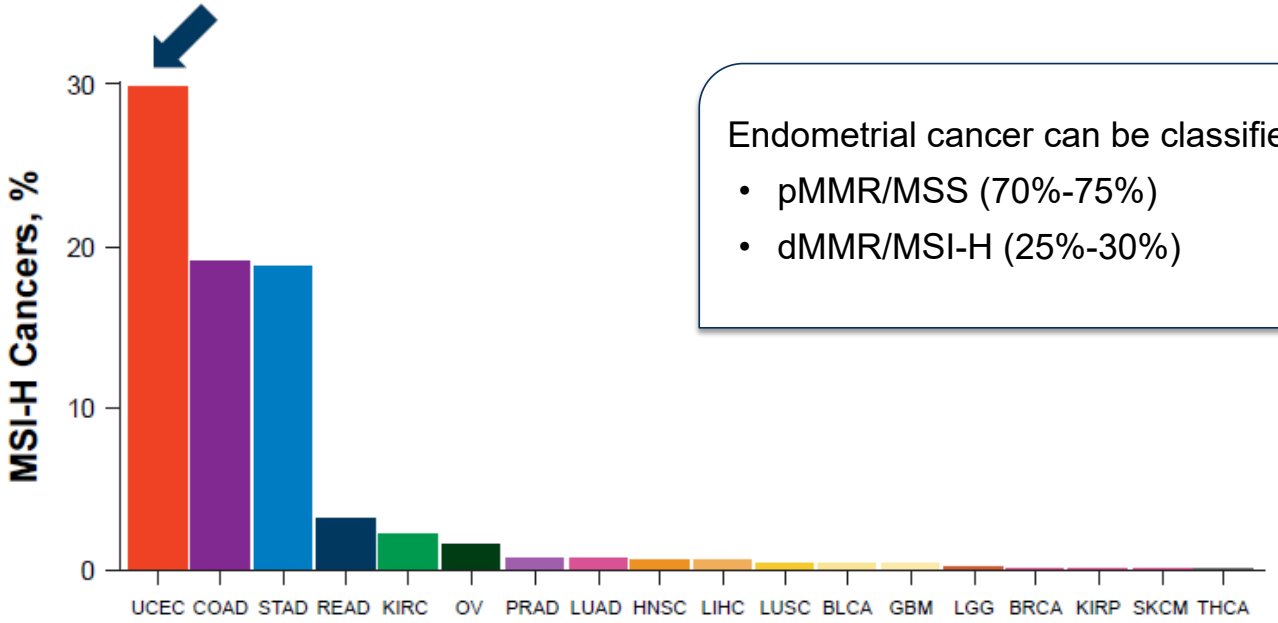
Repeat testing only when biology or treatment eligibility may have changed.

PART 2. Endometrial cancer

Molecular Classification

PART II · ENDOMETRIAL CANCER





Endometrial cancer can be classified as

- pMMR/MSS (70%-75%)
- dMMR/MSI-H (25%-30%)

DUO-E
RUBY Part 1
NRG-GY018
AtTEnd

dMMR

GOG-177

GOG-0209

1961
Progestin

2004
Doxorubicin, Cisplatin, Paclitaxel

2012
Carboplatin/Paclitaxel

2023–2024
Carboplatin/Paclitaxel + **Durvalumab** ± **Olaparib**
Carboplatin/Paclitaxel + **Dostarlimab**
Carboplatin/Paclitaxel + **Pembrolizumab**
Carboplatin/Paclitaxel + **Atezolizumab**

Do Not Wait for Hysterectomy

PART II · ENDOMETRIAL CANCER

Endometrial biopsy / curettage

↓ **immediately !**

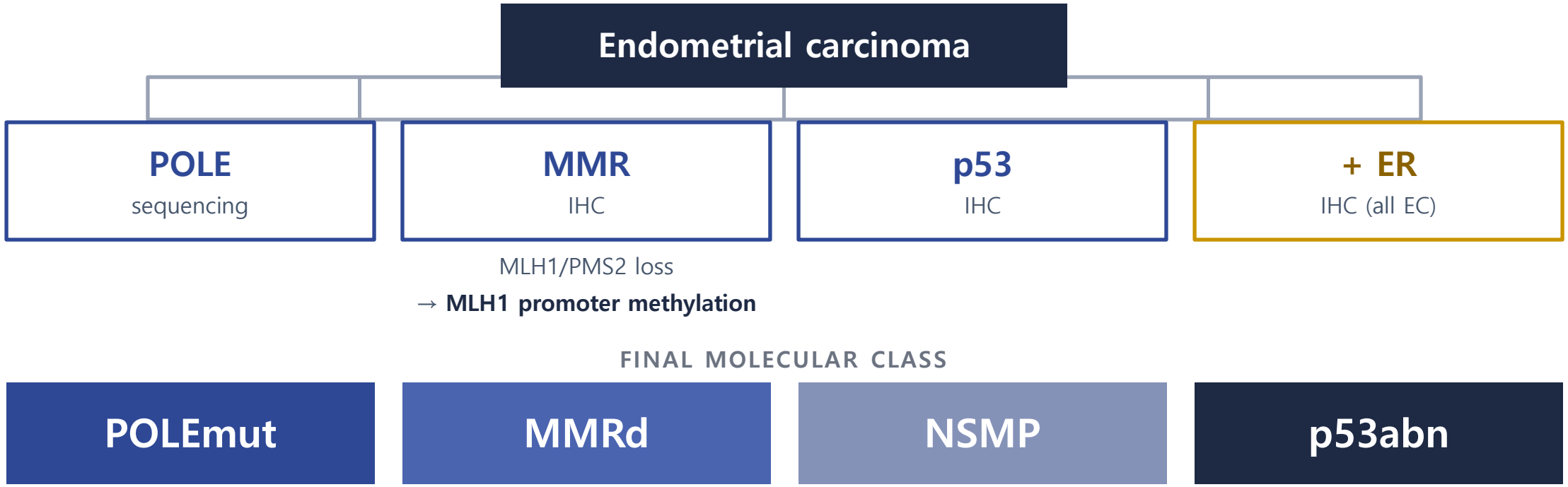
POLE	MMR	p53	ER

Molecular classification should start from the diagnostic specimen.

Concin N, et al. ESGO–ESTRO–ESP guidelines for endometrial carcinoma. Lancet Oncol. 2025;26:e423–e435. (all EC: IV, A · repeat on hysterectomy: IV, B)

A Practical Biopsy-Based Algorithm

PART II · ENDOMETRIAL CANCER — ESGO 2025



MULTIPLE CLASSIFIER RULE

POLE wins → MMRd wins over p53abn

Concin N, et al. Lancet Oncol. 2025;26:e423–e435.

MMR : Critical Biomarker

PART II · ENDOMETRIAL CANCER

STEP 1 — **MMR IHC**
MSH6 / PMS2 ± MSH2 / MLH1

↓

STEP 2 — **MSI-PCR**
If equivocal or heterogeneous staining

↓

STEP 3 — **MLH1 promoter methylation**
If MLH1/PMS2 loss

↓

STEP 4 — **Genetic counseling + germline testing**
If Lynch suspicion

2-antibody IHC approach
≈ 4-antibody approach

MLH1/PMS2 loss ≠ Lynch syndrome.
Methylation reflex first.

Concin N, et al. Lancet Oncol. 2025;26:e423–e435.

Growing Biomarker : HER2

PART II · ENDOMETRIAL CANCER

Advanced / recurrent p53abn EC

All serous carcinomas / carcinosarcomas

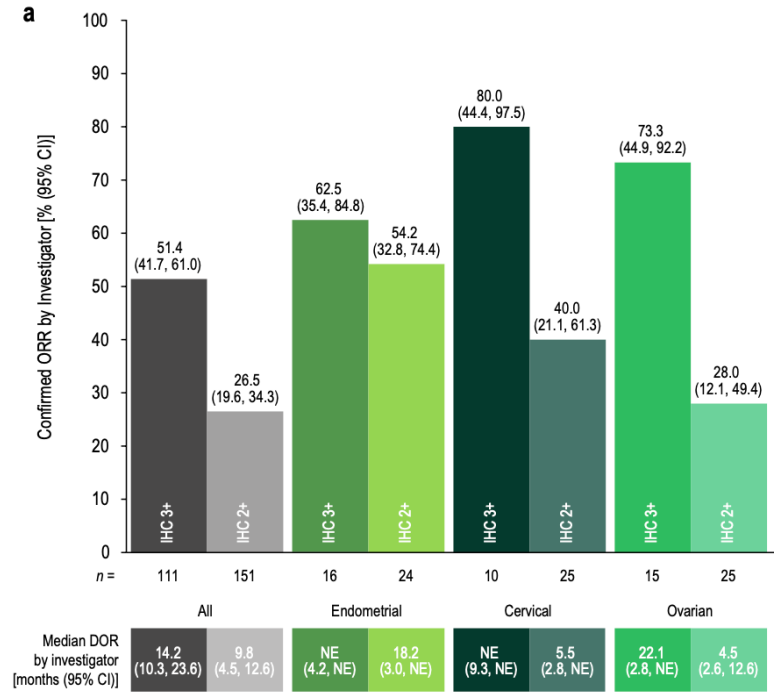
↓

HER2 IHC ("might be tested" · IV, C)

↓

0 – 1+	2+	3+
negative	→ Others : T-Dxd	→ Serous 1L: Trastzumab TC → Others : T-Dxd

Heterogenous / Dynamic biomarker : Dual block / Re-test



DESTINY Pan Tumor 02

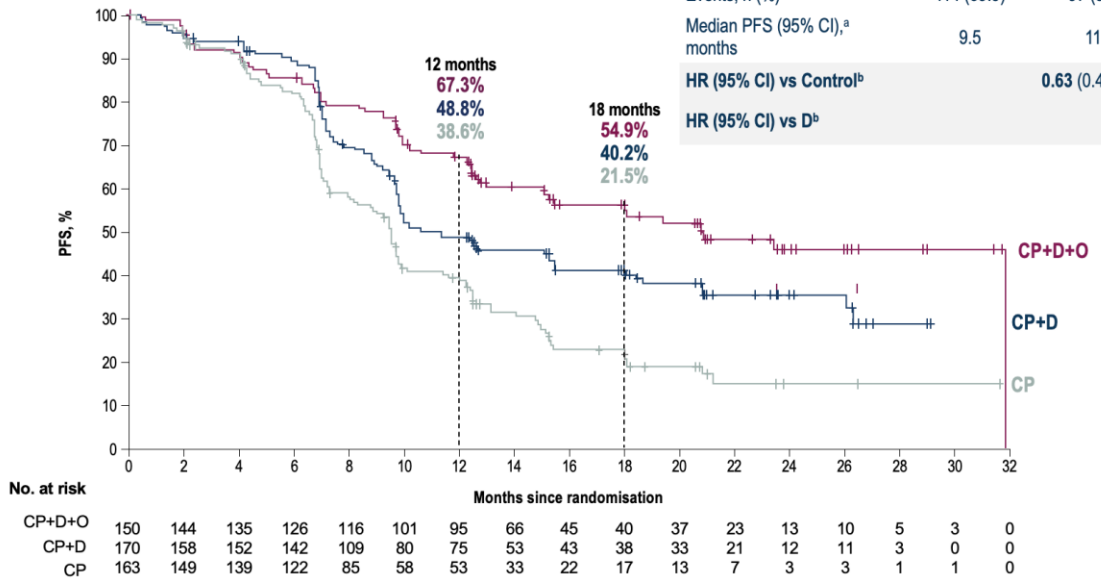
Concin N, et al. Lancet Oncol. 2025;26:e423–e435 (IV, C)

Growing Biomarker : PD-L1

PART II · ENDOMETRIAL CANCER

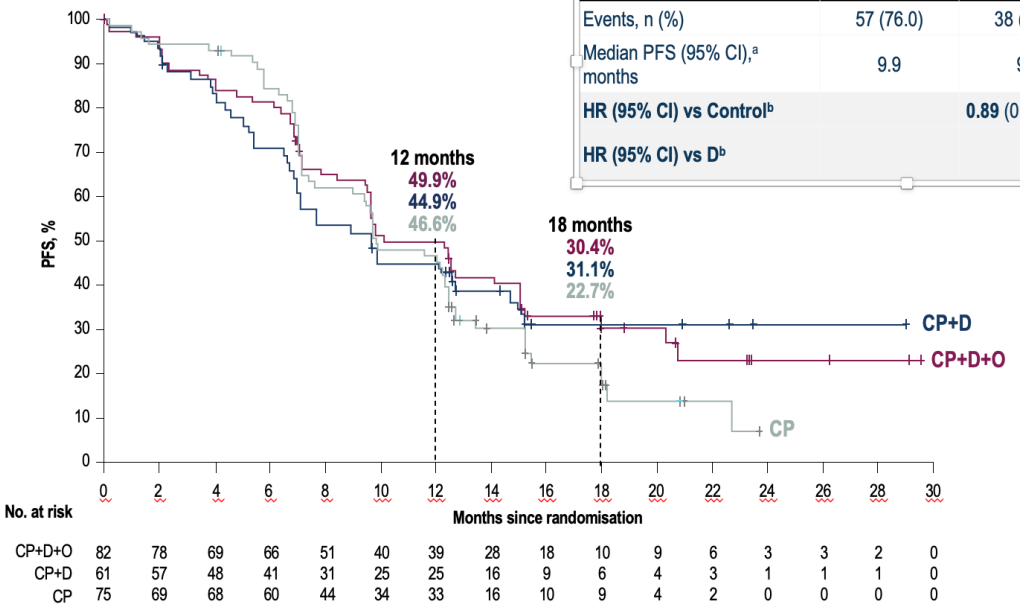
Prespecified exploratory analysis
PD-L1 positive (TAP>1%; 69% of population)

	CP N=163	CP+D N=170	CP+D+O N=150
Events, n (%)	114 (69.9)	97 (57.1)	68 (45.3)
Median PFS (95% CI),[a] months	9.5	11.3	20.8
HR (95% CI) vs Control[b]		**0.63** (0.48–0.83)	**0.42** (0.31–0.57)
HR (95% CI) vs D[b]			**0.67** (0.49–0.91)



Prespecified exploratory analysis
PD-L1 negative (TAP<1%; 31% of population)

	CP N=75	CP+D N=61	CP+D+O N=82
Events, n (%)	57 (76.0)	38 (62.3)	55 (67.1)
Median PFS (95% CI),[a] months	9.9	9.7	10.1
HR (95% CI) vs Control[b]		**0.89** (0.59–1.34)	**0.80** (0.55–1.16)
HR (95% CI) vs D[b]			**0.93** (0.61–1.41)



Concin N, et al. Lancet Oncol. 2025;26:e423–e435 (IV, C)

Endometrial Cancer: What Should Be Re-tested at Recurrence?

PART II · ENDOMETRIAL CANCER — RE-TESTING

Biomarker	Repeat?	Evidence / rationale
MMR	Consider	ESGO 2025 IV-B
HER2	Consider / test if treatment-relevant	Advanced / recurrent setting
ER	Reasonable if endocrine therapy considered	Treatment relevance
p53	Usually no	Molecular class generally established
POLE	Usually no	No established value of serial testing
PD-L1	No routine role	MMR is more clinically relevant
TMB	Selected cases only	Tumor-agnostic context

If feasible, repeat MMR on relapsed tissue.

ESGO 2025 · IV-B

Concin N, et al. Lancet Oncol. 2025;26:e423–e435 · Guzeloz et al. Medicina 2026 (small retrospective cohort)

PART 3. Cervical cancer

Cervical Cancer: A Different Molecular Paradigm

PART III · CERVICAL CANCER

AT DIAGNOSIS

Histology first

HPV-associated vs **HPV-independent**

Gastric · clear cell · mesonephric …

WHO 2020 / IECC · p16/HPV testing in ambiguous cases
HPV status / genotype → eligibility for HPV-targeted therapy

→

NEXT: THERAPEUTIC HPV VACCINES (INVESTIGATIONAL)

Peltopepimut-S (ISA101b) + cemiplimab

HPV16 E6/E7 synthetic long peptides · phase 2

Recurrent **HPV16-positive** CC after 1L chemo, N = 113

16.8% ORR · all responders SCC

≈ cemiplimab alone 16.4% (EMPOWER-Cervical 1, cross-trial)

→ HPV genotype becomes a trial-eligibility biomarker; HPV-independent tumors are not targets

Lorusso D, et al. Gynecol Oncol. 2025 (cemiplimab + peltopepimut-S, NCT04646005) · Tewari KS, et al. N Engl J Med. 2022 (EMPOWER-Cervical 1)

PD-L1: Test that It Changes Treatment

PART III · CERVICAL CANCER — RECURRENT / METASTATIC

Recurrent / metastatic cervical cancer

↓

PD-L1 CPS

↓ **CPS ≥ 1**

Pembrolizumab

+ platinum / taxane ± bevacizumab

LACC	1L	2L
KN-A18 Pem+CCRT	KN-826 Pem+TC±BEV (CPS≥1)	KN-158 Pem mono -(SQ) all comer -(non-SQ) CPS≥1

ESGO / ESTRO / ESP guidelines for the management of patients with cervical cancer

Beyond PD-L1: HER2

PART III · CERVICAL CANCER

HER2 IHC 3+

→ T-DXd tumor-agnostic option

Previously treated · no satisfactory alternative · accelerated approval (Apr 2024)

DESTINY-PanTumor02 enrolled IHC 2+ and 3+

DESTINY-PanTumor02 · Cervical cohort, N=40

ORR

2+ : 40% 3+ : 80%

investigator-assessed · phase II

DESTINY-PanTumor02, 2026 gynecologic cohort analysis

PART 4. Genetic counseling

Who Needs Germline Evaluation?

PART IV · GENETIC COUNSELING

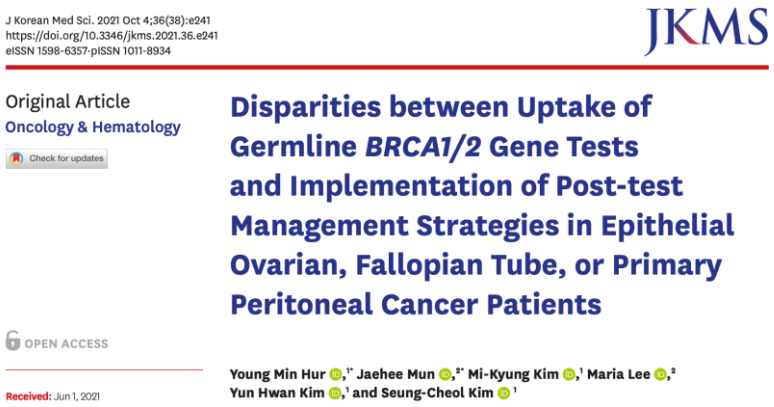
	Ovarian	Endometrial	Cervical
Routine germline relevance	**High**	**Tumor-directed**	Low
Trigger	All EOC	MMRd without MLH1 promoter methylation ± FH	Phenotype / FH
Main syndrome	HBOC / other OC genes	Lynch	Rare
Important exception	**Non-serous dMMR → Lynch**		

Not every gynecologic cancer needs germline testing —
but every gynecologic oncologist should recognize the trigger.

Konstantinopoulos PA, et al. J Clin Oncol 2020 · Concin N, et al. Lancet Oncol 2025 · Marchetti C, et al. ESGO consensus 2026 · FH, family history; PJS, Peutz–Jeghers syndrome

Korea: The Gap Is After the Test

PART IV · GENETIC COUNSELING — KOREAN 2-CENTER COHORT, 2009–2019, N=840



J Korean Med Sci. 2021 Oct 4;36(38):e241
https://doi.org/10.3346/jkms.2021.36.e241
eISSN 1598-6357-pISSN 1011-8934

JKMS

Original Article
Oncology & Hematology

Check for updates

Disparities between Uptake of Germline *BRCA1/2* Gene Tests and Implementation of Post-test Management Strategies in Epithelial Ovarian, Fallopian Tube, or Primary Peritoneal Cancer Patients

OPEN ACCESS

Received: Jun 1, 2021

Young Min Hur,[1*] Jaehee Mun,[2*] Mi-Kyung Kim,[1] Maria Lee,[2] Yun Hwan Kim,[1] and Seung-Cheol Kim[1]

54.0%

received germline BRCA testing

Advanced stage	Early stage
62.1%	37.4%

→

BRCA PV identified ↓

12.3%

had family cascade testing

J Korean Med Sci (Korean 2-center cohort) ·

Cascade Testing Prevents Cancer — Not Just Detects Mutations

PART IV · GENETIC COUNSELING

BRCA1/2

Risk-reducing salpingo-oophorectomy

Ovarian cancer–specific mortality

HR 0.21

95% CI 0.06–0.80

Lynch syndrome

Historical controlled surveillance cohort

CRC incidence

↓ 62%

8/133 vs 19/119 · 15-year follow-up

Lynch estimate derives from a historical non-randomized controlled cohort; contemporary residual CRC risk remains.

Domchek SM, et al. JAMA. 2010 · Järvinen HJ, et al. Gastroenterology. 2000

Genetic Counseling Step

PART IV · GENETIC COUNSELING — KOREAN 2-CENTER COHORT, 2009–2019, N=840

STEP 1

Germline P/LP in an MMR / BRCA gene

Report the exact gene + variant

VUS → no predictive testing

→

STEP 2 · DISCLOSURE

Pedigree + family letter

Start with first-degree relatives: parents, siblings, children

→

STEP 3 · RELATIVES

Test for the familial variant

Targeted (single-site) test

→

Positive → gene-specific surveillance & risk reduction

Negative → average-risk screening

Not tested → manage as at risk (category 2B)

WHAT CHANGES FOR A FEMALE CARRIER RELATIVE

- Abnormal bleeding → prompt endometrial biopsy
- Endometrial biopsy every 1–2 y from 30–35 y — may be considered
- ± Hysterectomy ± BSO timing by gene / Medication for RR

Multi-disciplinary counseling recommend !

NCCN Guidelines® Lynch Syndrome, Version 1.2026 — Strategies for Testing for LS; gene-specific risk management.

HBOC Management

Organ / domain	BRCA1	BRCA2	PALB2
Breast (screening)	MRI 25 y → + mammogram 30 y	MRI 25 y → + mammogram 30 y	MRI + mammogram 30 y
Ovary (RRSO)	**Recommended at 35–40 y**	May delay to 40–45 y	Consider at 45–50 y
Pancreas	MRI · EUS 50 y if FH*	MRI · EUS 50 y (no FH needed)	MRI · EUS 50 y if FH*
Prostate · skin	Consider PSA from 40 y / skin exam	Recommend PSA from 40 y / skin exam	Consider PSA from 40 y
Chemoprevention	OCs (ovary)	OCs (ovary)	Consider endocrine Tx.

* FH: ≥1 first-/second-degree relative with exocrine pancreatic cancer (same side); start at 50 y or 10 y before the earliest family case, whichever is earlier.
NCCN Guidelines® Genetic/Familial High-Risk Assessment: Breast, Ovarian, Pancreatic, and Prostate, Version 1.2027.

Lynch syndrome

Organ / domain	MLH1 / MSH2 / EPCAM	MSH6	PMS2
Endometrium (screening)	Endometrial biopsy from 30–35 y (q1–2 y)	Endometrial biopsy from 30–35 y (q1–2 y)	Endometrial biopsy from 30–35 y (q1–2 y)
Uterus · ovary (surgery)	**Consider TH + BSO at 40 y**	**TH at 40 y / BSO at 45–50 y**	TH ± BSO at 50 y (or after menopause)
Colon (colonoscopy)	**Start at 20–25 y (q1–2 y)**	Start at 30–35 y (q1–3 y)	Start at 30–35 y (q1–3 y)
Stomach · small bowel	EGD from 30–40 y (q2–4 y)	EGD from 30–40 y (q2–4 y)	Routine surveillance not recommended
Pancreas · other	Pancreas (if FH) / skin (MSH2)	Pancreas (if FH) / prostate from 40 y	Routine surveillance not recommended
Chemoprevention	Aspirin[1,2] / OCs · LNG-IUD	Aspirin / OCs · LNG-IUD	Aspirin / OCs · LNG-IUD

1. Burn J, et al. Cancer prevention with aspirin in hereditary colorectal cancer (Lynch syndrome), 10-year follow-up and registry-based 20-year data in the CAPP2 study: a double-blind, randomised, placebo-controlled trial.
2. Burn J, et al. Aspirin for cancer prevention in individuals with Lynch syndrome: first results from the CaPP3 multicentre, randomised, double-blind, non-inferiority trial.
TH, total hysterectomy; BSO, bilateral salpingo-oophorectomy; FH, family history. NCCN Guidelines® Lynch Syndrome, Version 1.2026.

Take Home Message

	Ovarian	Endometrial	Cervical
At diagnosis	g/s BRCA + HRD (+MMR, PD-L1, FRα, HER2)	POLE + MMR + p53 + ER + PD-L1	HPV + PD-L1
At recurrence	PSOC : Multi panel NGS PROC : PD-L1/FRα / HER2	MMR + HER2 + Multi panel NGS	PD-L1 + HER2 + Multi panel NGS
Treatment	PROC : KN B96, MIRV, T-Dxd	ICI, Len+PEM, T-Dxd	KN 826, KN-158, T-Dxd
Germline relevance → Genetic counseling	High	Lynch-directed	Usually low / phenotype-driven

Take Home Message

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Take Home Message

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