High risk and Metastatic/Recurrent Endometrial Cancer

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DECLARATION OF INTERESTS

I have the following financial relationships with ACCME defined ineligible companies to report over the past 24 months:

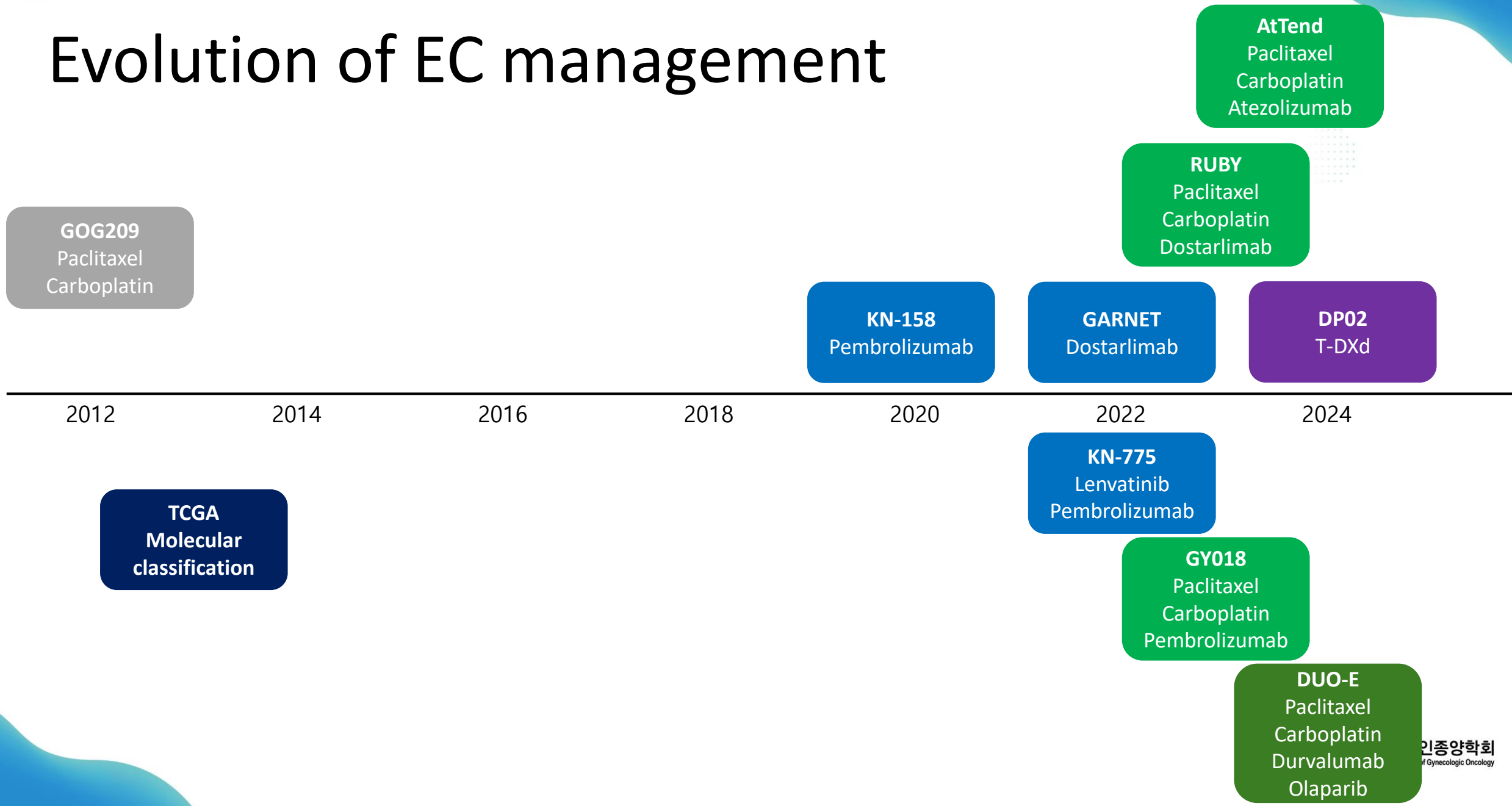
Honoraria/expenses for consulting/advisory boards from GSK

Funded research supported by Boryung, Hanmi, and Chong Kun Dang (Ongoing)

Contents

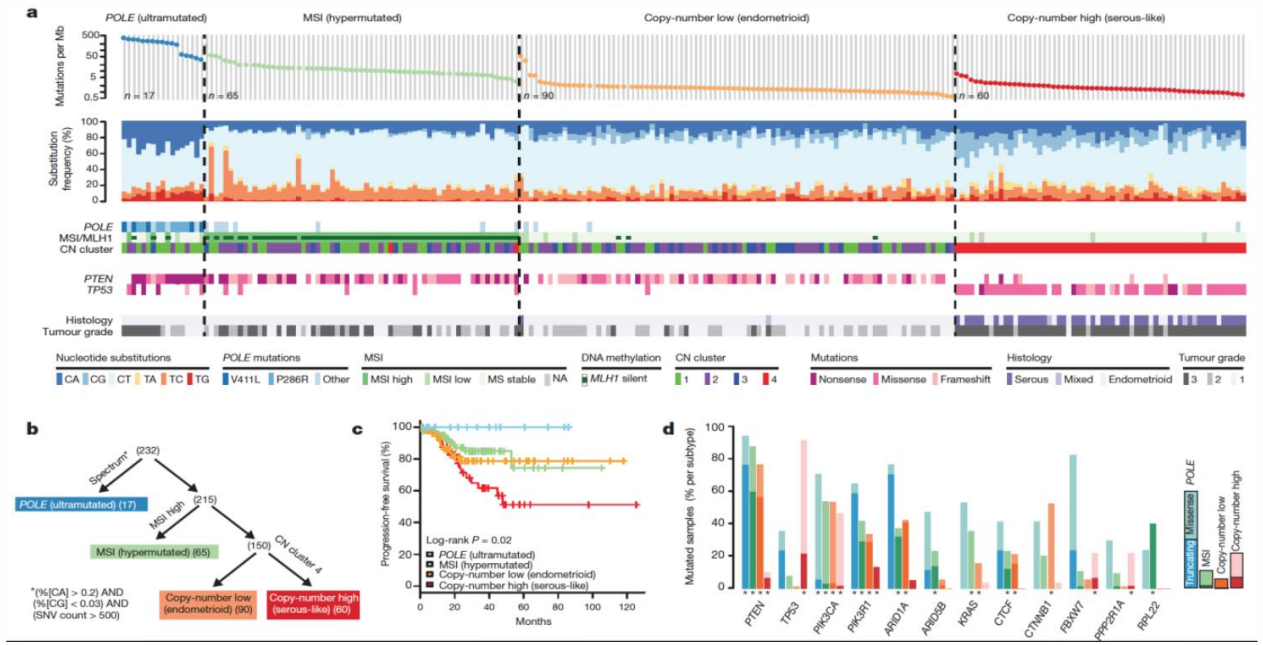
- Management landscape of endometrial cancer (EC)
- Adjuvant treatment in high-risk endometrial cancer
- Management of Recurrent/Metastatic disease

Evolution of EC management



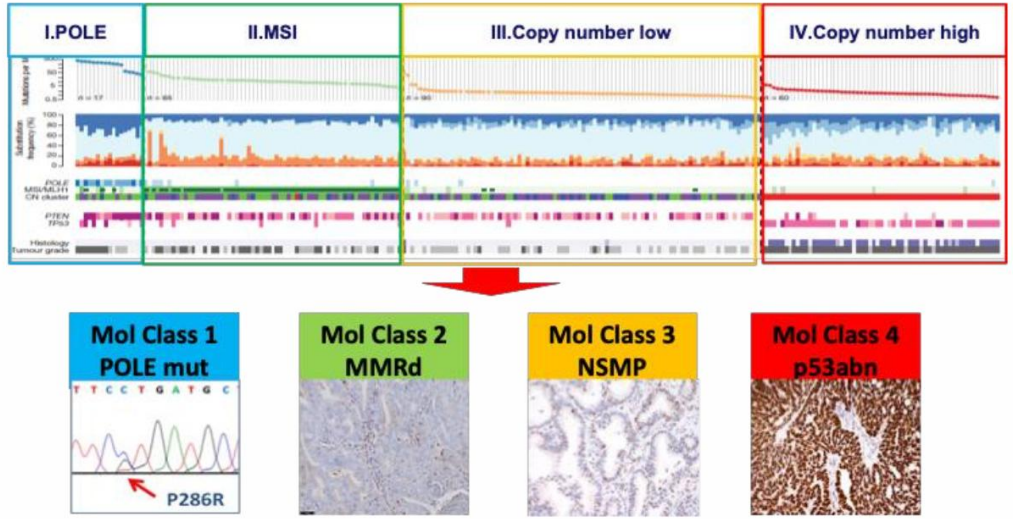
TCGA initiative: Emerging prospects in EC

The Cancer Genome Atlas: Endometrial Carcinoma



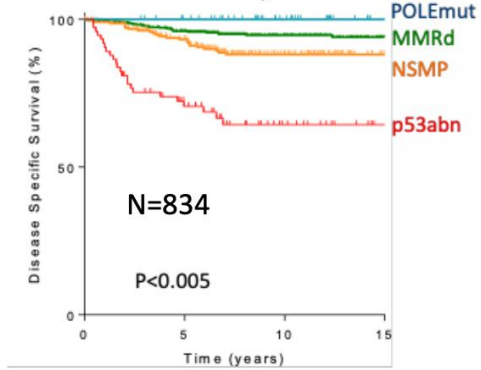
TCGA (Kandoth et al), Nature 2013

Surogate markers



High-intermediate risk

Stelloo et al, CCR 2016



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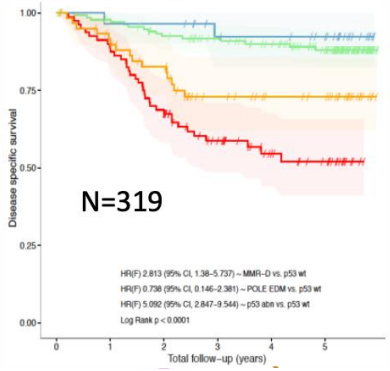
Talhouk et al, Cancer 2017



ESGO-ESTRO-ESP & ESMO guidelines

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
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 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
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

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

Table 2. EC risk groups

Risk group	Description[a]
Low risk	Stage IA (G1-G2) with endometrioid type (dMMR[b] and NSMP) and no or focal LVSI Stage I/II *POLE*mut cancer; for stage III *POLE*mut cancers[c]
Intermediate risk	Stage IA G3 with endometrioid type (dMMR and NSMP) and no or focal LVSI Stage IA non-endometrioid type (serous, clear-cell, undifferentiated carcinoma, carcinosarcoma, mixed) and/or p53-abn cancers without myometrial invasion and no or focal LVSI Stage IB (G1-G2) with endometrioid type (dMMR and NSMP) and no or focal LVSI Stage II G1 endometrioid type (dMMR and NSMP) and no or focal LVSI
High-intermediate risk	Stage I endometrioid type (dMMR and NSMP) any grade and any depth of invasion with substantial LVSI Stage IB G3 with endometrioid type (dMMR and NSMP) regardless of LVSI Stage II G1 endometrioid type (dMMR and NSMP) with substantial LVSI Stage II G2-G3 endometrioid type (dMMR and NSMP)
High risk	All stages and all histologies with p53-abn and myometrial invasion All stages with serous or undifferentiated carcinoma including carcinosarcoma with myometrial invasion All stage III and IVA with no residual tumour, regardless of histology and regardless of molecular subtype[b]

- First integration of histopathological and molecular features in risk groups:
  - POLE good
  - MMRd & NSMP intermediate
  - P53 poor

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Concin et al, Int J Gynecol Cancer 2021
Oaknin et al, Ann Oncol 2022;

FIGO 2009 versus FIGO 2023 staging systems for EC

FIGO 2009

anatomic tumor spread

FIGO 2023

tumor type, tumor grade, LVSI, and molecular alterations

FIGO 2009[2] (AJCC 8th ed)	FIGO 2023
Stage I	
Defined as tumor confined to the uterine corpus.	Defined now by a combination of the following features: histological type[a], myometrial invasion (presence and extent into inner vs outer half), absent or focal LVSI[b].
Subdivided as IA (myometrial invasion absent or <50% of the uterine wall) and IB (myometrial invasion ≥50%).	Categorization as IA vs IB as defined in FIGO 2009[2] now only applies to non-aggressive histological types with no or focal LVSI.
Distinction between absent and <50% myometrial invasion is not necessary.	For non-aggressive histological types with no or focal LVSI, reintroduces distinction between cancer confined to the endometrium (now IA1) vs <50% myometrial invasion (now IA2) vs ≥50% myometrial invasion (IB).
	For aggressive histological types, introduces stage IC (aggressive histological types without myometrial invasion), and considers any myometrial invasion as stage IIC.
	Introduces ovarian involvement as allowed if the following criteria are present: low grade endometrioid type; absent or superficial myometrial invasion (<50%); absent or focal LVSI; absence of additional metastases; the ovarian tumor is unilateral, limited to the ovary, without capsule invasion/rupture.
Stage II	
Defined as tumor confined to the uterus with invasion into the cervical stromal tissue.	Defined now by a combination of the following features: cervical stromal involvement, substantial LVSI[b], and aggressive histological tumor type with myometrial invasion.
	Stage II is now subdivided into IIA (cervical stromal invasion by non-aggressive histological type), IIB (substantial LVSI by non-aggressive histological type), and IIC (aggressive histological type with any myometrial invasion).
Stage III	
Defined as spread outside of the uterus other than bladder/intestinal lining, lymph nodes, and distant sites.	Defined as local and/or regional tumor spread.
Groups tubo-ovarian and serosal tumor involvement as stage IIIA.	Stage IIIA is now subdivided into IIIA1 (spread to ovary or fallopian tube) and IIIA2 (involvement of uterine subserosa or spread through uterine serosa). Introduces the concept of 'uterine subserosa'.
Defines vaginal and parametrial tumor involvement as stage IIIB.	Stage IIIB now includes pelvic peritoneum. It is subdivided into IIIB1 (metastasis or direct spread to vagina and/or parametria) and IIIB2 (metastasis to pelvic peritoneum).
Groups nodal micro- and macrometastasis as stage IIIC1 (pelvic) and IIIC2 (para-aortic).	Stage IIIC1 (pelvic nodal spread) is now subdivided into IIIC1i (micrometastasis) and IIIC1ii (macrometastasis). Stage IIIC2 (para-aortic nodal spread) is now subdivided into IIIC2i (micrometastasis) and IIIC2ii (macrometastasis).
Stage IV	
Groups abdominal peritoneal spread along with lungs, liver, brain, bone, and inguinal or extrapelvic lymph nodes above renal vessels (stage IV B).	Separates abdominal peritoneal spread (now IVB) from lungs, liver, brain, bone, and inguinal or extrapelvic lymph nodes above renal vessels (stage IVC).

*In FIGO 2023 stage I and II, *POLE*-mutant tumors are staged as IAm POLEmut and p53-abnormal tumors as IICm p53abn regardless of the anatomic spread, the degree of LVSI or histological type. No specific molecular profile (NSMP) and MMRd molecular subtypes do not affect tumor staging.

[a]Histological types:
- Non-aggressive histological types: FIGO grade 1 and 2 endometrioid.
- Aggressive histological types: FIGO grade 3 endometrioid, serous, clear cell, undifferentiated, dedifferentiated, mesonephric-like, gastrointestinal-type mucinous, carcinosarcoma.

[b]Lymphovascular space invasion (LVSI):
- Substantial: ≥5 vessels involved.
- Focal: <5 vessels involved.

1. Stage I & II: Non-anatomical parameters
- histological type and grade, LVSI, and molecular group

2. Stage III & IV: Subdivision of according to
- Location (vaginal vs parametrial)
- size (nodal micrometa vs macrometa)

3. Uterus and ovarian involvement
- IA3: "synchronous" malignancy
- IIIA1: spread to ovary or tube

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W Glenn McCluggage et al. IJGC 2023

ESGO-ESTRO-ESP guideline 2025

Low | Intermediate | High-Intermediate | High | Uncertain

2023 FIGO staging[T]			Molecular classification*				
			*POLE*mut	MMRd	NSMP low-grade+ERpos	NSMP high-grade/ERneg**	p53abn
I	**Confined to the uterine corpus**						
IA	IA1	Low-grade endometrioid, limited to polyp/endometrium (no myoinvasion)	IAm *POLE*mut				
	IA2	Low-grade endometrioid, myoinvasion <50%, no/focal LVSI	IAm *POLE*mut			**	IICm p53abn
	IA3	Low-grade endometrioid carcinoma of the endometrium & ovary#	IAm *POLE*mut			**	IICm p53abn
IB		Low-grade endometrioid, myoinvasion ≥50%, no/focal LVSI	IAm *POLE*mut			**	IICm p53abn
IC		High-grade histologies^, limited to polyp/endometrium	IAm *POLE*mut		n.a.		
II	**Confined to the uterus**						
IIA		Low-grade endometrioid, invasion of the cervical stroma	IAm *POLE*mut			**	IICm p53abn
IIB		Low-grade endometrioid, substantial LVSI***	IAm *POLE*mut			**	IICm p53abn
IIC		High-grade histologies^, myoinvasion	IAm *POLE*mut	Myoinvasion <50%, no/focal LVSI	n.a.		IICm p53abn
			IAm *POLE*mut	Myoinvasion ≥50%, no/focal LVSI			
			IAm *POLE*mut	Cervical stromal invasion, no/focal LVSI			
			IAm *POLE*mut	Substantial LVSI**			

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Concin et al, Lancet Oncol 2025

ESGO-ESTRO-ESP guideline 2025

Low | Intermediate | High-Intermediate | High | Uncertain

2023 FIGO staging[T]			Molecular classification*				
			*POLE*mut	MMRd	NSMP low-grade+ERpos	NSMP high-grade/ERneg**	p53abn
III	**Local and/or regional spread**						
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 and/or the parametria					
	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	Macrometastasis					
IV	**Locally advanced and/or metastatic disease**						
IVA		Invasion of the mucosa and/or the intestinal mucosa					
	Metastatic disease or residual disease after surgery						
III/IVA		With residual disease					
IVB		Peritoneal metastasis beyond the pelvis					
IVC		Distant metastasis					

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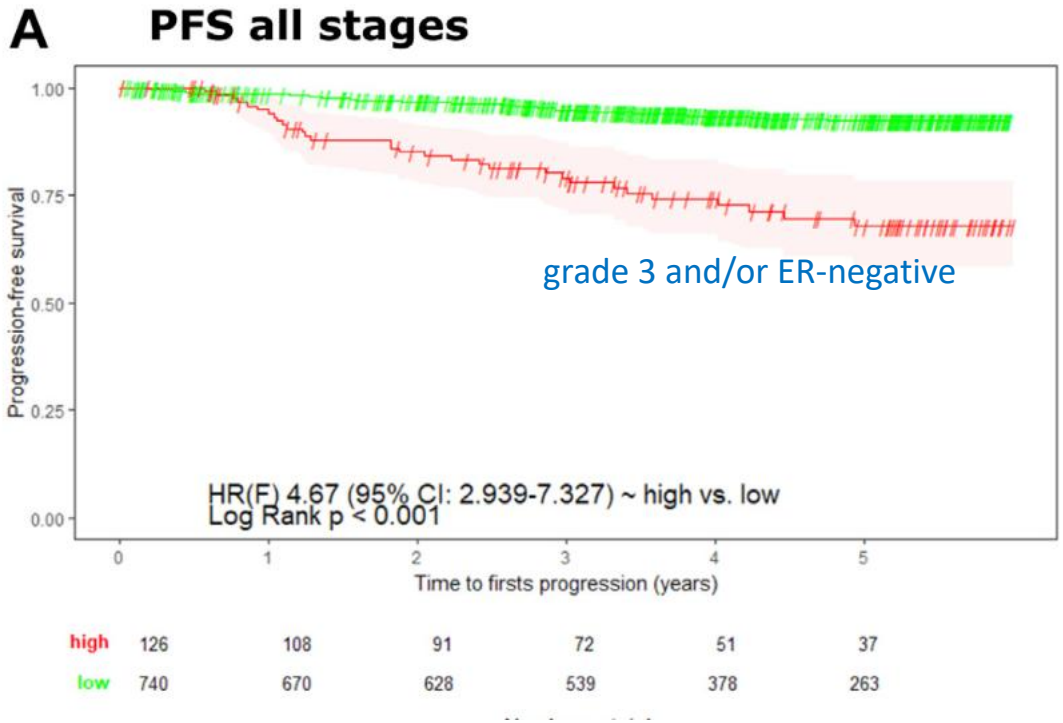
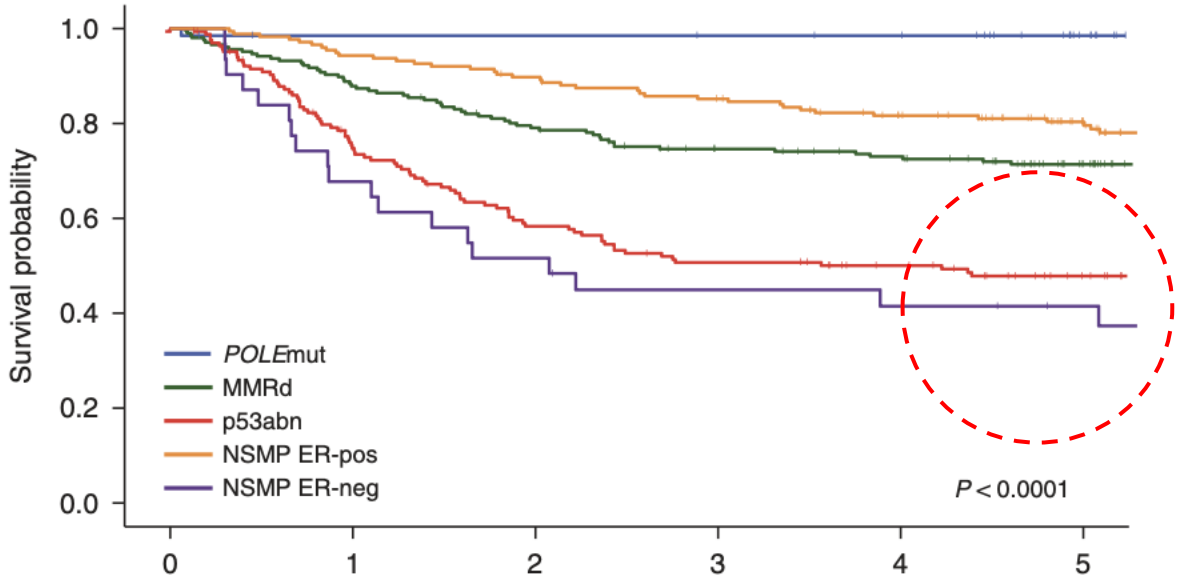
Concin et al, Lancet Oncol 2025

ESGO-ESTRO-ESP guideline 2025: summary

Risk Group	Recurrence Risk (5-yr)	Molecular Profile	Anatomical Extent & LVSI Status
Low Risk	**< 8%**	**POLEmut**	**Confined to the uterus** (with or without cervical invasion)
		MMRd or **NSMP** (low-grade/ER+)	Confined to endometrium/polyp OR **Myoinvasion < 50% AND no/focal LVSI**
		MMRd	**High-grade histology limited to endometrium/polyp (No LVSI)**
Intermediate Risk	**8–14%**	**MMRd** or **NSMP** (low-grade/ER+)	Myoinvasion ≥ 50% AND **no/focal LVSI**
		NSMP (low-grade/ER+)	**Cervical stromal invasion AND no/focal LVSI**
		MMRd	High-grade WITH Myoinvasion, BUT No cervical invasion AND No substantial LVSI
High–Intermediate Risk	**15–24%**	**MMRd**	**Cervical stromal invasion**
		MMRd or **NSMP** (low-grade/ER+)	**Substantial LVSI** (regardless of myoinvasion depth)
		MMRd	High-grade WITH myoinvasion **AND either Cervical invasion OR Substantial LVSI**
High Risk	**≥ 25%**	**p53abn** or **NSMP** (high-grade/ER-)	Any myoinvasion OR Cervical stromal invasion
		All types (except POLEmut)	Extra-uterine spread (Ovaries, Serosa, Vagina, Parametrium, Peritoneum, or Lymph nodes)
Uncertain Risk	**Unknown**	**p53abn** or **NSMP** (high-grade/ER-)	Limited to polyp or endometrium (No myoinvasion)
		POLEmut	Extra-uterine spread (Local, regional, or metastatic)

Role of ER status in NSMP group





- Strongest model within NSMP: (ER-neg OR grade 3) versus (ER-pos AND grade ½)
- Prognosis of NSMP ER-neg similar to p53abn

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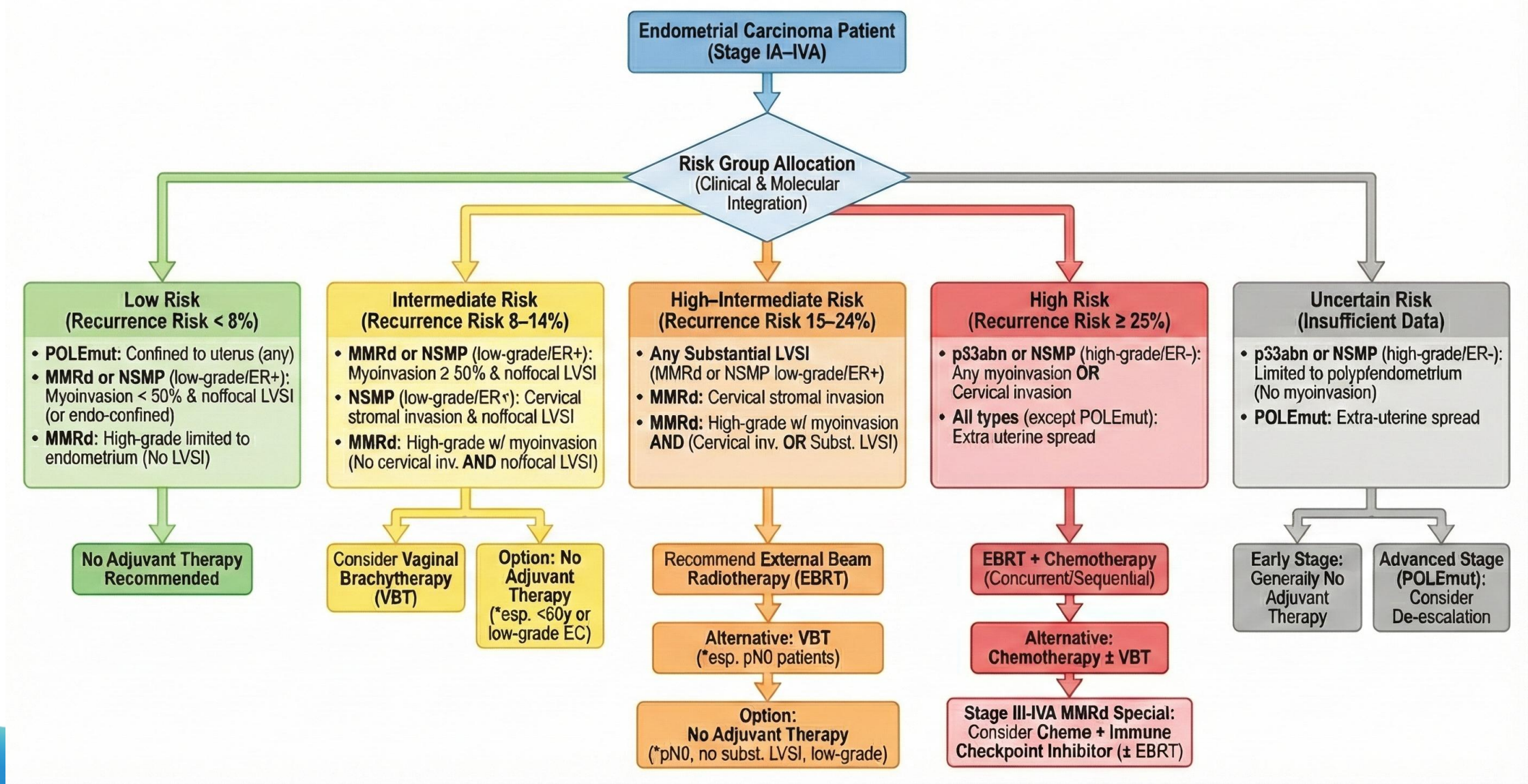
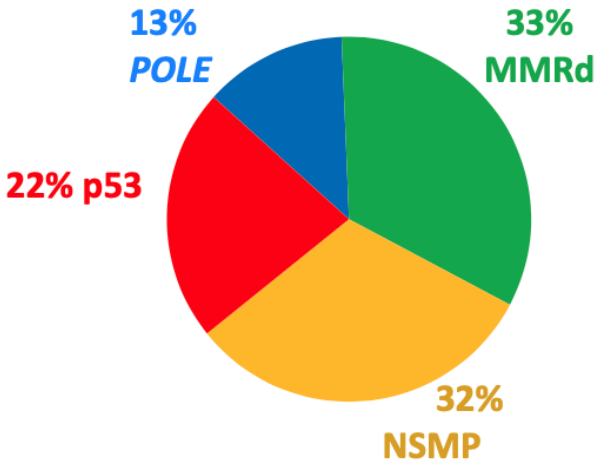
Jamieson et al. Modern Pathology 2023
Vermij et al. BJC 2023

Adjuvant treatment according to Risk groups

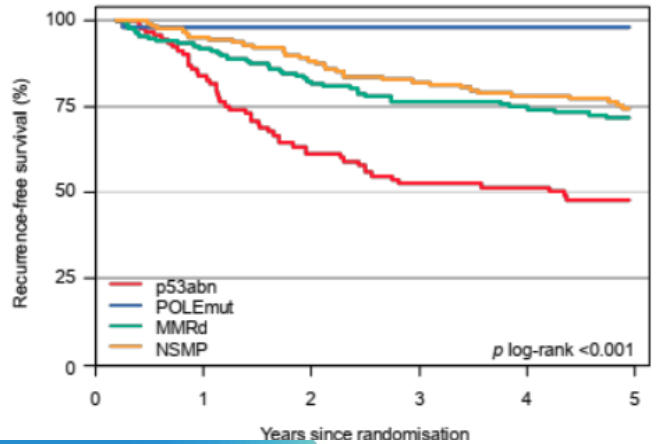


Molecualar groups in PORTEC-3

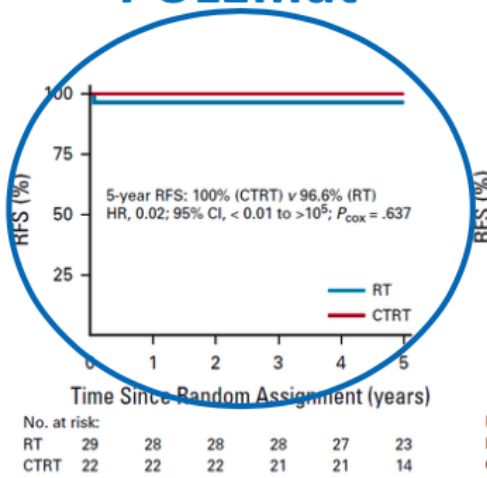
PORTEC-3 high-risk trial cohort
N=410



Recurrence free survival



POLEmut

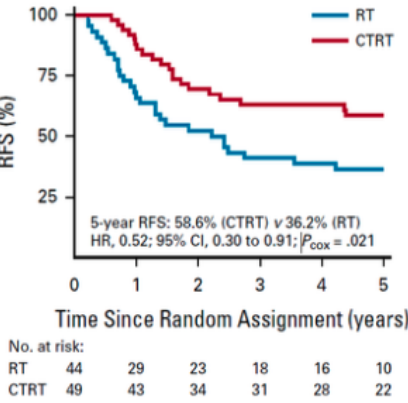


No. at risk:

RT	29	28	28	28	27	23
CTRT	22	22	22	21	21	14

does not relapse regardless of treatment

p53abn

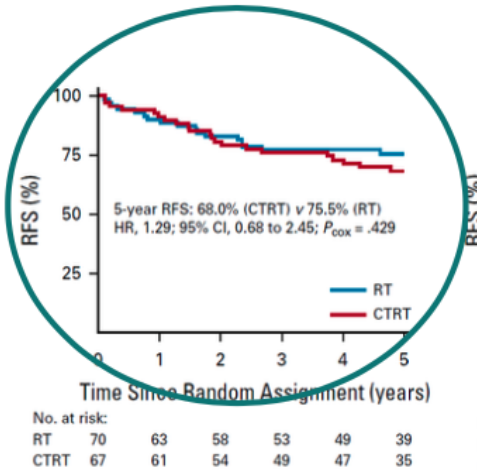


No. at risk:

RT	44	29	23	18	16	10
CTRT	49	43	34	31	28	22

worst prognosis but [greatest benefit from adjuvant CTX]

MMRd

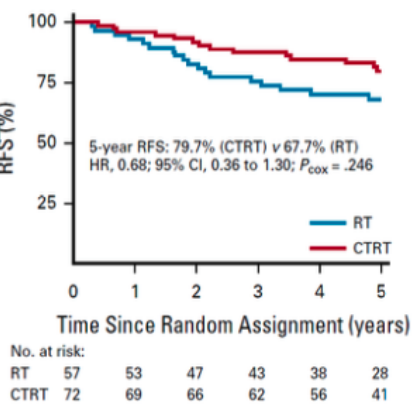


No. at risk:

RT	70	63	58	53	49	39
CTRT	67	61	54	49	47	35

intermediate prognosis , but [little benefit from adjuvant CTX]

NSMP



No. at risk:

RT	57	53	47	43	38	28
CTRT	72	69	66	62	56	41

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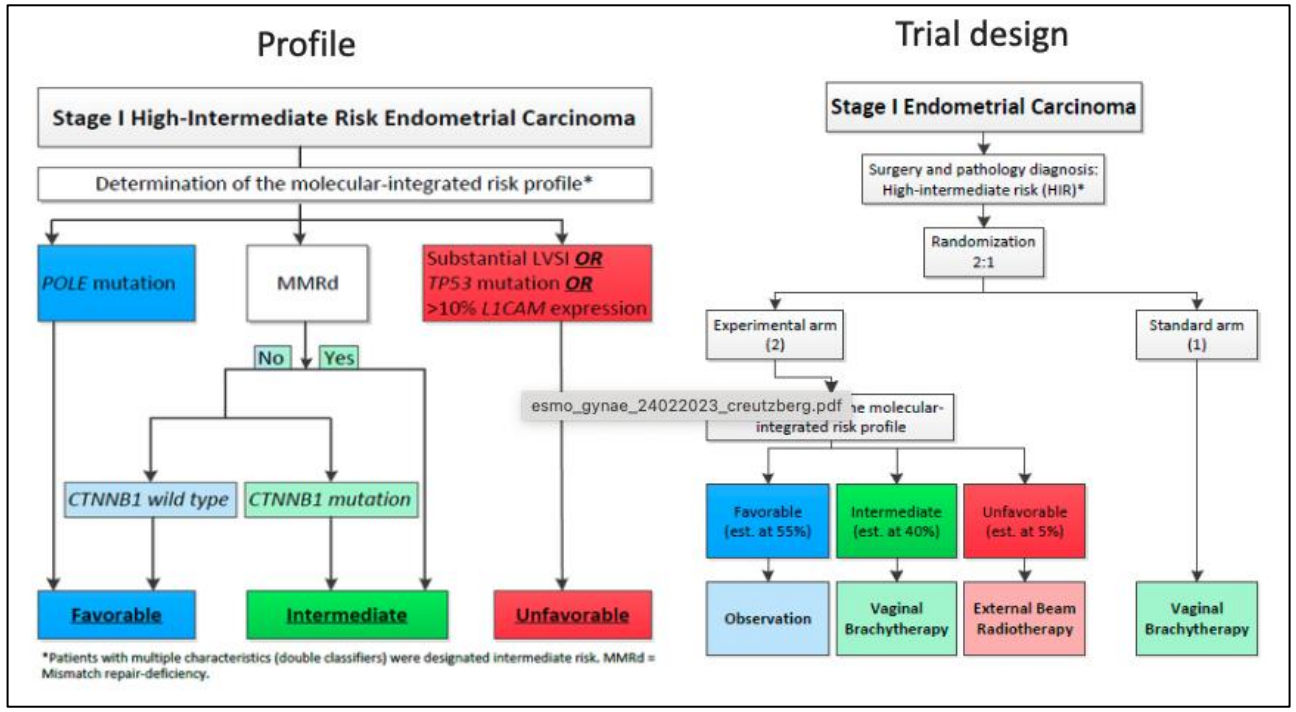
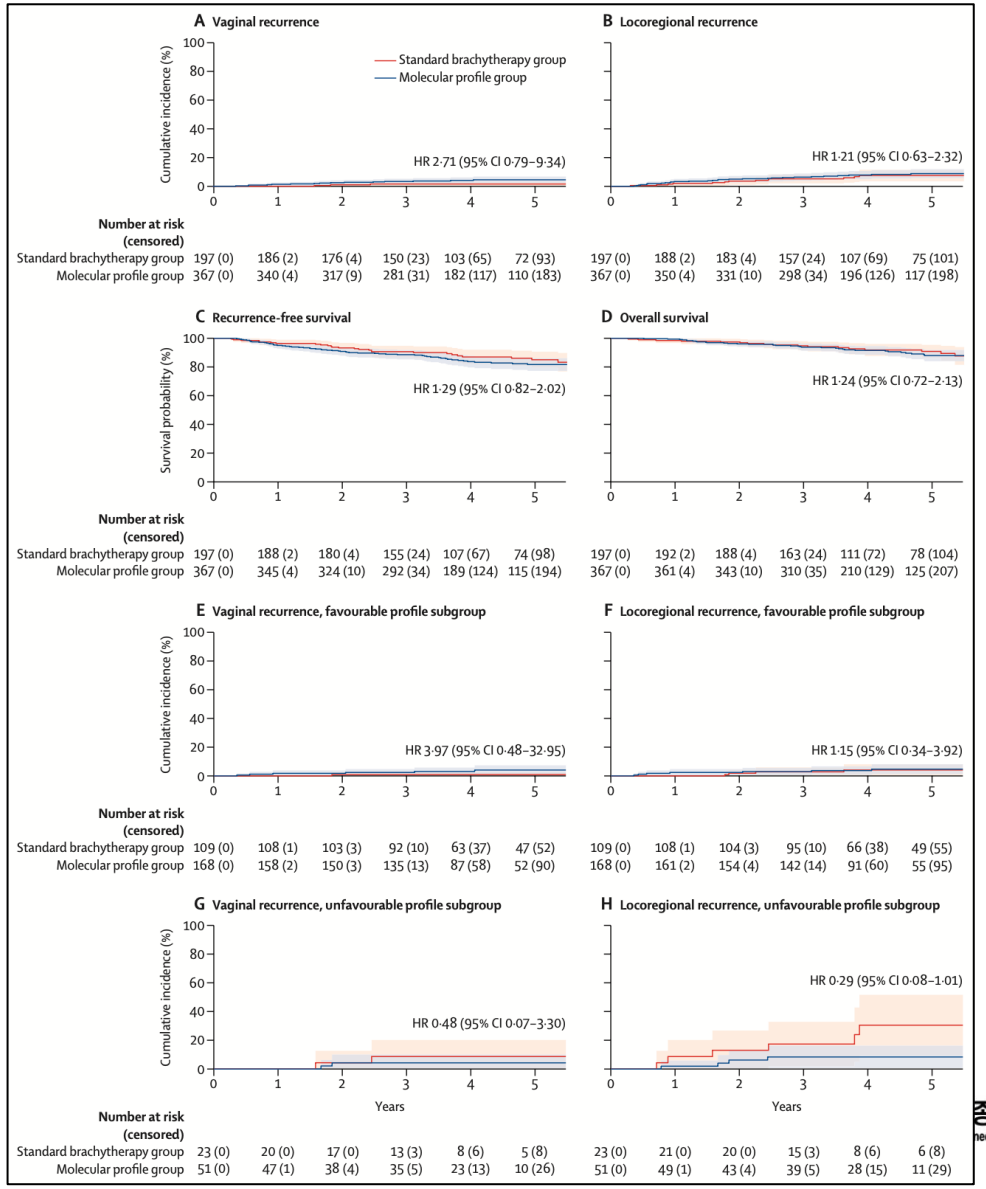
Korean Society of Gynecologic Oncology

Leon-Castillo et al, J Clin Oncol 2020

PORTEC-4a: molecular profile-based adjuvant Tx. in H-I risk group

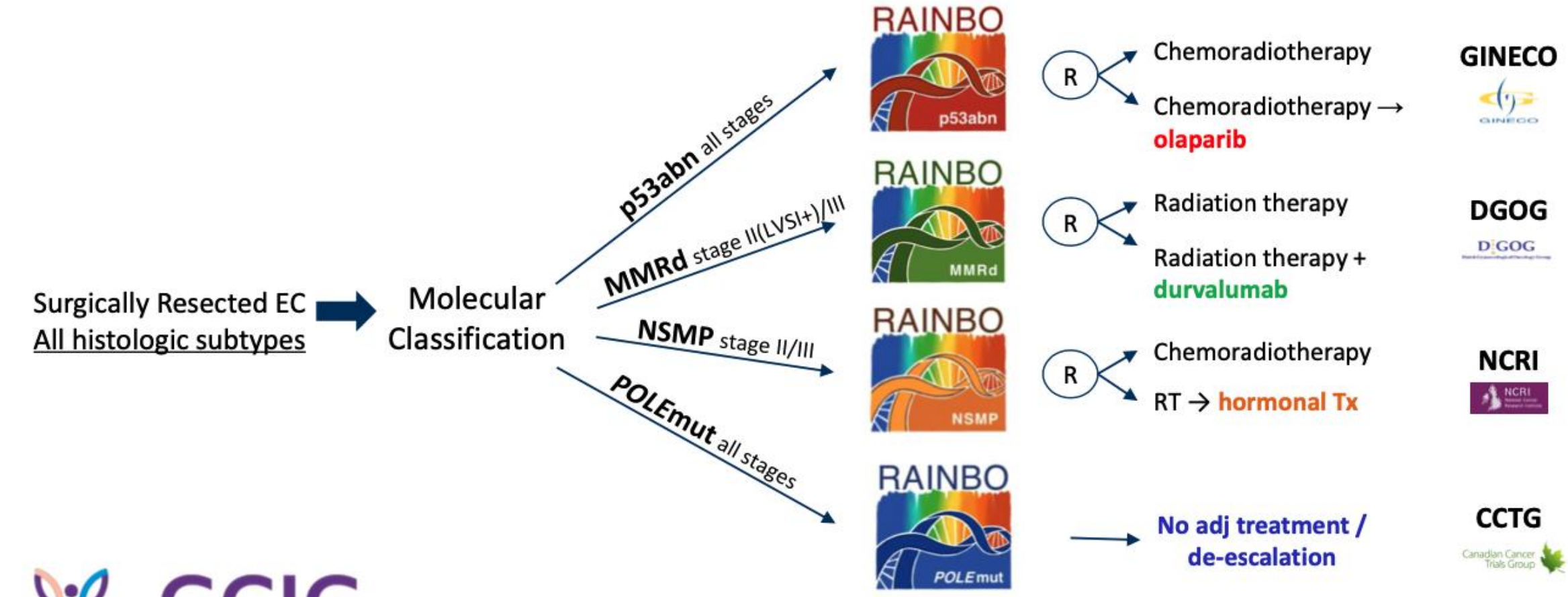


Individualized adjuvant treatment by molecular integrated risk profile spared **46% of patients with a favorable profile from adjuvant treatment**, and reduces both overtreatment and undertreatment.



Van den Heerik et al, Int J Gynecol Cancer 2020
Van den Heerik et al, Lancet oncol 2026

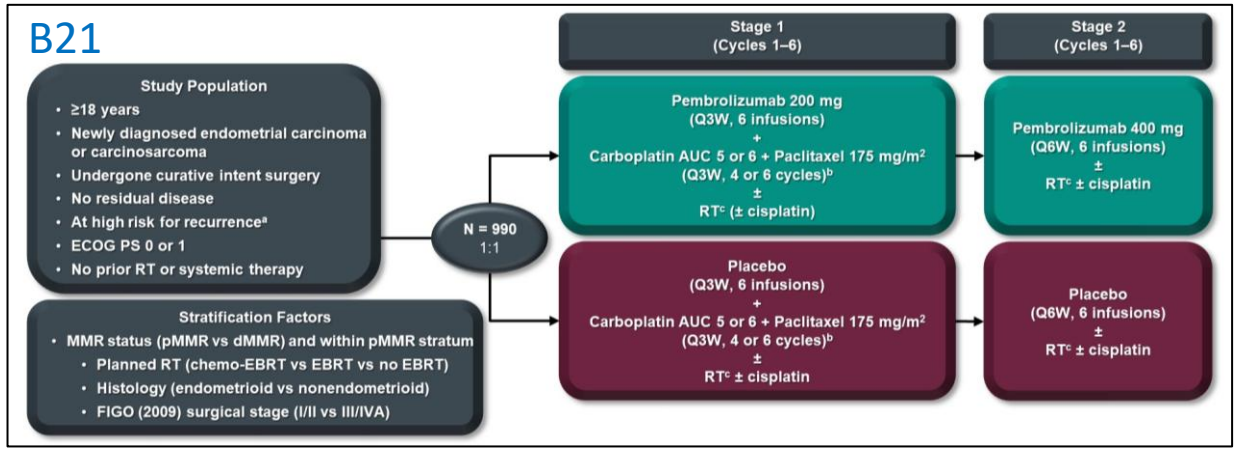
RAINBO: Refining Adjuvant treatment IN endometrial cancer Based On molecular features

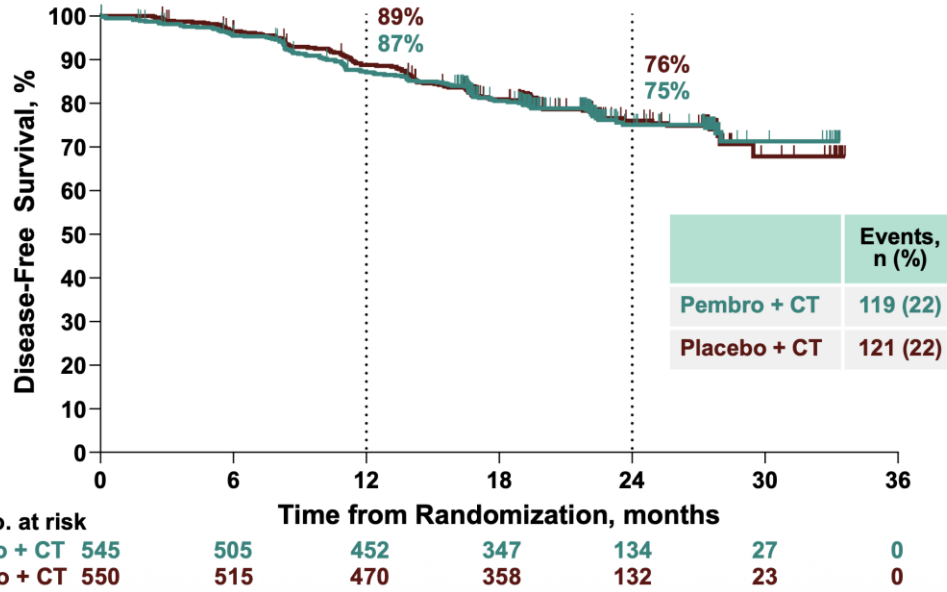


Primary endpoint 3-yr RFS

GCIG GYNECOLOGIC CANCER INTERGROUP

CTX+ICI in high risk EC?

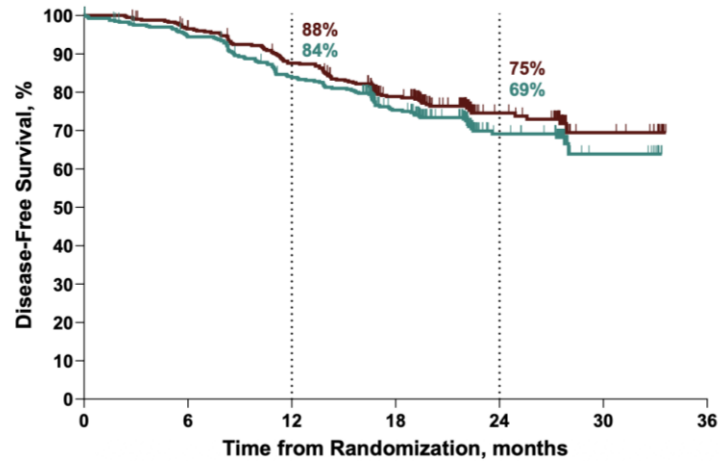




	Events, n (%)	Median (95% CI), mo	HR (95% CI)	*P* value
Pembro + CT	119 (22)	NR (NR–NR)	1.02 (0.79–1.32)	0.570
Placebo + CT	121 (22)	NR (NR–NR)		

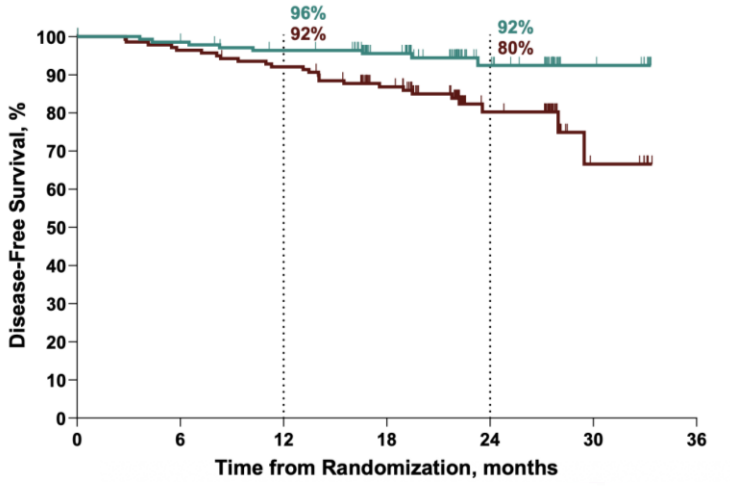
pMMR Subgroup

	Events, n (%)	Median (95% CI), mo	HR (95% CI)
Pembro + CT	111 (27)	NR (NR–NR)	1.20 (0.91–1.57)
Placebo + CT	96 (23)	NR (NR–NR)	



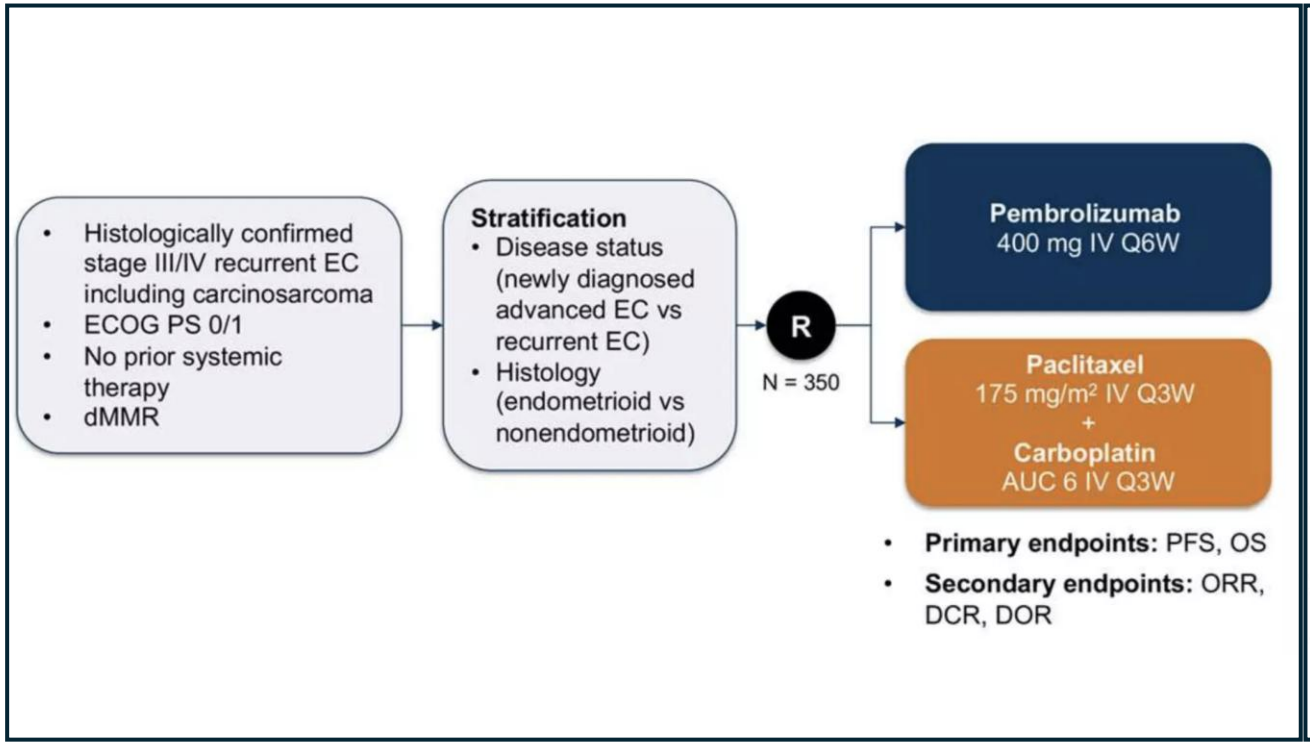
dMMR Subgroup

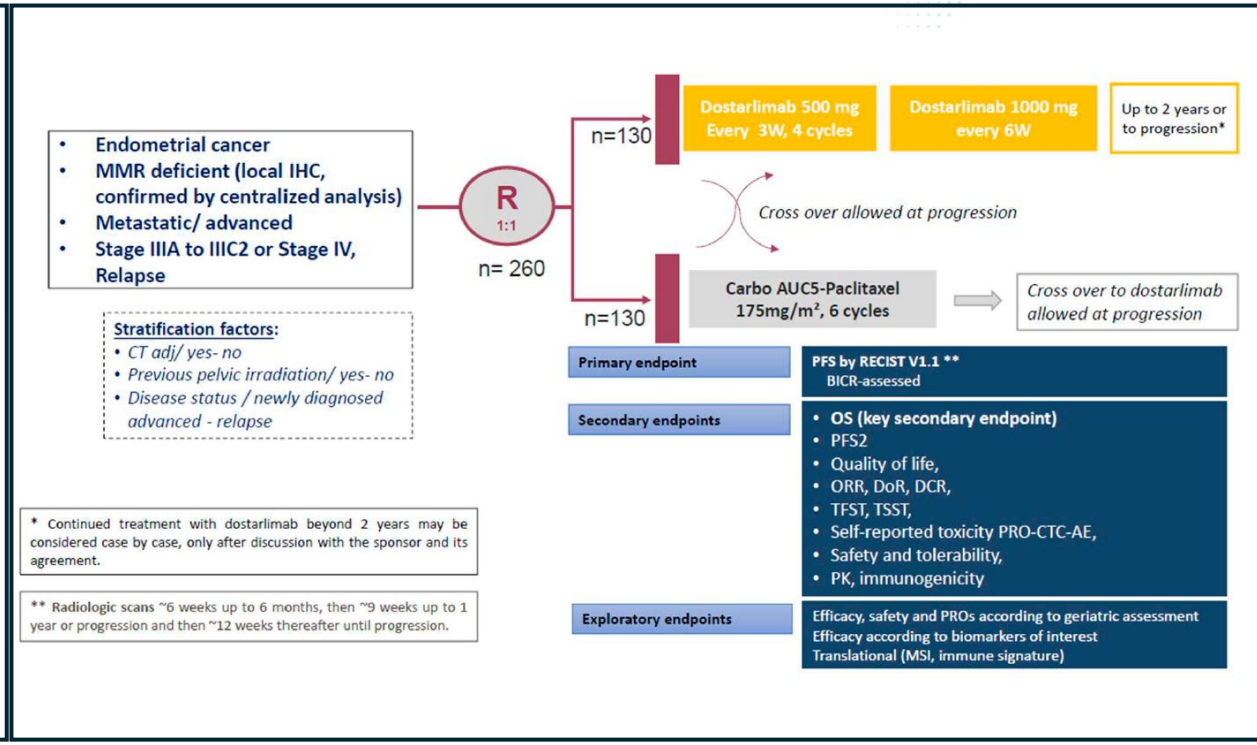
	Events, n (%)	Median (95% CI), mo	HR (95% CI)
Pembro + CT	8 (6)	NR (NR–NR)	0.31 (0.14–0.69)
Placebo + CT	25 (18)	NR (29.5–NR)	



Toon Van Gorp et al. ESMO 2024

Domenica, c96: ICI monotherapy in R/M EC





Paradigm-shifting data in metastatic or recurrent EC

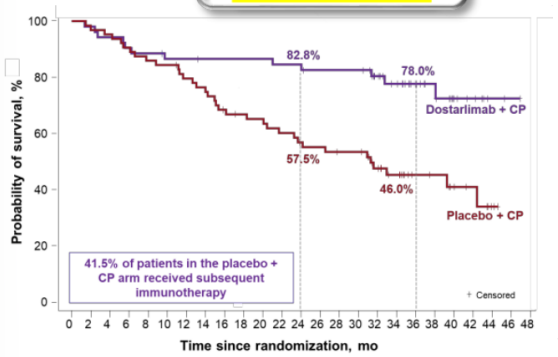
RUBY Part 1	RUBY Part 2	GY018	AtTEnd	DUO-E
• Dostarlimab • Chemotherapy	• Dostarlimab + Niraparib • Chemotherapy	• Pembrolizumab • Chemotherapy	• Atezolizumab • Chemotherapy	• Durvalumab • Durvalumab + Olaparib • Chemotherapy
• Statistically significant PFS dMMR and ITT, OS ITT	• Statistically significant PFS ITT and PFS pMMR	• Statistically significant PFS dMMR and pMMR	• Statistically significant PFS dMMR and ITT	• Statistically significant PFS ITT for durva and durva + ola
• **Not powered for pMMR**	• OS immature	• **Not testing for OS**	• pMMR didn't benefit • OS ITT immature	• **Not powered for pMMR or dMMR**

PFS and OS benefit of CTX+ICI in dMMR R/M EC

RUBY Part 1[1,2,5,8]

PFS HR 0.28 (95% CI, 0.16-0.50); *P*<0.001

OS HR 0.32 (95% CI, 0.17-0.63); *Nominal P*=0.0002

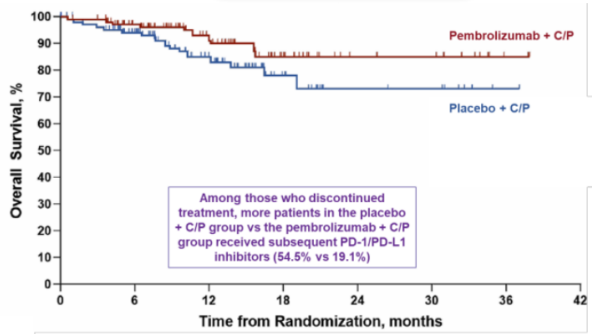


OS Data	Events, %	Median (95% CI), mo
Dostarlimab + C/P	22.6	NE (NE-NE)
Placebo + C/P	53.8	31.4 (20.3-NE)
OS data maturity	39.8%	
Median follow-up, mo	36.6	

GY018[3-5,9]

PFS HR 0.30 (95% CI, 0.19-0.48); *P*<0.001

OS HR 0.55 (95% CI, 0.25-1.19); *P*=0.0617

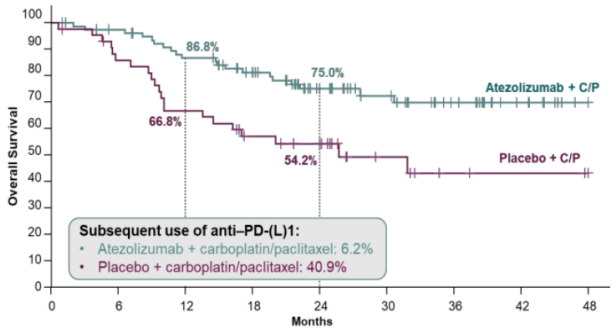


OS Data	Events, %	Median (95% CI), mo
Pembrolizumab + C/P	9.1	NR (NR-NR)
Placebo + C/P	15	NR (NR-NR)
OS data maturity	18%	
Median follow-up, mo	13.3-13.7	

AtTEnd[6,10]

PFS HR 0.36 (95% CI, 0.23-0.57); *P*=0.0005

OS HR 0.41 (95% CI, 0.22-0.76)

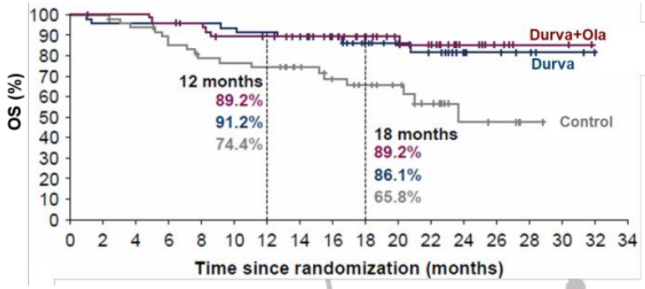


OS Data	Events, %	Median (95% CI), mo
Atezolizumab + C/P	24.6	NE (NE-NE)
Placebo + C/P	47.7	25.7 (13.5-NE)
OS data maturity	--	
Median follow-up, mo	--	

DUO-E[7,11]

PFS HR 0.42 (95% CI, 0.22-0.80); *Durva + C/P arm*

OS HR 0.34 (95% CI, 0.13-0.79) *Durva + C/P arm*



OS Data	Events, %	Median (95% CI), mo
Durvalumab + C/P	15.2	NR (NR-NR)
Placebo + C/P	36.7	23.7 (16.9-NR)
OS data maturity	21.7%	
Median follow-up, mo	--	

대한부인종양학회 Korean Society of Gynecologic Oncology

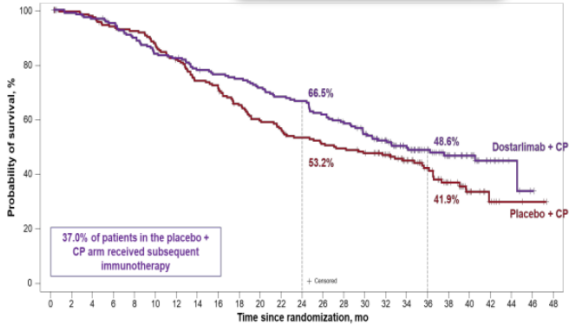
Slides by Dr. Mirza presented in Onco Summit 2024

PFS and OS benefit of CTX+ICI in pMMR R/M EC

RUBY Part 1[1,2,5,6]

PFS HR 0.76 (95% CI, 0.59-0.98)

OS HR 0.79 (95% CI, 0.60-1.04); nominal *P*=0.0493

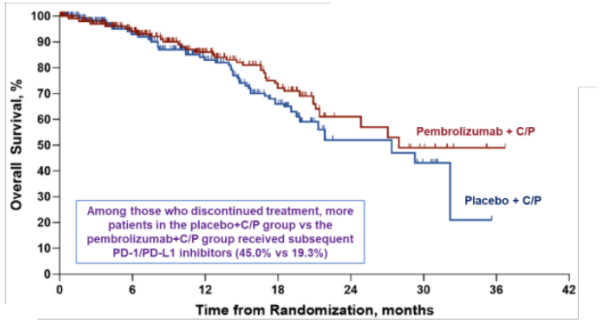


OS Data	Events, %	Median (95% CI), mo
Dostarlimab + C/P	50.5	34.0 (28.6-NE)
Placebo + C/P	59.2	27.0 (21.5-35.6)
OS data maturity	54.8%	
Median follow-up, mo	37.5	

GY018[3-5,7]

PFS HR 0.54 (95% CI, 0.41-0.71); *P*<0.001

OS HR 0.79 (95% CI, 0.53-1.17) P=0.1157

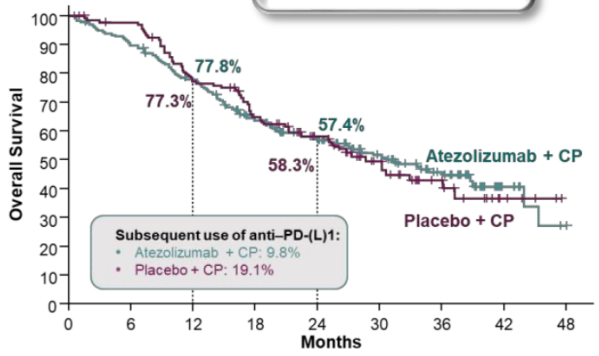


OS Data	Events, %	Median (95% CI), mo
Pembrolizumab + C/P	15.3	27.9 (21.4-NR)
Placebo + C/P	18.3	27.4 (19.5-NR)
OS Data maturity	27.2%	
Median follow-up, mo	8.4-8.8	

AtTEnd[6]

PFS HR 0.92 (95% CI, 0.73-1.16);

OS HR 1.00 (95% CI; 0.74-1.35)

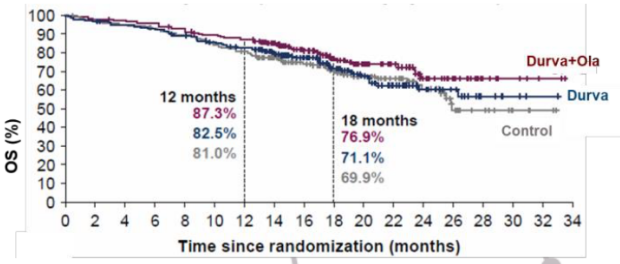


OS Data	Events, %	Median (95% CI), mo
Atezolizumab + C/P	47.2	31.5 (25.0-38.9)
Placebo + C/P	46.4	28.6 (22.4-37.2)
OS Data maturity	--	
Median follow-up, mo	--	

DUO-E[5,8]

PFS HR 0.77 (95% CI, 0.60-0.97); *Durva + C/P arm*

OS HR 0.91 (95% CI, 0.64-1.30) *Durva + C/P arm*



OS Data	Events, %	Median (95% CI), mo
Durvalumab + C/P	30.2	NR (NR-NR)
Placebo + C/P	33.3	25.9 (25.1-NR)
OS Data maturity	29.2%	
Median follow-up, mo	--	

대한부인종양학회 Korean Society of Gynecologic Oncology

Slides by Dr. Mirza presented in Onco Summit 2024

Benefit of PARPi addition to CTX+ICI

RUBY Part 2[1]

PFS

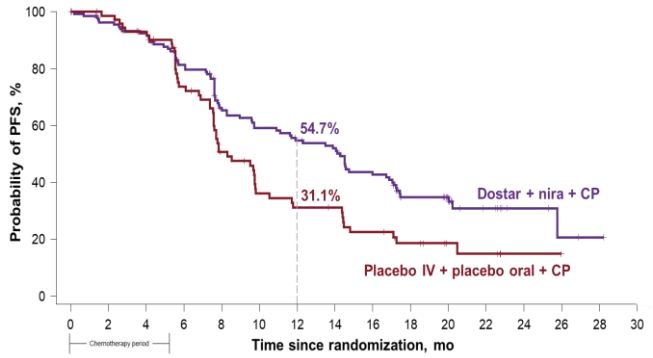
HR 0.63 (95% CI, 0.44-0.91); *P*=0.0060 Dostar + nira + C/P arm

HR 0.76 (95% CI, 0.59-0.98) Dostar + C/P arm

OS

The trial is ongoing for OS follow-up

HR 0.79 (95% CI, 0.60-1.04); nominal *P*=0.0493



	Events, %	Median (95% CI), mo
Dostarlimab + Niraparib + C/P	55.6	14.3 (9.7-16.9)
Placebo + C/P	71.6	8.3 (7.6-9.8)
PFS data maturity	61.1%	
Median follow-up, mo	19.1	

DUO-E[2,3]

PFS

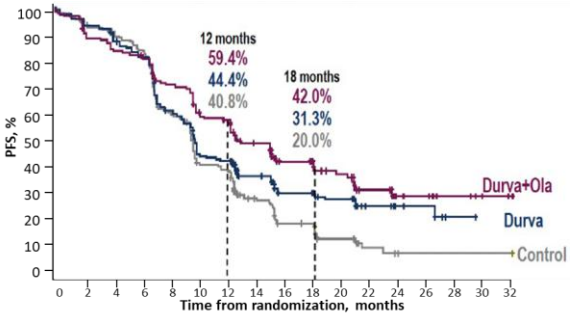
HR 0.57 (95% CI, 0.44-0.73); *Durva + Ola+ C/P arm*

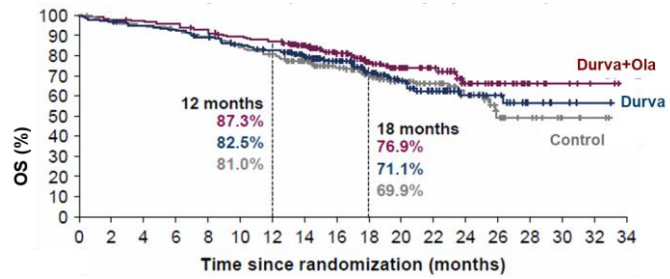
HR 0.77 (95% CI, 0.60-0.97); *Durva + C/P arm*

OS

HR 0.69 (95% CI, 0.47-1.00) *Durva + Ola + C/P arm*

HR 0.91 (95% CI, 0.64-1.30) *Durva + C/P arm*





	Control (N=192)	Durva (N=192)	Durva+Ola (N=191)
Events, n (%)	148 (77.1)	124 (64.6)	108 (56.5)
Median PFS (95% CI),* months	9.7 (9.2–10.1)	9.9 (9.4–12.5)	15.0 (12.4–18.0)
HR (95% CI) vs Control†		0.77 (0.60–0.97)	0.57 (0.44–0.73)
HR (95% CI) vs Durva†			0.76 (0.59–0.99)

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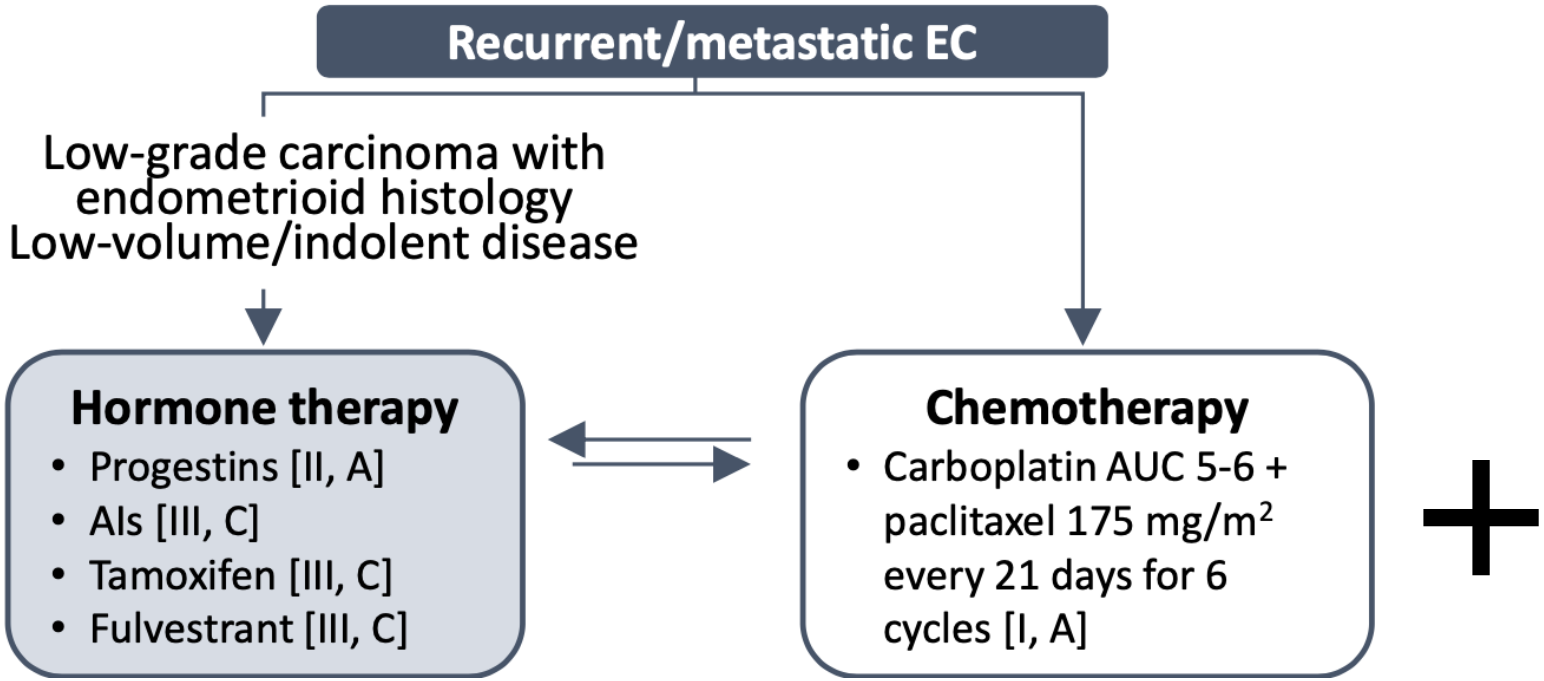
Slides by Dr. Mirza presented in Onco Summit 2024

1st line systemic treatment in R/M EC



+

All comer

Pembrolizumab (except for carcinosarcoma)
Dostarlimab

dMMR

Durvalumab

pMMR

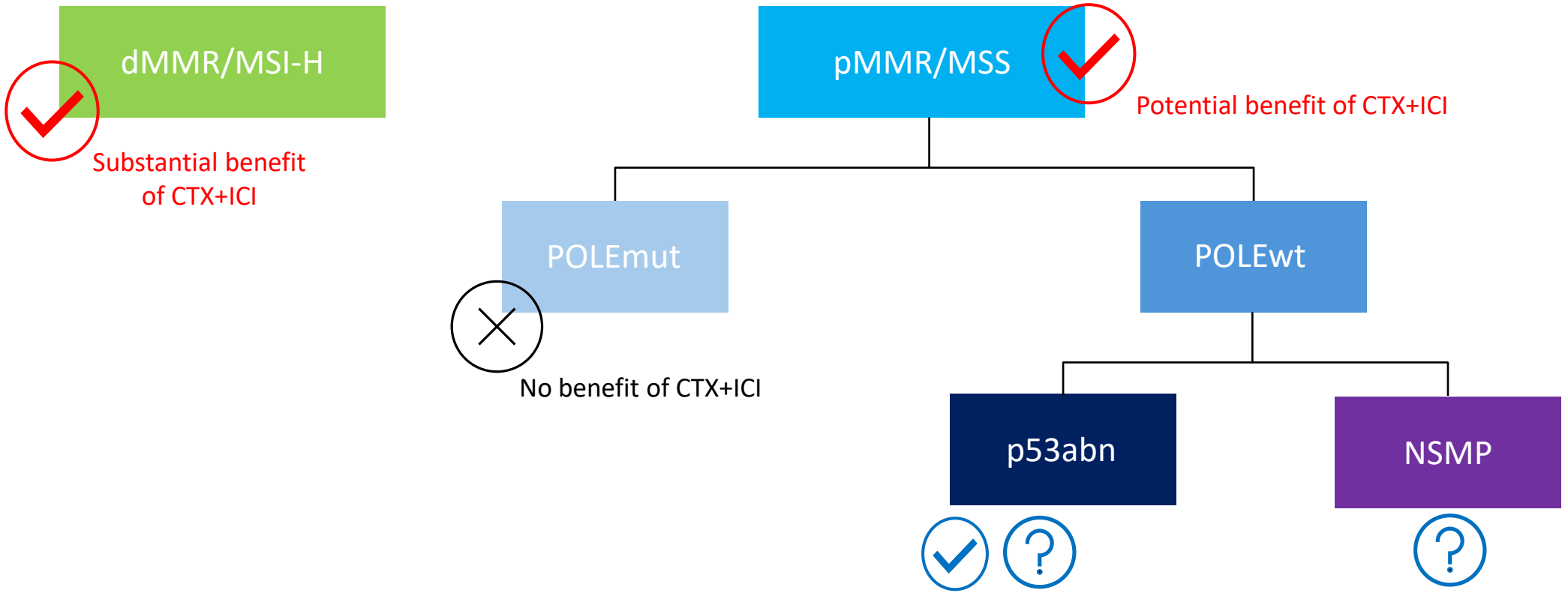
Durvalumab followed by Durvalumab/Olaparib

HER2+

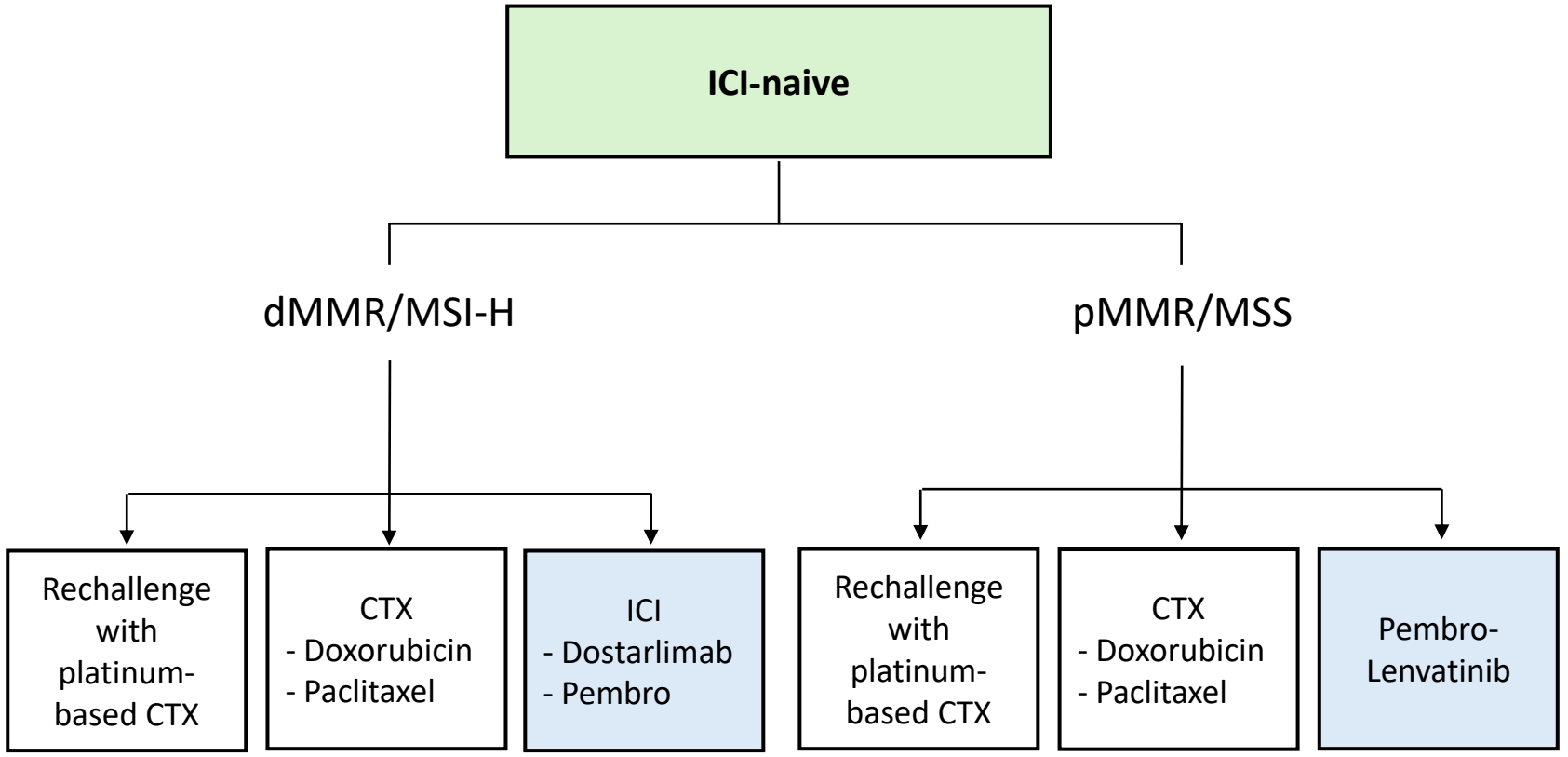
Trastzumab

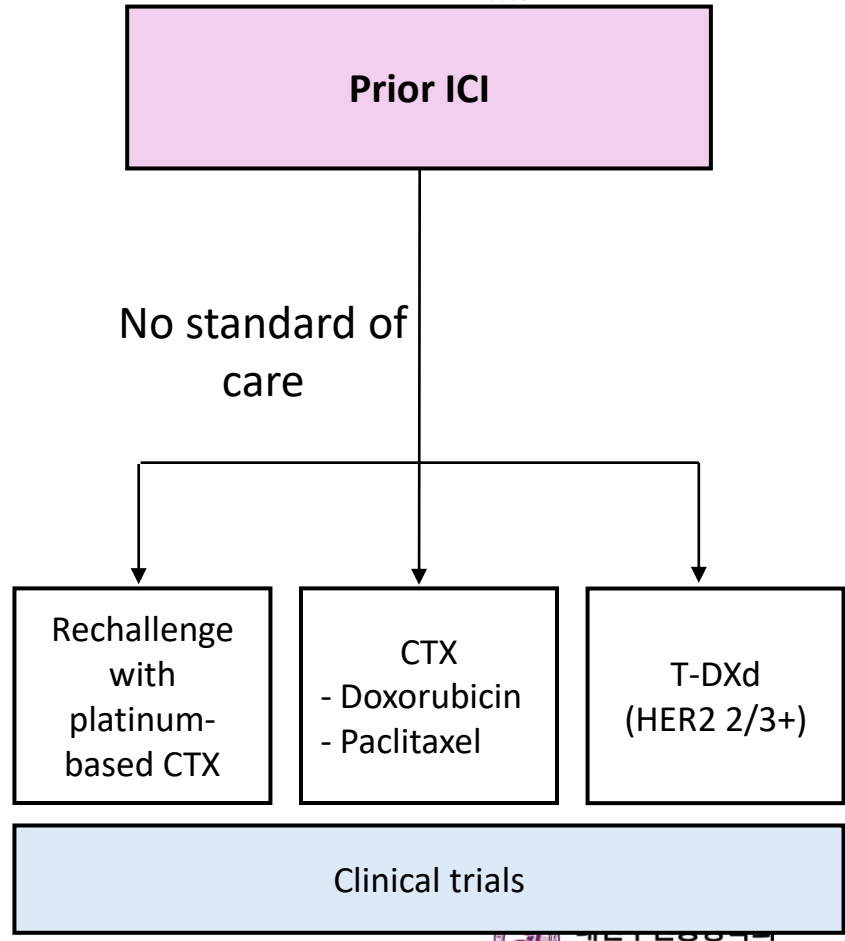
S. Koppikar et al. ESMO open 2023

CTX+ICI for metastatic or recurrent EC according to molecular classification



2nd line systemic therapy for recurrent EC





2nd line systemic therapy for recurrent EC

Endometrial cancer

Adjuvant therapy

Low risk
- **POLEmut**: confined to Ut
- **MMRd** or **NSMP** (low-grade/ER+): Conf. EM or MI<50% and no/fo. LVSI
- **MMRd**: high-G limited to EM

→ **No adjuvant Tx**

Intermediate risk
MMRd or NSMP (low-G/ER+)
MI ≥ 50% AND no/focal LVSI
NSMP (low-grade/ER+)
Cx stromal inv. AND no/focal LVSI
MMRd: High-G WITH MI, BUT No Cx inv. AND No sub. LVSI
MMRd: High-G WITH MI AND either Cx inv. OR Sub. LVSI

→ **Vaginal brachytherapy or No adjuvant Tx**

High-Intermediate risk
- dMMR: Cx stromal Inv.
- **MMRd** or **NSMP** (low-grade/ER+): Substantial LVSI
- **MMRd:** High-grade WITH myoinvasion AND either Cx inv. OR Sub. LVSI

→ **EBRT**

High risk
- **p53abn/NSMP (high-grade/ER-)**: Any myoinvasion OR Cx stromal inv.
- **All types** (except POLEmut): Extra-uterine spread

→ **CTX±RT**

Metastatic or residual dz after surgery
- Measurable dz, stage III-IV, any IVB
- clear, carcinosarcoma, serous, mixed IIIC2-IVB (dostarlimab)
- dMMR? (pembrolizumab)

1st line systemic therapy

Carboplatin/Paclitaxel

Pembrolizumab (except for carcinosarcoma)

Dostarlimab

Durvalumab (dMMR)

Durvalumab/Olaparib (dMMR)

Trastzumab (HER2+ serous or carcinosarcoma)

2nd line systemic therapy

ICI-naive

Pembro/Dostar (dMMR/MSI-H)

Lenvatinib/Pembro (pMMR/MSS)

Platinum-based CTX

Other CTX (paclitaxel/doxorubicin)

Prior ICI

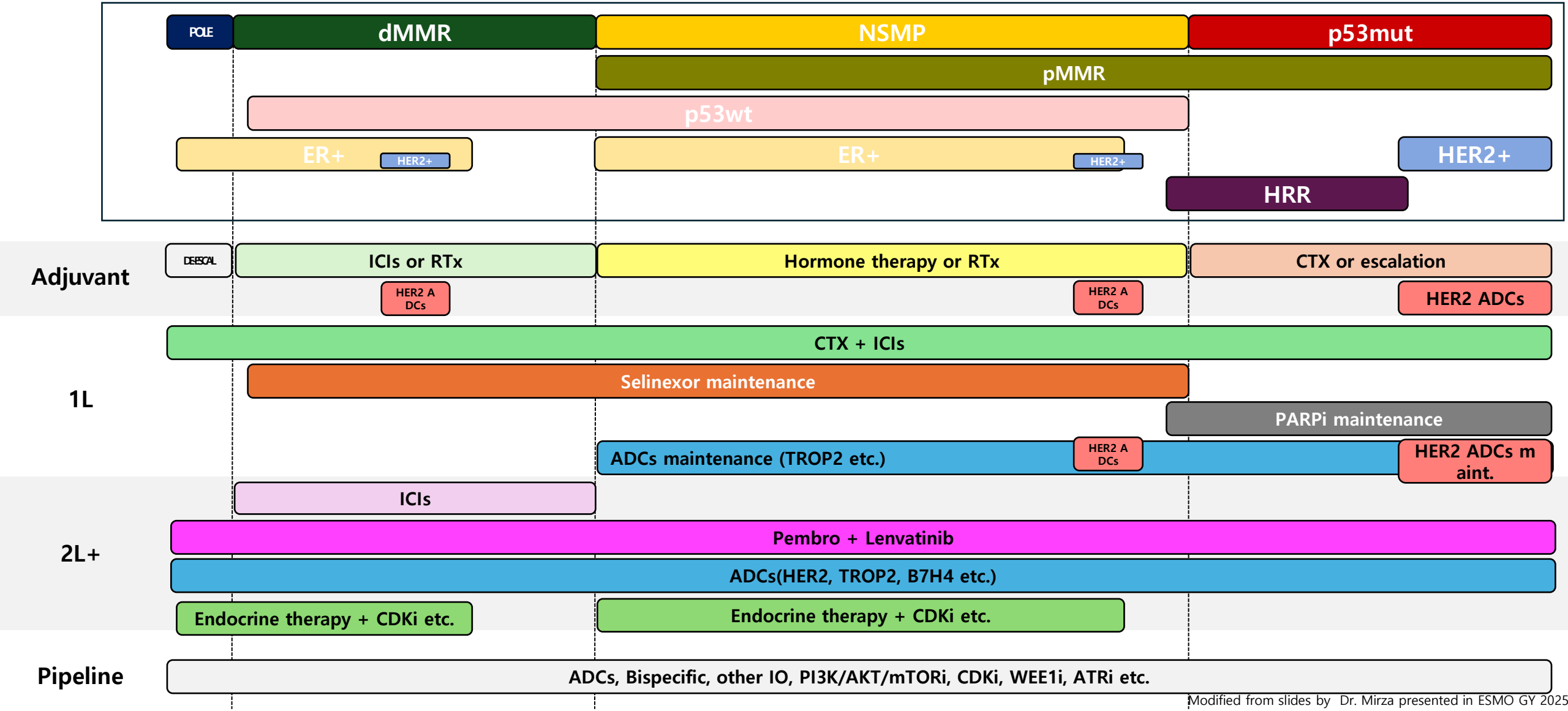
T-DXd (HER2 2/3+)

Clinical trials

Platinum-based CTX

Other CTX (paclitaxel/doxorubicin)

EC Tx. strategies according to molecular profile



Modified from slides by Dr. Mirza presented in ESMO GY 2025

www.sgo.or.kr

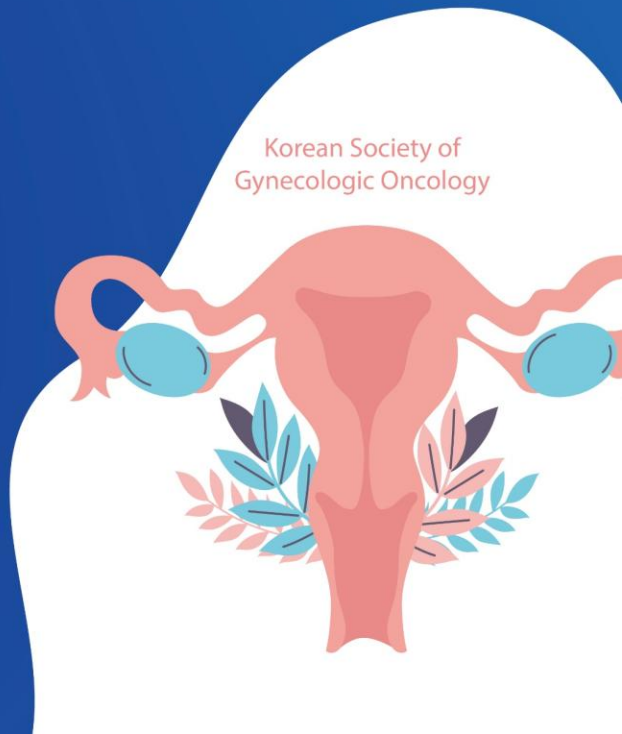
2026년 대한부인종양학회 제7회 동계학술대회 with Chemo-TIP Review

일자 2026년 1월 17일 (토)

장소 세종대학교 컨벤션센터

Thank you for your attention!

대한부인종양학회
Korean Society of Gynecologic Oncology



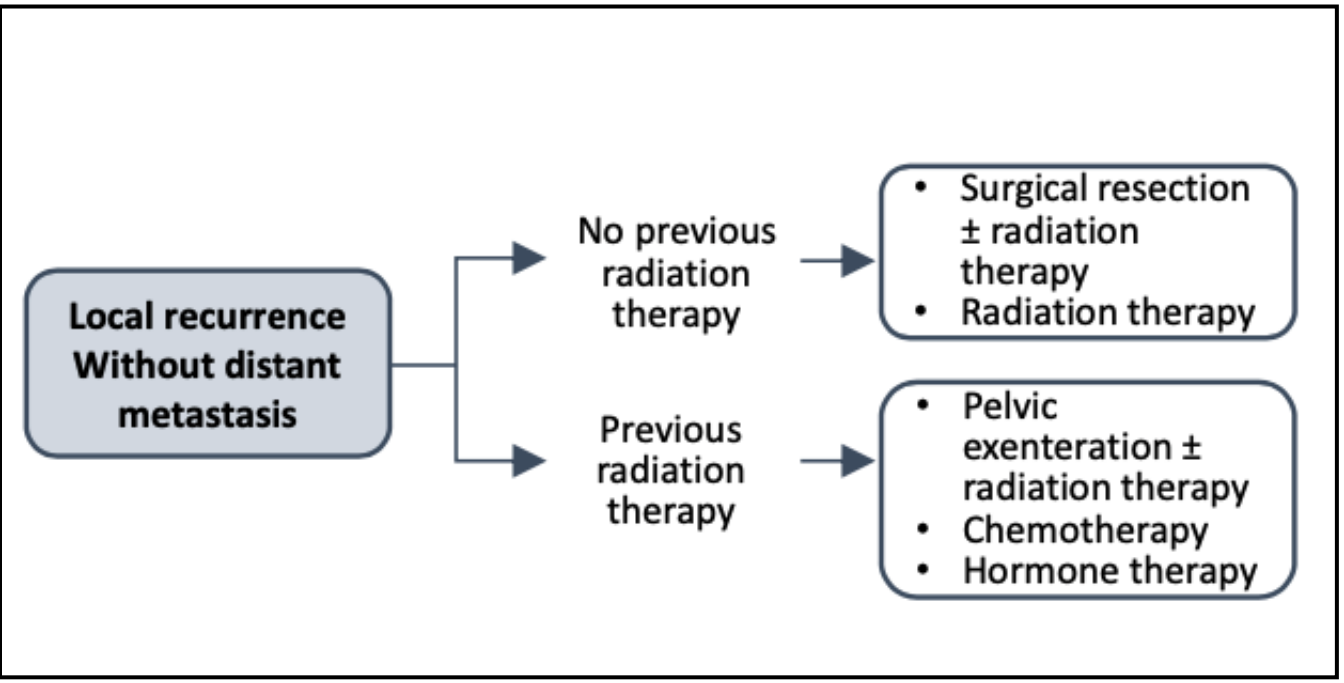
Back-up: Molecular profile of EC

	Endometrioid	Endometrioid	Endometrioid	Serous & High-grade Endometrioid	Carcinosarcoma	Clear cell
	POLE-ultramutated	MSI-hypermutated	MSS CN-low	CN-high serous-like	NA	NA
Mutational load						
SCNA load						
MSI	Mixed MSI	MSI high	MSI low	MSI low		
Grade	1, 2, 3	1, 2, 3	1, 2	3	High	High
ER status	ER+ ; ER+	ER+ ; ER-	ER+			
TP53 mutation	35%	low	low	90%	60-90%	35%
PI3K alterations	PTEN M+ (94%) PIK3CA M+ (71%) PIK3R1 M+ (65%)	PTEN M+ (75-85%) PIK3CA M+ (50-55%) PIK3R1 M+ (30-40%)		PTEN (11%) PIK3CA A+ (45%) PIK3CA M+ (35%) PIK3R1 M+ (12%)	PTEN M+ (19%) PIK3CA M+ (35%) PIK3CA A+ (14%)	PTEN loss (80%) PIK3CA (18%)
KRAS mutation	>50%	35%	low		17%	0%
ERBB alterations	0	low	low	ErbB2 A+ 30-40% (serous)	ErbB2 A+ (13%) ErbB3 A+/M+ (13%)	ErbB2 M+ (12%)
FGFR amplification or mutation	FGFR1 A+/M+ (7%) FGFR2 A+/M+ (13%) FGFR3 A+/M+ (5%)				FGFR3 A+ (20%)	
Wnt/βcatenin			CTNNB1 M+ (>50%)			
Others	ARID1A M+ (75%) PD1/PD-L1 over-expr. POLE exonuclease domain mutations	ARID1A M+ (35-40%) PD1/PD-L1 overexpr.	ARID1A M+ (35-40%)	PPP2R1A M+ (20%) FBXW7 M+ (20% of UC) HRD (15-20%)	HRD (22-53%) ARID1A (25%) PPP2R1A (28%) FBXW7 M+ (35%) CCNE1 A+ (42%) Sox17 A+ (25%)	ARID1A (25%) TERT promoter mutations

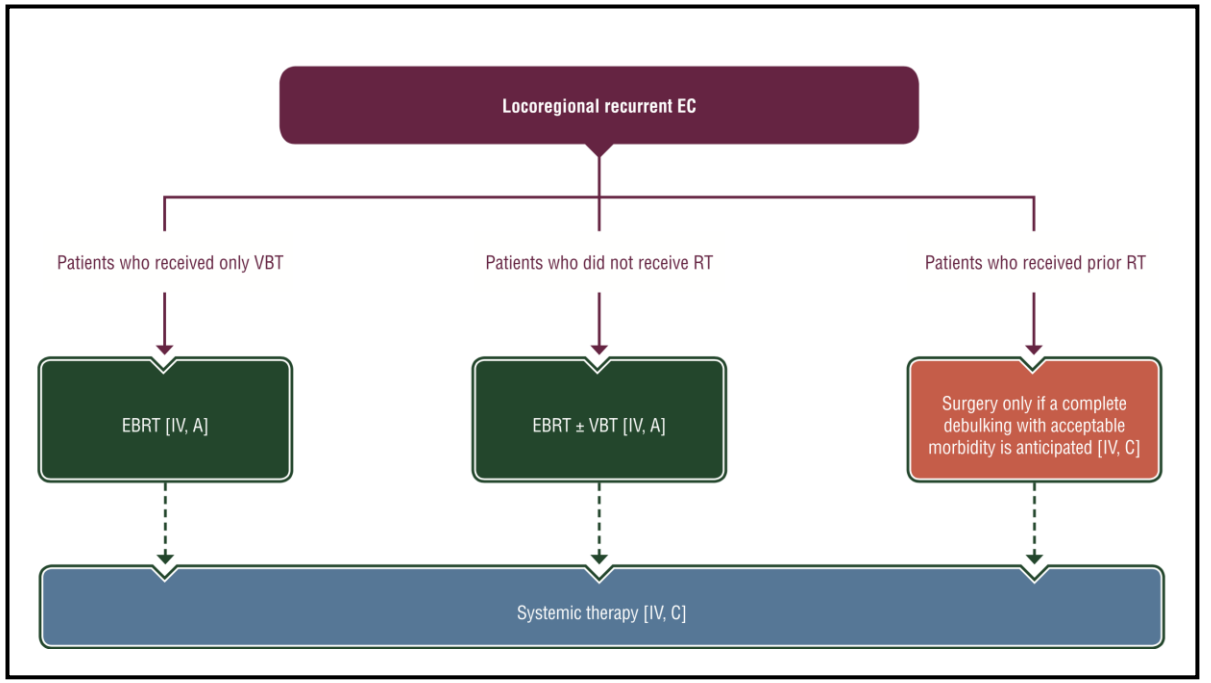
Morice et al. Lancet 2016; Jamieson et al JNCCN 2023

Back-up: Treatment for loco-regional recurrence

KSGO guideline



ESMO guideline



KSGO 2020 guideline
Oaknin et al, Ann Oncol 2022