

子宫内膜癌术后辅助放疗的选择

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2021-07-20

子宫内膜癌

发生率和死亡率都在上升

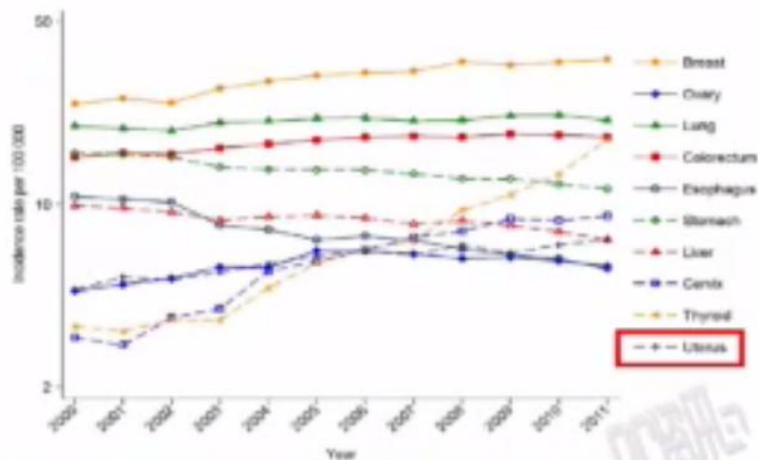
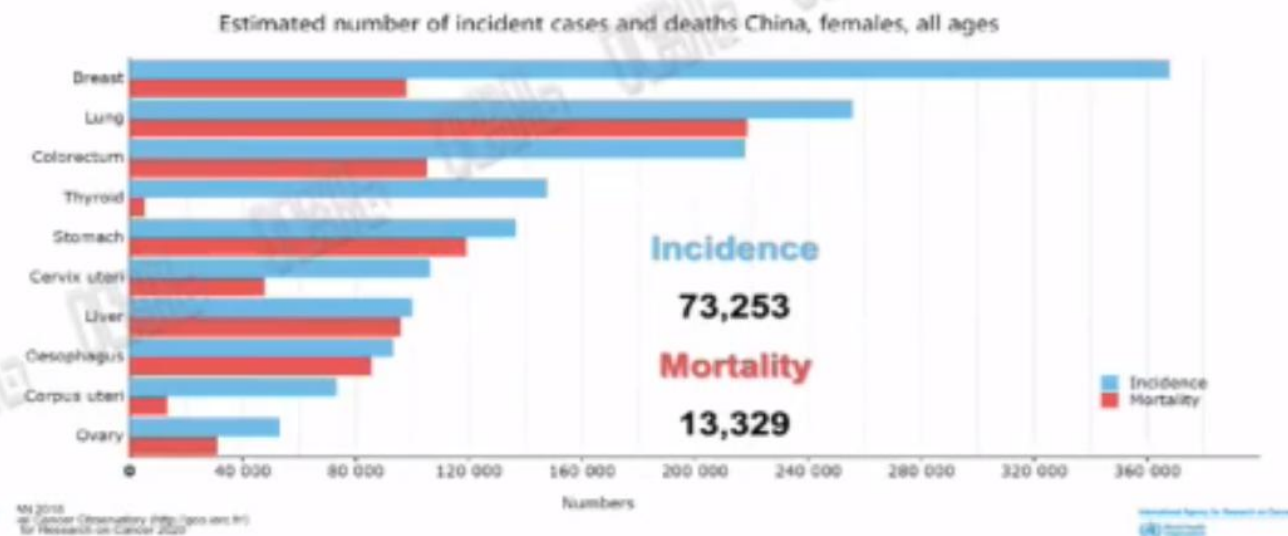


FIGURE 6. Trends in Incidence Rates (Age-Standardized to the Segi Standard Population) for Selected Cancers for Females: China, 2000 to 2011.



- 继宫颈癌之后第二个常见的妇科恶性肿瘤，约占妇科恶性肿瘤的20%~30%¹
- 我国的发病率不断上升，且有年轻化趋势²
- 中国³

发病人数 73253人/年
死亡人数 13329人/年

子宫内膜癌治疗指南

- 中国：
卫建委的诊疗规范
妇科恶性肿瘤临床实践指南
- 美国：
NCCN、ASTRO、ASCO、ABS
- 欧洲：
ESMO、ESMO-ESGO-ESTRO

.....

原则：

手术为主，辅助放疗、化疗、内分泌治疗、
靶向、免疫.....



American Society of Clinical Oncology



The American College of
Obstetricians and Gynecologists
WOMEN'S HEALTH CARE PHYSICIANS



Society of Gynecologic Oncology

ENSEMBLE,
EN RÉSEAU
POUR VAINCRE
LE CANCER



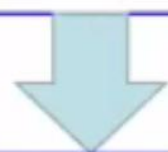
American
Brachytherapy
Society

重要的RCT研究

- ✓ GOG-33 (美国 1977-)
- ✓ Aalders (欧洲 1980-)
- ✓ GOG-99 (美国 1998-)
- ✓ PORTEC-1 (欧洲)
- ✓ PORTEC-2 (欧洲)
- ✓ Sorbe B et al (欧洲 2005-)
- ✓ ASTEC/EN.5 (英国+加拿大 1996-)
- ✓ GOG-122 (美国)
- ✓ PORTEC-3 (欧洲)
- ✓ GOG0249 (美国)
- ✓ GOG0258 (美国)
- ✓ PORTEC-4 (欧洲)
-

影响预后因素

- 分期
- 病理分型: EEC或NEEC
- 组织学分级: G1、G2、G3
- 肌层浸润
- 年龄
- LVSI



低危 (LR)、低中危 (LIR)、
中危 (IR)、高中危 (HIR)、
高危 (HR)、晚期

Risk classifications

ASCO

Journal of Clinical Oncology

Risk Group	PORTEC ¹⁰	GOG-99 ^{11*}	ESMO, ESGO, and ESTRO Consensus ²
Low	EEC, any age, grade 1-2 tumor, < 50% invasion	EEC, no invasion	EEC, grade 1-2 tumor, < 50% invasion, LVSI negative
Low-intermediate	EEC, grade 1-2 tumor, age < 60 years, ≥ 50% invasion	EEC, not high-intermediate	EEC, grade 1-2 tumor, ≥ 50% invasion, LVSI negative
High-intermediate	EEC, grade 1-2 tumor, age ≥ 60 years, ≥ 50% invasion	EEC, age ≥ 70 years with one factor or ≥ 50 years with two factors: grade 3 tumor, ≥ 66% invasion, or LVSI	EEC, grade 3 tumor, < 50% invasion, any LVSI
	EEC, grade 3 tumor, age ≥ 60 years, < 50% invasion	EEC, any age, with all factors: grade 3 tumor, ≥ 66% invasion, and LVSI	EEC, grade 1-2 tumor, LVSI positive, any invasion
High	EEC, grade 3 tumor, ≥ 50% invasion	Stage II-III EEC	EEC, grade 3 tumor, ≥ 50% invasion, any LVSI
	Stage II-III EEC	Stage I-III NEEC	Stage II-III EEC, no residual disease
	Stage I-III NEEC (serous/clear cell)		NEEC (serous, clear cell, undifferentiated, carcinosarcoma)
Advanced/ metastatic	Stage IV	Stage IV	Stage III with residual disease and stage IVa
			Stage IVb

研究设计：随机、多中心研究

N = 645

入组标准：
FIGO IA-IB
Endometrioid
G1-G2



随机分配

观察组(n = 326): 单纯手术

实验组(n = 319): 手术+VBT

主要结果:

➤ 26例(4.0%)复发,
局部复发率2.6%
远处复发率1.4%;

➤ 阴道残端复发率
单纯手术: 3.1%,
手术+VBT: 1.2% (p = 0.114)

*1988年分期:

IA病变局限于子宫内膜

IB病变浸润 $<1/2$

IC病变浸润 $>1/2$

总体复发率较低，且VBT未能降低阴道残端复发率，建议观察



All staging in guideline is based on updated FIGO staging. ([See ST-1](#))

CLINICAL FINDINGS (Endometrioid Histology)^a

Surgically staged:
Stage I^e →

HISTOLOGIC GRADE/ADJUVANT TREATMENT^{g,h,m}

FIGO Stage	Histologic Grade	Adjuvant Treatment
IA	G1, G2	Observation preferred or Consider vaginal brachytherapy if lymphovascular space invasion (LVSI) and/or age ≥60 y ⁿ
	G3	Vaginal brachytherapy preferred or Consider observation if no myoinvasion or Consider EBRT if high-intermediate risk (HIR) ^o (category 2B)
IB	G1	Vaginal brachytherapy preferred ^o or Consider observation if no other adverse risk factors ^{o,p}
	G2	Vaginal brachytherapy preferred or Consider EBRT if HIR ^o or Consider observation if no other adverse risk factors ^q
	G3	RT (EBRT and/or vaginal brachytherapy) ± systemic therapy ^q (category 2B for systemic therapy)

^a[See \(UN-1\)](#) for classification of uterine neoplasms.

^eThe degree of surgical staging to assess disease status depends on preoperative and intraoperative findings. Multidisciplinary expertise is recommended.

^g[See Principles of Evaluation and Surgical Staging \(ENDO-C\)](#).

^h[See Principles of Radiation Therapy for Uterine Neoplasms \(UN-A\)](#).

ⁱ[See Systemic Therapy for Endometrial Carcinoma \(ENDO-D\)](#).

^mInitiate EBRT as soon as the vaginal cuff is healed, preferably no later than 12 weeks after surgery.

ⁿVaginal brachytherapy strongly suggested if two risk factors present.

^oIf HIR per GOG 249: age 50–69 y with two risk factors or age <50 y with three risk factors, or age ≥70 y with one risk factor. Risk factors include grade 2 or 3, depth of invasion to outer half, and LVSI.

^pPotential adverse risk factors: age ≥60 y, depth of invasion, and/or LVSI. [See Discussion](#) for additional information on adverse risk factors.

^qRisk factors that would lead to EBRT ± systemic therapy are: age, LVSI, and depth of myoinvasion. Risk factors are continuous variables. Risk of recurrence is higher with older age (especially >60 y), extensive LVSI, and deeper myoinvasion (>50%). Also, when there are more risk factors present, the risk of recurrence is higher. [See Systemic Therapy for Endometrial Carcinoma \(ENDO-D\)](#).

I期子宫内膜癌——LR

Risk Group	PORTEC ¹⁰	GOG-99 ^{11*}	ESMO, ESGO, and ESTRO Consensus ²
Low	EEC, any age, grade 1-2 tumor, < 50% invasion	EEC, no invasion	EEC, grade 1-2 tumor, < 50% invasion, LVSI negative

- **低危组：** IA期， G1/G2, 子宫内膜样腺癌， 不伴有LVSI、 年龄<60岁
- 复发风险： <5%

术后不推荐辅助治疗

I期子宫内膜癌术后放疗——LIR、IR、HIR

Risk Group	PORTEC ¹⁰	GOG-99 ^{11*}	ESMO, ESGO, and ESTRO Consensus ²
Low-intermediate	EEC, grade 1-2 tumor, age < 60 years, $\geq$ 50% invasion	EEC, not high-intermediate	EEC, grade 1-2 tumor, $\geq$ 50% invasion, LVSI negative
High-intermediate	EEC, grade 1-2 tumor, age $\geq$ 60 years, $\geq$ 50% invasion	EEC, age $\geq$ 70 years with one factor or $\geq$ 50 years with two factors: grade 3 tumor, $\geq$ 66% invasion, or LVSI	EEC, grade 3 tumor, < 50% invasion, any LVSI
	EEC, grade 3 tumor, age $\geq$ 60 years, < 50% invasion	EEC, any age, with all factors: grade 3 tumor, $\geq$ 66% invasion, and LVSI	EEC, grade 1-2 tumor, LVSI positive, any invasion

观察**vs**体外放疗：体外放疗降低局部复发，不改变总生存

	入组标准	术式	分组	局部复发率	生存率
PORTEC-1 2000	714例 IB期, G2-3 IC期, G1-2	TAH-BSO	观察 VS EBRT	14% 4% P<0.001	85% 81% NS
GOG-99 2004	392例 IB, IC, IIA	TAH-BSO + LA		12% 3% P<0.1	86% 92% NS
ASTEC/EN.5 2009	789例 IA/IB期, G3 IC期	TAH-BSO + LA (30%)		6% (BT 50%) 3% (BT 50%) P<0.02	84% 84% NS

PORTEC-1

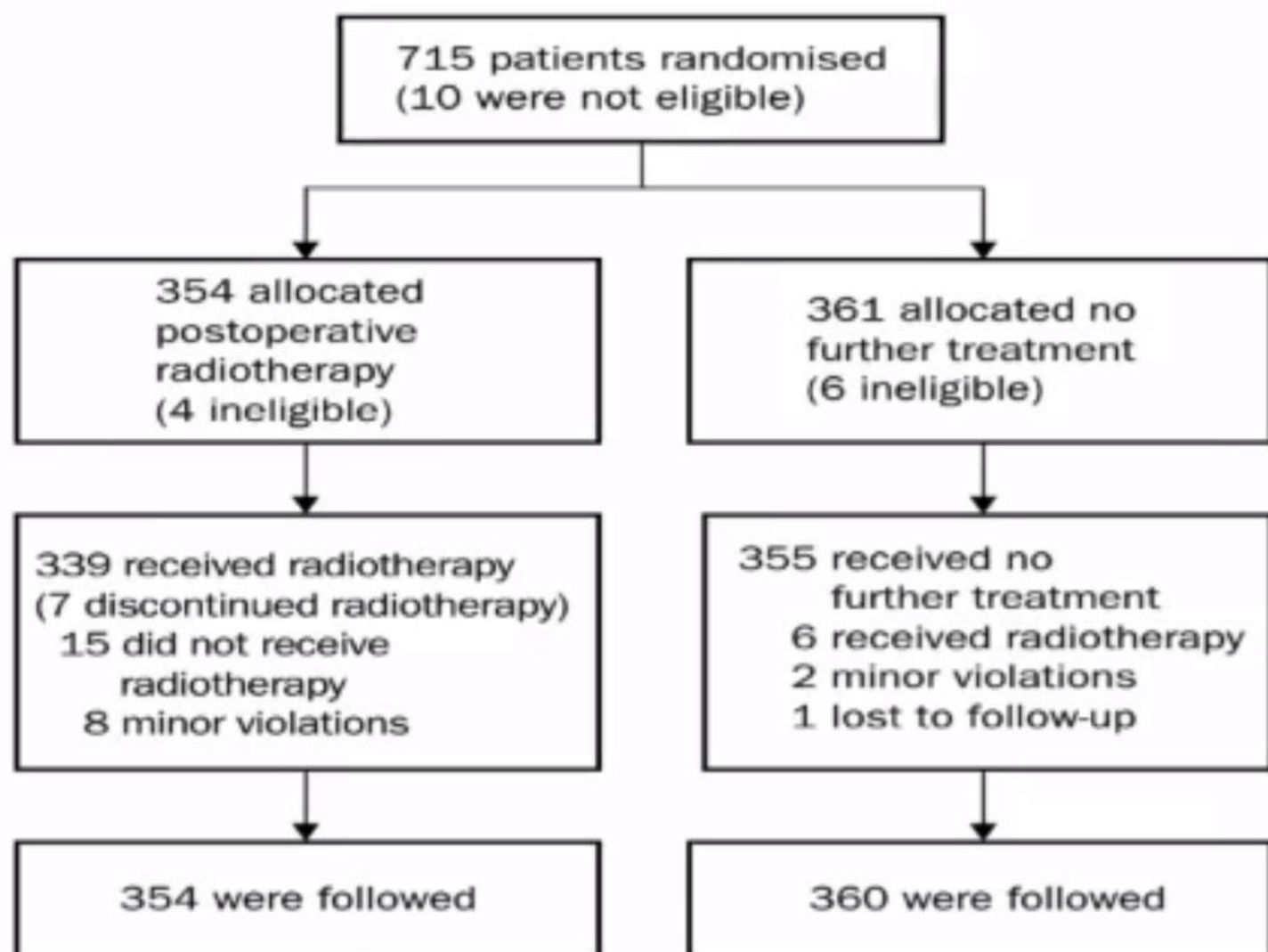


Figure 1: **Trial profile**

入组标准：I期

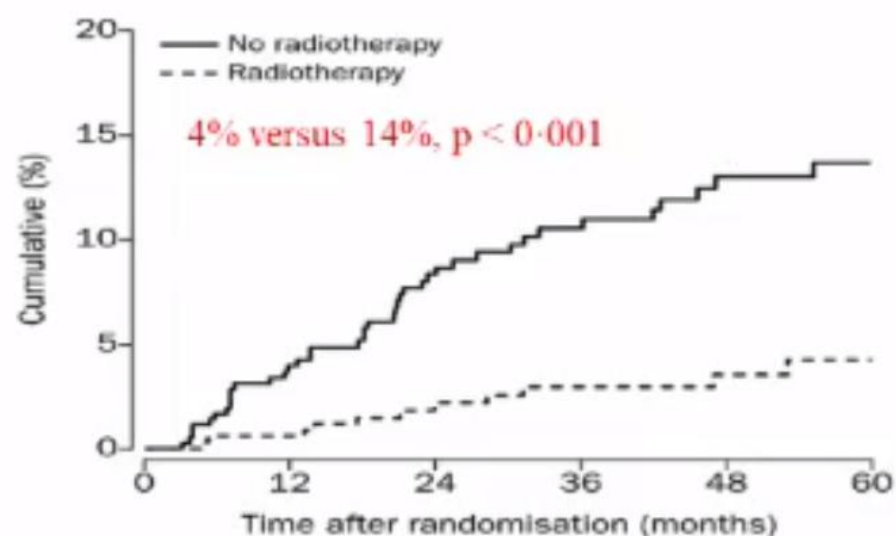
➤ 深肌层浸润；

➤ G2；

➤ G3、浅肌层浸润

中位随访52个月

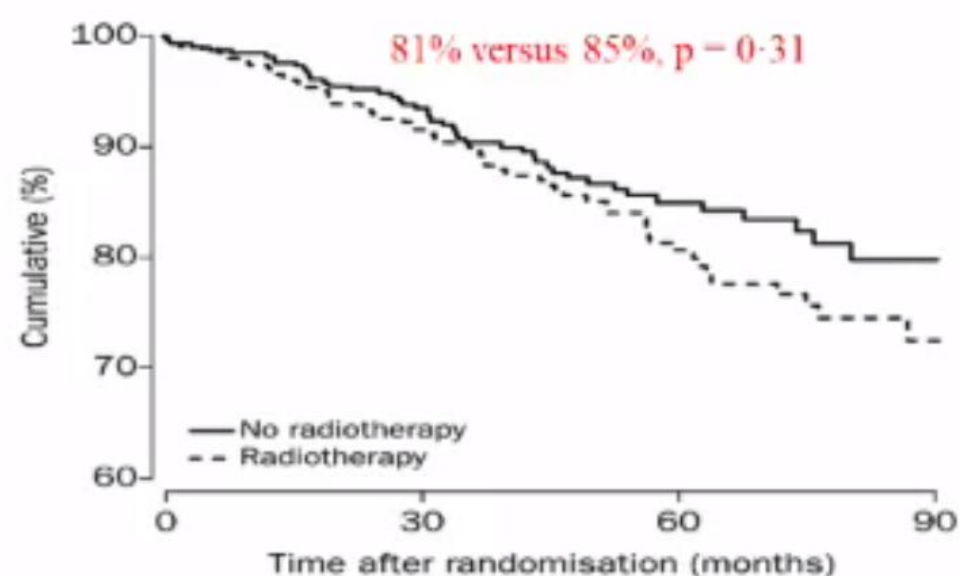
PORTEC-1: EBRT降低5年局部复发率, 不改善生存率



Numbers at risk

Radiotherapy	354	338	284	219	161	109
No radiotherapy	360	328	271	210	159	115

Figure 2: **Probability of locoregional (vaginal or pelvic) relapse for patients assigned to postoperative radiotherapy or no further treatment**



Numbers at risk

Radiotherapy	354	260	111	24
No radiotherapy	360	257	125	23

Figure 3: **Probability of survival for patients assigned to postoperative radiotherapy or no further treatment**

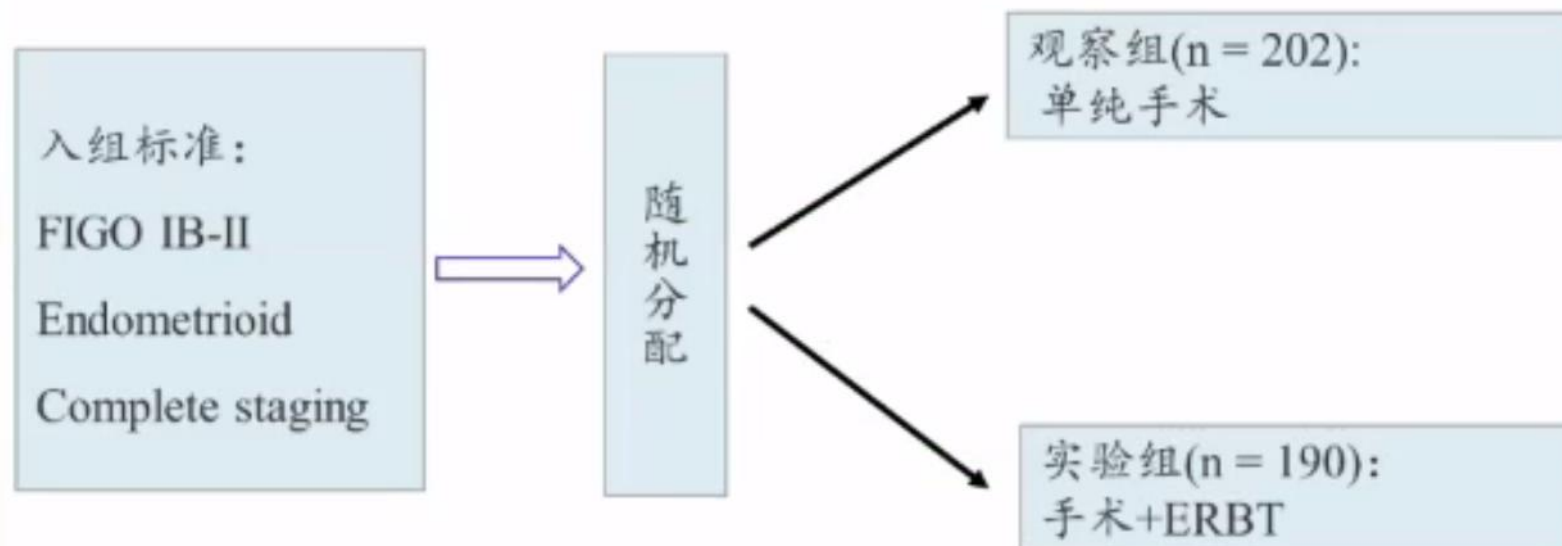
PORTEC-1: 影响预后的主要为>60岁、G3, 未进一步分层分析 (HIR)

	Locoregional relapse		Death due to endometrial cancer	
	Hazard ratio (95% CI)	p	Hazard ratio (95% CI)	p
Age ≥ 60	3.2 (1.3–7.5)	0.003	3.1 (1.2–8.0)	0.02
Invasion $\geq 50\%$	1.8 (0.9–3.8)	0.11	1.9 (0.8–4.4)	0.16
Grade 1	0.77 (0.4–1.6)	0.50	0.45 (0.2–1.3)	0.15
Grade 3	2.2 (0.8–5.8)	0.11	4.9 (1.9–12.5)	0.0008
No radiotherapy	3.9 (2.0–7.6)	<0.0001	0.76 (0.4–1.4)	0.37

Hazard ratio describes relative hazard of failure per unit time, for age ≥ 60 years compared with <60 years; for myometrial invasion $\geq 50\%$ compared with <50%; for grade 1 and 3 compared with grade 2; for no radiotherapy compared with postoperative radiotherapy.

GOG-99 trial

N = 392



主要结果:

- 中位随访69月, 49例复发, 32例疾病相关死亡;
- 2年累计复发率12% VS. 3% (HR: 0.42; P = 0.007);
- 4年累计生存率86% VS. 92% (HR: 0.86; P = 0.557);
- **主要获益人群: HIR组**
- 放疗主要降低了盆腔和阴道残端复发。

- *1988年分期IA病变局限于子宫内膜
IB病变浸润 $<1/2$
IC病变浸润 $>1/2$

GOG-99 trial: HIR获益更明显

➤ HIR定义:

G2-G3、LVSI、>2/3肌层受累

>50岁至少2个危险因素、>70岁至少1个危险因素.

GOG-99 trial: HIR组获益更明显

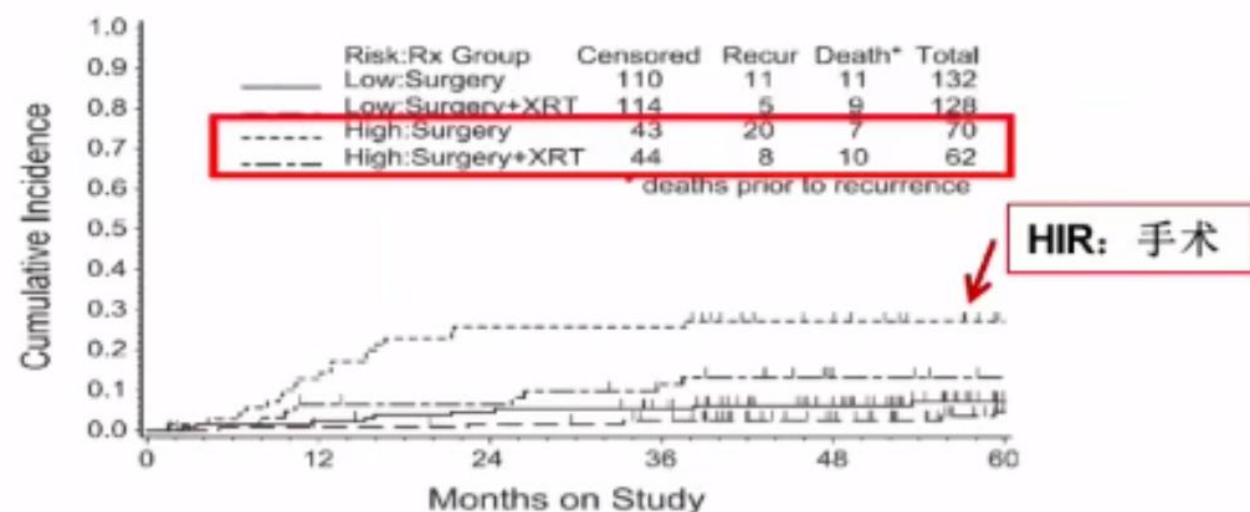


Fig. 3. Cumulative incidence of recurrence by randomized treatment group and risk group.

All	31	13		0.42 (0.25,0.73)
High risk		20	8	0.42 (0.21,0.83)
Low risk		11	5	0.46 (0.19,1.11)

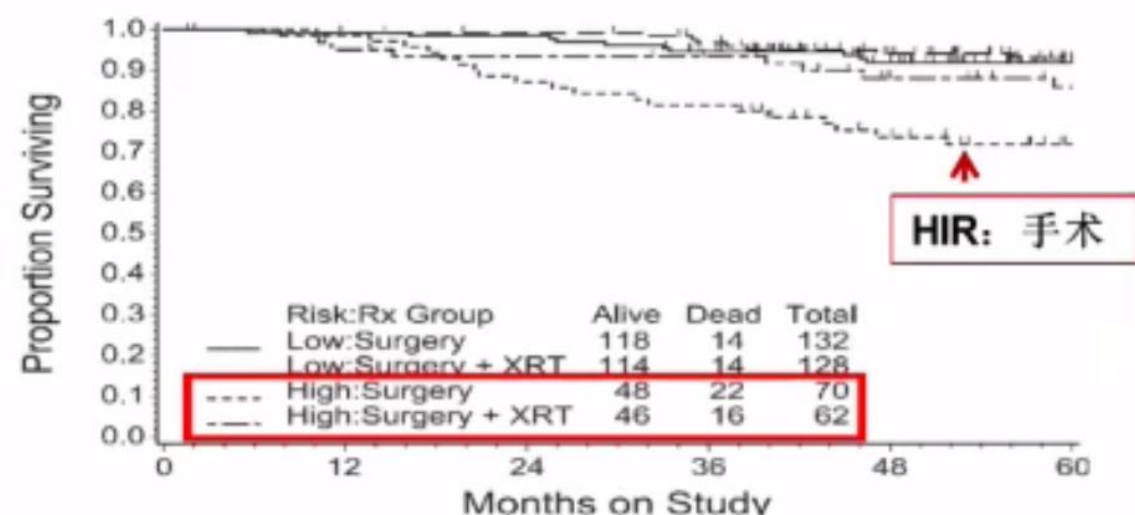


Fig. 4. Survival by randomized treatment group and risk group.

All	17	15		0.93 (0.52,1.67)
High risk		14	8	0.60 (0.29,1.24)
Low risk		3	7	2.38 (0.77,7.42)

H.M. Keys, et al., Gynecol. Oncol. 92 (3) (2004) 744-751.

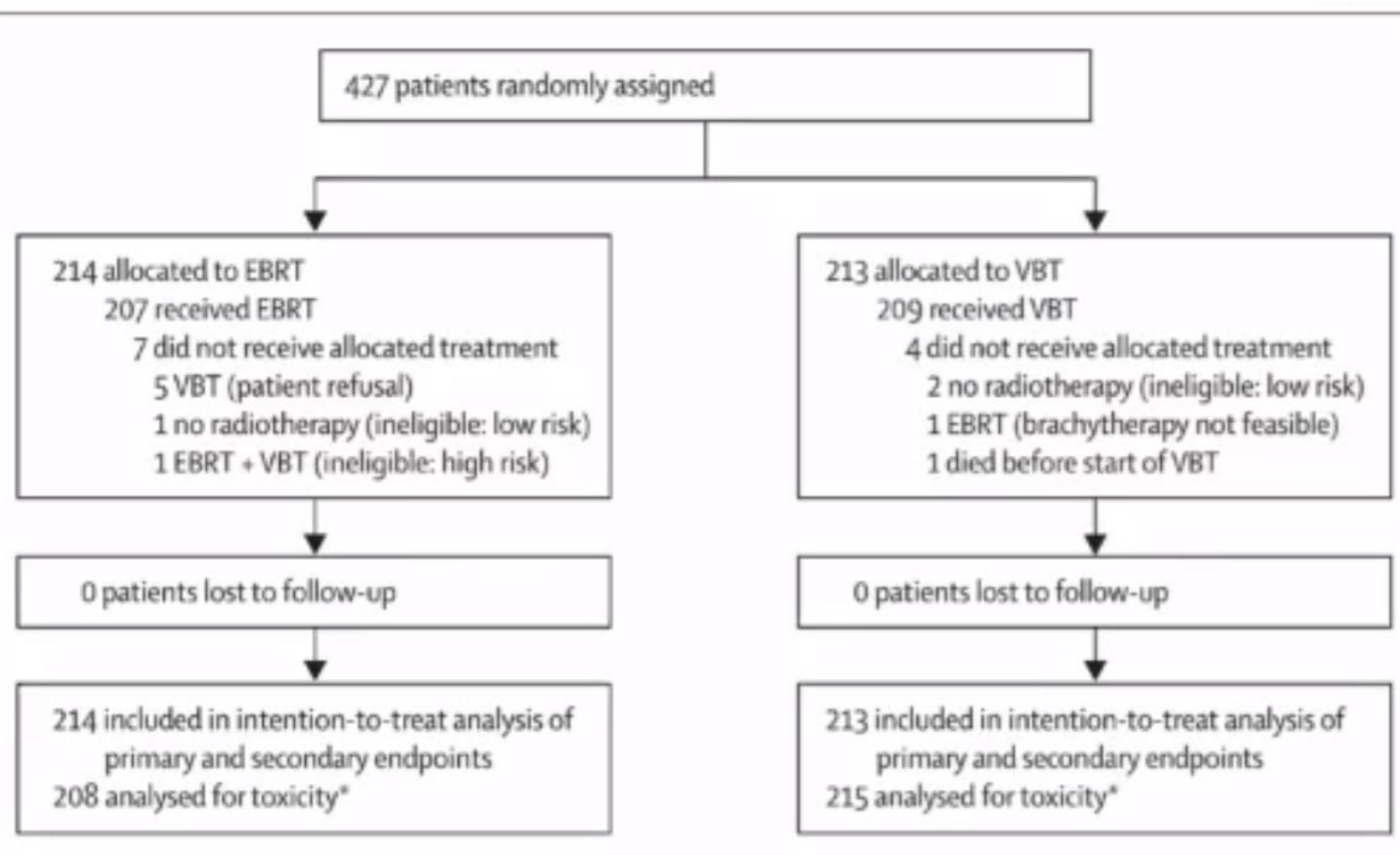
I期子宫内膜癌术后放疗——LIR、IR、HIR

PORTEC-1: HIR (年龄>60岁、G3)
——体外放疗获益

GOG-99 : HIR (G2/G3、LVSI、>2/3肌层受累)
年龄>50岁至少2个危险因素
年龄>70岁至少1个危险因素
——体外放疗获益

I期EEC: 体外放疗降低局部复发, 不改变总生存, HIR更获益

PORTEC-2: VBT vs EBRT——（非劣性研究）



入组标准:

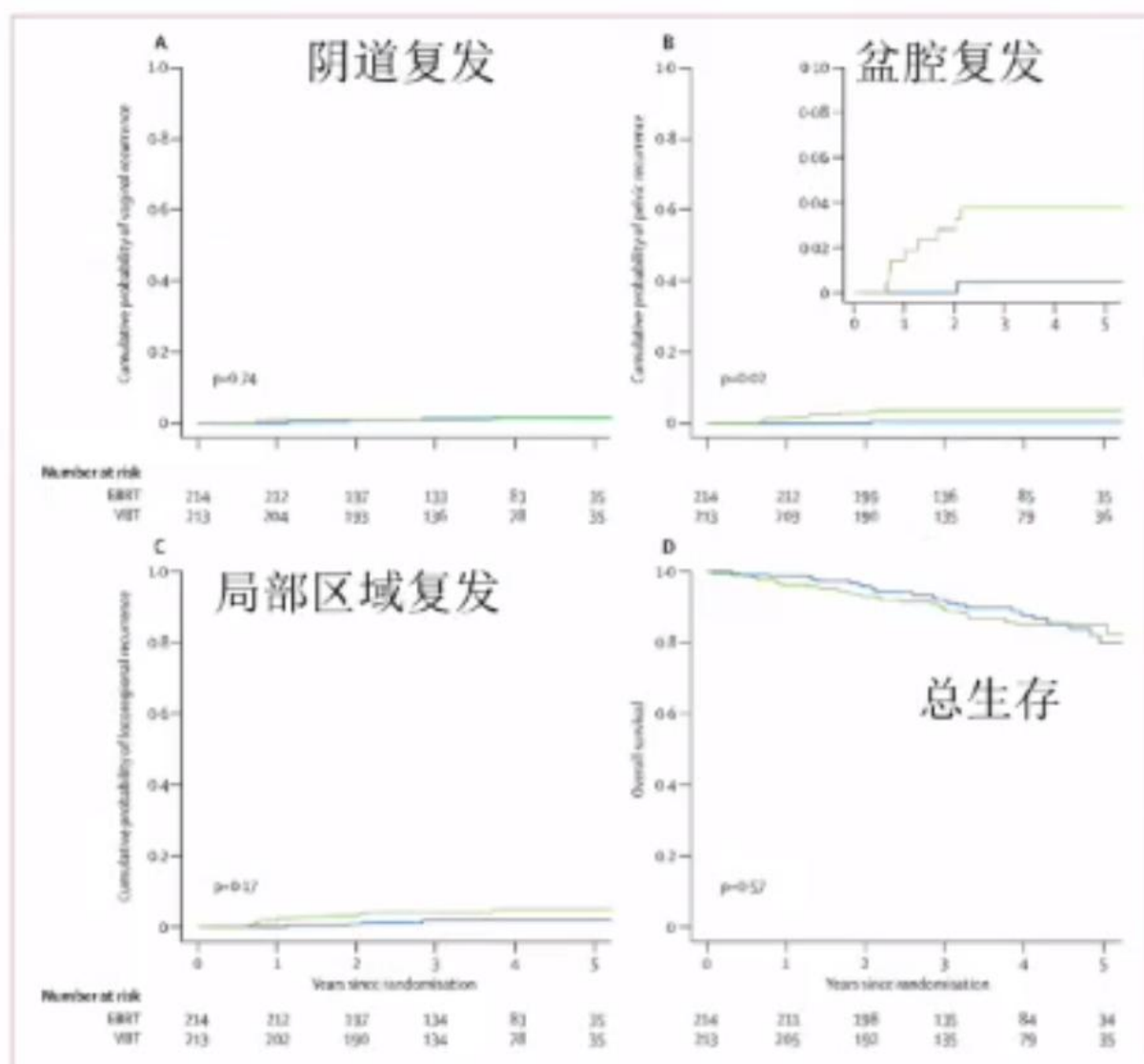
- 60 岁且G3或 IC期, G1-G2;
- IIA (除外G3伴深肌层浸润)

*1988年分期IIA病变只浸润宫颈腺体

其中80%为IC期,
中位随访45月

	近距离	体外	P值
阴道复发	1.8%	1.6%	0.74
局部区域复发	5.1%	2.1%	0.17
单纯盆腔复发	3.8%	0.5%	0.02
病理重阅后分析无差异			
远处转移	8.3%	5.7%	0.46
总生存	84.8%	79.6%	0.57
无病生存	82.7%	78.1%	0.74
消化道副反应	12.6%	53.8%	

- DFS、OS、局部局域复发无差异
- 盆腔复发 **EBRT < BT**
- 副反应: **G1-2**消化道反应 **EBRT > BT**



I期HIR伴有其他因素 - II期子宫内膜癌术后放疗

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Death from all causes (time-to-event data)	2	334	Hazard Ratio (Random, 95% CI)	0.91 [0.60, 1.39]
1.1 EBRT vs no additional treatment	1	132	Hazard Ratio (Random, 95% CI)	0.73 [0.38, 1.40]
1.2 EBRT vs no additional treatment (VBT balanced across groups)	1	202	Hazard Ratio (Random, 95% CI)	1.07 [0.61, 1.88]
2 Death from all causes	3	429	Risk Ratio (M-H, Random, 95% CI)	0.88 [0.63, 1.22]
2.1 EBRT vs no additional treatment	1	132	Risk Ratio (M-H, Random, 95% CI)	0.82 [0.48, 1.42]
2.2 EBRT vs no additional treatment (VBT balanced across groups)	2	297	Risk Ratio (M-H, Random, 95% CI)	0.91 [0.60, 1.38]
3 Endometrial carcinoma-related deaths (time-to-event data)	2	334	Hazard Ratio (Random, 95% CI)	0.84 [0.51, 1.40]

- I期IB且G3
- II期（宫颈间质受侵）
- 中高危：中危合并其它危险因素（>60岁，LVSI等）

EBRT降低死亡风险，降低盆腔复发率，改善OS趋势

I期HIR伴有其他因素 -II期子宫内膜癌术后放疗

- EBRT? vs EBRT+BT?
- EBRT后的阴道复发率
 - 2.3%、1.6% (PORTEC-1、PORTEC-2)、1% (JGOG)
 - 其中高危组复发 2% (Creutzberg et al)
- EBRT+BT 后的复发率
 - 1.9% (Sorbe et al)
- EBRT+BT vs EBRT
 - 阴道复发率 (6% vs 7.7%, $P=0.74$)
 - 盆腔控制率 (96% vs 94%, $P=NS$)
 - 毒性 (18.6% vs 3.8%, $P=0.01$)
 - 继发肿瘤发生率 (3.48% vs 2.71%)

Creutzberg CL, van Putten WL, Wärlam-Rodenhuis CC, et al. Outcome of high-risk stage IC, grade 3, compared with stage I endometrial carcinoma patients: The Post-operative Radiation Therapy in Endometrial Carcinoma Trial. *J Clin Oncol* 2004;22:1234-1241.

Sorbe B, Horvath G, Andersson H, Boman K, Lundgren C, Pettersson B. External pelvic and vaginal irradiation versus vaginal irradiation alone as postoperative therapy in medium-risk endometrial carcinoma—a prospective randomized study. *Int J Radiat Oncol Biol Phys* 2012;82:1249-1255.

Randall ME, Wilder J, Greven K, Raben M. Role of intracavitary cuff boost after adjuvant external irradiation in early endometrial carcinoma. *Int J Radiat Oncol Biol Phys* 1990;19:49-54.

Greven KM, D'Agostino RB Jr, Lanciano RM, Corn BW. Is there a role for a brachytherapy vaginal cuff boost in the adjuvant management of patients with uterine-confined endometrial cancer? *Int J Radiat Oncol Biol Phys* 1998;42:101-104.

I-II期子宫内膜癌术后放疗——LIR

- 低-中危组：IA期，G1/G2，子宫内膜样腺，伴有LVSI或年龄大于60岁
——可考虑行近距离放疗减少阴道复发



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All staging in guideline is based on updated FIGO staging. [\(See ST-1\)](#)

CLINICAL FINDINGS
(Endometrioid
Histology)^a

HISTOLOGIC GRADE/ADJUVANT TREATMENT^{g,h,m}

FIGO Stage	Histologic Grade	Adjuvant Treatment
IA	G1, G2	Observation preferred or Consider vaginal brachytherapy if lymphovascular space invasion (LVSI) and/or age ≥ 60 y ⁿ
	G3	Vaginal brachytherapy preferred or Consider observation if no myoinvasion or Consider EBRT if high-intermediate risk (HIR) ^o (category 2B)

Surgically staged:
Stage I^e →

I-II期子宫内膜癌术后放疗——LIR、IR、HIR

- 中危： IA (G3)、IB (G1/G2)，无LVSI，年龄<60，
——EBRT与BT减少阴道复发等效
——更推荐BT



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All staging in guideline is based on updated FIGO staging. [\(See ST-1\)](#)

CLINICAL FINDINGS
(Endometrioid
Histology)^a

Surgically staged:
Stage I^b →

HISTOLOGIC GRADE/ADJUVANT TREATMENT^{a,h,m}

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	G3	Vaginal brachytherapy preferred or Consider observation if no myoinvasion or Consider EBRT if high-intermediate risk (HIR) ^o (category 2B)
IB	G1	Vaginal brachytherapy preferred ^o or Consider observation if no other adverse risk factors ^{o,p}
	G2	Vaginal brachytherapy preferred or Consider EBRT if HIR ^o or Consider observation if no other adverse risk factors ^{o,p}

I-II期子宫内膜癌术后放疗——LIR、IR、HIR

● 中-高危组:

IA(G3)、IB₁(G1/G2) 合并LVSI或高龄

——EBRT降低盆腔复发率, 有改善OS趋势

——推荐EBRT降低盆腔复发率

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All staging in guideline is based on updated FIGO staging. [\(See ST-1\)](#)

HISTOLOGIC GRADE/ADJUVANT TREATMENT^{9,h,m}

FIGO Stage	Histologic Grade	Adjuvant Treatment
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	G3	Vaginal brachytherapy preferred or Consider observation if no myoinvasion or Consider EBRT if high-intermediate risk (HIR) ^o (category 2B)
IB	G1	Vaginal brachytherapy preferred ^o or Consider observation if no other adverse risk factors ^{o,p}
	G2	Vaginal brachytherapy preferred or Consider EBRT if HIR ^o or Consider observation if no other adverse risk factors ^{o,p}
	G3	RT (EBRT and/or vaginal brachytherapy) $\pm$ systemic therapy ^q (category 2B for systemic therapy)

HR

Risk Group	PORTEC ¹⁰	GOG-99 ^{11*}	ESMO, ESGO, and ESTRO Consensus ²
High	EEC, grade 3 tumor, ≥ 50% invasion	Stage II-III EEC	EEC, grade 3 tumor, ≥ 50% invasion, any LVSI
	Stage II-III EEC	Stage I-III NEEC	Stage II-III EEC, no residual disease
	Stage I-III NEEC (serous/clear cell)		NEEC (serous, clear cell, undifferentiated, carcinosarcoma)

包括:

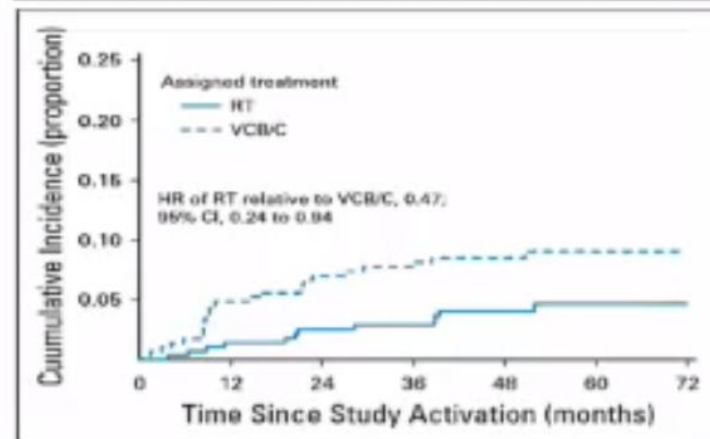
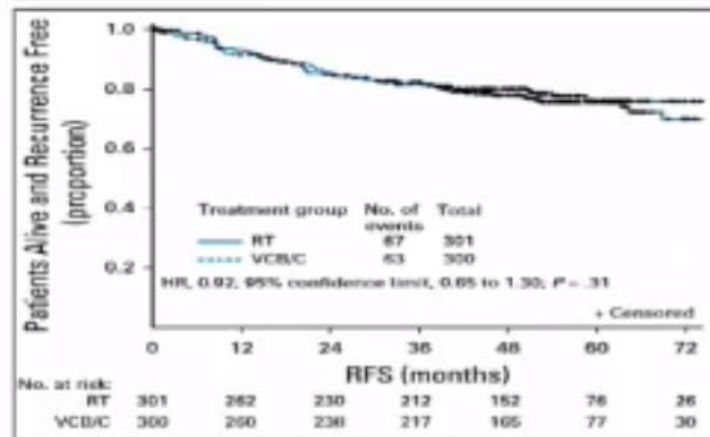
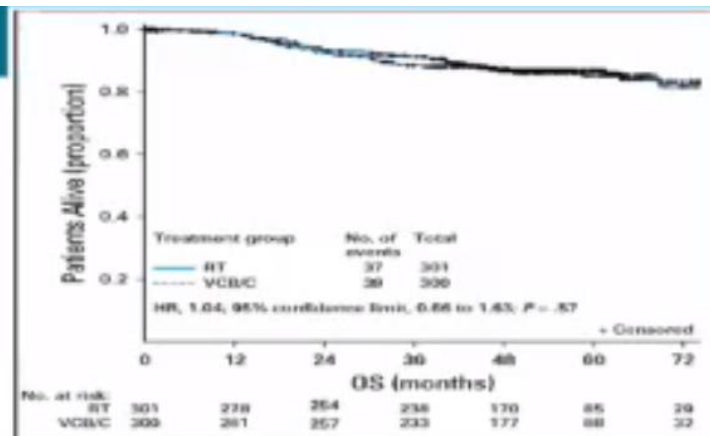
- 早期**EEC**: **IB且G3**
II期（宫颈间质受侵）
- 晚期**EEC**: **III及IV期**
- **NEEC**: 浆液性癌（任何分期）
透明细胞癌（任何分期）
癌肉瘤（任何分期）

盆腔复发率>15%，远处转移风险增加

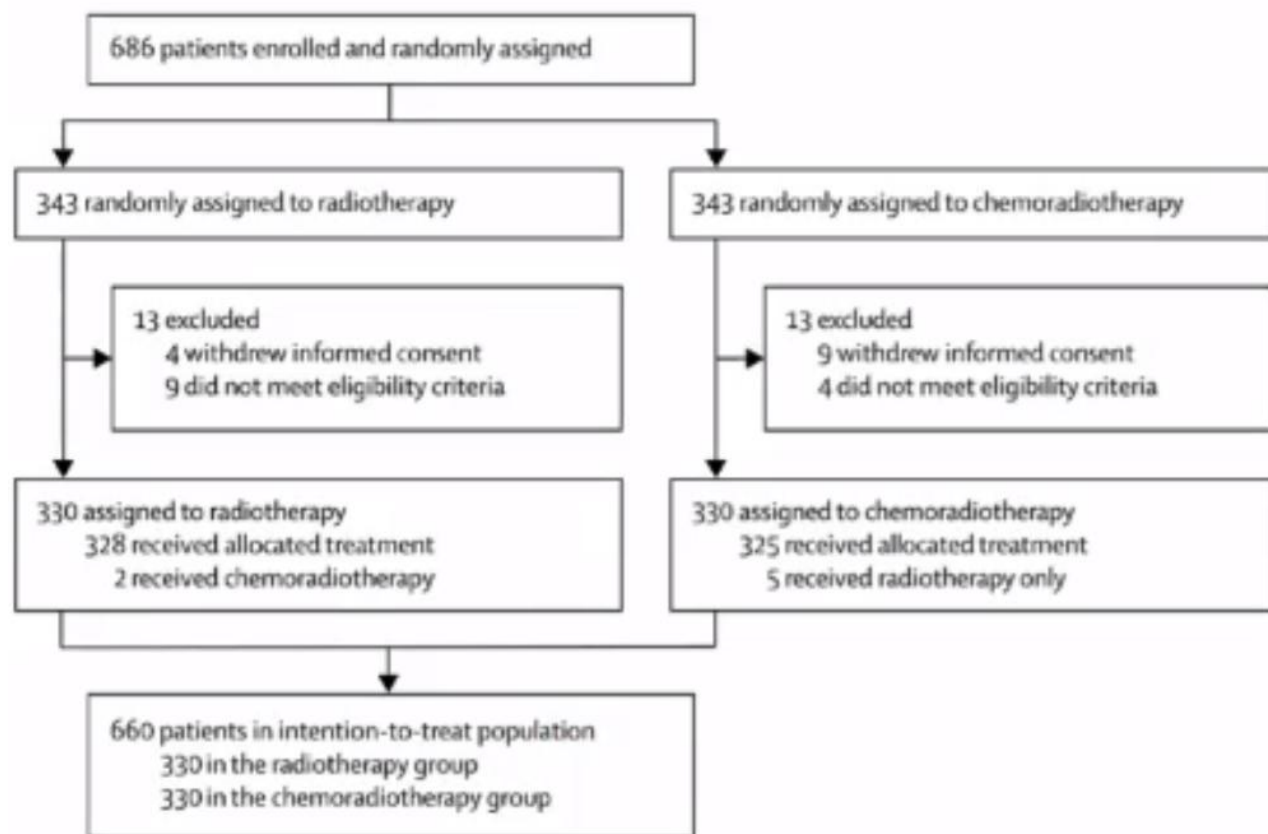
ESMO-ESOG-ESTRO
ASTRO
ASCO
NCCN

HR——GOG-0249

- I期高中危、II期 EC, I-II期浆液性或透明细胞癌
- EBRT±BT vs BT+紫杉醇联合卡铂3程
- 入组601pts: 298 vs. 302
- 结果:
 - 5y-OS 87% vs 85%, RFS 76% vs 76% (阴道及远转率相当)
 - 盆腔区域复发率在化疗组联合BT 中略高 (9% vs 4%)
 - 副反应: 急性期化疗组略高 (>G3 62% vs 11%), 远期反应相当
- 早期高危患者, 术后单纯放疗有效、安全,
化疗没有体现优势!



HR—PORTEC-3



入组标准:

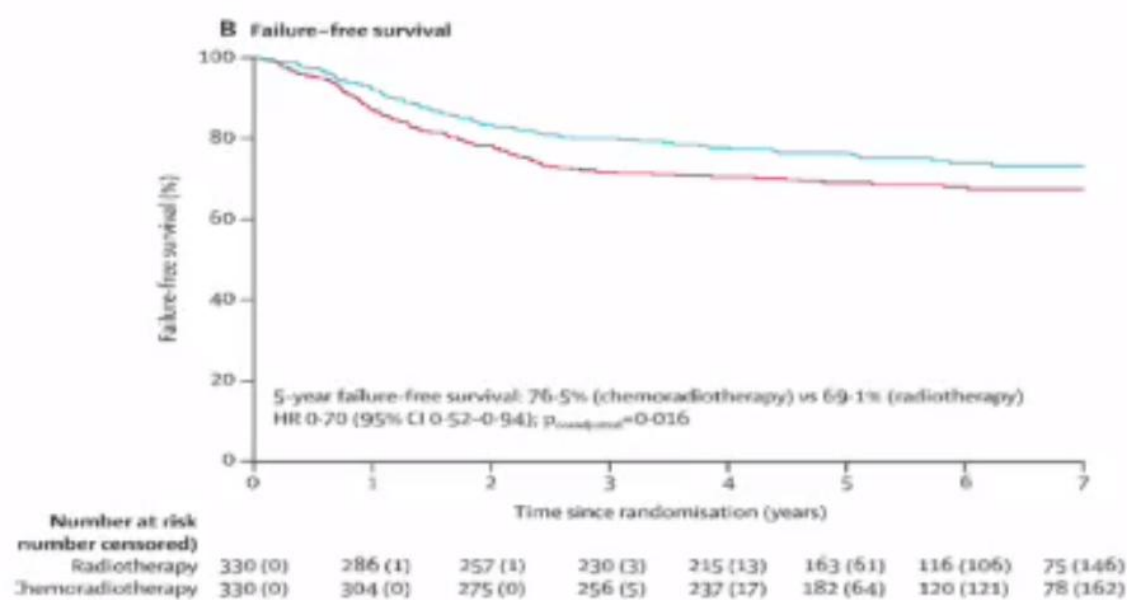
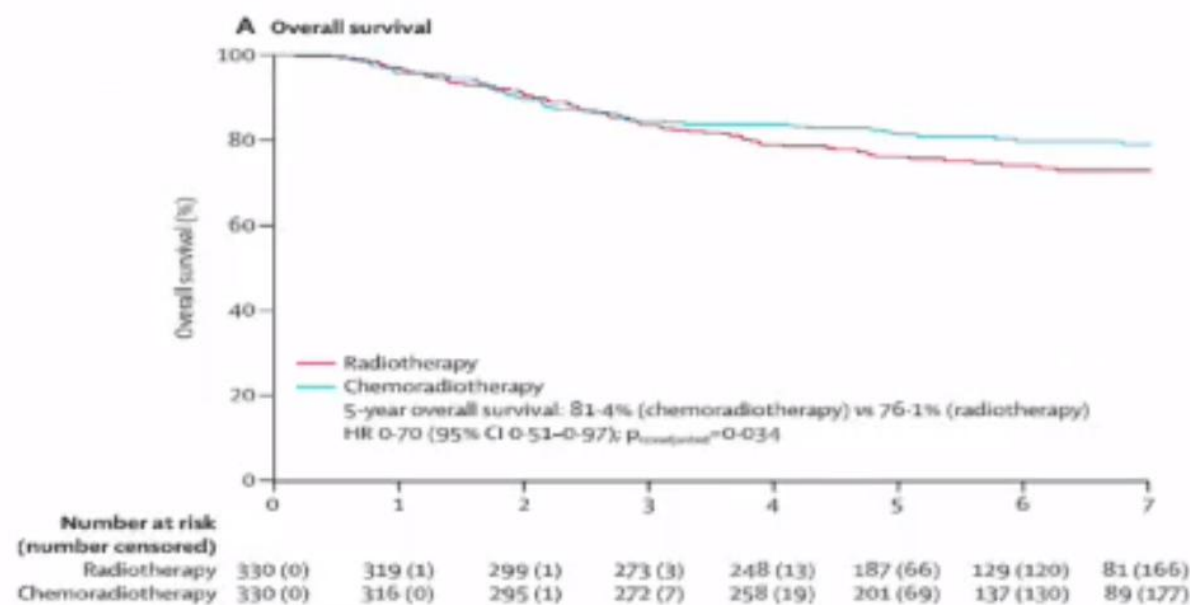
- IA G3+LVSI EEC;
- IB+G3 EEC;
- II-III C EEC;
- I-III Non-EEC

◆ 盆腔体外放疗 vs. 顺铂同期放化疗+TC4周期

● 中位随访72.6个月

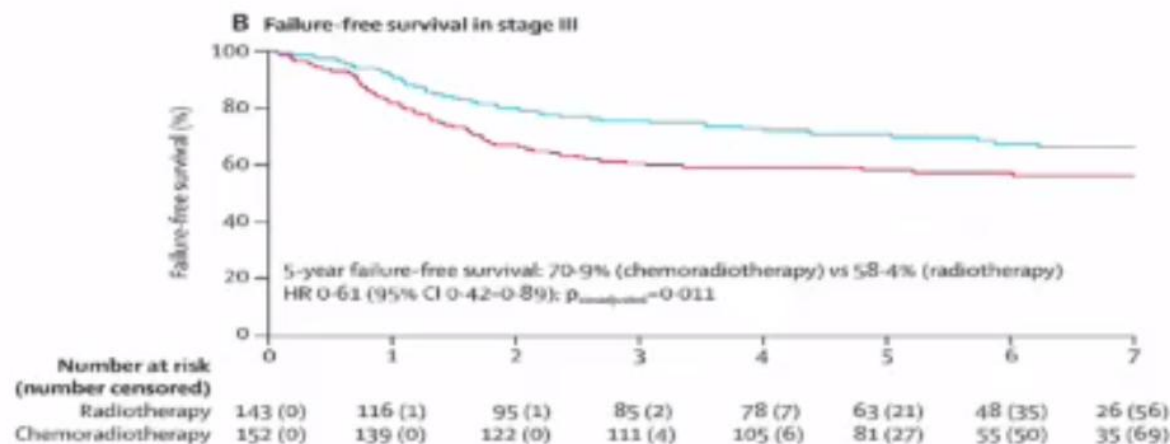
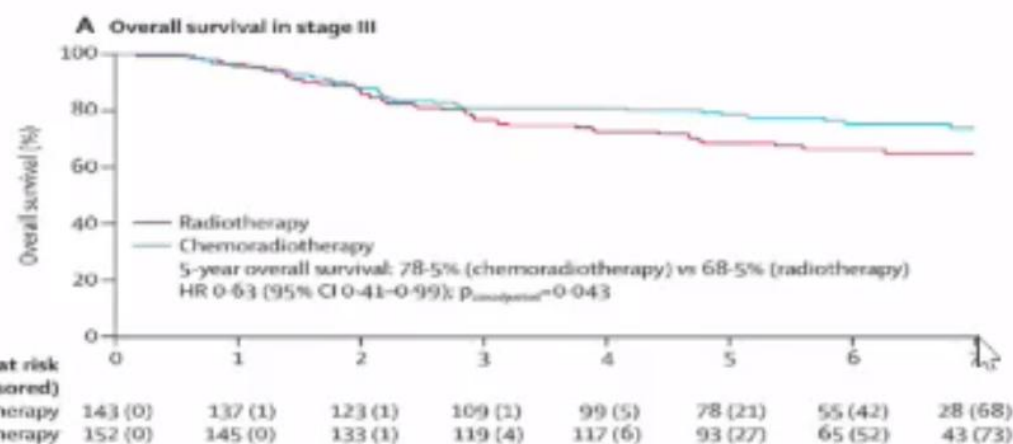
HR—PORTEC-3

- 两组患者盆腔控制率高，仅有1.2%的患者有阴道或盆腔复发
- CTRT+CT组可明显降低患者的远处复发率（21.4% vs 29.1%, $p = 0.016$ ），改善患者的5年OS（81.4% vs 76.1%, $p = 0.034$ ）



PORTEC-3: CTRT vs RT

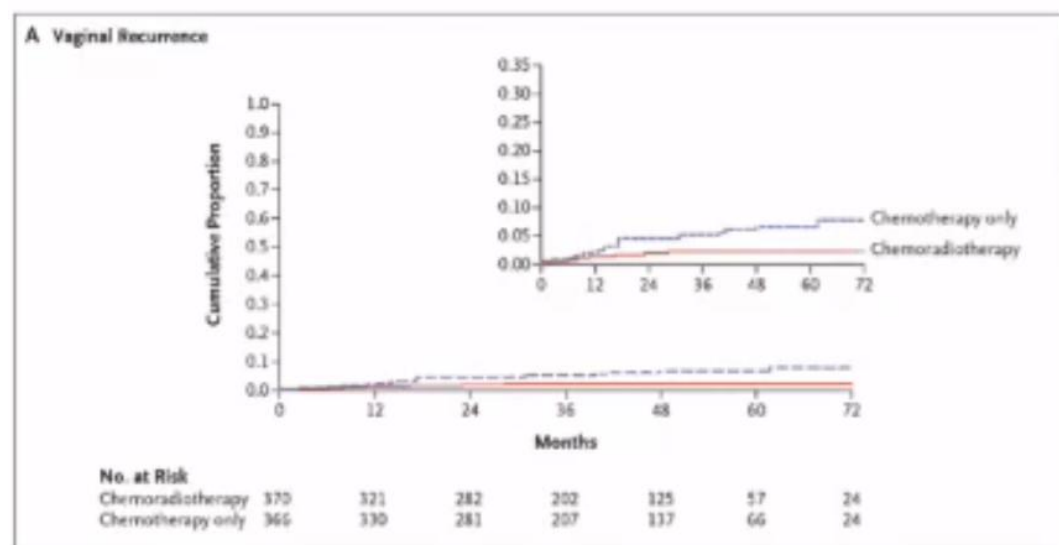
- I-II期HR患者FFS和OS无显著差异 (81.3% vs 77.3%, $p = 0.54$; 83.8% vs 82.0%, $p = 0.50$) .
- CTRT+CT组使III期患者的5年OS改善10% ($p = 0.0043$) ,FFS改善12.5% ($p = 0.011$)
- 副反应: 化疗组高 (急性期>G3 60% vs 12%), (远期>G2 8% vs 4%) $p < 0.0001$
- 5年RFS 76%, 远处转移是治疗失败的主要原因



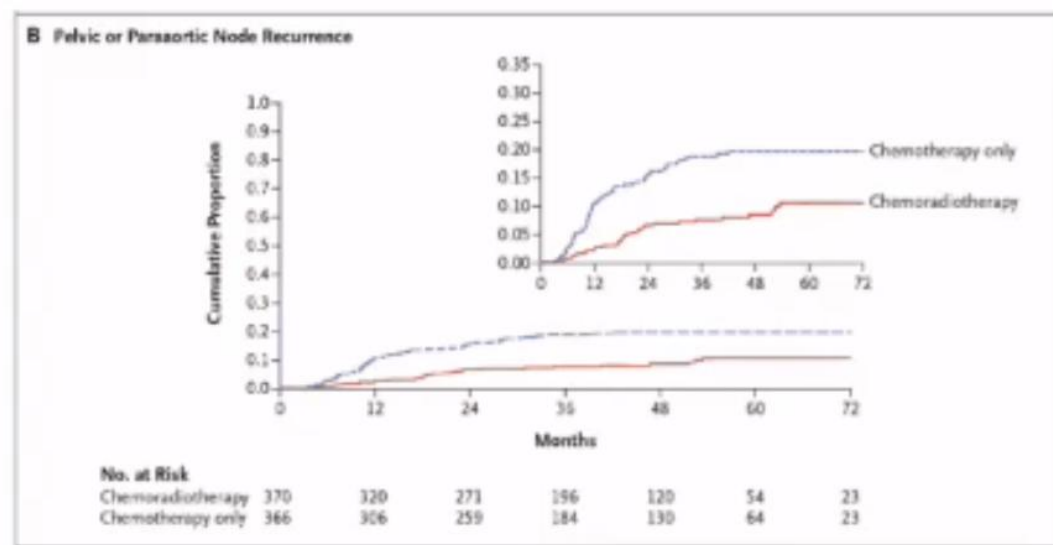
HR——GOG-0258

- **III-IVA期EC、浆液癌、透明细胞癌，残存病灶小于2cm或I-II期浆液癌、透明细胞癌伴腹水细胞学阳性**
- **CCRT+TC化疗4程 vs TC化疗6程**
- **入组 804pts: 370 vs 360**
- **中位随访时间47个月**
- **结果:**
 - 单纯化疗组的阴道残端及盆腔复发率略高
 - 同步放化疗+化疗组的远处转移率略高
 - 两组生存无差异

- 单纯化疗组：阴道残端及盆腔复发率略高



7% vs 2%

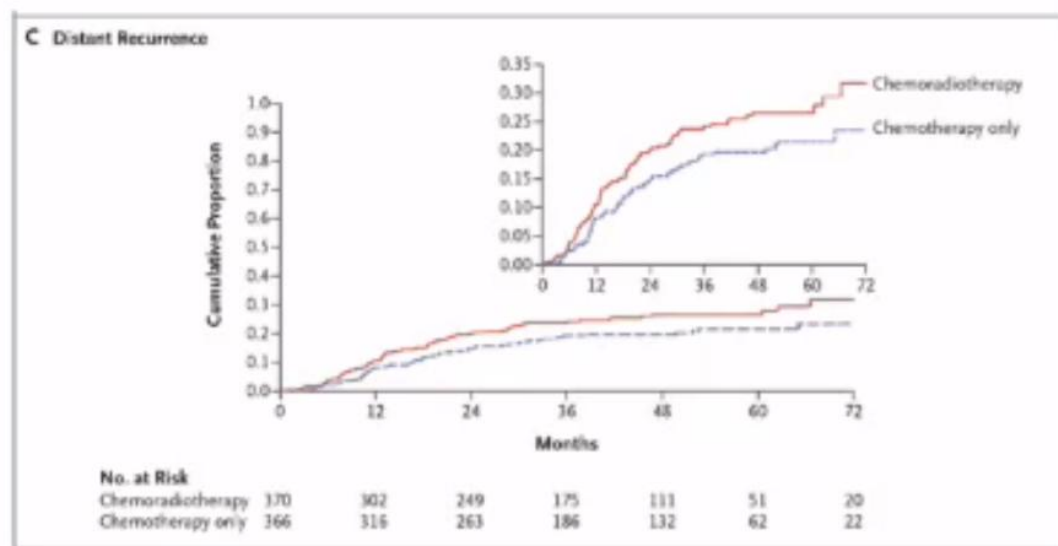


20% vs 11%

D. Matei, V. et al., N. Engl. J. Med. 380 (24) (2019) 2317-2326.

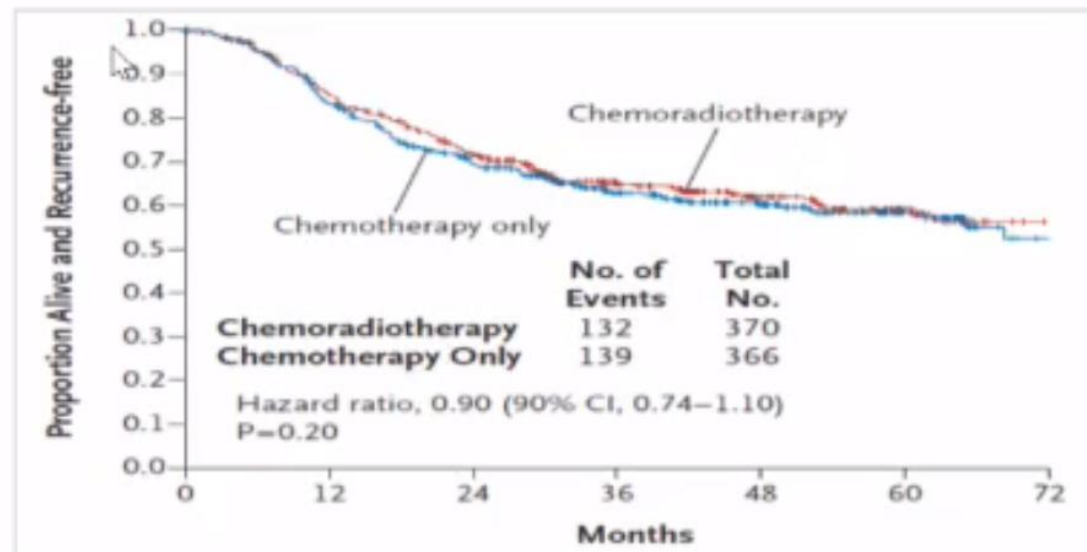
HR——GOG-0258

- 同步放化疗+化疗组的远处转移率略高



27% vs 21%

- RFS 无差异



59% vs 58%



NCCN Guidelines Version 1.2021 Endometrial Carcinoma

All staging in guideline is based on updated FIGO staging. ([See ST-1](#))

CLINICAL FINDINGS (Endometrioid Histology)^a

Surgically staged:
Stage I^e →

HISTOLOGIC GRADE/ADJUVANT TREATMENT^{g,h,m}

FIGO Stage	Histologic Grade	Adjuvant Treatment
IA	G1, G2	Observation preferred or Consider vaginal brachytherapy if lymphovascular space invasion (LVSI) and/or age ≥60 y ⁿ
	G3	Vaginal brachytherapy preferred or Consider observation if no myoinvasion or Consider EBRT if high-intermediate risk (HIR) ^o (category 2B)
IB	G1	Vaginal brachytherapy preferred ^o or Consider observation if no other adverse risk factors ^{o,p}
	G2	Vaginal brachytherapy preferred or Consider EBRT if HIR ^o or Consider observation if no other adverse risk factors ^q
	G3	RT (EBRT and/or vaginal brachytherapy) ± systemic therapy ^q (category 2B for systemic therapy)



NCCN Guidelines Version 1.2021 Endometrial Carcinoma

All staging in guideline is based on updated FIGO staging. ([See ST-1](#))

CLINICAL FINDINGS
(Endometrioid
Histology)^a

HISTOLOGIC GRADE/ADJUVANT TREATMENT^{g,h,m}

Surgically staged:^e
Stage II^{r,s}

FIGO Stage	Histologic Grade	Adjuvant Treatment
II	G1–G3	EBRT (preferred) and/or vaginal brachytherapy ^t ± systemic therapy (category 2B for systemic therapy)

[See Surveillance \(ENDO-9\)](#)



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NCCN Guidelines Version 1.2021 Endometrial Carcinoma

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All staging in guideline is based on updated FIGO staging. ([See ST-1](#))

CLINICAL FINDINGS
(Endometrioid Histology)^a

ADJUVANT TREATMENT^{g,h}

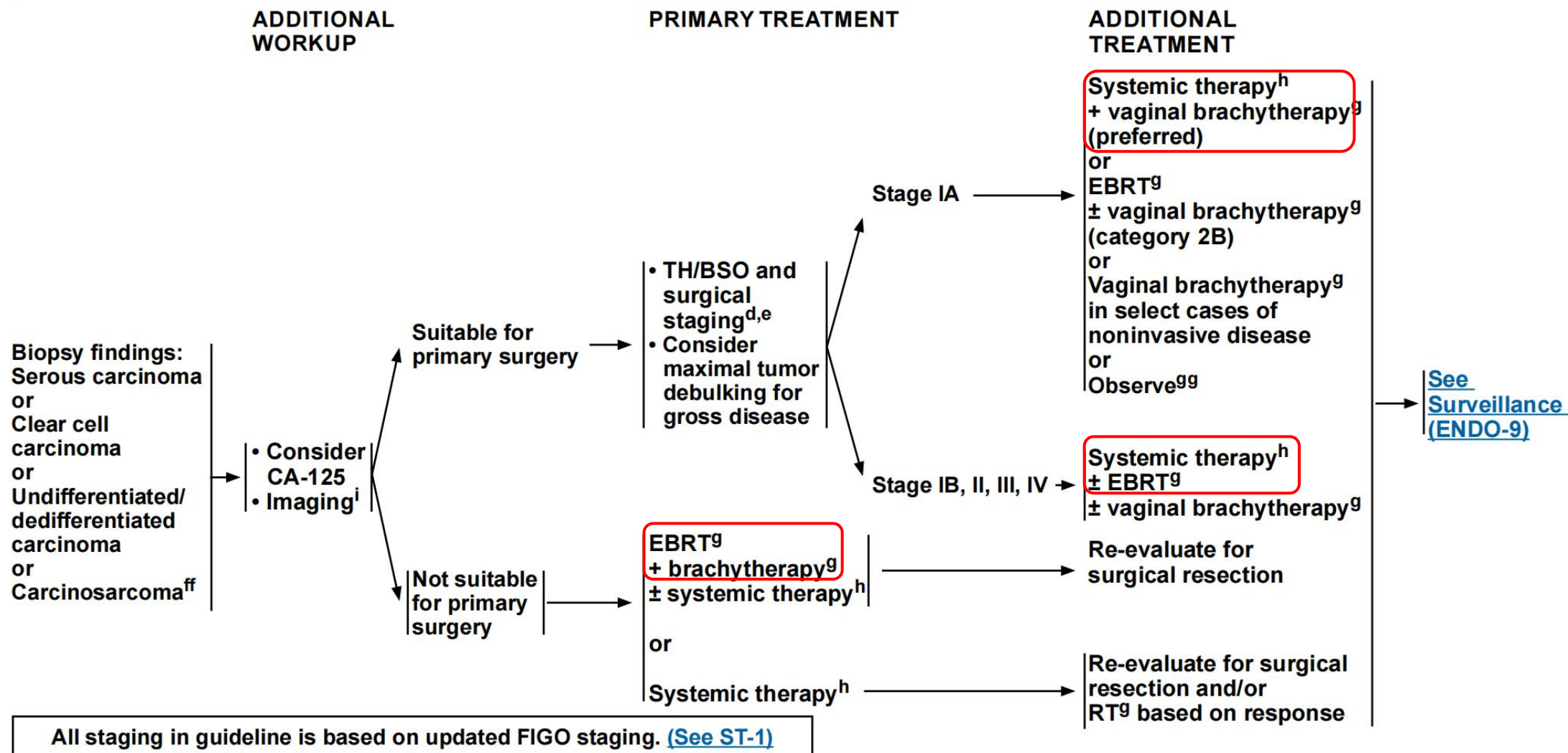
Surgically staged:^e
Stage III, IV^u



Systemic therapy
± EBRT
± vaginal brachytherapy^v



NCCN Guidelines Version 1.2021 Endometrial Carcinoma



HR

- GOG-0249: EBRT±BT vs BT+TC化疗

- ✓ I期高中危、II期 EC, I-II期浆液性或透明细胞癌
- ✓ 5y-OS 、RFS 相当
- ✓ 盆腔区域复发率在化疗组联合BT 中略高

➤ 早期高危患者，术后单纯放疗有效、安全，化疗没有体现优势

- PORTEC-3: EBRT vs CCRT+TC化疗

- ✓ IA G3+LVSI EEC、IB+G3 EEC、II-IIIC EEC、I-III Non-EEC
- ✓ I-II期HR患者FFS和OS无显著差异
- ✓ CTRT+CT组使III期患者的5年改善OS、FFS

➤ 远处转移是治疗失败的主要原因

- GOG-0258: CCRT+TC化疗 vs TC化疗

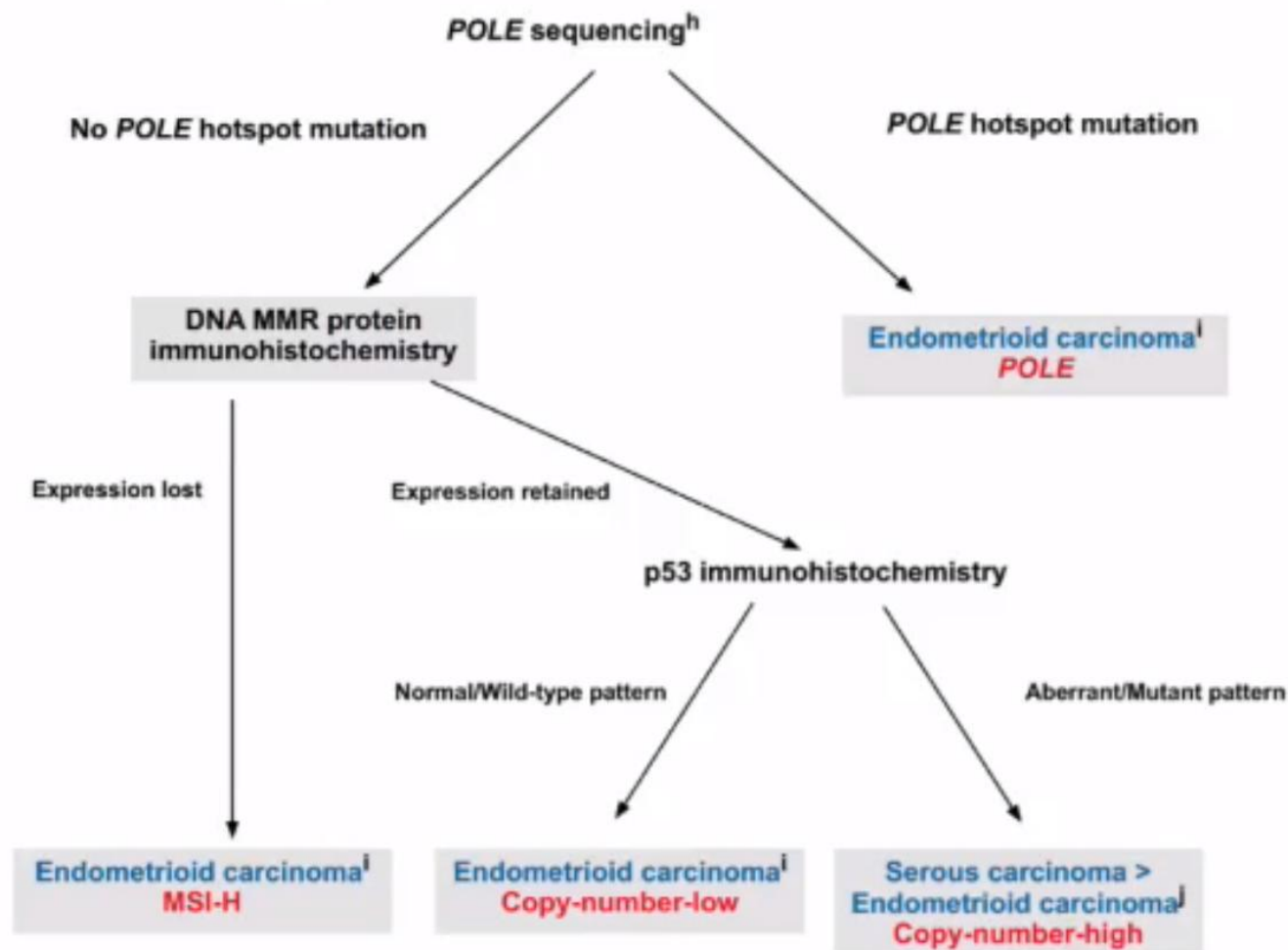
- ✓ III-IVA期EC、浆液癌、透明细胞癌，
- ✓ 两组生存无差异
- ✓ 单纯化疗组的阴道残端及盆腔复发率略高
- ✓ 同步放化疗+化疗组的远处转移率略高

如何选择？

——放疗？化疗？放疗化疗？

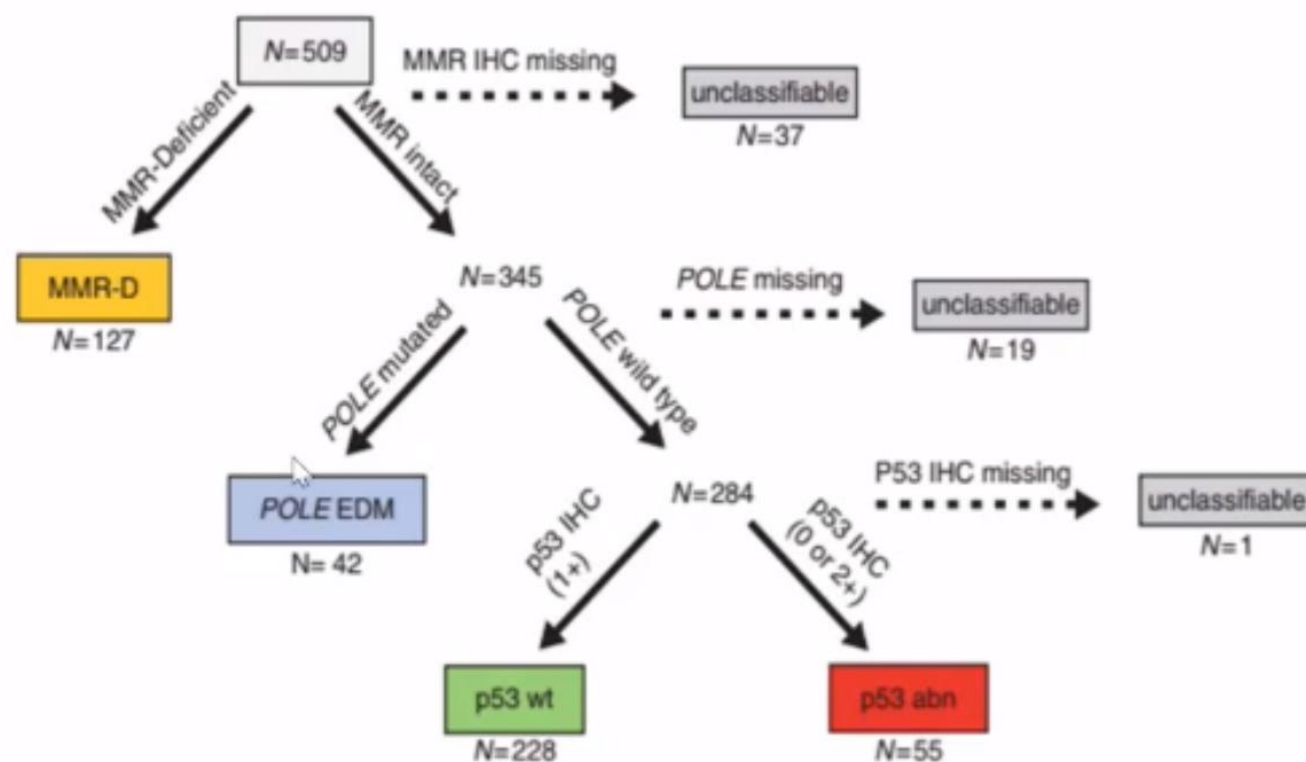
——分子分型？

TCGA分型流程

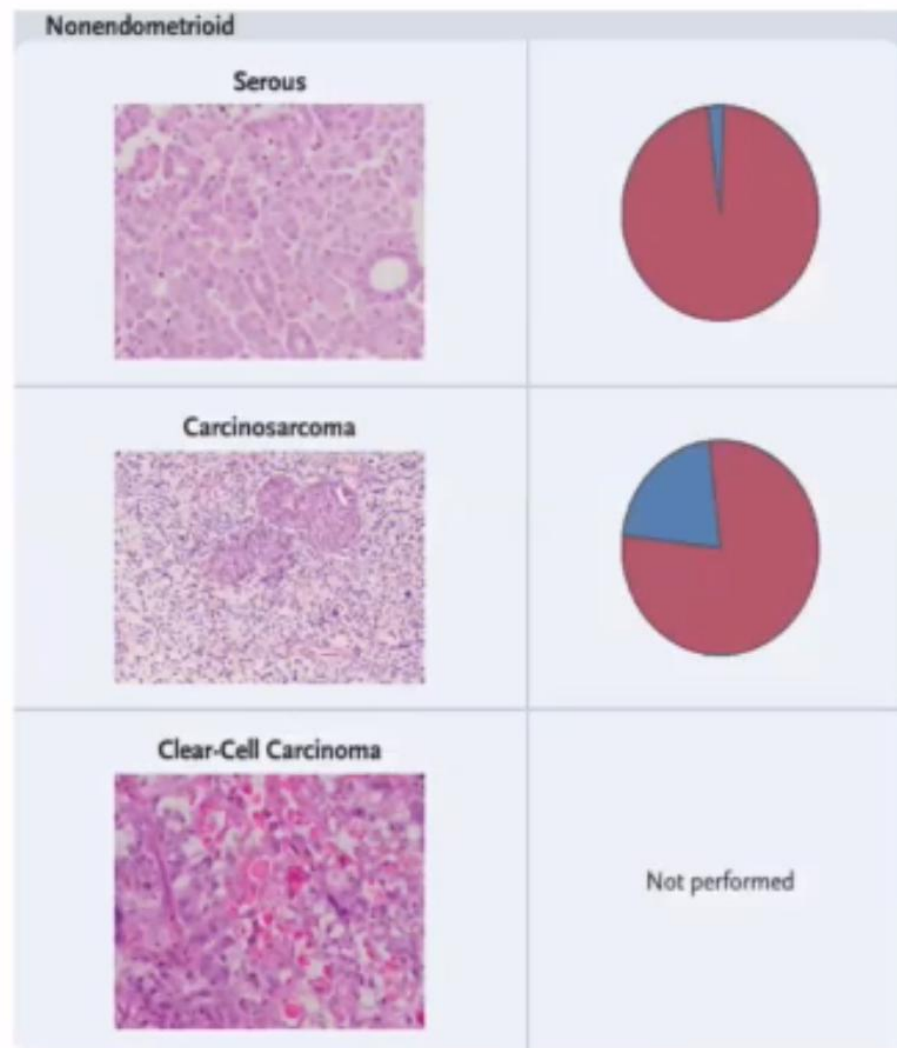
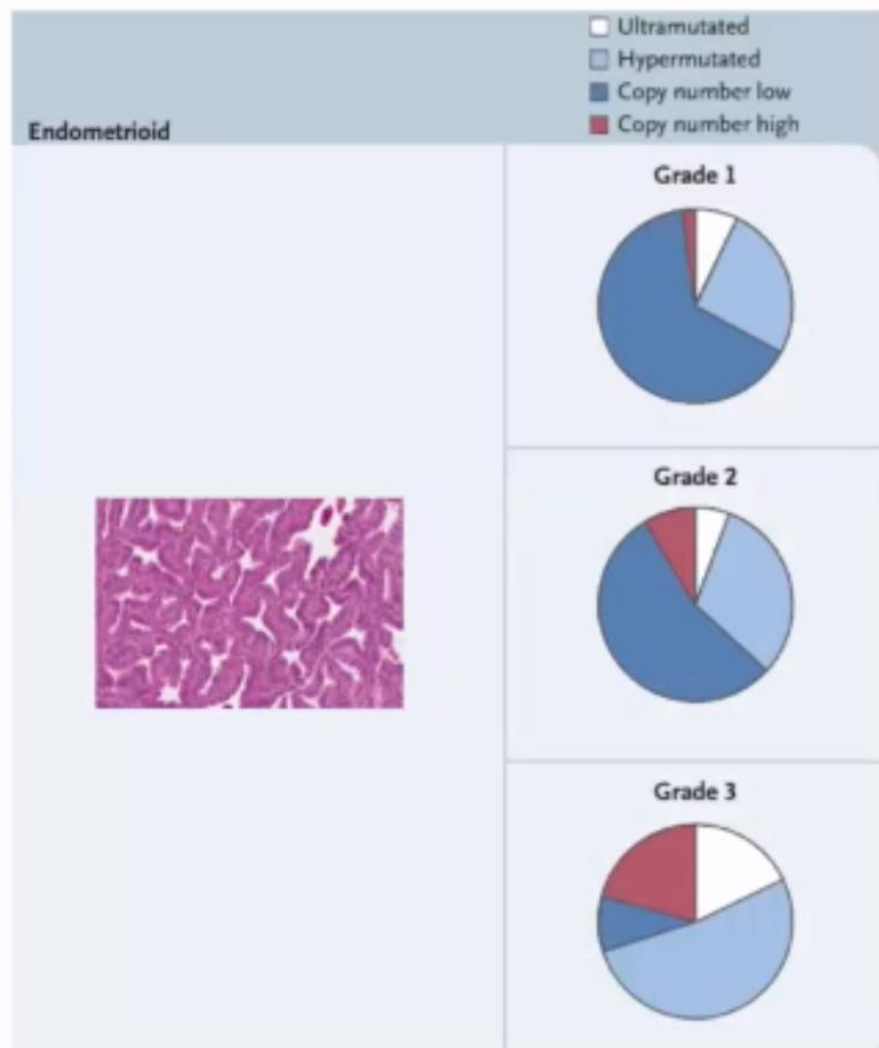


ProMisE分型

A



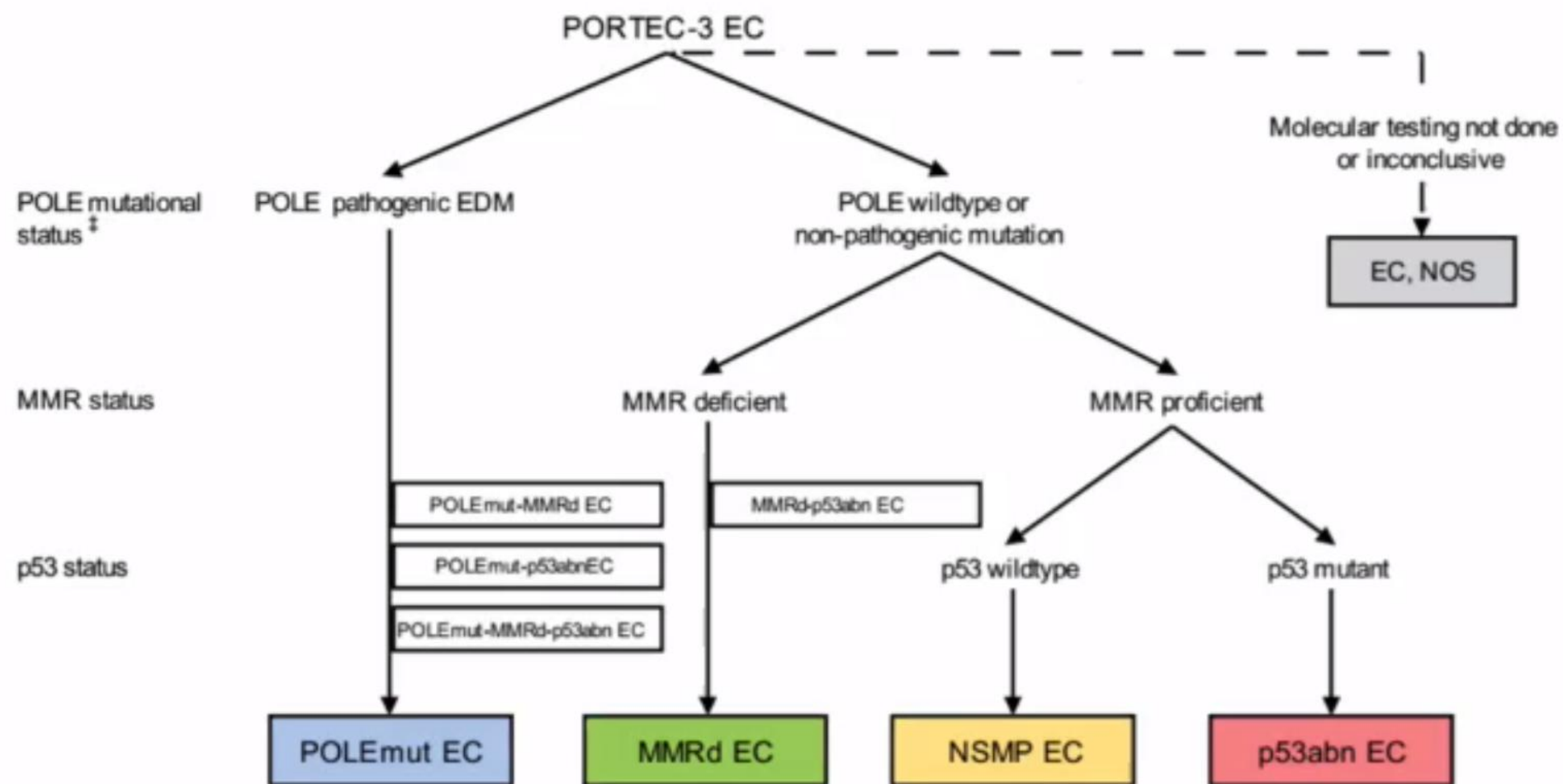
病理类型和分子分型的关系



Kandoth C, et al. Nature, 2013,497(7447):67-73.

PORTEC-3设计思路

EBRT vs CCRT+TC化疗



PORTEC-3分子分型

EBRT vs CCRT+TC化疗

- 2019年ESMO首次报道了PORTEC-3分子分型的结果，对410例行p53、MMR、POLE基因分析：
 - ✓ p53突变型（P53abn）92例（22%）
 - ✓ POLE突变型52例（13%）
 - ✓ MMRd 137例（33%）
 - ✓ 无突变型（NSMP）129例（32%）；
- 5年PFS: **p53abn 50%, POLEmut 98%**, MMRd 74%, NSMP 76% ($p < 0.0001$);
- 对于p53突变者，CTRT+TC化疗组与RT组5年PFS分别为61%和37% ($p = 0.017$);
- 对于MMR缺陷者，两组5年PFS无明显差异

PORTEC-3分子分型

Table: LBA63 Recurrence-free survival by molecular subgroup

	Events	5-year estimate %	HR (95% CI)	P value of HR
p53abn EC				
RT	28	37,2	1	
CTRT	20	61,1	0,50 (0,28-0,88)	0,017
POLEmut EC				
RT	1	96,6	1	
CTRT	0	100	0,02 (<0,01->10 ⁴)	0,632
MMRd EC				
RT	17	75,8	1	
CTRT	18	72,4	1,15 (0,59-2,22)	0,687
NSMP EC				
RT	19	68,9	1	
CTRT	17	81,2	0,71 (0,37-1,37)	0,311

EBRT vs CCRT+TC化疗

结论:

- 高危型EC, p53abn更可能从化疗中获益;
- POLEmut HREC 两组5年PFS: 97-100%;
- MMRd和NSMP型未能从额外CT中获益

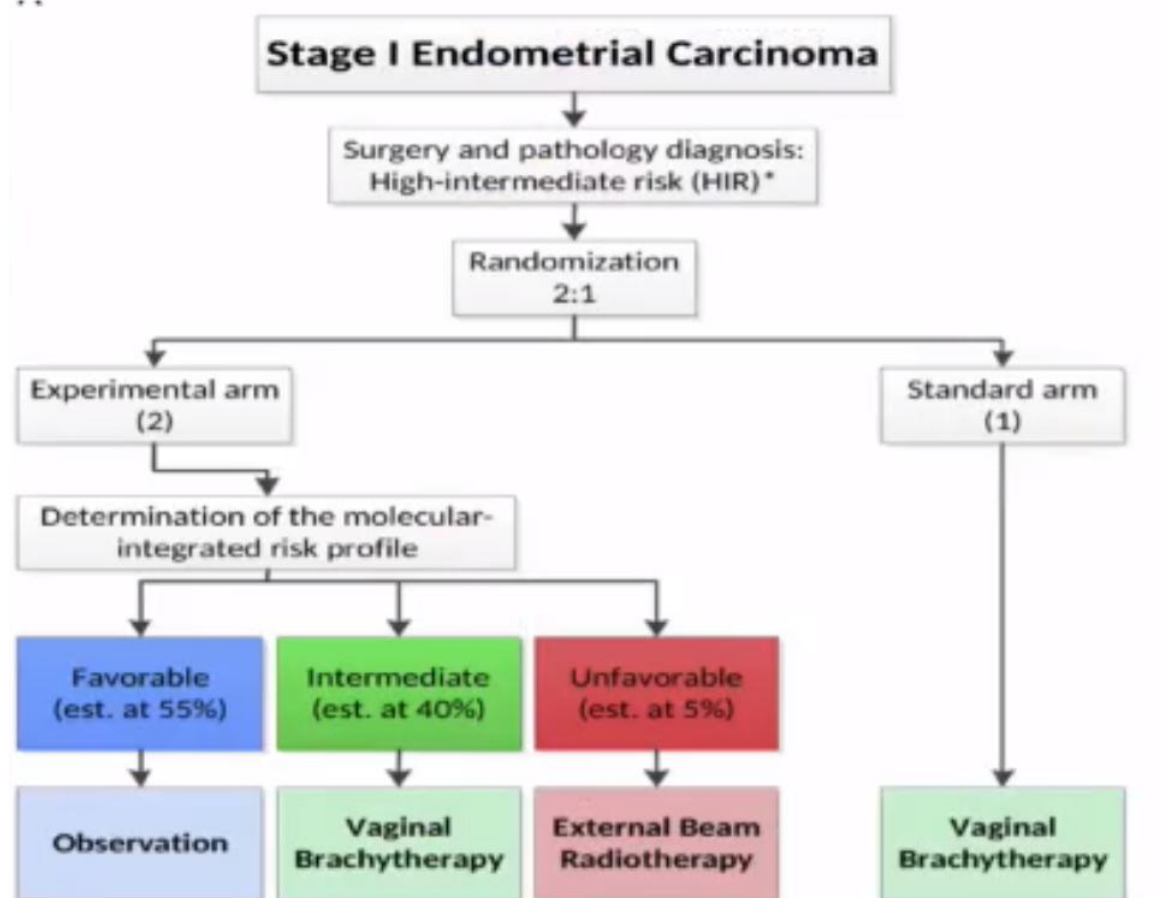
P53abn型是否需要增加治疗强度?

POLEmut型降低治疗强度?

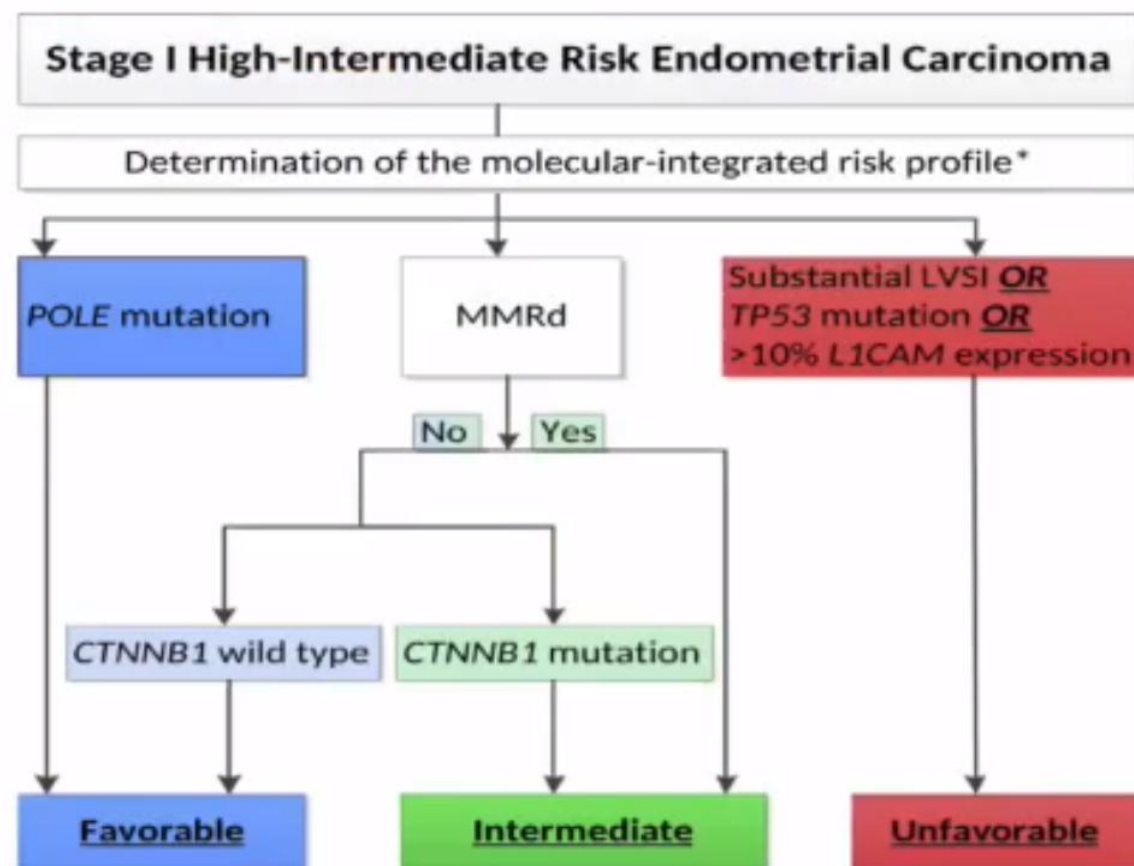
LBA63 Molecular classification of the PORTEC-3 trial for high-risk endometrial cancer: Impact on adjuvant therapy

C.L. Creutzberg¹, A. Leon-Castillo², S.M. de Boer¹, M.E. Powell³, L.R. Miles⁴, H.J. Mackay⁵, A. Leary⁶, H.W. Nijman⁷, N. Singh⁸, P. Pollock⁹, A. Fyles¹⁰, C. Haie-Meder¹¹, V.T.H.B.M. Smit¹², R.J. Edmondson¹², H. Putter¹³, H.C. Kitchener¹², E.J. Crosbie¹², M. de Bruyn⁷, R. Nout¹, T. Bosse²

PORTEC-4a trial-期待结果!



*High-intermediate risk (HIR) endometrial cancer: stage IA (with invasion) and grade 3; stage IB, grade 1 or 2; with either age ≥ 60 or substantial lymph-vascular space invasion (LVSI); stage IB, grade 3 without LVSI; or stage II (microscopic) with grade 1. Est = estimated.



*Patients with multiple characteristics (double classifiers) were designated intermediate risk. MMRd = Mismatch repair-deficiency. For details, see text.

Fig. 1. A – Study design of the PORTEC-4a trial. B – Decision tree of the molecular-integrated risk profile.

B.G. Wortman, et al., Gynecol. Oncol. 151 (1) (2018) 69-75.

2020 ESGO/ESTRO/ESP 推荐（纳入分子分型）

Risk Group	Molecular Classification Unknown	Molecular Classification Known ^{Δ,*}
Low	Stage IA endometrioid + low-grade** + LVSI negative or focal	- Stage I-II POLEmut 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, undifferentiated 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

《中国妇科恶性肿瘤临床实践指南》第六版

——由中华医学会妇科肿瘤学分会组织编写，人民卫生出版社出版



- **Ia期G1-2：低危组**

- 无淋巴脉管间隙浸润、年龄 <60 岁，——推荐术后观察

- **Ia期G1-2：低-中危组**

- 合并淋巴脉管间隙浸润、年龄 ≥ 60 岁——术后可考虑腔内放疗，减少阴道复发

- **Ia期G3及Ib期G1-2：中危组**

- 复发中75%在阴道残端，放疗不改善OS，EBRT与BT减少阴道复发同等效果——术后腔内放疗，减少阴道复发
- 无淋巴脉管间隙浸润、年龄 <60 岁——术后可以观察（低级别证据）

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● Ib期G3、II期G1-3：中-高危组

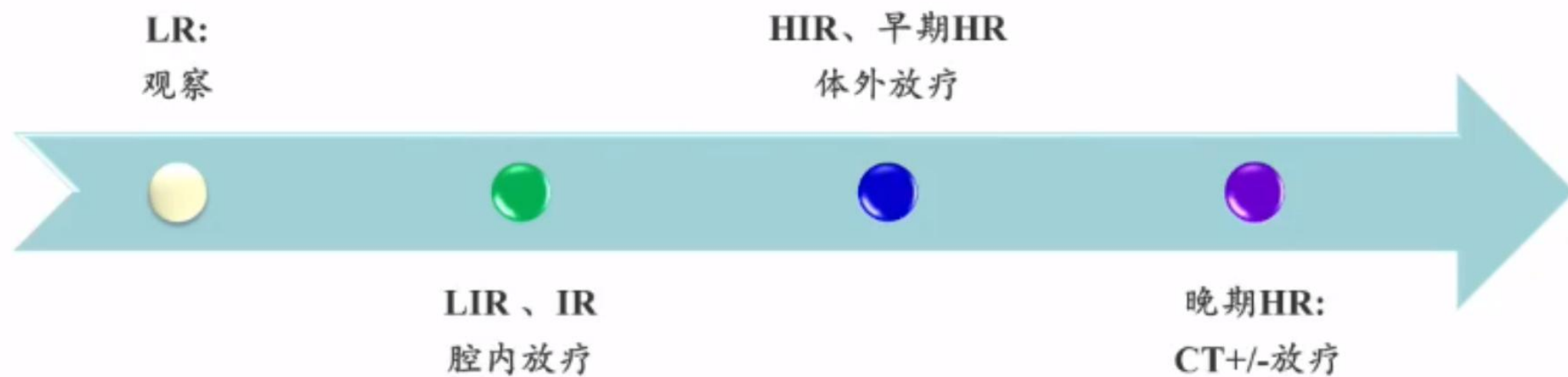
- 局部区域复发↑，EBRT降低死亡风险，降低盆腔复发率，改善OS趋势
——阴道腔内照射和/或盆腔外照射±化疗
- II期G3——推荐盆腔外照射±阴道内照射±化疗

● III及IV期子宫内膜样腺癌、及特殊病理类型（浆液性癌、透明细胞癌）：高危组

- 盆腔复发率>15%，远处转移风险增加
- 放疗减少盆腔复发，
- 化疗减少远处转移，改善总生存

小结——

子宫内膜癌术后放疗选择



根据——患者身体条件、手术情况、病理类型、分子分型——细化治疗

Thank you for your attention!