



8th Annual

LEAD 2026

LEADERSHIP
EMPOWERMENT
DEVELOPMENT

Enriching Experiences for Leaders in Hematology and Oncology

SEPT
18-19,
2026

Clinical Updates in Gynecologic Malignancies

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Disclosures

No relevant financial relationships to disclose.

Background

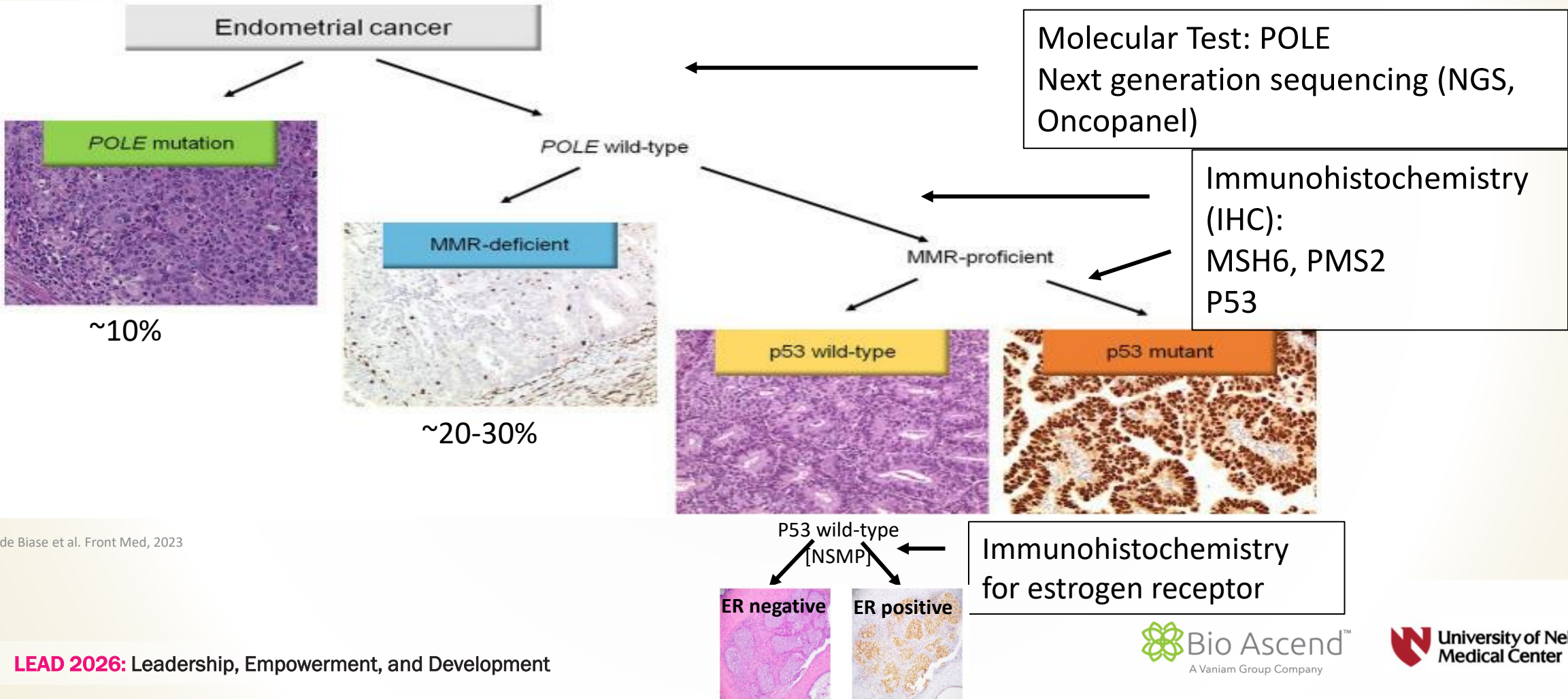
- In recent years there has been remarkable progress in the treatment approaches for gynecologic tumors.
- The combination of modern radiotherapy techniques with systemic treatment options including the addition of immunotherapy has revolutionized treatment protocols.
- Deeper insights and utilization of molecular profiling, in conjunction with pathological risk factors, is allowing for more effective and personalized treatment strategies.

Agenda

Text	Topic
I	Endometrial Cancer
IA	Updates in Staging
IB	Treatment in Early-Stage Endometrial Cancer
IC	Treatments in Advanced Endometrial Cancer
II	Cervical Cancer
IIA	Treatment in Early-Stage Cervical Cancer
IIB	Treatment in Locally Advanced Cervical Cancer
III	Survivorship

Endometrial Cancer

Molecular Classification



Staging

Stage	FIGO 2009	FIGO 2023
Stage I	Tumor confined to the corpus uteri	Confined to the uterus corpus and ovary [simultaneous primaries]
IA	No or <50% MMI	Disease limited to the endometrium OR non-aggressive histology (low-grade endo <50% MMI no or focal LVSI OR good prognosis
IA1	-	Non-aggressive histology in endometrial polyp OR confined to endometrium
IA2	-	Non-aggressive histology <50% MMI no or focal LVSI
IA3	-	Low-grade endometrioid carcinoma limited to uterus and ovary
IB	≥ 50% MMI	Non-aggressive histology with invasion of ≥50% MMI and no or focal LVSI
IC	-	Aggressive histology limited to polyp or confined to the endometrium
Stage II	Tumor invades cervical stroma, but does not extend beyond the uterus	Invasion of cervical stroma with extrauterine extension OR substantial LVSI OR aggressive histology types with MMI
IIA	-	Invasion of the cervical stroma of non-aggressive histology
IIB	-	Substantial LVSI of non-aggressive histology
III	Local and/or regional spread of tumor	Local and/or regional spread of the tumor of any histology
IIIA	Tumor invades serosa of corpus uteri and/or adnexa	Invasion of uterine serosa, adnexa, or both by direct extension or metastasis
IIIA1	-	Spread to ovary or fallopian tube except when meeting Stage IA3 criteria
IIIA2	-	Involvement of uterine subserosa or spread through the uterine serosa
IIIB	Vaginal and/or parametrial involvement	Metastasis or direct spread to the vagina and/or to the parametria or pelvic peritoneum
IIIB1	-	Metastasis or direct spread to the vagina and/or the parametria
IIIB2	-	Metastasis to the pelvic peritoneum
IIIC	Metastases to pelvic and/or PA nodes	Metastasis to the pelvic or para-aortic lymph nodes or both
IIIC1	Positive pelvic nodes	Metastasis to the pelvic lymph nodes
IIIC1i	-	Micrometastasis
IIIC1ii	-	Macrometastasis
IIIC2	Positive PA nodes +/- positive pelvic nodes	Metastasis to para-aortic lymph nodes up to the renal vessels, with or without metastasis to the pelvic lymph nodes
IIIC2i	-	Micrometastasis
IIIC2ii	-	Macrometastasis
IV	Tumor invades bladder and/or bowel mucosa and/or distant metastases	Spread of the bladder mucosa and/or intestinal mucosa and/or distant mets
IVA	Tumor invasion of bladder and/or bowel mucosa	Invasion of the bladder mucosa and/or the intestinal/bowel mucosa
IVB	Distant metastases, including intra-abdominal metastases and/or inguinal nodes	Abdominal peritoneal metastasis beyond the pelvis
IVC	-	Distant mets including to any extra- or intra-abdominal lymph nodes above the renal vessels, lung, liver, brain, or bone

Berek. Int J Gynaecol Obstet. 2023

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Treatment Approaches: Early-Stage Adjuvant Treatment Trials

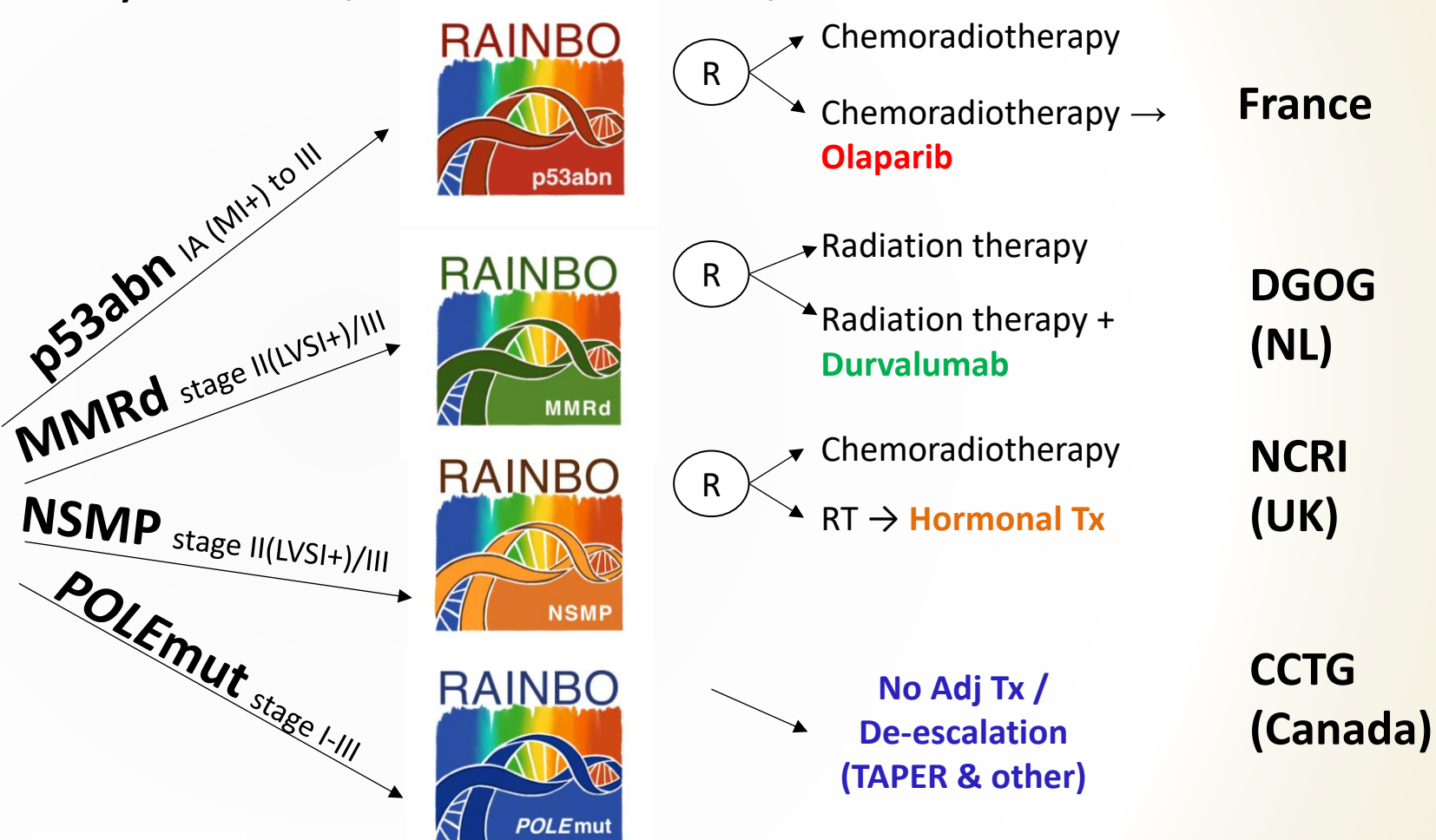
	GOG 99 1987-1995 Obs vs EBRT	PORTEC 1 1990-1997 Obs vs EBRT	ASTEC/EN.5 1996-2005 Obs vs EBRT	PORTEC 2 2002-2006 VBT vs EBRT	GOG 249 2009-2013 VBT+Chemo vs EBRT [3D or IMRT 45–50.4 Gy in 25-28 fx]
N	392	714 (569 with central path)	905	427 (all with central path)	601
Median f/u	5.8 yrs	10 yrs	4.8 yrs	3.7 yrs	4.4 yrs
Eligibility	IB-occult II	IB G2-3, IC G1-2	IA G3, IB G3, IC-IIB	IB G3, IC G1-2, IIA	Stage I Endometrioid Histology: Age 70+ w 1 RF, 50+ w 2 RF, 18+ w 3RF; Stage II endometrioid; Stage I or II serous (15%) or clear cell (5%)
LN dissection	Yes	No	Yes (30%)	No	Yes
VC brachy	No	No	Yes (53%)	Yes (50%)	Yes
Pelvic + vaginal recurrence	12% vs 3% (SS) (26% vs 6% for HIR)	14% vs 5% (SS)	6.1% vs 3.2% (SS)	5.1% vs 2.1% (NS)	Para-aortic nodal or pelvic recurrences: 9% vs 4% (SS); Vaginal or distant recurrences (NSS) with 2.5% and 1.8% respectively
DM	6.4% vs 5.3% (NS)	8% vs 7% (NS)	6.8% vs 7.5% (NS)	8.3% vs 5.7% (NS)	RFS 76%/76% (NS)
OS	86% vs 92% (NS)	66% vs 73% (NS)	84% vs 84% (NS)	85% vs 80% (NS)	85% vs 87% (NS)

Refining Adjuvant treatment IN endometrial cancer Based On molecular profile (RAINBO) DGOG/transPORTEC/ENGOT-en14

RAINBO program supported by GCIG and coordinated by TransPORTEC.

Allocates patients with surgically resected endometrial cancer to 4 international academic sub-trials each led by one Gyn-Onc national clinical trial group.

Eligible histotypes: endometrioid, serous, clear cell, un/dedifferentiated, mixed and carcinosarcoma



RAINBO Research Consortium Int J Gynecol Cancer 2023

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PORTEC 4a

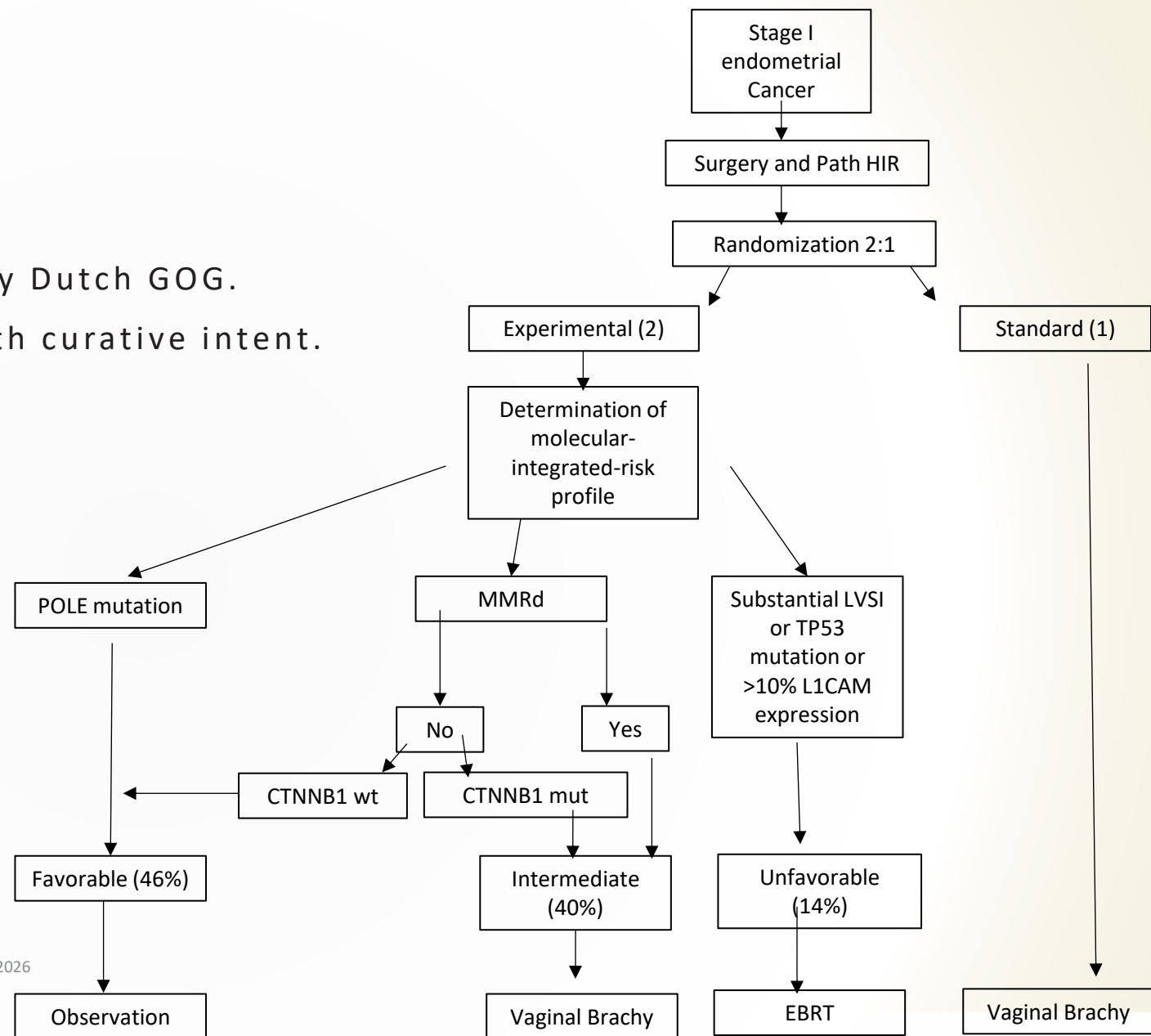
Prospective, multicenter, ph III study. Led by Dutch GOG.
500 women randomized (2:1). Treatment with curative intent.

Primary endpoint: Vaginal Recurrence.

Inclusion Criteria:

Women ≥ 18 yrs, TLH/TAH BSO
Endometrioid endometrial cancer with
High-intermediate risk features:
Stage IA, gr 3 (any age, +/- LVSI)
Stage IB, gr 1 or 2 age ≥ 60 yrs
Stage IB, gr 1 or 2, +LVSI
Stage IB, gr 3, -LVSI
Stage II (microscopic), gr 1

Wortman et al. Gynecol Oncol, 2018; van den Heerik et al. Int J Gynecol Cancer 2020. van den Herrik Lancet Oncol 2026



PORTEC 4a - Results

June 1, 2016 – Dec 24, 2021. N=564. MFU = 58.1 mo

NSMP (59% [97% were estrogen receptor positive]), MMRd (29%), POLE (9%), p53abn (3%).

23 vaginal recurrences were reported [64% were simultaneous pelvic, distant or both, while 36% were isolated vaginal recurrence].

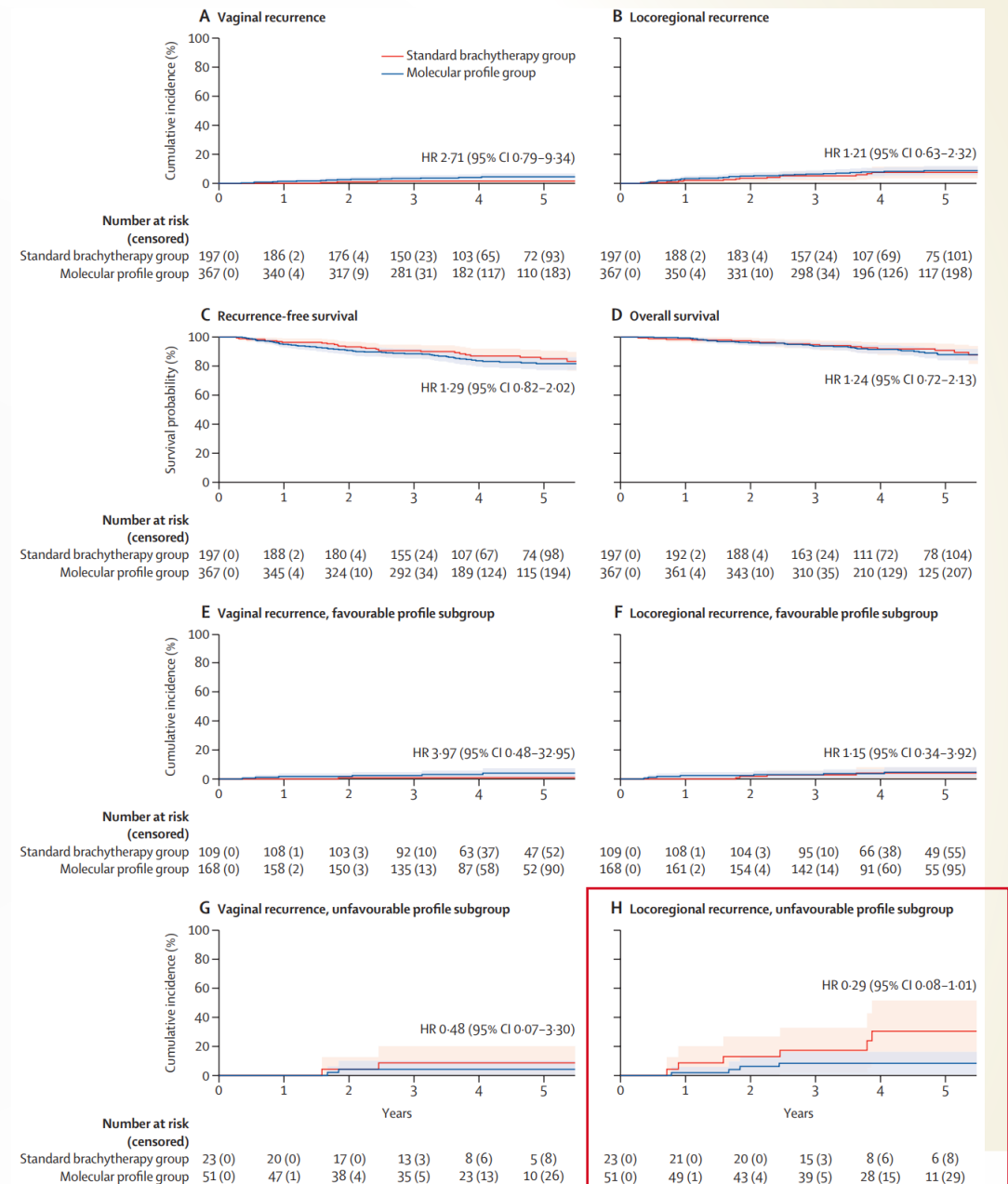
The 5yr cumulative incidence of vaginal recurrence was 4.5% in molecular and 1.6% in standard, below the 7.0 equiv margin.

Recurrence free survival was 81.7% in molecular and 85.1% in standard group. 5y OS 88% vs 90.9%.

In the unfavorable risk profile CI vaginal recurrence 4.3% vs 8.7%. Locoregional recurrence 8.4% vs 30.5%.

Eight grade 3 or above GU toxicities were related to treatment. No differences were seen between groups in the short or long term.

van den Herrik Lancet Oncol 2026



Treatment Approaches: Advanced-Stage Treatment Trials

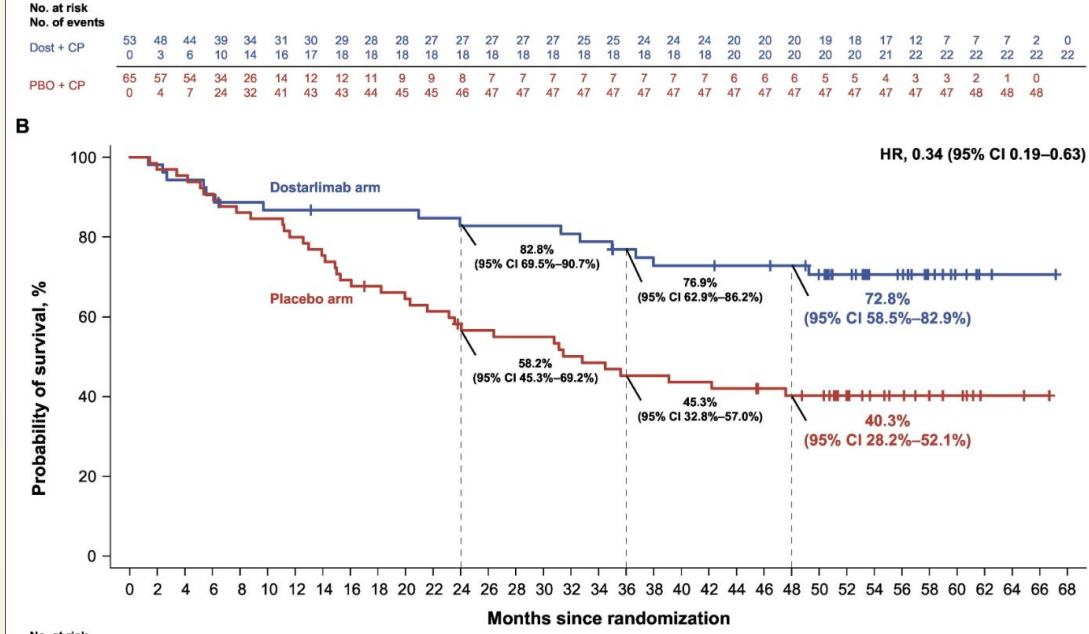
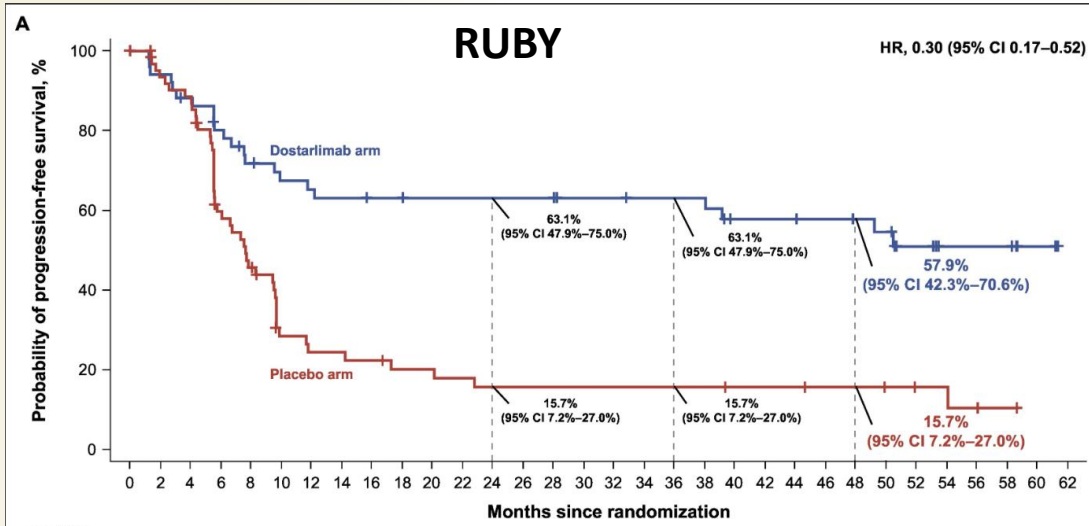
	PORTEC 3	GOG 258	Ruby	GY-018	B21
N	660 [Molecular Classification in 411 (62%)]	733	494	816	1092
Primary endpoint	FFS and OS	RFS	PFS	PFS	DFS and OS
Median f/u	10.1 yrs (121.2 mo)	112	25.4 mo	12 mo dMMR 7.9 mo pMMR	23.7 mo Pembro 24.1 mo Placebo
Eligibility	G3 endometrioid with IA w +LVSI/or IB Stage II-III endometrioid Stage I-III serous/clear cell	Stage I-II serous/clear cell with positive cytology Stage III-IVA endometrioid Stage III-IVA serous/clear cell	Stage III w measurable dz, IIC1 carcinosarc, serous, clear cell, mixed hist, IIC2 or IV, or first recurrence.* ECOG PS 0-1	Measurable disease (stage III or IVA) or Stage IVB or recurrent endometrial cancer. ECOG PS 0, 1, 2	Newly diag endometrial carcino or carcinosarcoma s/p surg w/o res dz. I/II w MMI non endometrioid. I/II w MMI any hist TP53m, III/IVA any hist. No prior RT or syst tx.
Treatment	ChemoEBRT f/b Carbo/paclitaxel (pelvis 48.6 Gy w cis 50 mg/m2 wk 1&4 f/b Carbo/paclitaxel x4) Vs. EBRT: pelvis 48.6 Gy	Pelvis 45 Gy w cis 50 mg/m2 wk 1&4 Carbo/paclitaxel x4 (up to 15 Gy boost) Vs. Carbo/paclitaxel x6	Dostarlimab IV 500 mg or placebo 6C q3w w P 175 mg/m2+ C 5 mg/mL/min, f/b up to 3y maint Dostarlimab IV 1000 mg q6w	Pembrolizumab 200 mg IV or placebo 6C q3w along w P/C f/b up to 14 maint cycles of Pembro 400 mg IV q6w (1.5y)	Pembrolizumab or placebo 6C q3w along w P/C f/b maintenance
Outcomes	CRT/RT 5Y VR 2%/2%; PR 6%/8% 5Y RFS 77%/69% 10Y RFS 72.8%/67.4% (adjusted HR 0.74 [95% CI 0.56–0.98], p=0.034. 5YOS 81%/76%; 10YOS 74.4%/67.3% [5Y OS Stage III 78.5%/68.5% 10Y 69.5%/56.1%; in serous pts 71.4%/58.2%; 57.1%/48.7%}	CRT/CT 5Y VR 2%/7%; P/PAR 11%/20% 5Y RFS 58%/59%; 5Y DR 27% vs 21%	2yPFS d-MMR-MSI-H 61.4%/15.7%; 2y PFS p-MMR-MSS 28.4%/18.8% Overall pop 2YPFS 36.1%/18.1%; 2YOS was 71.3%/56.0%. 2YOS p-MMR 66.5%/53.2%; 3YOS p-MMR 48.6%/41.9% MFU 55 mo 4y PFS d-MMR-MSI-H 57.9%/15.7%; 4y OS 72.8%/40.3%.	Stratified dMMR/pMMR PFS pembro vs placebo dMMR 74%/38% [HR 0.30, 95% CI 0.19-0.48; p<0.001] pMMR 60%/55% [HR 0.54, 95% CI 0.41-0.71; p<0.001] 49mo FU Pembro +CP reduced risk of death by 44% dMMR 78.6%/60.4% [HR 0.56; 95% CI 0.34-0.92] pMMR 40.7%/39.5% [HR 0.86; 95% CI 0.69-1.08] NSS	Stratify by MMR status, planned RT, Endo vs Not, Stage I/II vs III/IVA. DFS rate 75%/76% [HR 1.02 95% CI 0.79-1.32; p=0.570] dMMR favored pembro [HR 0.31, 95% CI 1.14-0.69] pMMR [HR 1.20, 95% CI 0.91-1.57]

Browel Pract Radiat Oncol 2026; Post et al. Lancet Oncol 2025;

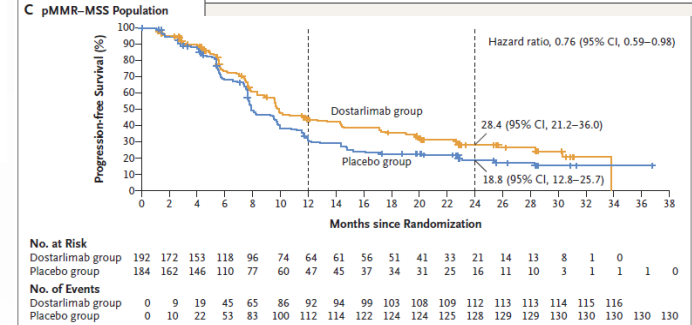
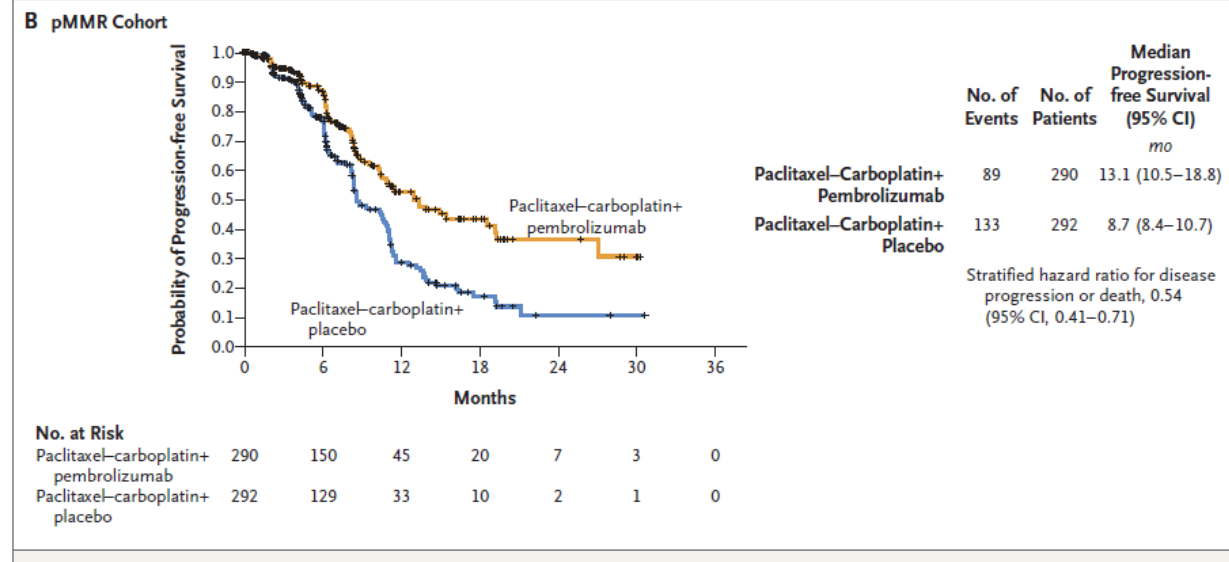
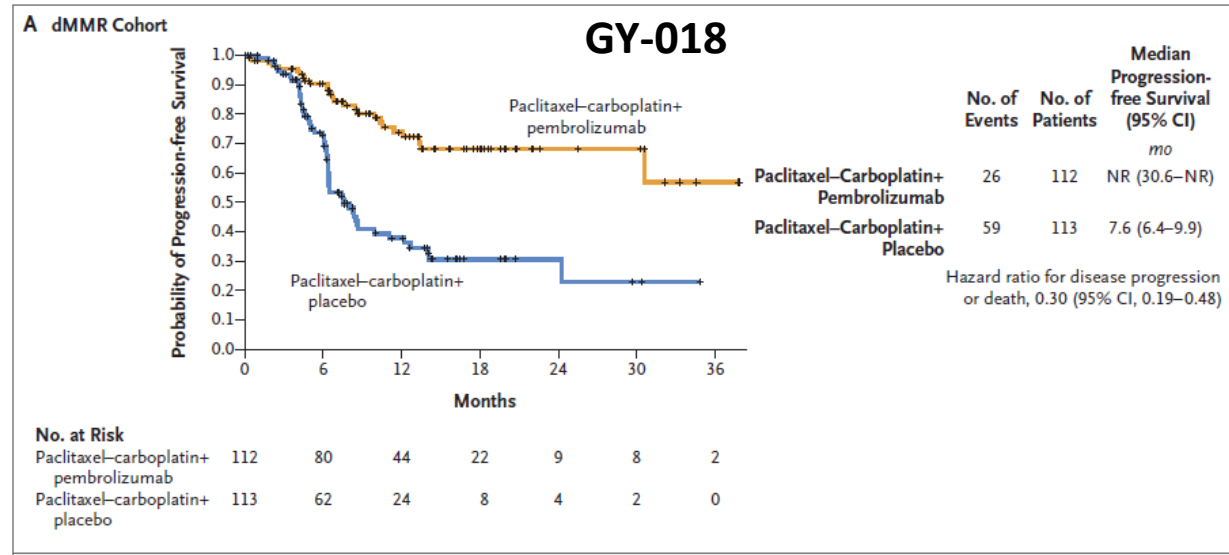
*With low potential for cure by radiation therapy or surgery alone or in combination.

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d-MMR/MSI-H



Mirza et al. N Engl J Med 2023; Powell et al. Gynecol Oncol 2026

LEAD 2026: Leadership, Empowerment, and Development

p-MMR/MSS



KEYNOTE-B21 / ENGOT-en11 / GOG-3053

Primary outcomes: **Disease free survival & overall survival**

Eligibility:

Newly diagnosed endometrial carcinoma or carcinosarcoma s/p curative surgery w/o residual dz.

FIGO 2009

- Stage I/II w MMI non endometrioid
- Stage I/II w MMI any histology TP53m
- Stage III/IVA any histology

No prior RT or systemic tx

R
A
N
D
O
M
I
Z
E

EBRT
VBT
No RT

Chemotherapy alone

Carbo paclitaxel x 6 cycles + placebo

$\pm RT$
 $\pm Cis$

Carbo paclitaxel
Pembro 200mg x 6 cycles →
Pembro 400mg x 6 cycles

$\pm RT$
 $\pm Cis$

Stratified by MMR status, planned radiation, histology, FIGO 2009 staging.

Results:

Jan 10 2021 – Oct 31 2022.
1095 total 545 pembro 550 placebo

MFU 23.7 mo pembro 24.1 placebo

RT received by 67% in both groups.
Greater proportion in placebo got subsequent pembro.

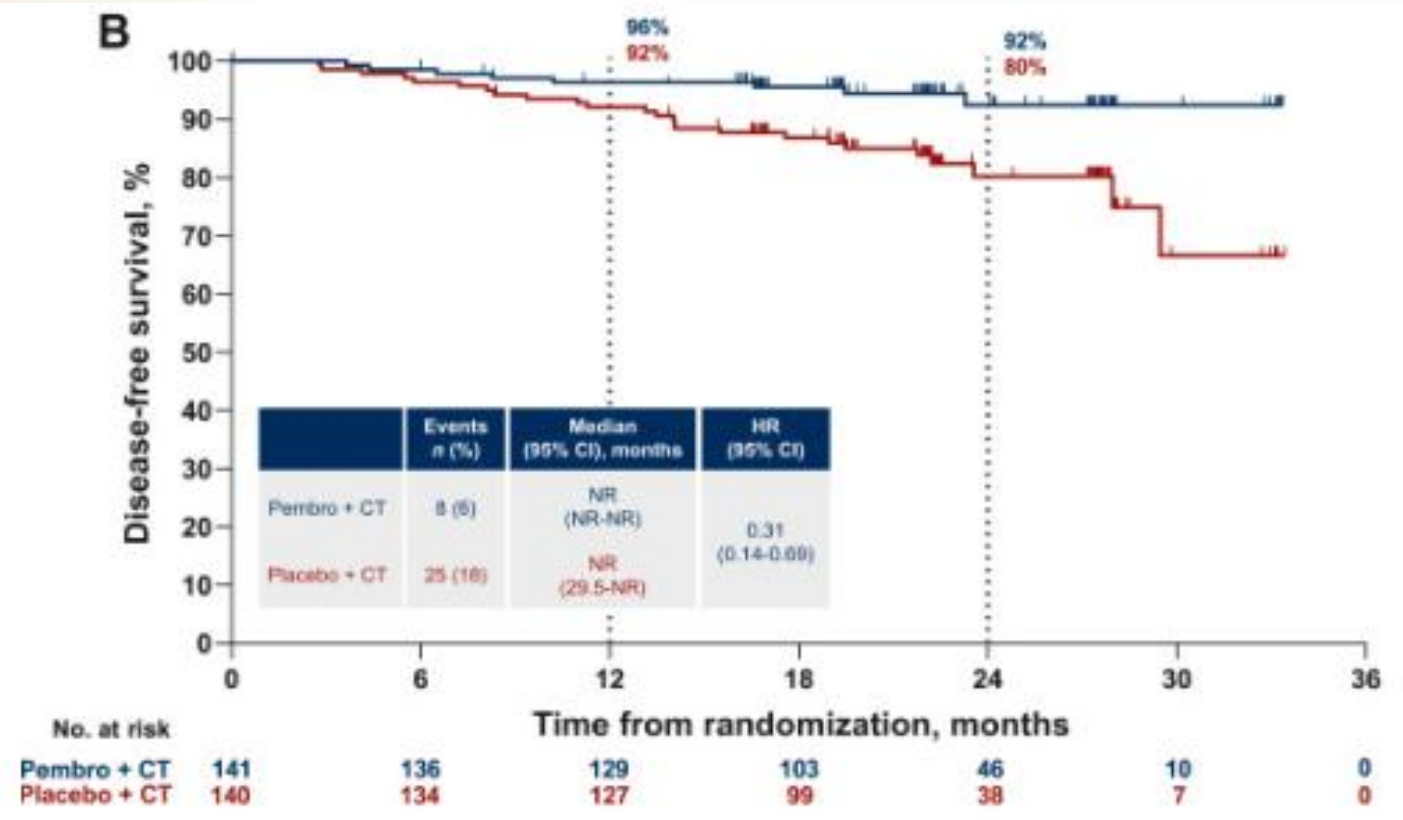
DFS rate 75% and 76% [HR 1.02
95% CI 0.79-1.32; p=0.570]

dMMR favored pembro [HR 0.31,
95% CI 1.14-0.69]

pMMR [HR 1.20, 95% CI 0.91-1.57]

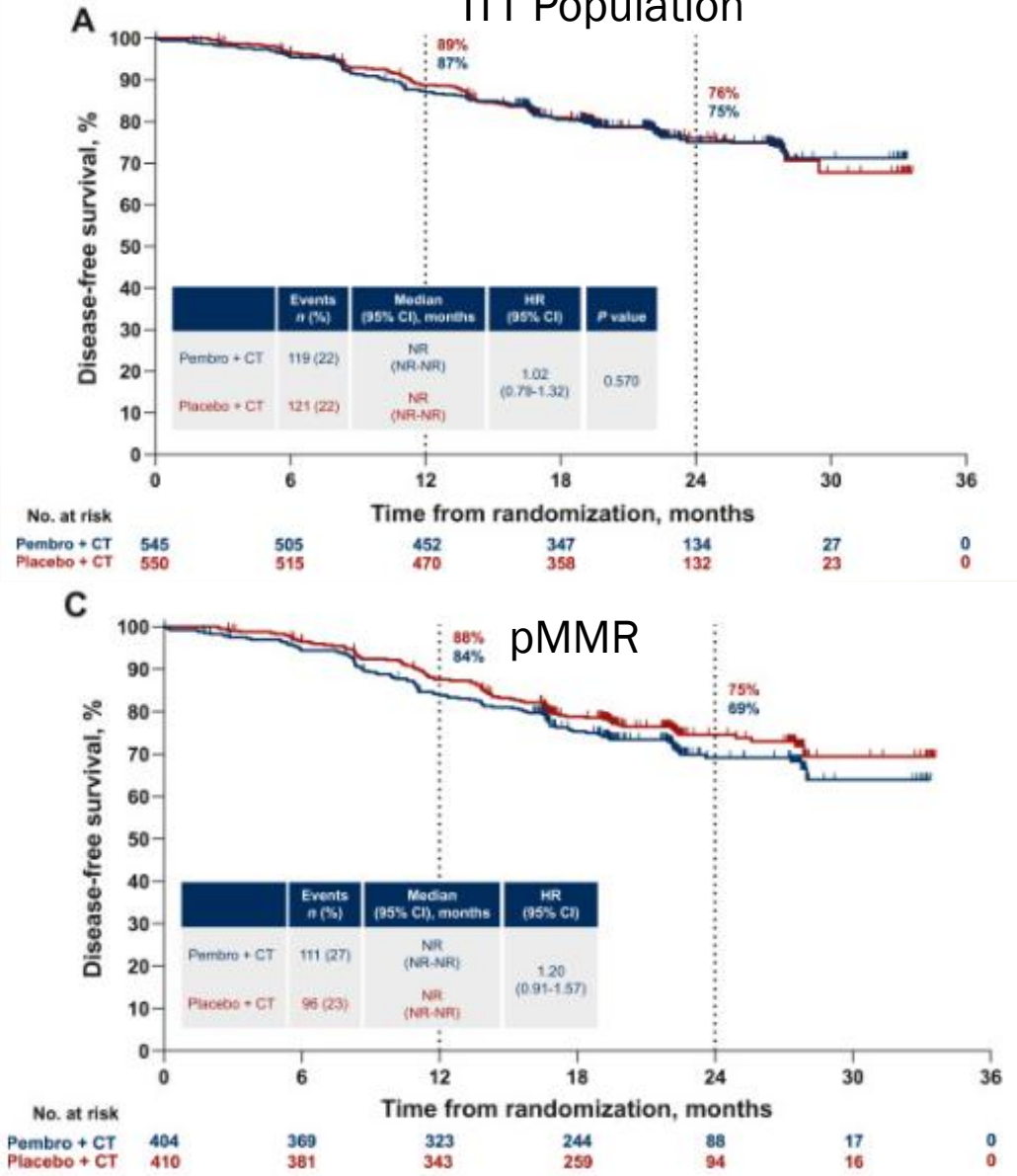
KEYNOTE B21 - Results

dMMR



Gorp et al. Ann Oncol. 2024

ITT Population



Cervical Cancer

Case

30F presents with post-coital bleeding. No hx HPV vaccination. HIV neg. Pregnancy neg.

Physical exam:

Large, 6 cm fungating mass.

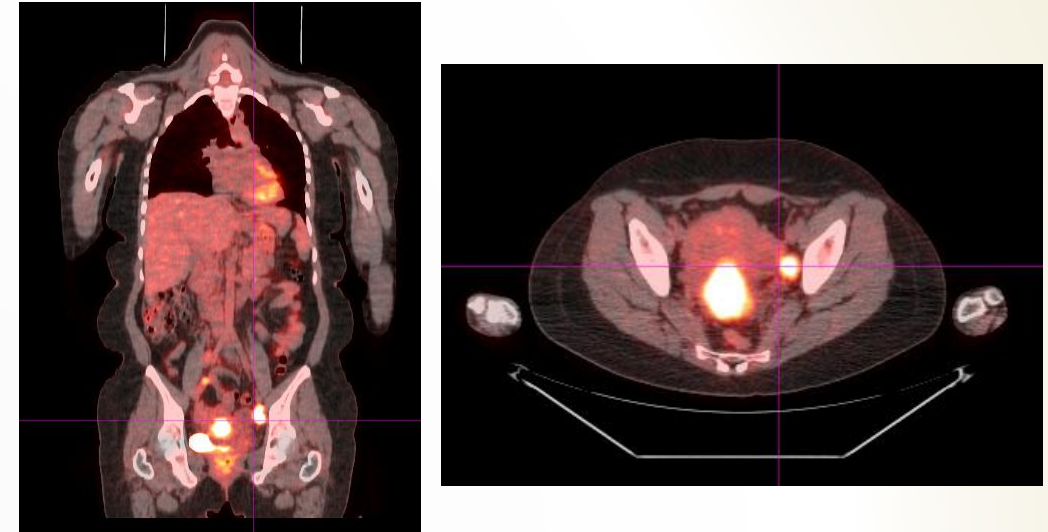
Disease extension from cervix to proximal 1/3 vagina with involvement of vaginal fornices.

Palpable bilateral parametrial involvement.

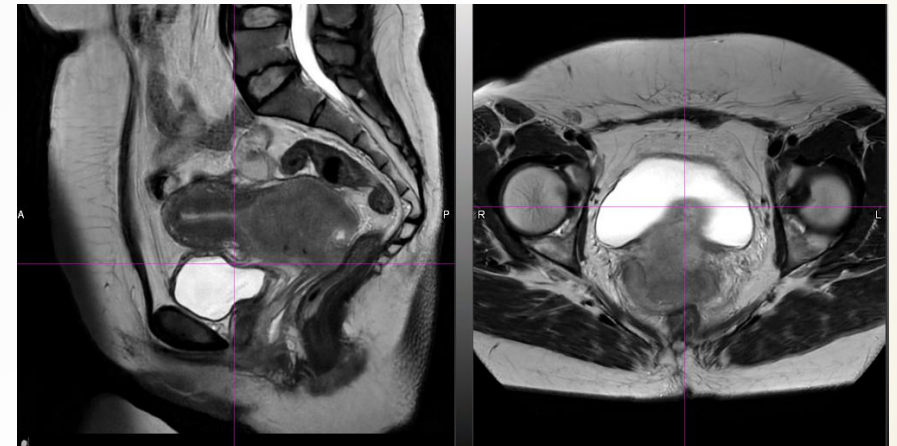
Concern for potential involvement of the bladder and rectal mucosa based on imaging.

Biopsy consistent with invasive squamous cell carcinoma, moderately differentiated, positive for p16, PD-L1 CPS >1

PET CT



MRI Pelvis T2 Sequence



Staging

Stage	FIGO 2014	FIGO 2018
IA IA1 IA2 IB IB1 IB2 IB3	Confined to the cervix (microscopic) ≤ 5 mm depth and ≤ 7 mm width ≤ 3 mm depth ≤ 7 mm width > 3 mm depth and not < 5 mm depth and ≤ 7 mm width Clinical lesion ≥ 5 mm depth confined to the cervix ≤ 4 cm maximum diameter > 4 cm maximum diameter -	Confined to the cervix ≤ 3 mm depth > 3 mm depth and ≤ 5 mm depth Clinical lesion ≥ 5 mm depth confined to the cervix ≤ 2 cm maximum diameter > 2 cm and ≤ 4 cm maximum diameter > 4 cm maximum diameter
II IIA1 IIA2 IIB	Beyond the uterus but not involving the lower one-third of the vagina or pelvic sidewall Upper two-thirds of the vagina and ≤ 4 cm Upper two-thirds of the vagina and > 4 cm Parametrial involvement	Beyond the uterus but not involving the lower one-third of the vagina or pelvic sidewall Upper two-thirds of the vagina and ≤ 4 cm Upper to thirds of the vagina and > 4 cm Parametrial invasion
III IIIA IIIB IIIC1 IIIC2	Lower third of the vagina, pelvic sidewall and ureters (hydronephrosis and non-functioning kidney) Lower one-third of the vagina but no extension to sidewall Pelvic sidewall, or hydronephrosis/non-functioning kidney - -	Lower vagina, pelvic sidewall, ureters, and lymph nodes Lower one-third of the vagina Pelvic sidewall Pelvic lymph node involvement Para-aortic lymph node involvement
IV IVA IVB	Clinical involvement of adjacent and distant organs Rectal or bladder involvement Distant organs outside the pelvis	Adjacent and distant organs Rectal or bladder involvement Distant organs outside the pelvis

Salva et al. Int J Gynecol Cancer 2020

Treatment Algorithm – Early-Stage Treatment Trials

LACC trial – RCT of minimally invasive (laparoscopic or robot assisted) vs open abdominal radical hysterectomy in IA1 (+LVI), IA2, or IB1 cervical cancer.

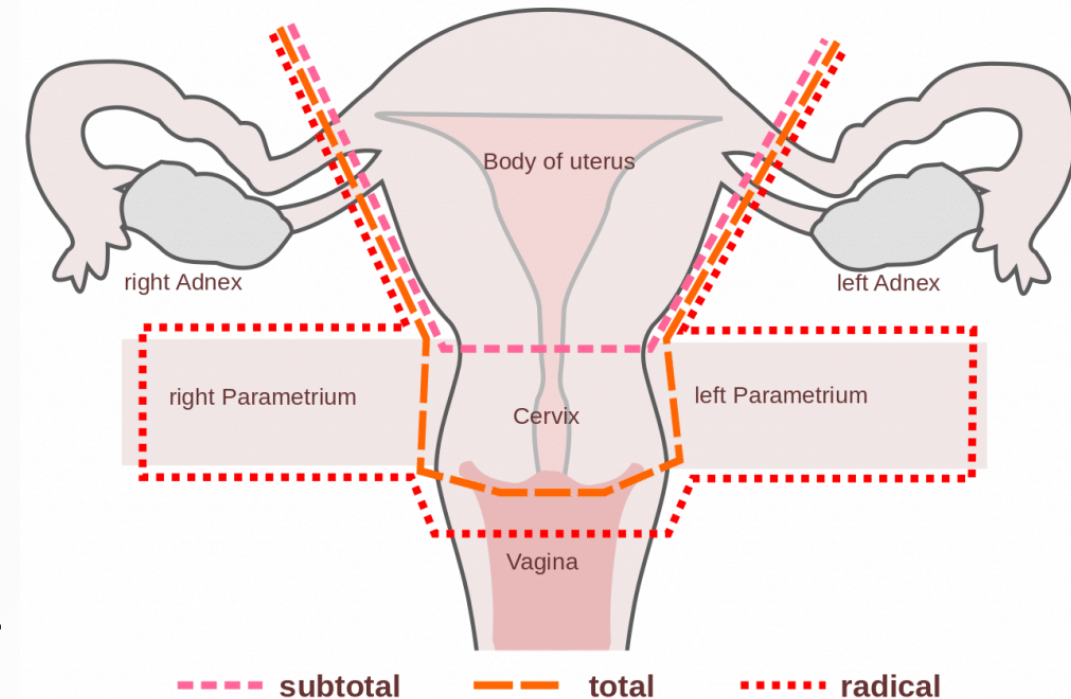
631 patients 4.5y FU - DFS 86% vs 96.5%. A difference of -10.6 percentage points crossing the lower boundary of non-inferiority of -7.2.

MIS lower rate of DFS and OS compared to open.

SHAPE Trial – RCT of simple vs rad hysterectomy in $\leq$ IB1.

700 pts – 3Y Pelvic recurrence rate 2.52% vs 2.17% (NSS), no difference in OS, fewer complications including lower risk of urinary incontinence or retention in simple hyst.

Ramirez PT et al. NEJM. 2018; Plante M et al. NEJM. 2024.

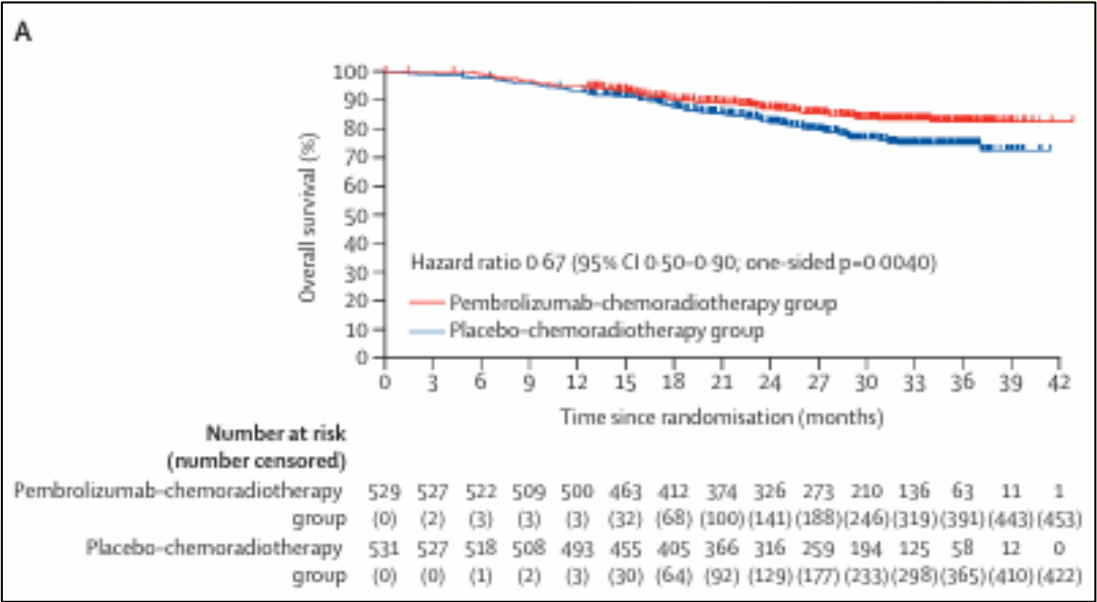
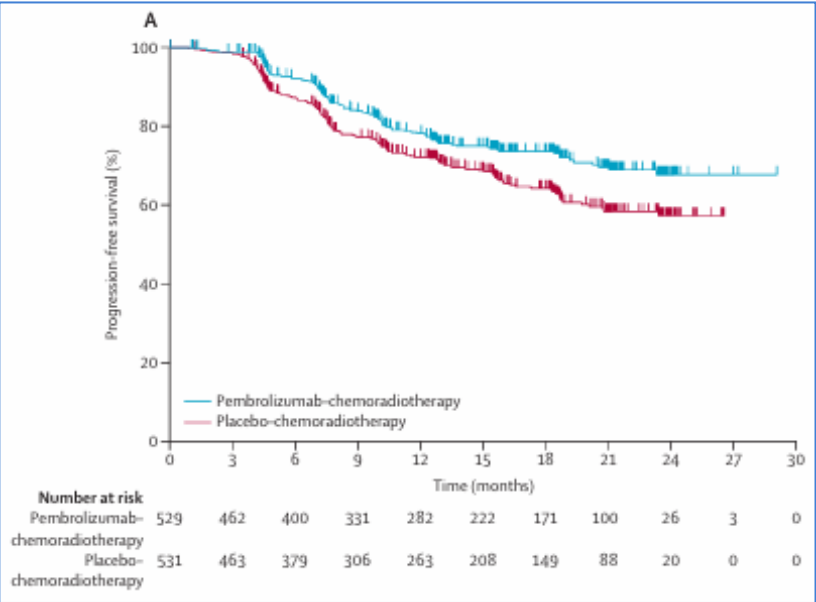


Treatment Approaches: Locally Advanced Cervical Cancer

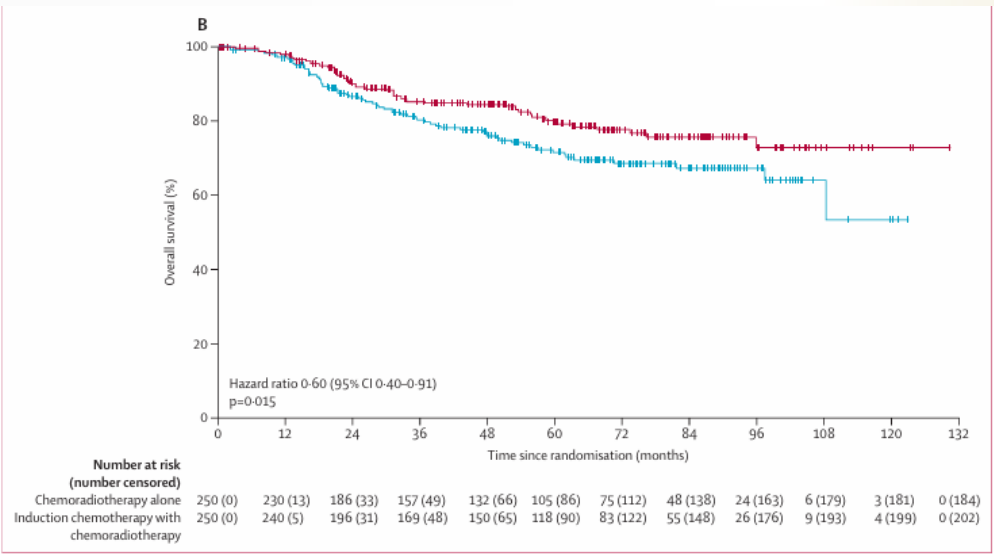
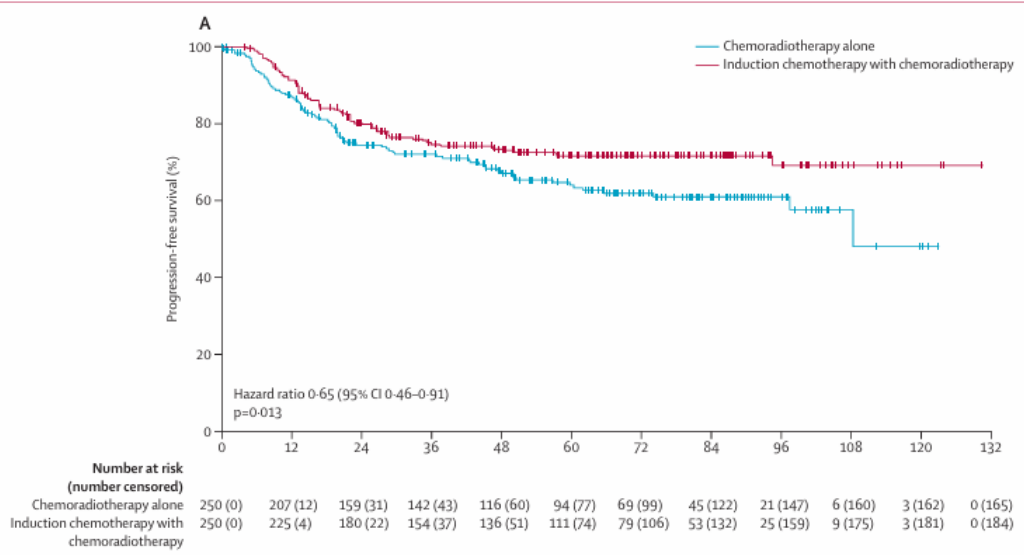
	GOG 120	KEYNOTE A18	INTERLACE	GY 037
N	526	1060	500	336
Primary endpoint	PFS and OS	PFS by RECIST 1.1 and OS	PFS and OS	PFS
Median f/u	106 mo	41.9 mo	67 mo	Ongoing
Eligibility	Untreated, invasive squamous, adenosquamous, or adenocarcinoma of the cervix (confirmed by central pathologic review), stages IIB, III, and IVA.	FIGO 2014 Stage IB2-IIB (node positive) or Stage III-IVA (node positive or negative). RECIST 1.1 measurable or non-measurable dz. Treatment naïve.	FIGO 2008 stage IB1 disease with nodal involvement, or stage IB2, IIA, IIB, IIIB, or IVA disease.	TNM T3 and T4 disease, N0-2, ECOG PS 0-1,, no prior tx.
Treatment	Group 1: Cisplatin 40 mgm2 QW 6C Group 2: Cisplatin 50 mg/m2 on days 1 and 29 f/b fluorouracil 4g/m2 given as a 96-hr infusion d 1 & 29, and 2 g/m2 of oral hydroxyurea twice weekly for 6 weeks Group 3: 3 g of oral hydroxyurea per square meter twice weekly for 6 wks	Cisplatin 40 mg/m2 QW x 5C + concurrent EBRT f/b brachy boost + Pembro 200 mg Q3W x 5 C or Placebo f/b maint Pembro or Placebo 400mg Q6w x 15C	Induction chemo Q1W Carbo AUC 2 and Paclitaxel 80 mg/m2 for 6 weeks f/b Cisplatin 40 mg/m2 QW x 5C + concurrent EBRT (45.0-50.4 Gy in 20-28fx) f/b brachy boost (to EQD2 78-86 Gy) or concurrent chemo/EBRT + brachy boost alone.	Induction chemotherapy C/P Q1W for 6 wks with concurrent pembrolizumab f/b CCRT w pembrolizumab and pembrolizumab maintenance, or standard CCRT with pembrolizumab f/b pembrolizumab maintenance.
Outcomes	30mo PFS 63%/62%/42% 5Y PFS 58%/57%/35% 10Y PFS 46%/43%/26% 30mo OS 70%/70%/53% 5Y OS 60%/61%/40% 10Y OS 53%/53%/34%	2Y PFS 70.6%/59.7% [HR 0.72, 95% CI 0.59-0.87, p=0.0020] 3Y PFS 64.3%/55.6% [HR 0.73, 95% CI 0.57-0.94, 2Y OS 87%/81% (NSS) 3Y OS 81.8%/74.4% HR 0.73 (p=0.0040) 4Y OS 75.4%/70.2%	5Y PFS 72%/64% [HR 0.65, 95% CI 0.46-0.91, p=0.013] 5Y OS 80%/72% [HR 0.60, 95% CI 0.40-0.91, p=0.015]	Actively Accruing

Results

KEYNOTE A18

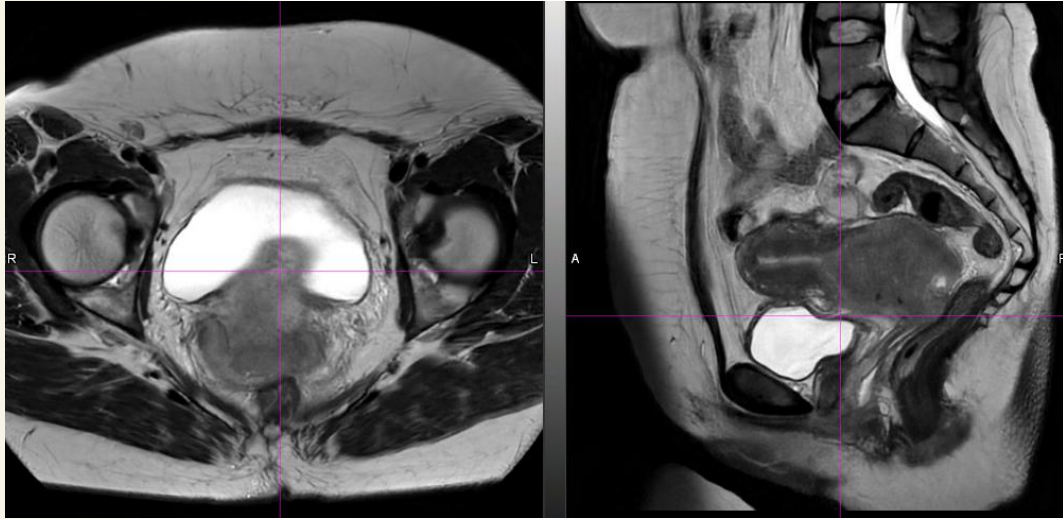


INTERLACE

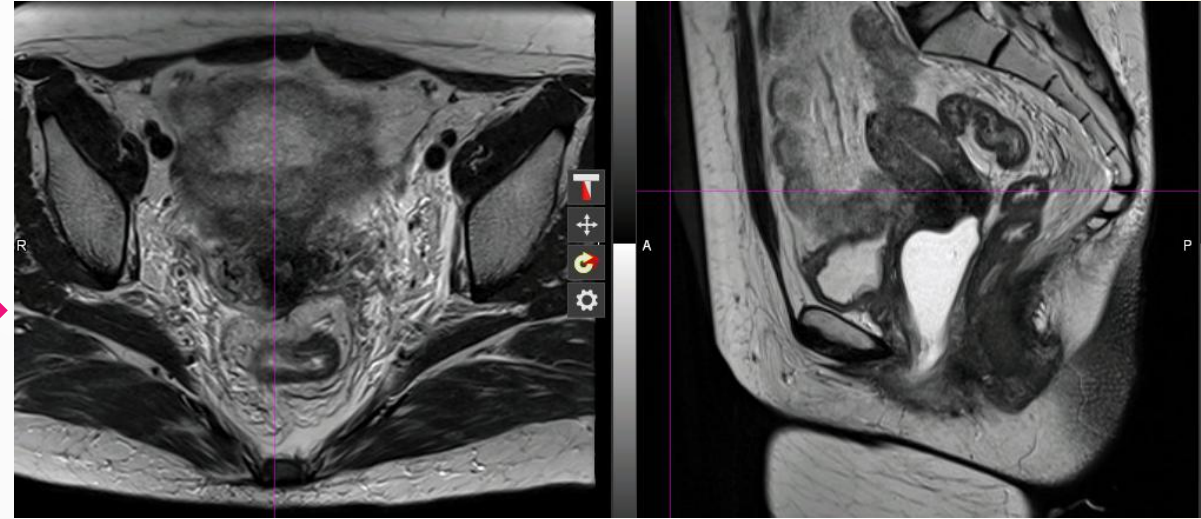


Lorusso et al. The Lancet. 2024. Duska et al. JCO. 2025. McCormack et al. The Lancet. 2024.

Case – Response

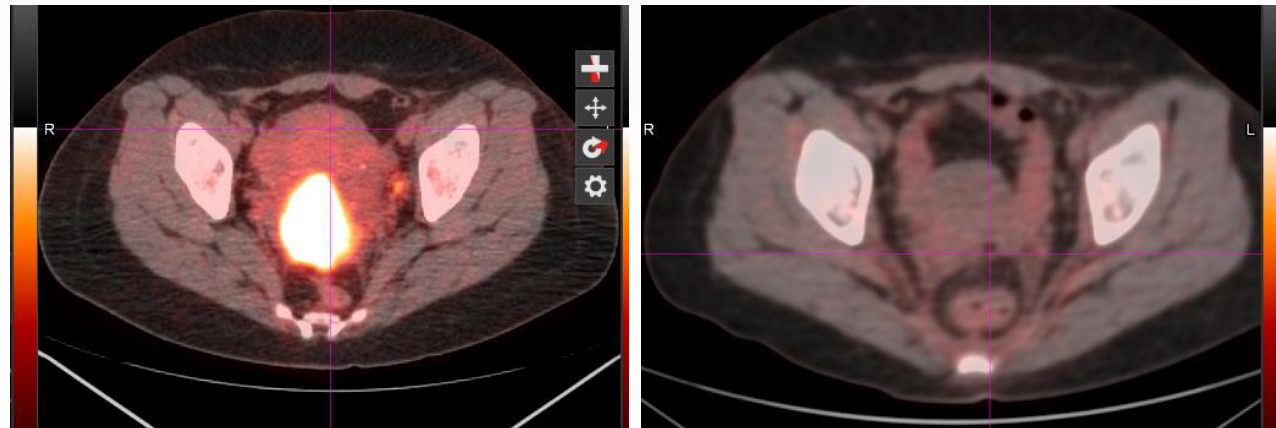


Prior to Pembro+Chemo+EBRT treatment initiation



Prior to Brachytherapy treatment initiation

3 Month Post Treatment PET-CT
Patient feeling well. No residual
vaginal bleeding or pain



Evolving Treatment Timeline

1999 National Cancer Institute attesting to survival benefits conferred through platinum-based chemoradiation for LACC

2021 Pembrolizumab combined with chemo +/- Bev as first line treatment for PD-L1+ recurrent metastatic cervical cancer KEYNOTE 861

2024 Pembrolizumab concurrently and following CRT significantly improved PFS in newly diagnosed high-risk LACC

NRG 037: Neoadjuvant Pembrolizumab and Chemotherapy and Chemoradiation vs. Chemoradiation Followed by Pembrolizumab for Locally Advanced Cervical Ca.

20yrs

2018 Pembrolizumab receives FDA approval in PD-L1 recurrent metastatic cervical cancer KEYNOTE 158

2023 CALLA Durvalumab concurrently and following CRT showed no significant improvement in PFS for newly diagnosed LACC

January 12, 2024 US Food and Drug Administration approved pembrolizumab with chemoradiotherapy in LACC (restricted label to FIGO 2014 Stage III-IVA Cervical Carcinoma)

Survivorship

Sexual Health and Survivorship

Sexual health is a critical component of cancer care survivorship, impacted by all forms of curative management.

Patients treated for pelvic malignancies report significant rates of sexual dysfunction which negatively impact quality of life.

Data on aids and interventions for sexual dysfunction is limited.

Guideline recommendations on devices for vaginal health are limited to academic literature reviews, practice surveys, and small observational studies, focused mainly on education.

Consider:

Dilator timing, frequency, and duration.

Use of lubrication and vaginal moisturizers (containing hyaluronic-acid).

Ongoing assessment and reinforcement at subsequent visits.



M Katz et al. J Sex Med 2026

Take Away Points

- Recent years have shown remarkable breakthrough in utilization of multimodality treatment approaches including surgery, chemotherapy, immunotherapy, and adaptive radiation to improve outcomes in patients with gynecologic malignancies.
- New approaches are coming down the pipeline, and it is our responsibility to know how to best incorporate our evolving understanding of molecular markers and tumor histopathology to existing data to provide the optimal treatment strategy for each patient.
- At the end of the day remember why we do this...



Thank You!

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