Adjuvant Treatment in Endometrial Cancer

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Adjuvant Treatment Selection Endometrial Cancer

- All Completed Clinical Trials in Endometrial Cancer are Based on Clinico-Pathological Risk Factors
- Treatment Selections based on Molecular risk features based on various subgroup and posthoc analysis.
- Prospective trials report PORTEC 4a expected in 2025-2026
- Rainbo Studies with Molecular classification beginning.
- Treatment Selection based on Standard Pathology
    - Adaptations based on molecular information

FIGO staging :Endometrial Cancer Report 2018

FIGO CANCER REPORT 2018

WILEY

Cancer of the corpus uteri

Frédéric Amant[1,2,3,*] | Mansoor Raza Mirza[4] | Martin Koskas[5] | Carien L. Creutzberg[6]

TABLE 1 Cancer of the corpus uteri.

FIGO Stage	
I[a]	Tumor confined to the corpus uteri
IA[a]	No or less than half myometrial invasion
IB[a]	Invasion equal to or more than half of the myometrium
II[a]	Tumor invades cervical stroma, but does not extend beyond the uterus[b]
III[a]	Local and/or regional spread of the tumor
IIIA[a]	Tumor invades the serosa of the corpus uteri and/or adnexae[c]
IIIB[a]	Vaginal involvement and/or parametrial involvement[c]
IIIC[a]	Metastases to pelvic and/or para-aortic lymph nodes[c]
IIIC1[a]	Positive pelvic nodes
IIIC2[a]	Positive para-aortic nodes with or without positive pelvic lymph nodes
IV[a]	Tumor invades bladder and/or bowel mucosa, and/or distant metastases
IVA[a]	Tumor invasion of bladder and/or bowel mucosa
IVB[a]	Distant metastasis, including intra-abdominal metastases and/or inguinal nodes)

extensive LVSI is found.[6] The distinction made using LVSI status could be more relevant than the distinction between Stages IA and IB for predicting survival in Stage I endometrial cancer.[7]

3 | PROGNOSTIC TUMOR CHARACTERISTICS FOR HIGH-RISK DISEASE

Its early presentation following postmenopausal bleeding results in a generally good prognosis, but it should be treated using evidence-based protocols, and where appropriate, by expert multidisciplinary teams. Four main histopathologic criteria are recommended to determine high-risk disease:

1. Tumor grade 3 (poorly differentiated).
2. Lymphovascular space invasion.
3. Nonendometrioid histology (serous, clear cell, undifferentiated, small cell, anaplastic, etc.).
4. Cervical stromal involvement.

Amant, Int J Gynecol Obst 2018

Early Stage
(Localized)
(Stage I/II)

Low Risk

Intermediate Risk

High Intermediate Risk

High Risk

Advanced Stage (Localised)
Stage III/IVA

Postoperative Risk Stratification

Risk Grouping

	Low	Intermediate	High
Pathological features	Stage I <50% MI Grade I-II	>50% invasion Grade I or II <50% invasion/grade III LVSI/ Age>60	Stage II-IV Serous Clear Cell
5 year recurrence rate	2-10%	20-25%	30-65%

Low Risk Endometrial Cancer can be cured with surgery alone.

All effort of risk stratification is to identify patients that will benefit from treatment modulation

Within this group 20-25% incidence of recurrence without any adjuvant treatment.

Risk Groupings for Endometrial Cancer (2016)

	FIGO Stage	Grade	LVSI	Histology
Low Risk	I <50% Myometrial invasion	I/II	LVSI-	Endometroid
Intermediate	I =/>50% Myometrial Invasion	I/II	LVSI-	Endometroid
High Intermediate	I< 50 % myometrial invasion I, any depth	III I/II	LVSI+/- LVSI +	Endometroid
High	I =/>50% Myometrial Invasion Stage II Stage III	III Any Grade Any Grade	LVSI-/+ Any LVSI Any LVSI	Endometroid Any Any
Advanced	Stage III Incomplete surgery	Any Grade	Any LVSI	Any

ESMO-ESGO-ESTRO Report 2016

SEER database: Lymphadenectomy Dissection rates

	LN Dissection Rate SEER Database
1988-1991	31%
1992-1995	40%
1996-1999	47%
2000-2003	53%
Use of LN Dissection N=42184 patients	0.81 (> 11 node removal HR 0.74 (p<0.0001)

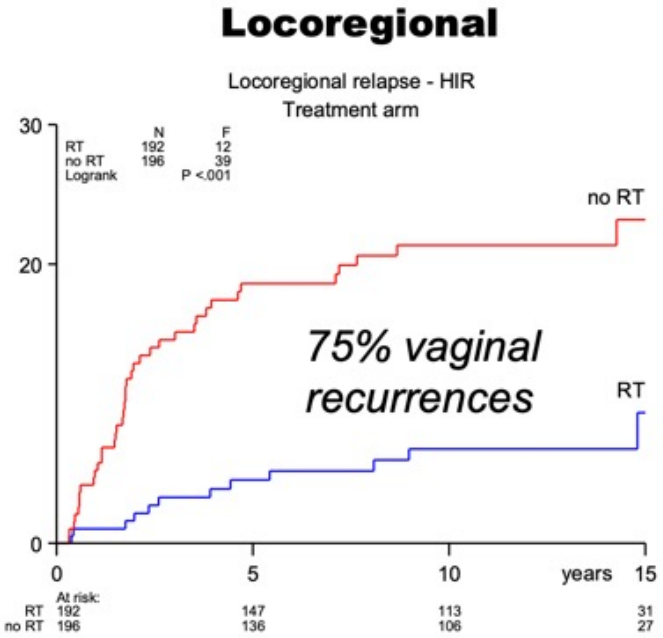
ESMO ESGO ESTRO Guidelines,2016

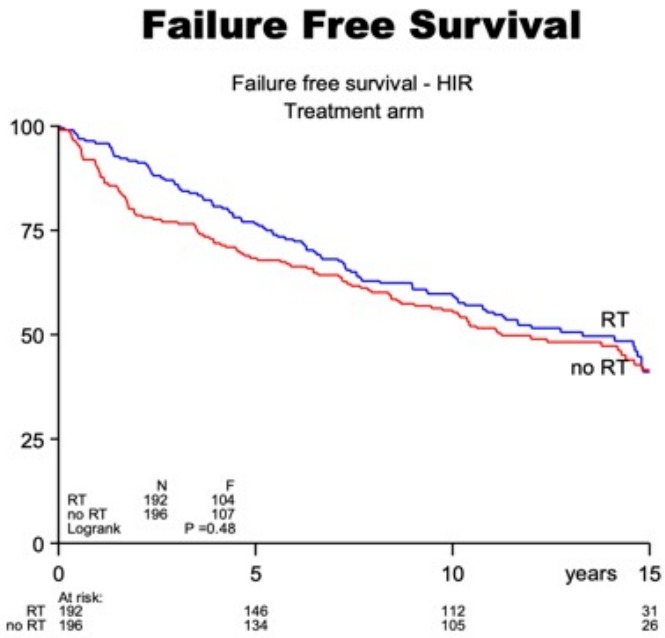
Treatment Allocation
Early stage
(Intermediate-High)

Randomized Trials on Adjuvant Radiation

	PORTEC-1	GOG 99	ASTEC/EN.5	PORTEC-2
Risk	Intermediate Risk	Intermediate risk group	Intermediate High and High Risk (15%)	High Intermediate Tisk
Surgical Staging	No	Yes	Some	No
Randomisation	Obs vs. EBRT	Obs vs. EBRT	Obs vs EBRT	EBRT vs. BT
Number	714	448	905	427
Pelvic Failure	15.5% vs 6% (HIR:20% vs 5%)	13% vs 4% (4% in LIR and 19% in HIR)	6.1% vs 3.2%	5.1% vs 2.1%
Grade ≥III GI toxicity	2.6% EBRT 0.5% No RT	2.6% 0.4%	7% EBRT 3% EBRT/VB	2% EBRT 1% VB
Life threatening Late Toxicity	1% (surgical intervention)	1.3%	1% (RT arm)	None

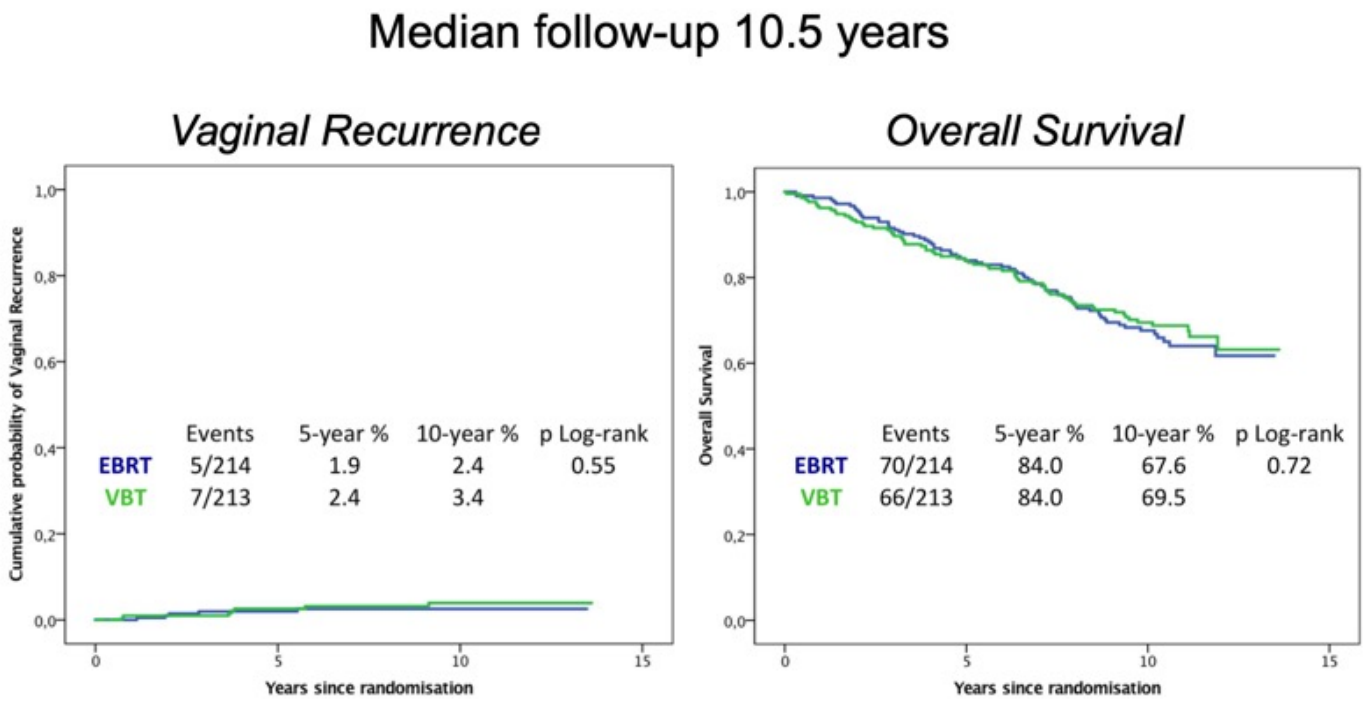
PORTEC -1 15 year follow up





Creutzberg, IJROBP,2011

PORTEC-2 10 year follow up



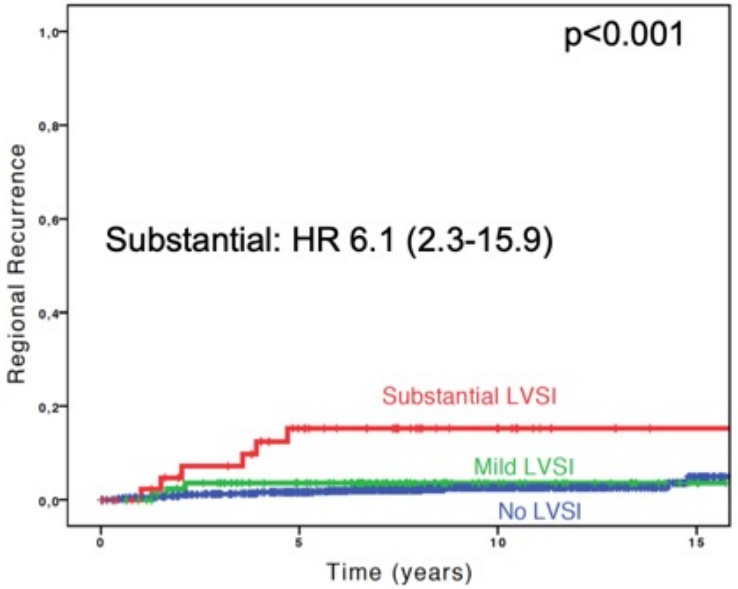
Wortman BJC 2010

LVSI

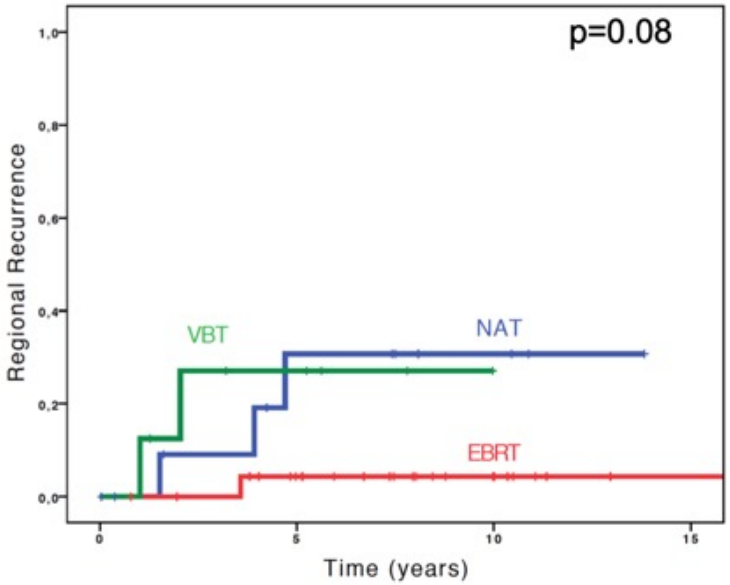
- Pelvic nodal recurrence

5%

All 954 patients



Substantial LVSI: 46 patients

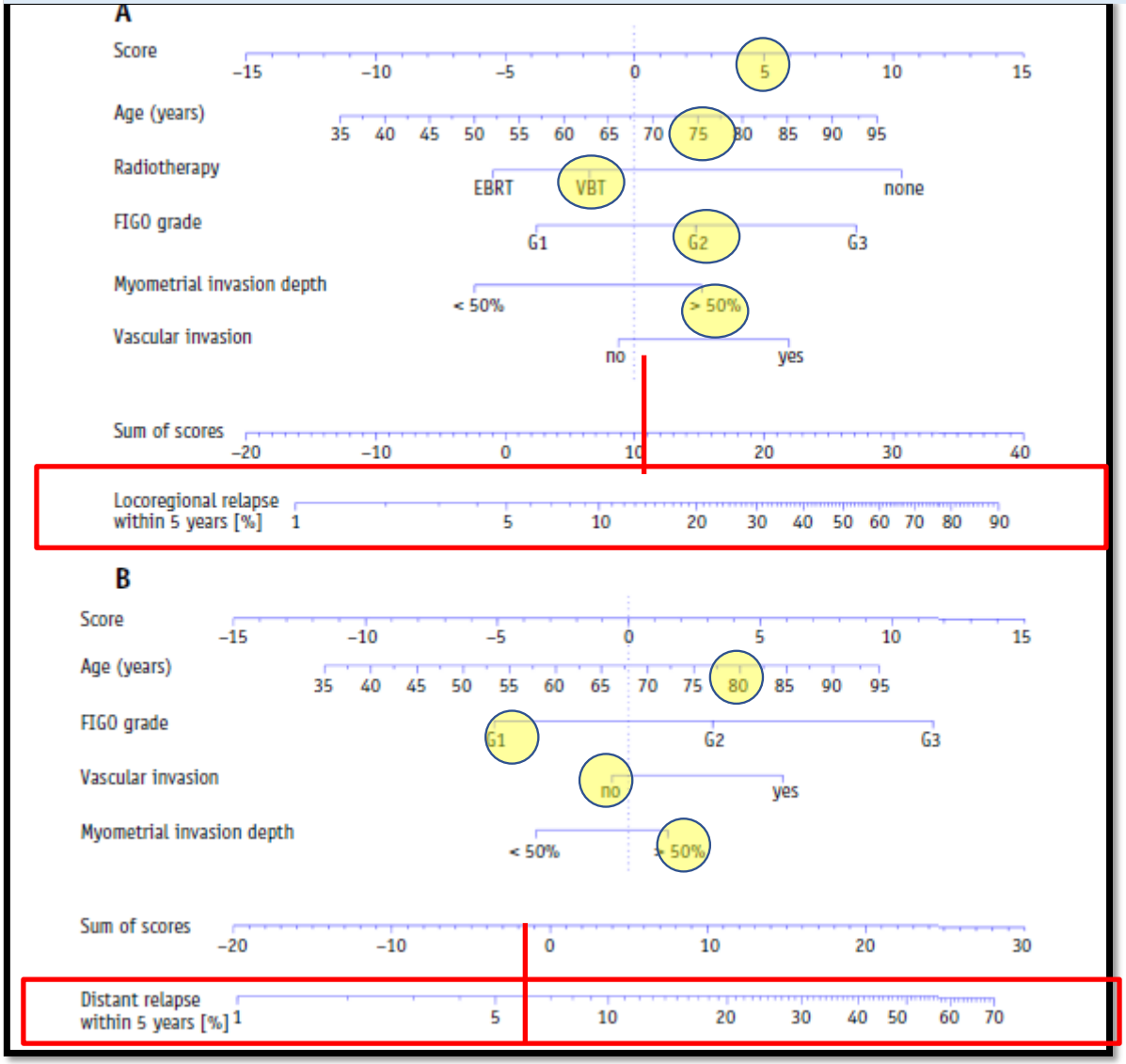


Bosse, EJC 2015, Nout ASTRO 2014

Summary: Adjuvant RT Trials in Early Stage Endometrial Cancer

- Low Risk Patients (2009 FIGO IA gr I/II) may be observed.
- Low and High Intermediate Risk: (Age >60, IA Gr III/ IB Grade I-II) may be treated with brachytherapy alone.
- LVSI + may be considered for EBRT due to risk of PLN disease.

Nomograms for risk of relapse



PORTEC -1

PORTEC -2 Trials

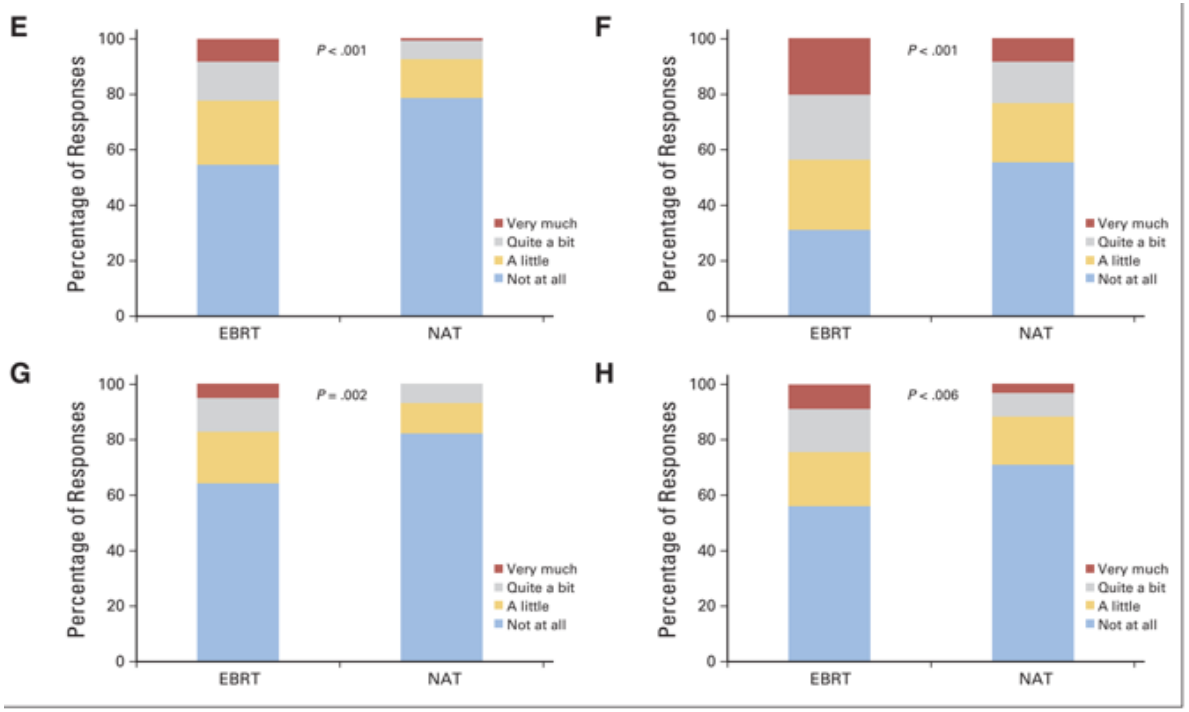
Intermediate Risk Patients (Endometroid)

No LN Dissection

Need external validation as 3/4th of the patients included to make these nomograms have received adjuvant RT.

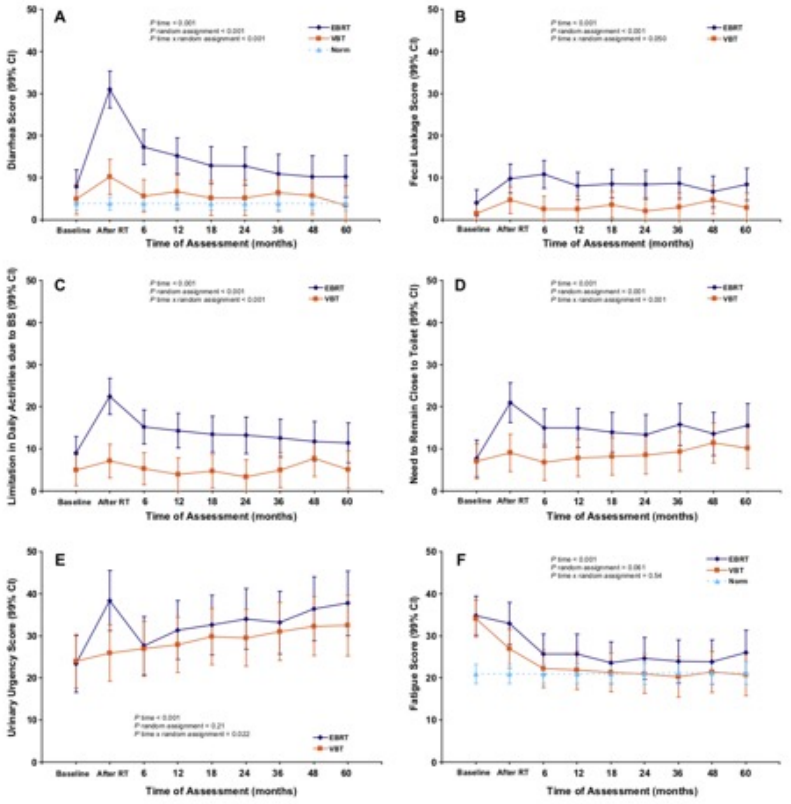
Creutzberg, IJROBP 2014

Impact of Postoperative RT on QOL
PORTEC I and II Trial : EBRT vs BT



Diarrhoea, Fecal Urgency, Fecal Leakage, Limitation of ADL

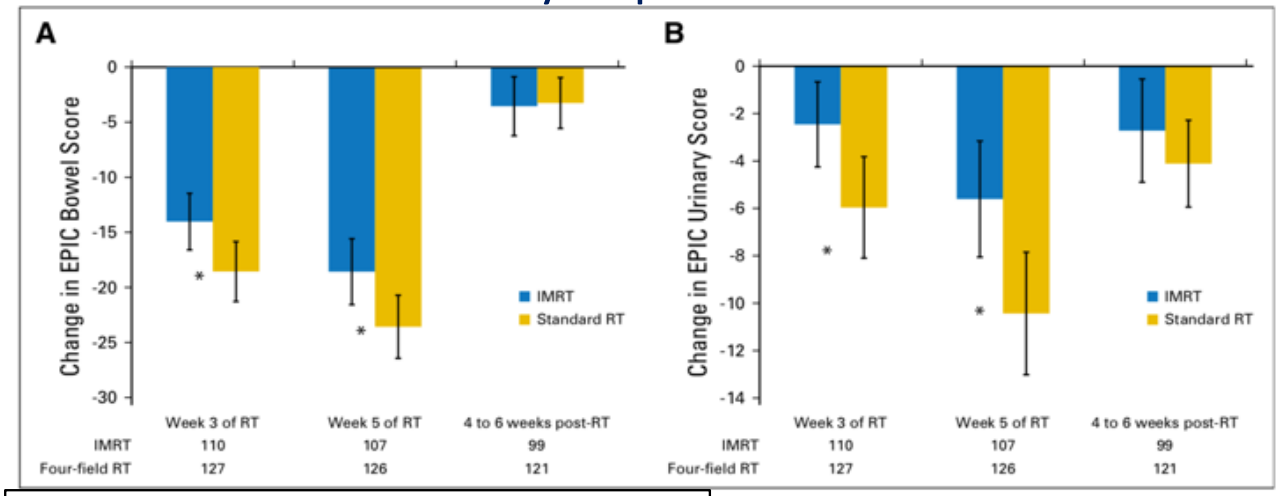
Nout RA, JCO 2011

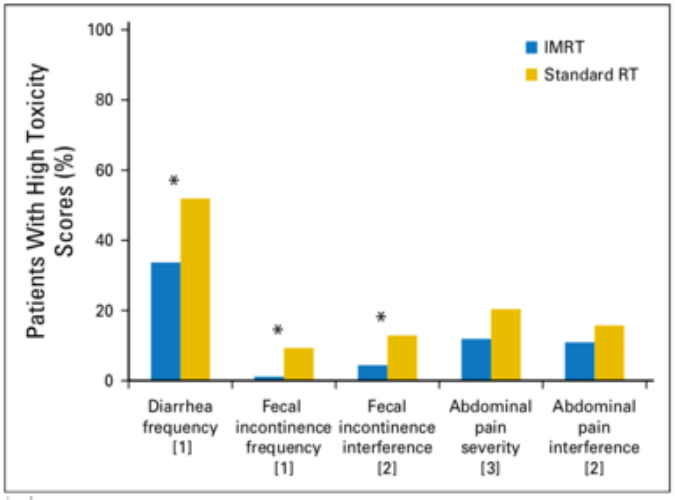


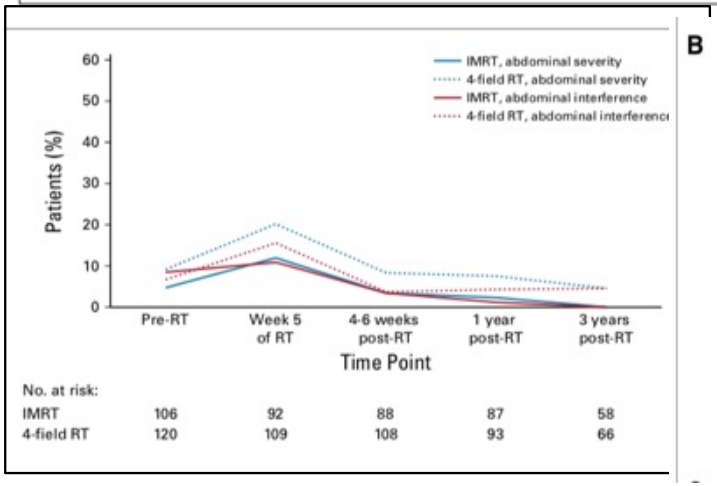
Nout RA, Eur J Cancer 2012

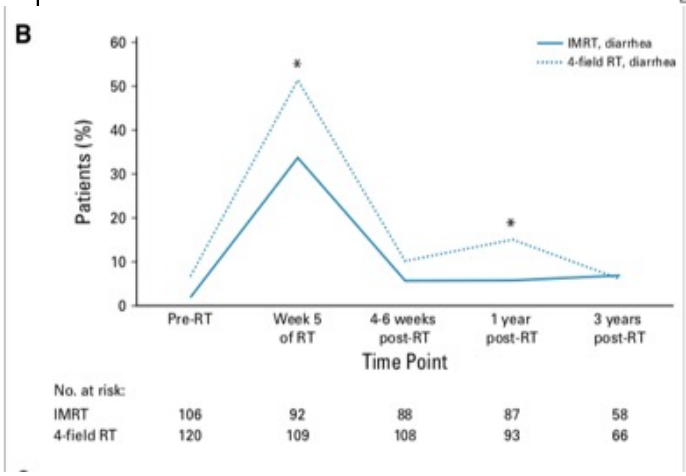
TIME -C NRG Study

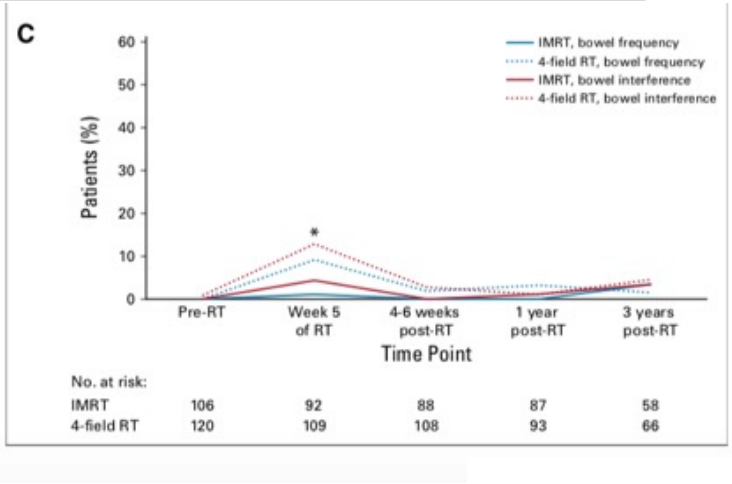
Early Impact on RT. No benefit at long term follow up







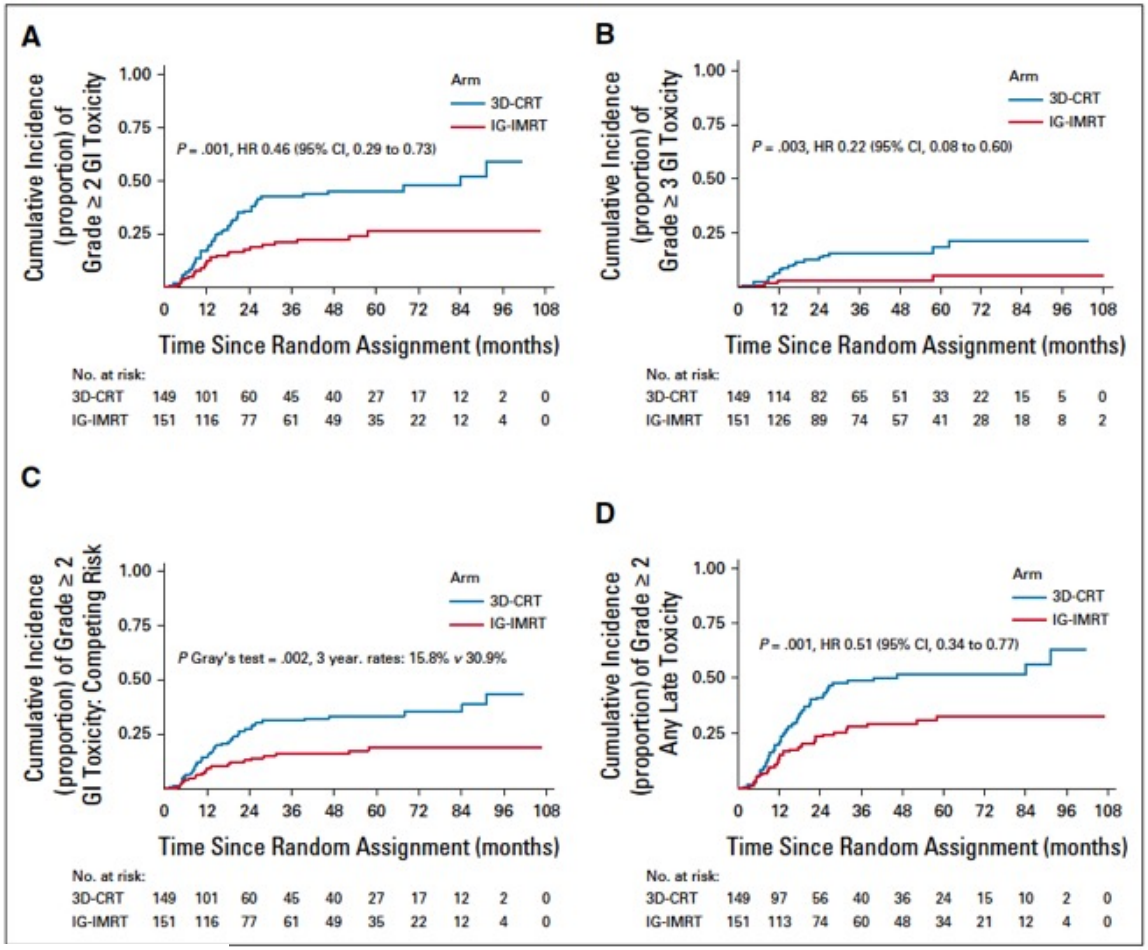




Klopp JCO 2018

Yeung, JCO 2020

Physician Reported Adverse Effects: PARCER Phase III IMRT Trial



Chopra, JCO,20121

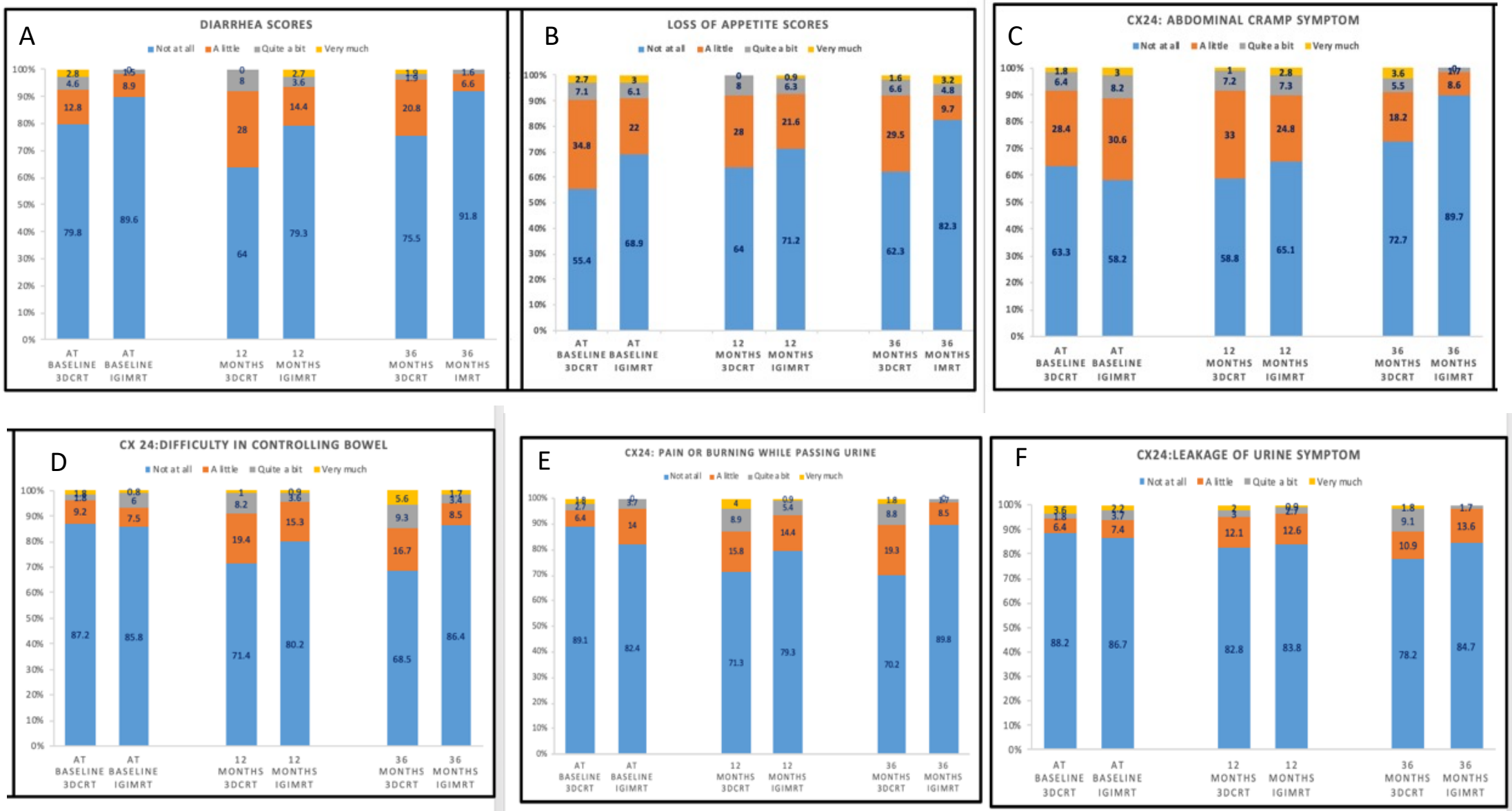

A
DIARRHEA SCORES
Not at all
A little
Quite a bit
Very much
100%
90%
80%
70%
60%
50%
40%
30%
20%
10%
0%
2.8
4.6
12.8
79.8
1.5
8.9
89.6
0
8
28
64
2.7
3.6
14.4
79.3
1.9
1.9
20.8
75.5
1.6
6.6
91.8
AT BASELINE 3DCRT
AT BASELINE IGIMRT
12 MONTHS 3DCRT
12 MONTHS IGIMRT
36 MONTHS 3DCRT
36 MONTHS IMRT
B
LOSS OF APPETITE SCORES
Not at all
A little
Quite a bit
Very much
2.7
7.1
34.8
55.4
3
6.1
22
68.9
0
8
28
64
0.9
6.3
21.6
71.2
1.6
6.6
29.5
62.3
3.2
4.8
9.7
82.3
AT BASELINE 3DCRT
AT BASELINE IGIMRT
12 MONTHS 3DCRT
12 MONTHS IGIMRT
36 MONTHS 3DCRT
36 MONTHS IMRT
C
CX24: ABDOMINAL CRAMP SYMPTOM
Not at all
A little
Quite a bit
Very much
1.8
6.4
28.4
63.3
3
8.2
30.6
58.2
1
7.2
33
58.8
2.8
7.3
24.8
65.1
3.6
5.5
18.2
72.7
1.7
8.6
89.7
AT BASELINE 3DCRT
AT BASELINE IGIMRT
12 MONTHS 3DCRT
12 MONTHS IGIMRT
36 MONTHS 3DCRT
36 MONTHS IGIMRT
D
CX 24:DIFFICULTY IN CONTROLLING BOWEL
Not at all
A little
Quite a bit
Very much
1.8
9.2
87.2
0.8
6
7.5
85.8
1
8.2
19.4
71.4
0.9
3.6
15.3
80.2
5.6
9.3
16.7
68.5
1.7
3.4
8.5
86.4
AT BASELINE 3DCRT
AT BASELINE IGIMRT
12 MONTHS 3DCRT
12 MONTHS IGIMRT
36 MONTHS 3DCRT
36 MONTHS IGIMRT
E
CX24: PAIN OR BURNING WHILE PASSING URINE
Not at all
A little
Quite a bit
Very much
1.8
2.7
6.4
89.1
3.7
14
82.4
4
8.9
15.8
71.3
0.9
5.4
14.4
79.3
1.8
8.8
19.3
70.2
1.7
8.5
89.8
AT BASELINE 3DCRT
AT BASELINE IGIMRT
12 MONTHS 3DCRT
12 MONTHS IGIMRT
36 MONTHS 3DCRT
36 MONTHS IGIMRT
F
CX24:LEAKAGE OF URINE SYMPTOM
Not at all
A little
Quite a bit
Very much
3.6
1.8
6.4
88.2
2.2
3.7
7.4
86.7
2
3
12.1
82.8
0.9
2.7
12.6
83.8
1.8
9.1
10.9
78.2
1.7
13.6
84.7
AT BASELINE 3DCRT
AT BASELINE IGIMRT
12 MONTHS 3DCRT
12 MONTHS IGIMRT
36 MONTHS 3DCRT
36 MONTHS IGIMRT

Fig 4 A- F

Special Considerations for EBRT

Patients with Familial Lynch Syndrome or HNPCC

Post Total Proctocolectomy and Ileo Rectal Anastomosis

Dual Pelvic Primary (Rectum and Endometrial Cancer)

Does Chemotherapy in addition to radiation improve survival in early stage high risk patients?

Systemic Chemotherapy Trials: Endometrial Cancer

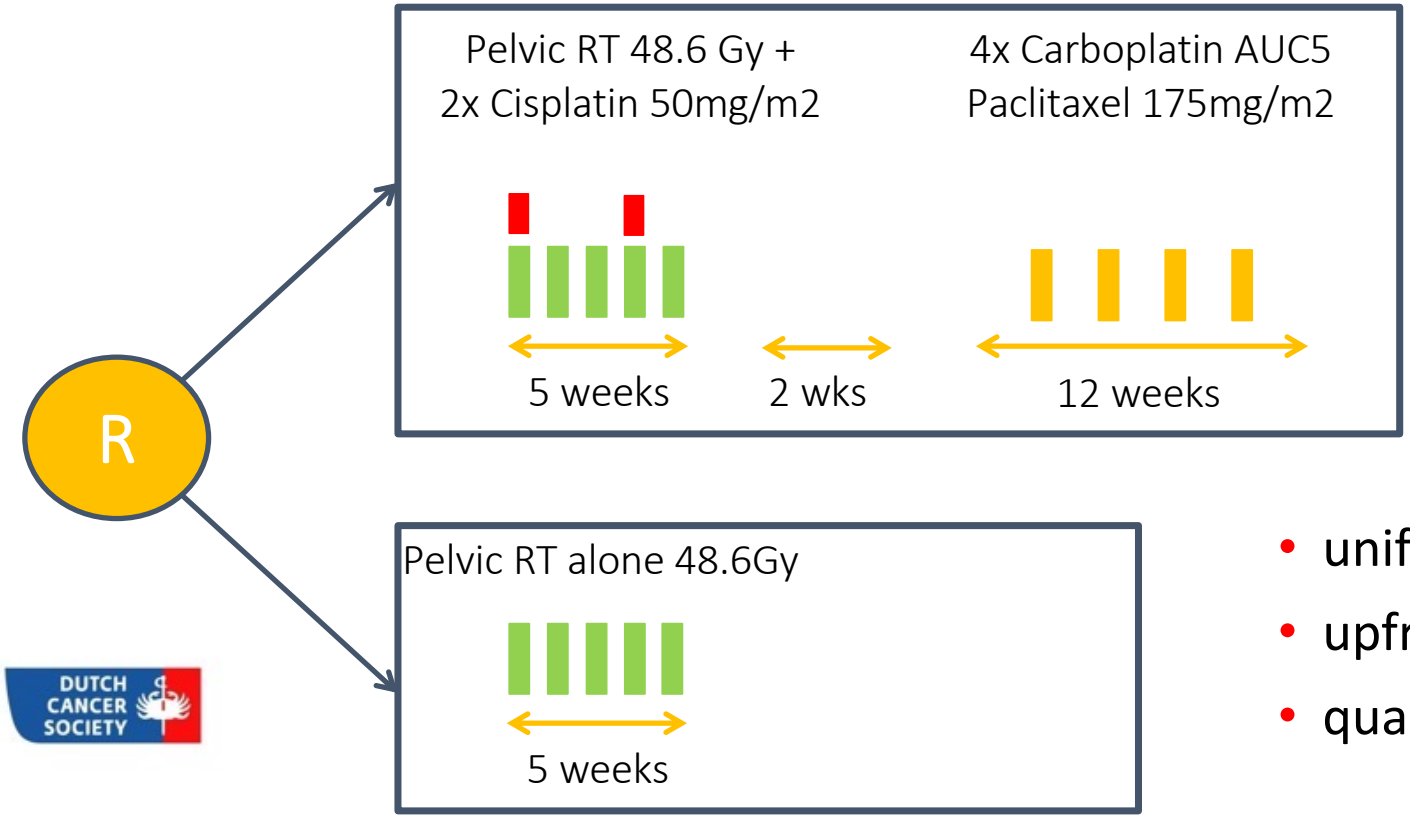
	NSGO/EORTC	MaNGO/ILIADE III	Maggi R
Number	383	156	345
Randomization	RT vs RT+CT	RT vs RT+CT	RT vs Chemo
Stage	Stage I-III, Grade II-III Type II (High Intermediate/ High)	Stage IIB,IIIA-C (High)	IC Grade III II G3>50% MI Stage III (High Risk)
PFS	24% vs 15% (p-0.04)	32% vs 19%(NS)	No difference in PFS
	PFS (8%, p=0.0009) 5% difference in OAS not significant or CSS (&%) not significant		

Small Representation of Stage I/II high risk tumours in above trials

Addition of Systemic chemotherapy not considered to be of important towards OS

PORTEC-3

- 686 stage I High risk, stage II/III Endometrial Cancer

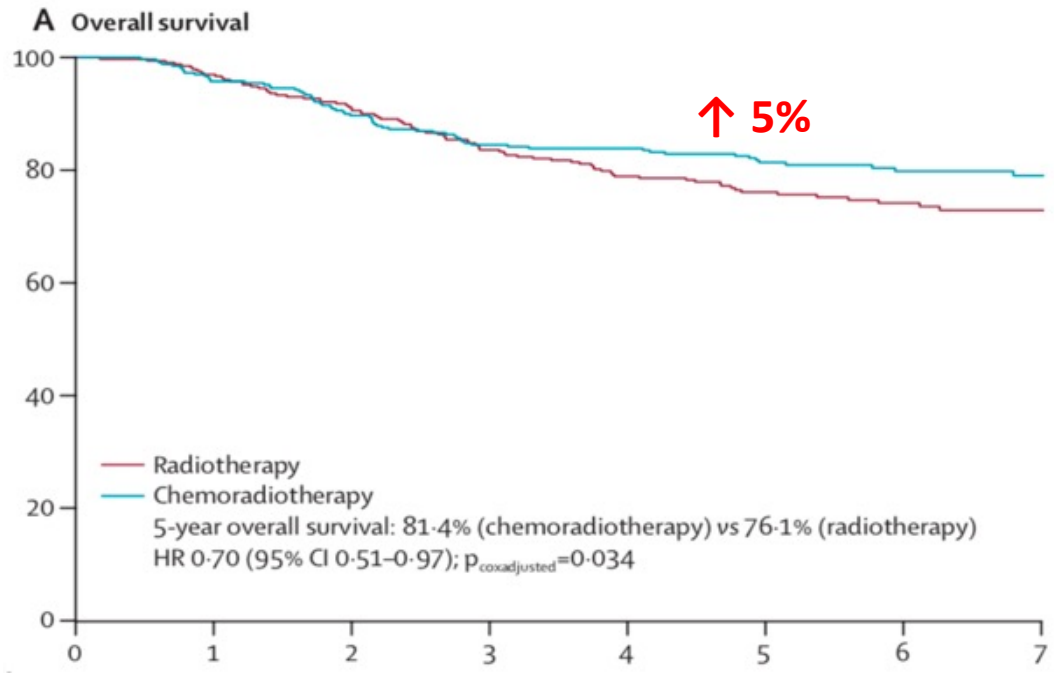


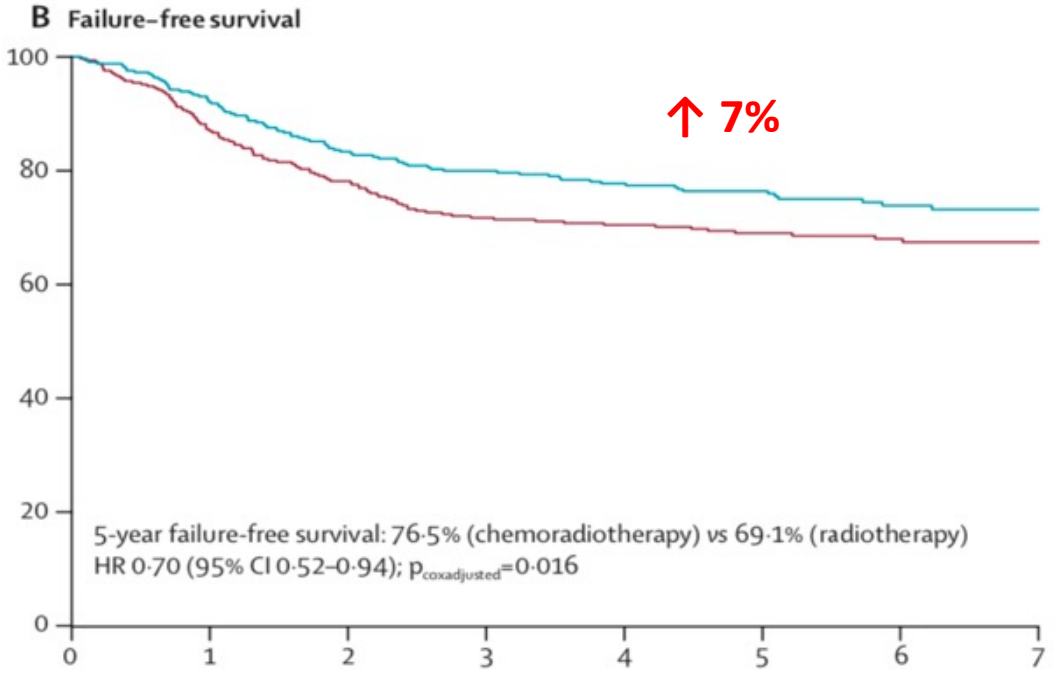
- uniform treatment schedule
- upfront pathology review
- quality of life analysis

De Boer et al. Lancet Oncol 2018

Courtesy: R Nout, PORTEC Group

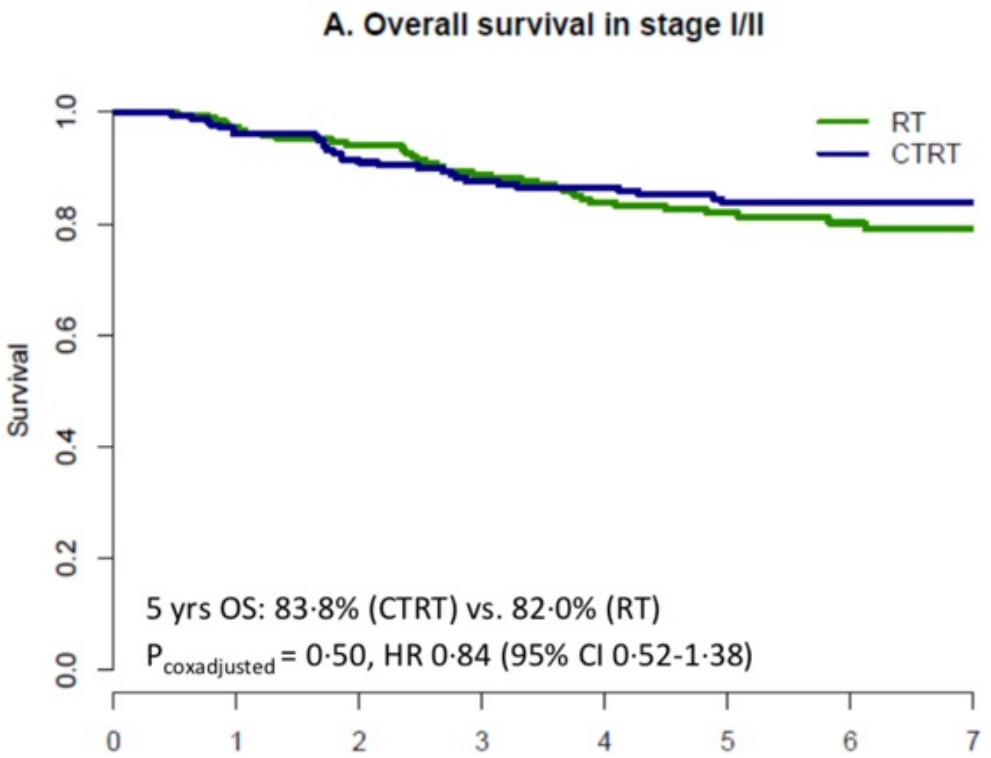
PORTEC-3: overall & failure free survival

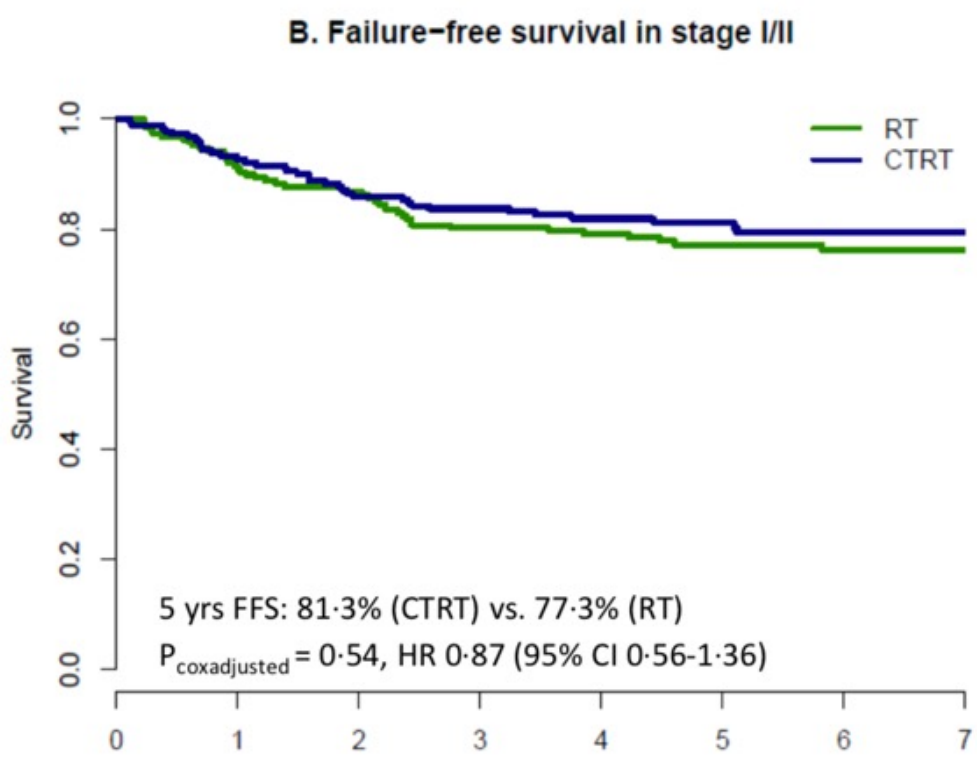




de Boer et al, Lancet Oncology 2019

PORTEC-3: stage I/II





- Stage I/II: no significant difference in Overall or Failure Free Survival

de Boer et al, Lancet Oncology 2019

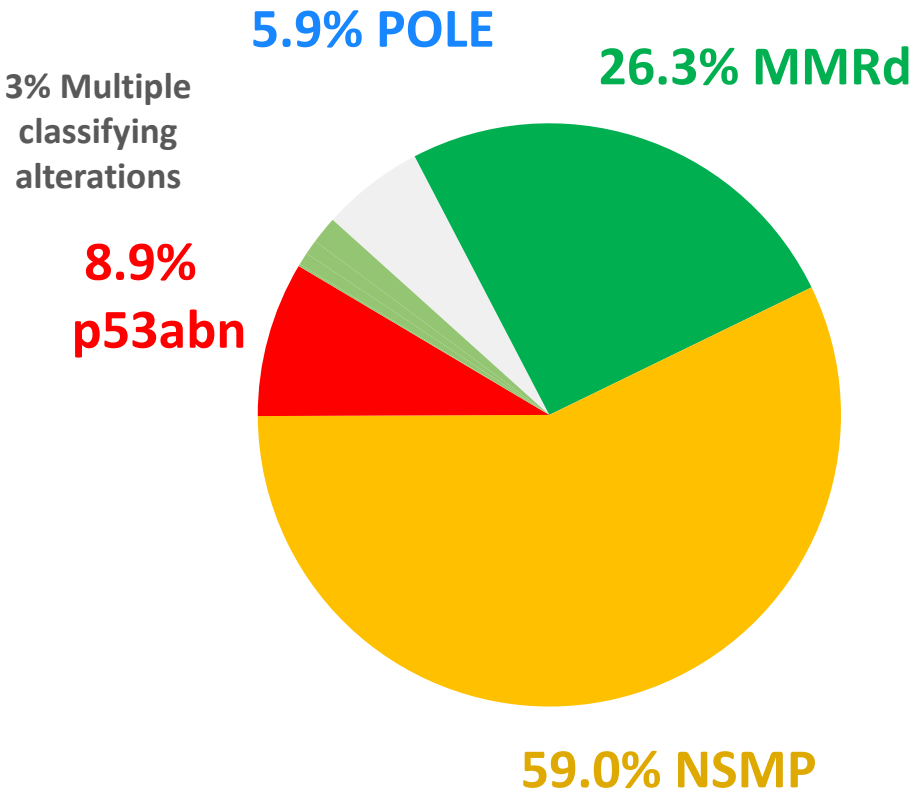
	Patient Population	N	Randomization	Primary Endpoint	Results
PORTEC III ASCO	High Risk Stage I Grade III LVSI, Stage II-III Type II Histology	660	RT+CT F/B Chemo RT Alone	5 yr OS 5 yr FFS	82% vs 77%(p=0.18) 76% vs 69% (p=0.07) * 9-10% stageIII Unplanned
GOG 249	High Risk Stage I Stage II Stage I-II serous	601	Vaginal Brachy+Chemo (p+cx 3) Vs Pelvic RT+/-BT	RFS	VCB+Chemo not superior 82% at 3 yrs 91% OS at 3 yrs Higher PA node in VB+chemo Higher Toxicity
GOG/NRG High Risk	Stage III-IV Optimally debulked Stage I-II Serous (Essentially Stage IIIC)	813	Cisplatin+RT f/b chemo vs Pacli Carbo	5yr RFS	No difference in 5 yr RFS or OS Survival/QOL awaited
JGOG 2403	High Risk,Stage I Grade III LVSI Stage II-III Type II Histology Stage IV no mets outside abdomen	788	Doxo+CDDP Docetaxel+CDDP Pacli+Carbo ? No RT	5 year PFS	No difference in 5 yr PFS and OS Toxicity profile better with Docetaxel+Platinum

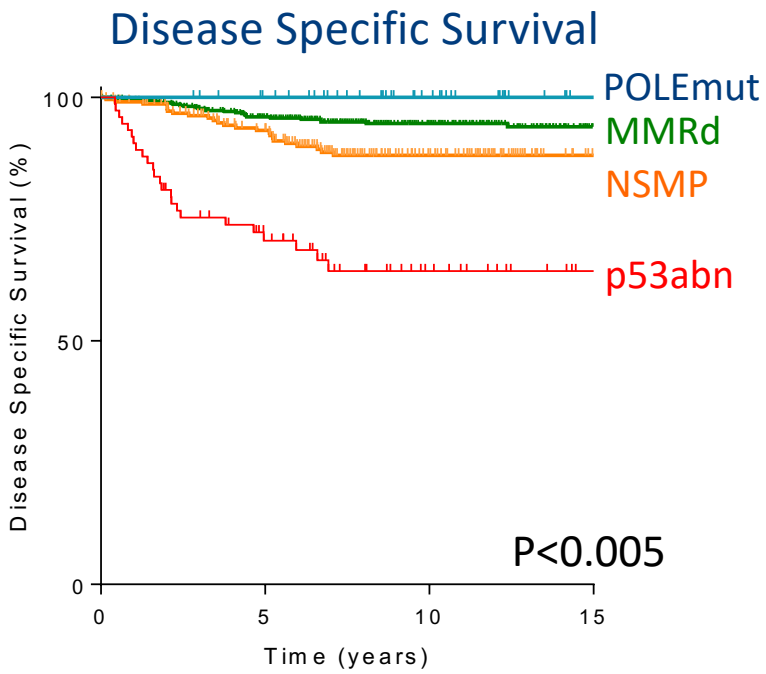
Molecular Classification Endometrial Cancer

	POLE (Ultramutated)	MSI (Hypermutated)	Copy Number Low (NSMP)	Copy Number High
Copy Number Aberrations	Low	Low	Low	High
Microsatellite Instability	Mixed MSI High,Low,Stable	High Lynch Associated	Stable	Stable
Mutation Rate	Very High	High	Low	Low
Genes Commonly Mutated	POLE PTEN PI3KCA PI3KR1 FBXW7 ARID1A KRAS ARIDSB	PTEN RPL22 KRAS PIK3CA PIK3R1 ARID1A	PTEN CTNNB1 PIK3CA	TP53 PIK3CA
Histological Type	Endometroid	Endometroid	Endometroid	Serous, Endometroid,Mixed
Tumour Grade	Grade I-III	Grade I-III	Grade I-II	Grade III
Progression Free Survival	**Good**	**Intermediate**	**Intermediate**	**Poor**

Lancet Oncology 2014

PORTEC-1&2 (N=834 HIR, endometrioid)





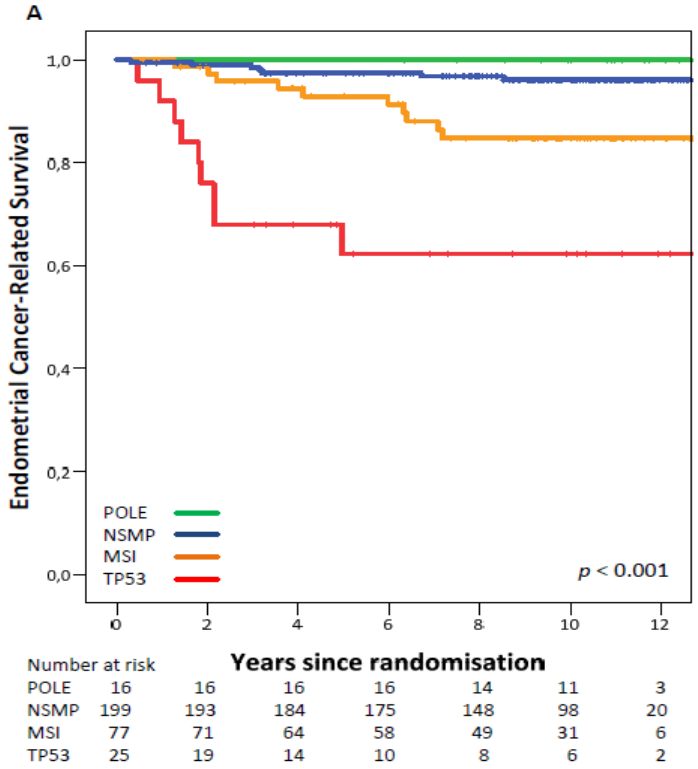
High-intermediate risk

Stelloo et al, CCR 2016

Surrogate markers improve prognostic accuracy in low stage, **intermediate risk** endometrial cancer

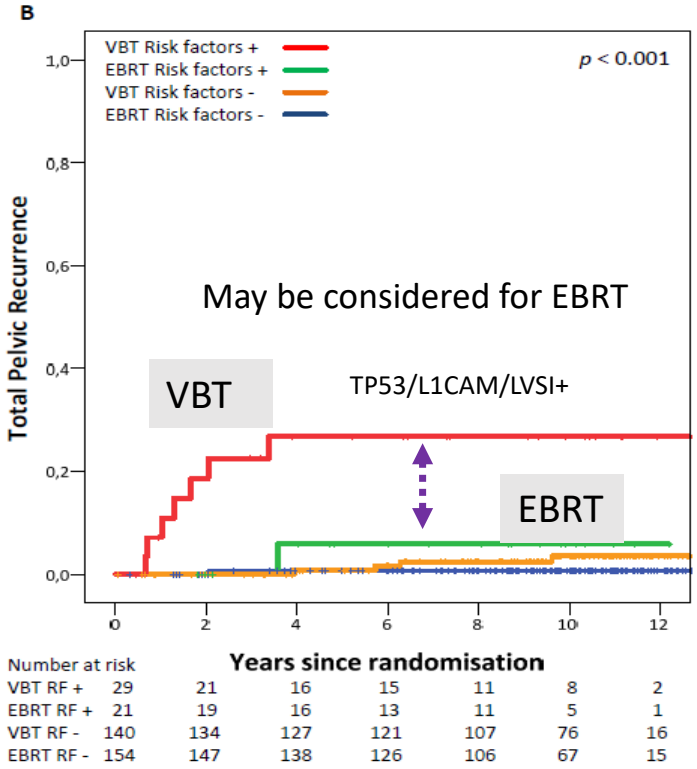
PORTEC-2 trial – 10-year results "HIR"

Endometrial Cancer Related Survival



Number at risk							
POLE	16	16	16	16	14	11	3
NSMP	199	193	184	175	148	98	20
MSI	77	71	64	58	49	31	6
TP53	25	19	14	10	8	6	2

Pelvic Recurrence



Number at risk							
VBT RF +	29	21	16	15	11	8	2
EBRT RF +	21	19	16	13	11	5	1
VBT RF -	140	134	127	121	107	76	16
EBRT RF -	154	147	138	126	106	67	15

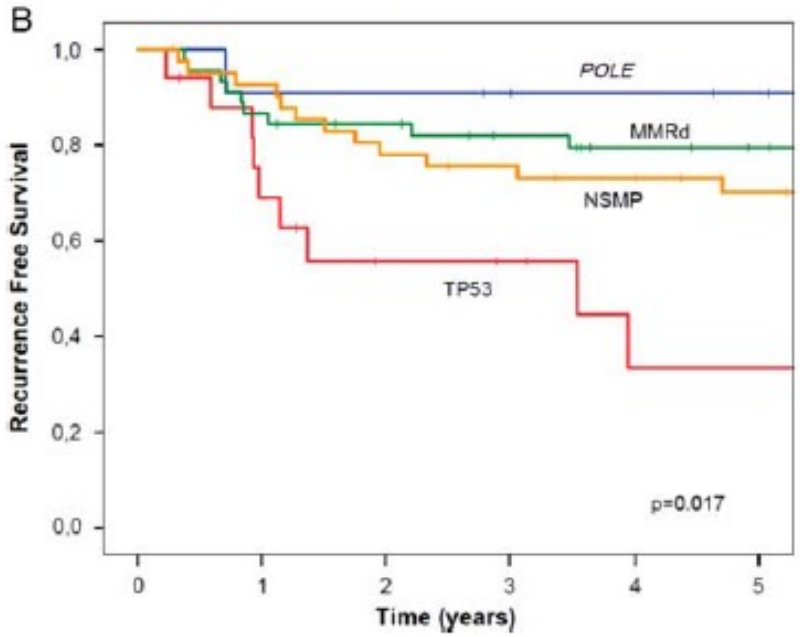
- EBRT provides better pelvic control in patients with molecular risk factors or substantial LVSI
- These findings support treatment based on molecular integrated risk profiles

Wortman et al, BJC 2018

Molecular classification of high grade EC

N=381; international collaboration

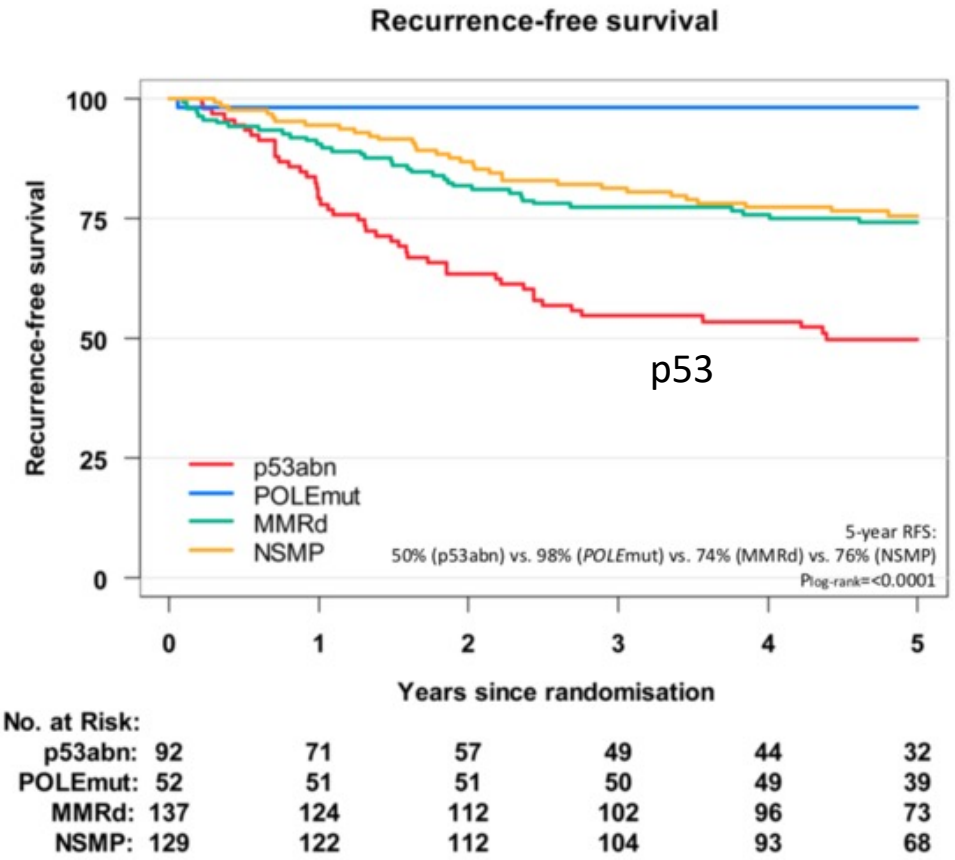
Stage I grade 3



- Molecular classification refines the prognosis of grade 3 endometrial cancer
- Prognostic independent from stage
- Grade 3 endometrial cancer is **not** a homogeneous ‘high risk’ cohort

Bosse et al, Am J Surg Pathol 2018

PORTEC-3: molecular subgroups (N=410)



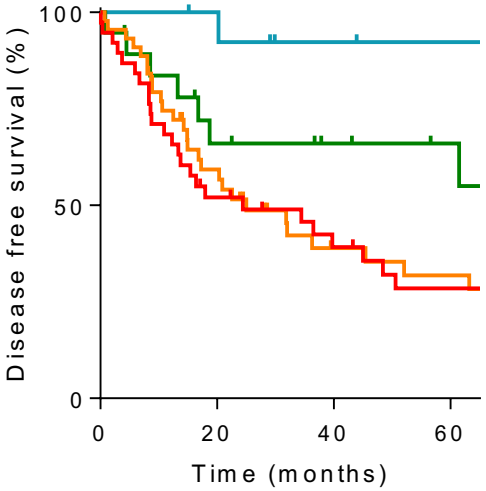
	Events	5-year estimate, %	HR (CI95%)	p-value
p53abn EC				
RT	28	37.2	1	
RT-CT	20	61.1	0.50 (0.28-0.89)	0.017
POLEmut EC				
RT	1	96.6	1	
RT-CT	0	100	0.02 (<0.01->10^4)	0.632
MMRd EC				
RT	17	75.8	1	
RT-CT	18	72.4	1.15 (0.59-2.22)	0.687
NSMP EC				
RT	19	69.9	1	
RT-CT	17	81.2	0.71 (0.37-1.37)	0.311

Creutzberg et al, Presented at ESMO 2019

Slide Courtesy: R Nout

Non-Endometrioid by surrogate marker

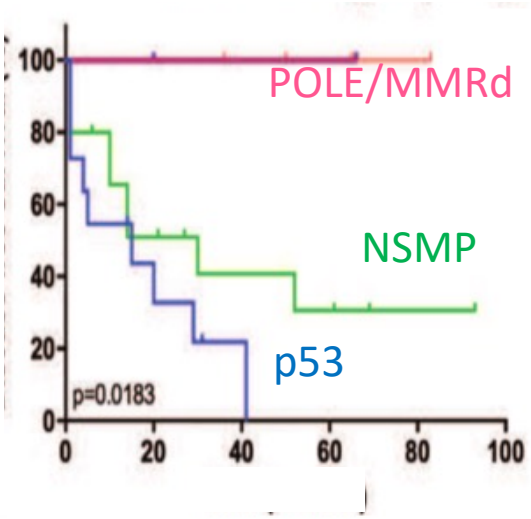
N=116



High-risk Endometrial Carcinomas

Stelloo et al, Mod Path 2015

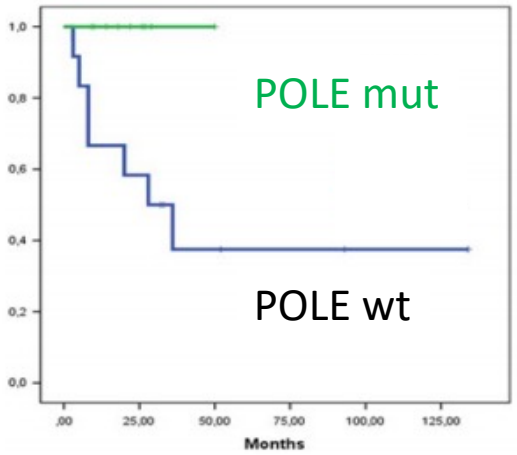
N=32



Clear Cell Endometrial Carcinomas

DeLair et al, J Path 2017

N=21

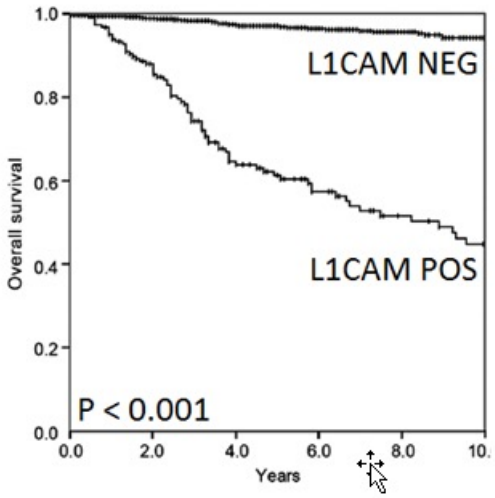


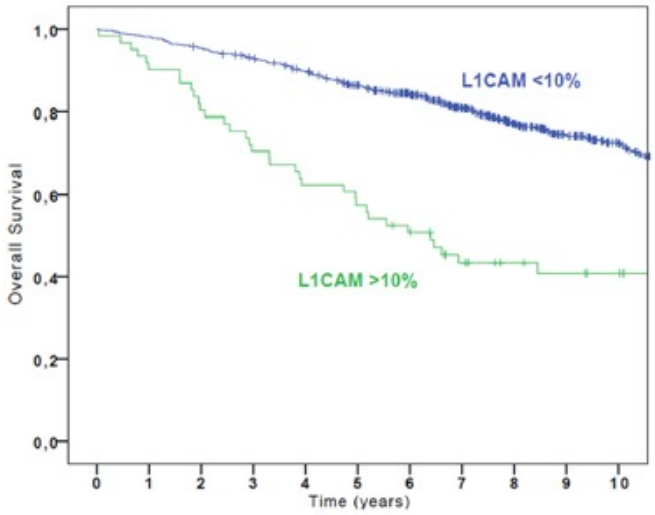
Un/Dedifferentiated Carcinomas

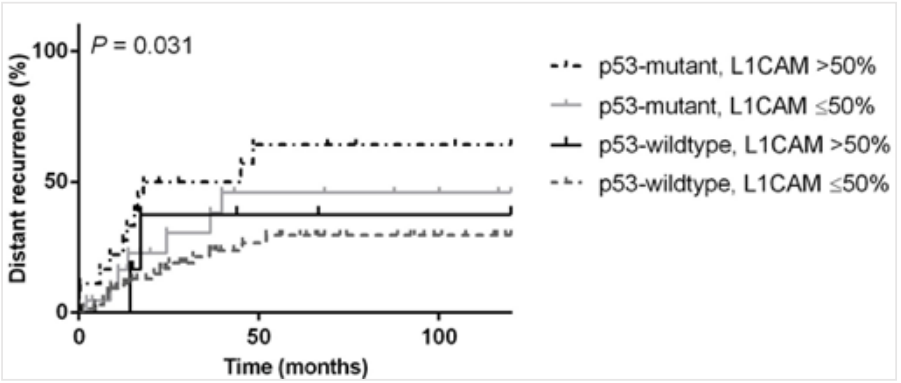
Espinosa et al, AJSP 2017

Prognostic refinement **may** be generalizable to high-risk and non-endometrioid histotypes – larger cohorts required!

Prognostic value of L1- cell adhesion molecule (L1-CAM)







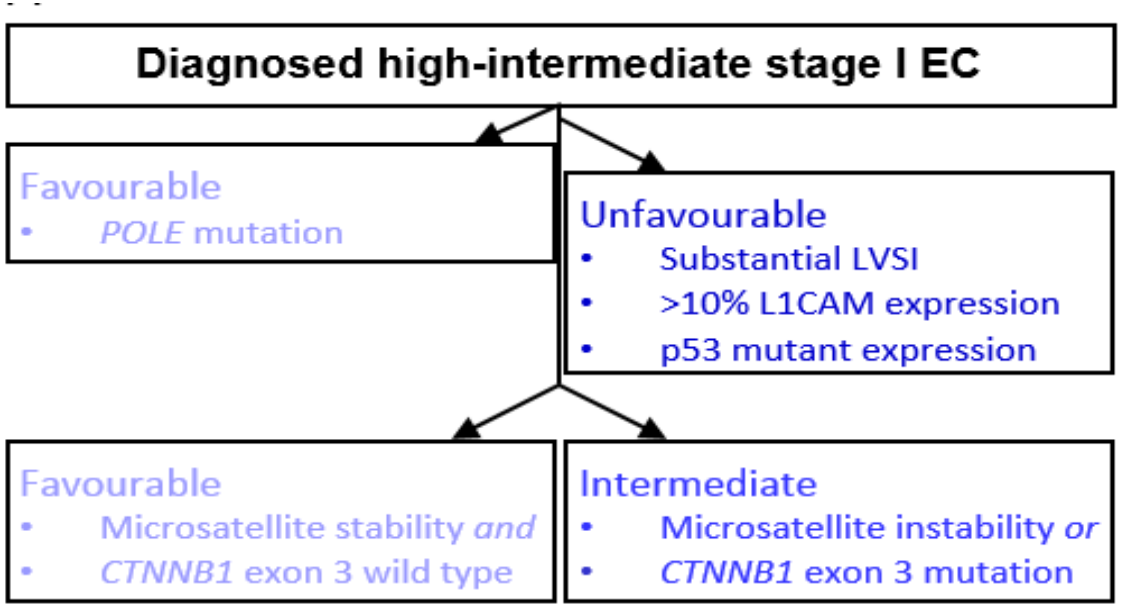
L1-CAM independent from TP53 mutation

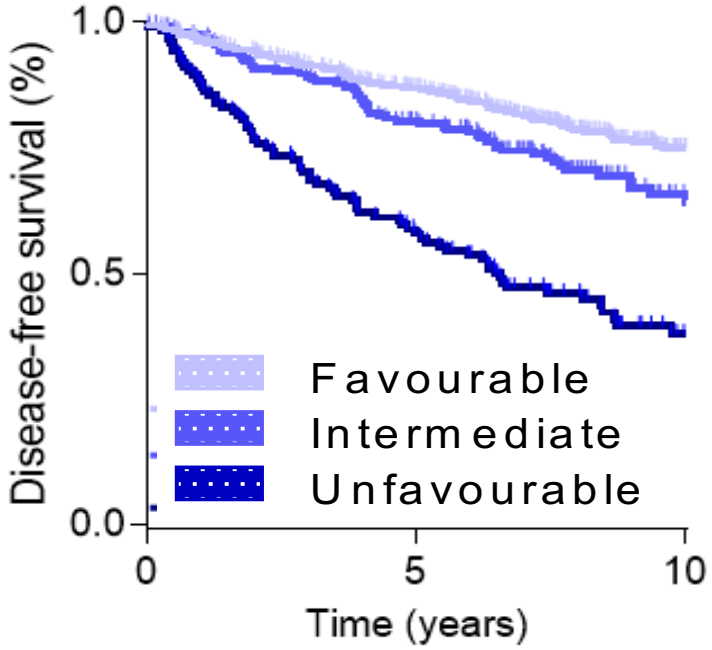
L1-CAM overexpression is a strong negative prognostic factor, associated with EMT

- About 7-10% of EC are L1CAM+
- More often L1CAM+ in grade 3, p53+, non-endometrioid cancers
- Independent from TP53 mutation
- Combined p53-mutant and L1-CAM expression more unfavorable than either one

Zeimet, JNCI 2013; Bosse, Eur J Cancer 2014; Van der Putten, Br J Cancer 2016; van Gool, Mod Path 2015

Molecular integrated risk profile PORTEC-1 and 2

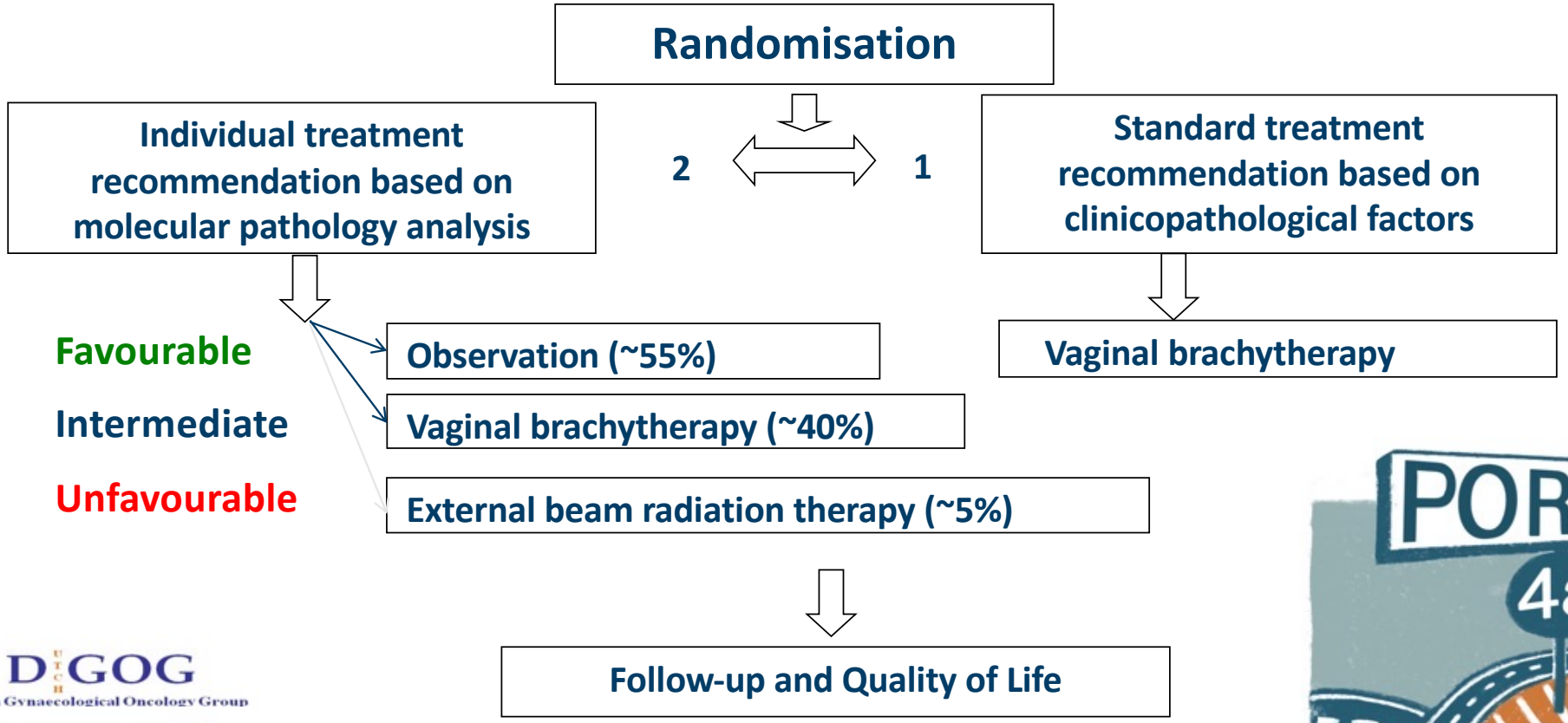




- **55%** of high-intermediate risk patients reclassified to **favourable**
- **15%** of high-intermediate risk patients reclassified to **unfavourable**

Stelloo et al, Clinical Cancer Research 2016

PORTEC-4a: molecular integrated vs standard indications for adjuvant treatment



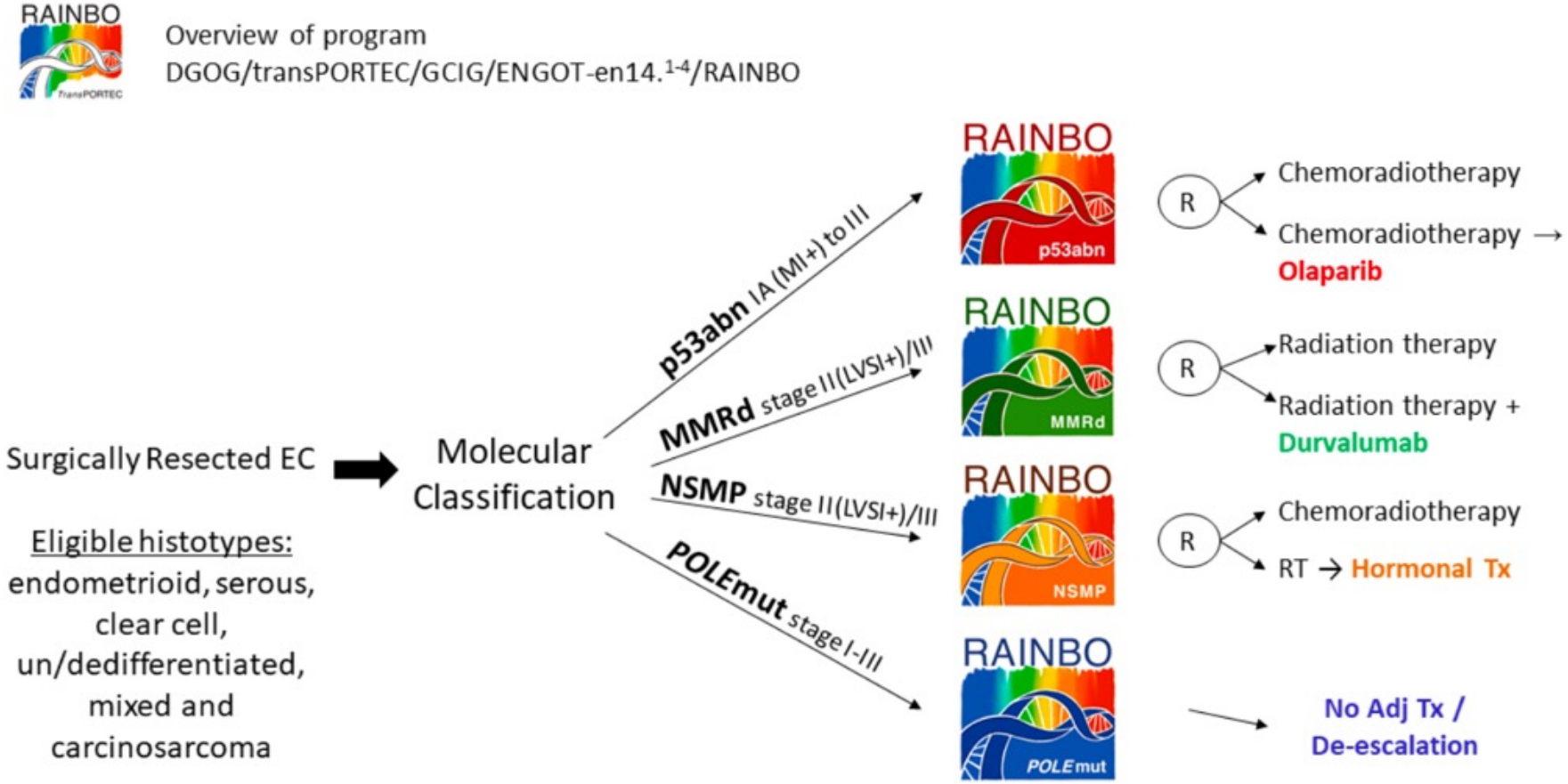
Courtesy: Nout R

Molecular Risk Based Treatment Selection

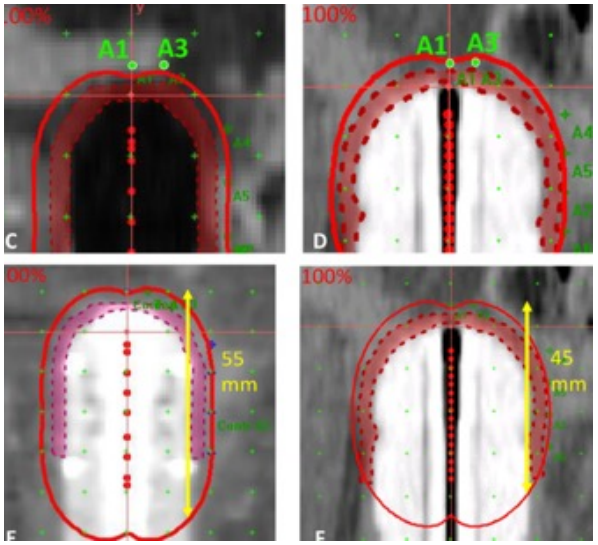
Risk group	Molecular classification unknown	Molecular classification known*†
Low	► Stage IA endometrioid + low-grade‡ + LVSI negative or focal	► Stage I–II ***POLEmut*** endometrial carcinoma, no residual disease ► Stage IA **MMRd/NSMP** endometrioid carcinoma + low-grade‡ + LVSI negative or focal
Intermediate	► 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, 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

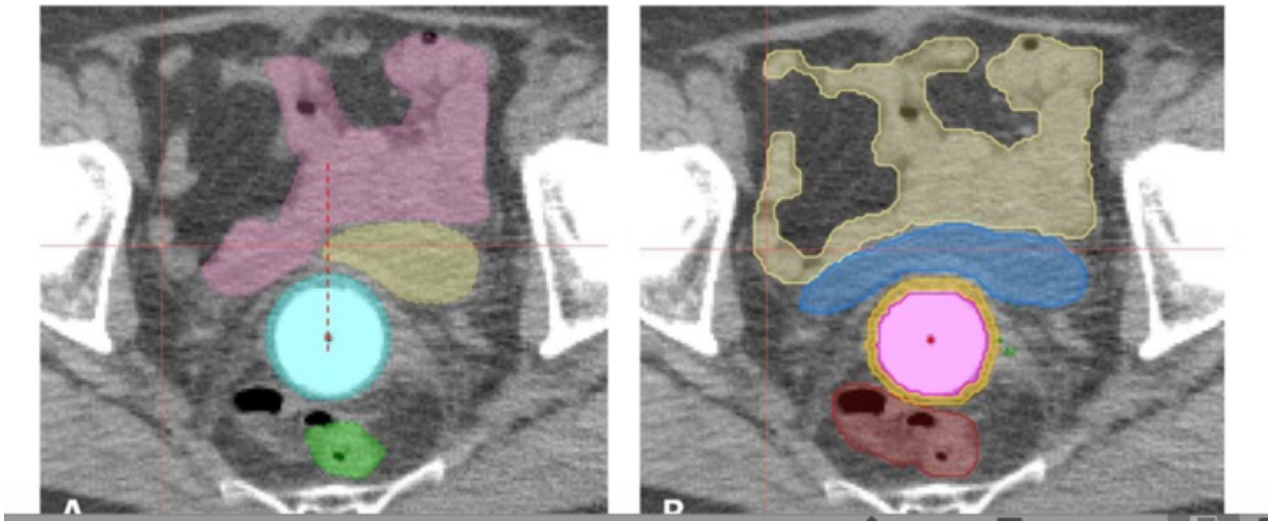
Rainbo Trial

(Refining Adjuvant Treatment using Molecular Classification for Endometrial Cancer: trans PORTEC Platform Trial)



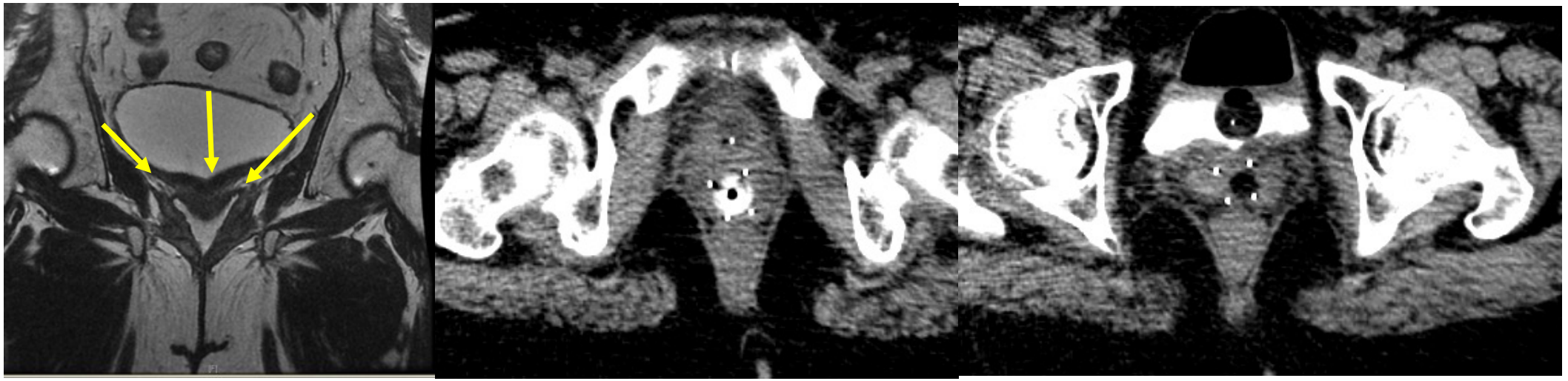
Brachytherapy for Endometrial Cancers Adjuvant, Medically Inoperable and Recurrent



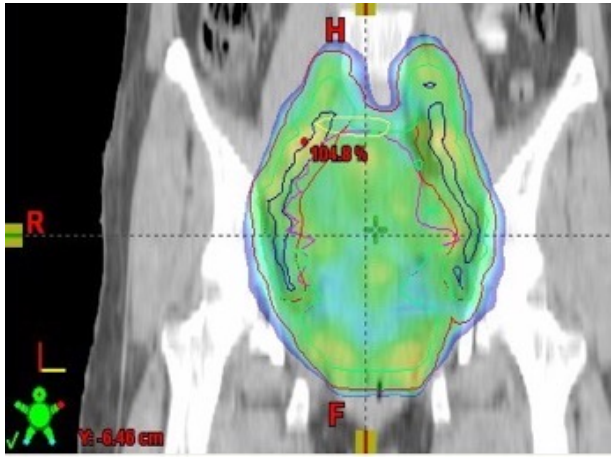


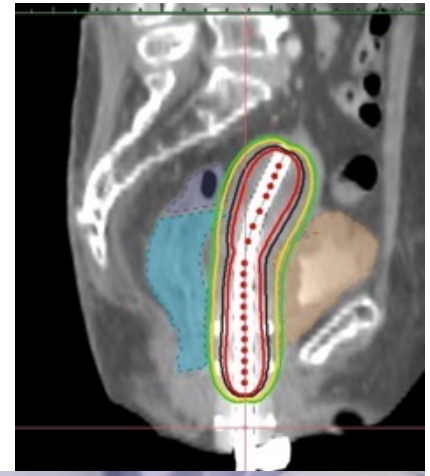
Adjuvant Vaginal BT: 7 Gy x 3 # delivered in 3 weeks

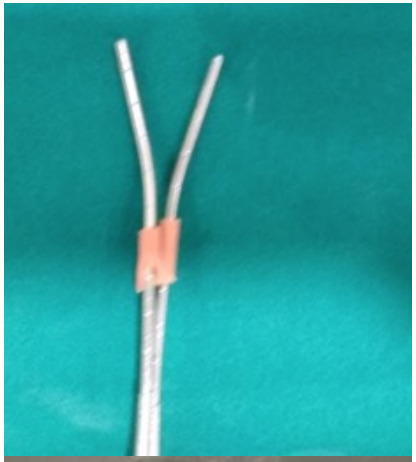
Wortman, Radiotherapy and Oncology

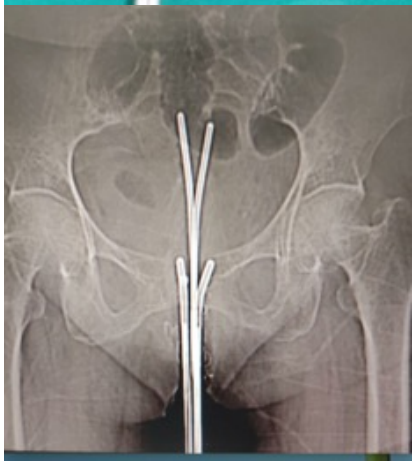


Radical Radiotherapy in Endometrial Cancers

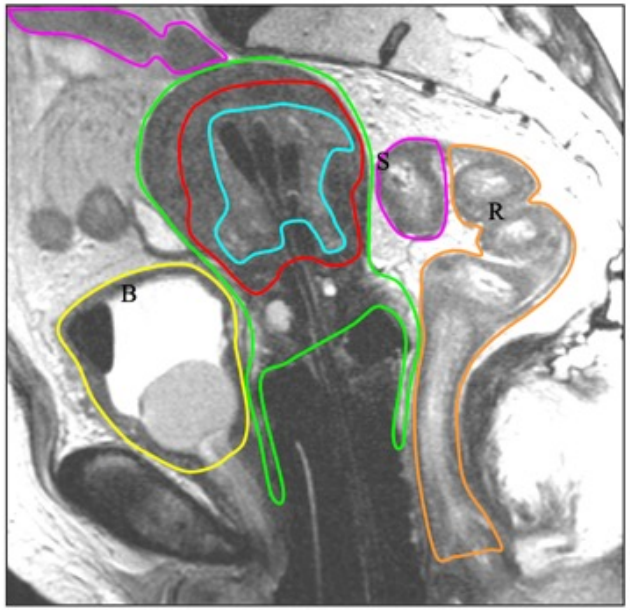


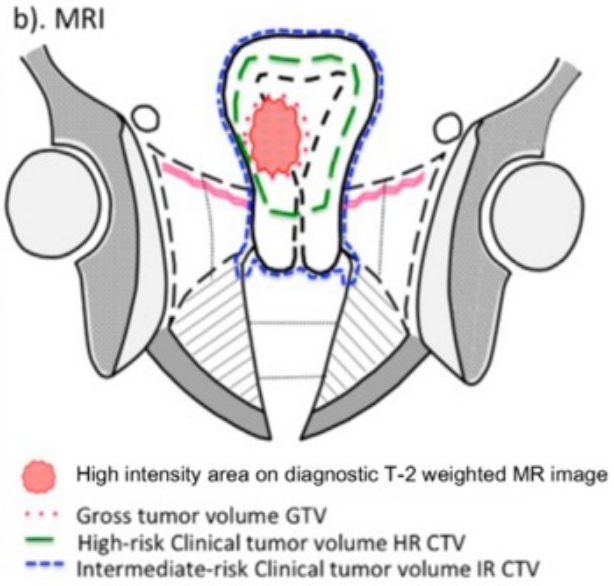






Target Concept for Medically Inoperable Endometrial Cancers





- CTV: whole uterus, cervix and upper 1/3 of vagina
  - Take all information into account (colposcopy, imaging) to delineate GTV
  - Depending of pattern of spread parametrial and paravaginal tissue may be included

GEC ESTRO Handbook 2nd Ed. Chapter 17: Endometrial cancer

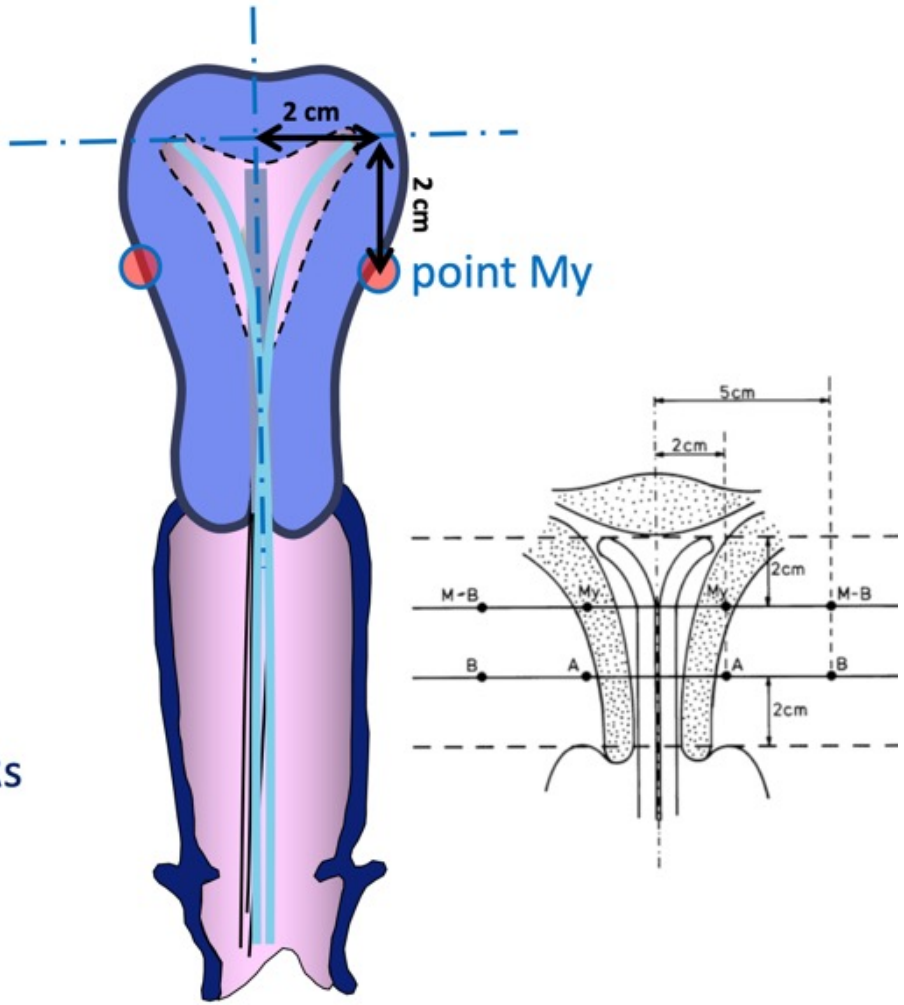
Treatment Planning

Applicator Reconstruction
- One-channel
- two-channel or other

Define point My (Starting point)

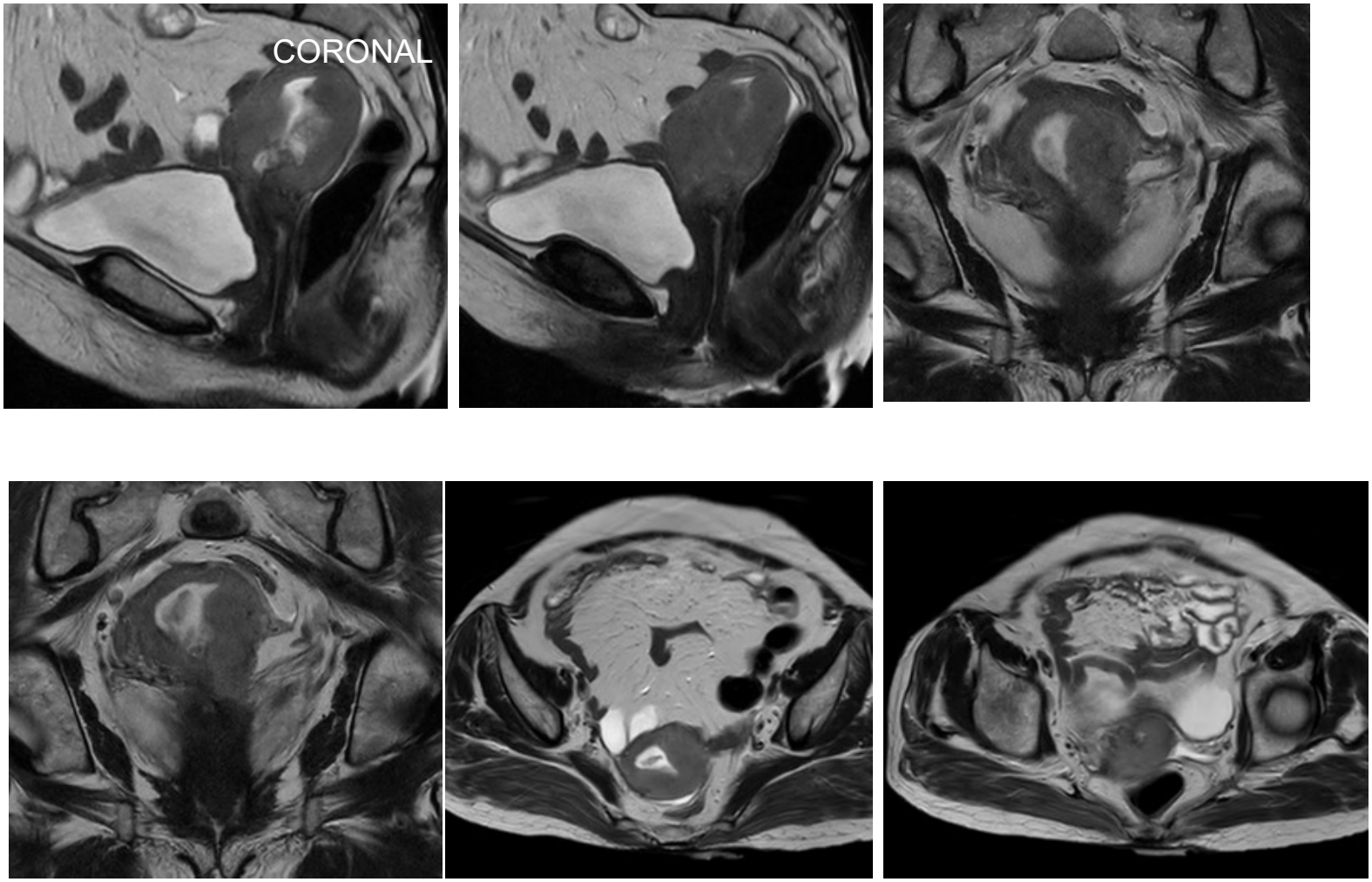
Activate Source position and Normalize to point(s) My

Optimize dwells according to target and OARs



Slide Courtesy Nout R

T2 W MRI (At Diagnosis)



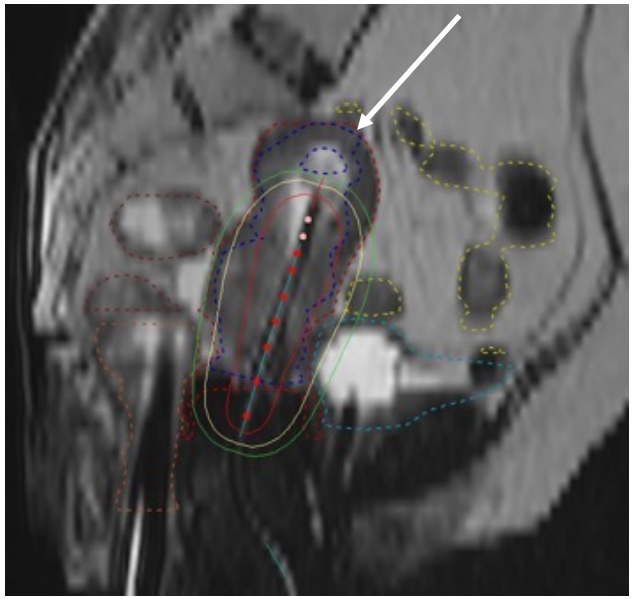
BT Treatment Planning (Possible Option A)

Standard Intracavitary plan (7 cm tandem/ 22 mm ring)

Prescription Dose: 7 Gy/

ROI	Dose (1#)	EQD2 (4#)
GTV D98	3.8 Gy	63 $Gy_{4.5}$
CTV D90	1.8 Gy	50.6 $Gy_{4.5}$
BLADDER D2cc	6.1 Gy	87.6 Gy_3
RECTUM D2cc	3.7 Gy	63 Gy_3
SIGMOID D2cc	3.3 Gy	59.8 Gy_3
BOWEL D2cc	4.4 Gy	69.2 Gy_3

Unacceptable target doses



Standard Intracavitary plan

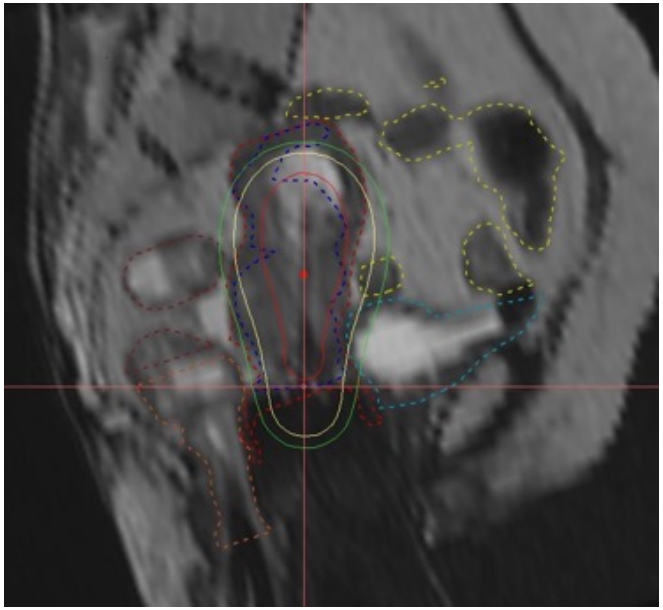
All EQD2 Calculations (Alpha/Beta=4.5)

BT Treatment Planning (Possible Option B)

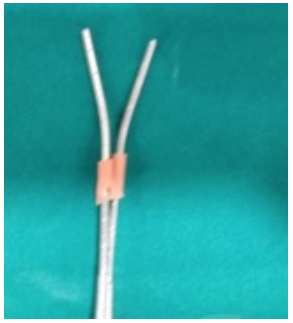
”Simulated “Rotte-Y” Plan)

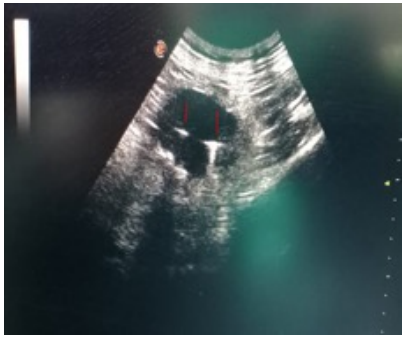
ROI	Dose (1#)	EQD2 (4#)
GTV D98	4.4 Gy	67.7 $Gy_{4.5}$
CTV D90	4.3 Gy	67 $Gy_{4.5}$
BLADDER D2cc	5.4 Gy	79.5 Gy_3
RECTUM D2cc	3.1 Gy	58.3 Gy_3
SIGMOID D2cc	3.8 Gy	64 Gy_3
BOWEL D2cc	5 Gy	75 Gy_3

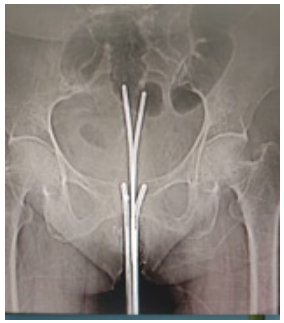
Rotte-Y Simulation Plan

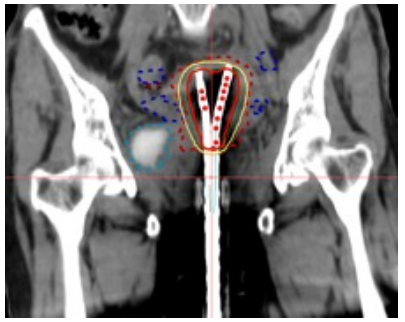


Acceptable target and OAR doses.

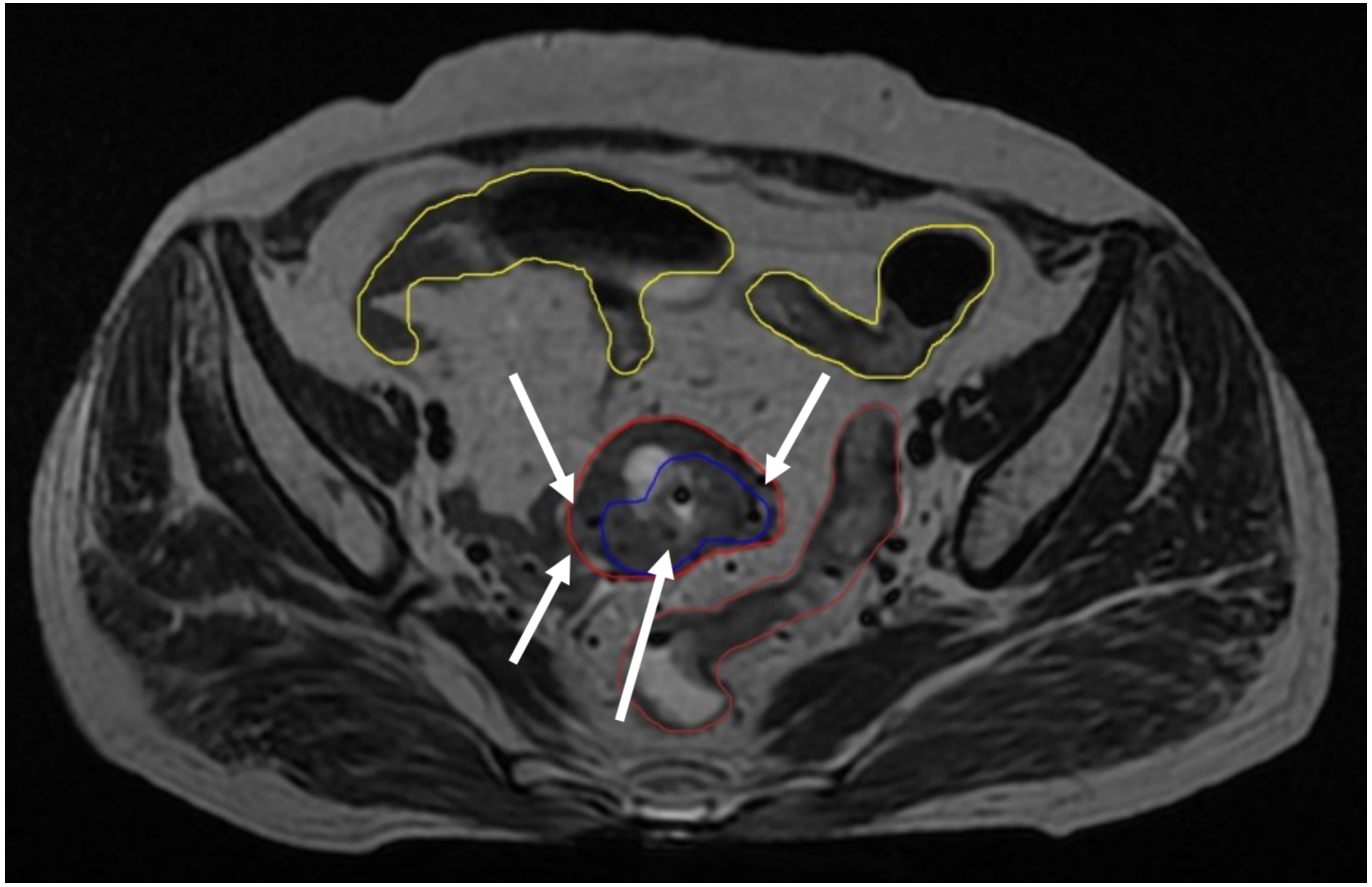








Venezia : Additional Needles in Fundus (8 cm)

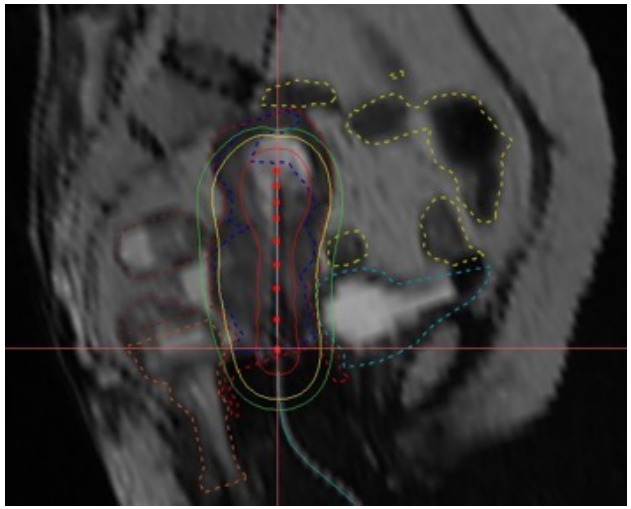


BT Treatment Planning (Actual Treatment Plan)

IC+IS with parallel and oblique needles

ROI	Dose (1#)	EQD2 (4#)
GTV D98	4.9 Gy	71.9 $Gy_{4.5}$
CTV D90	5 Gy	72.8 $Gy_{4.5}$
BLADDER D2cc	5.4 Gy	79.5 Gy_{3}
RECTUM D2cc	3.9 Gy	64.7 Gy_{3}
SIGMOID D2cc	4.3 Gy	68.3 Gy_{3}
BOWEL D2cc	4.2 Gy	67.4 Gy_{3}

Acceptable target and OAR doses

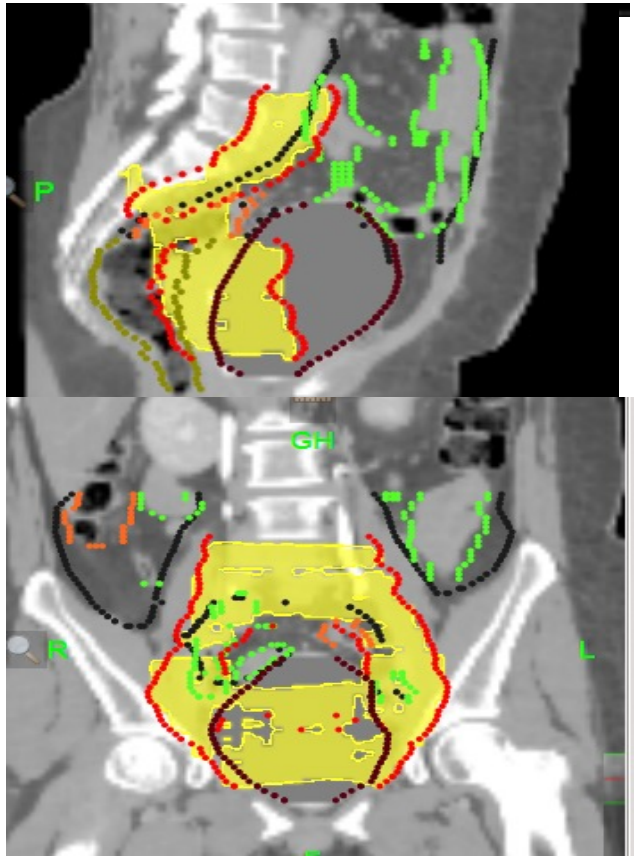


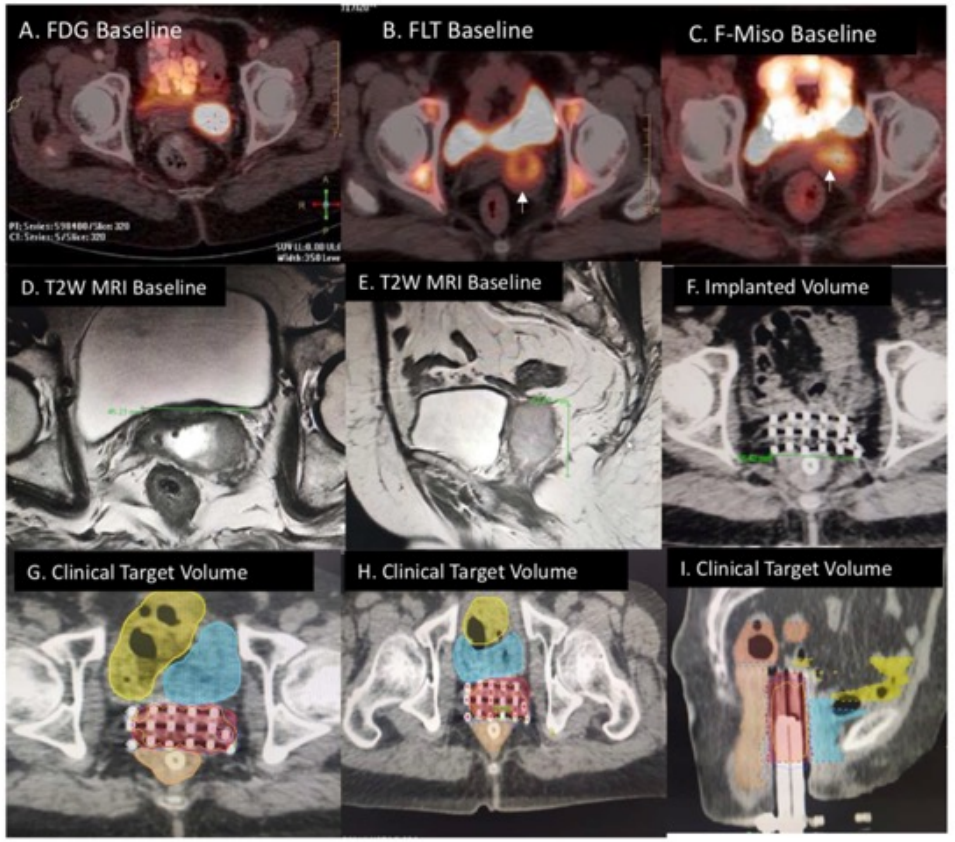
IC + IS with parallel and oblique needles

Comparative Plans

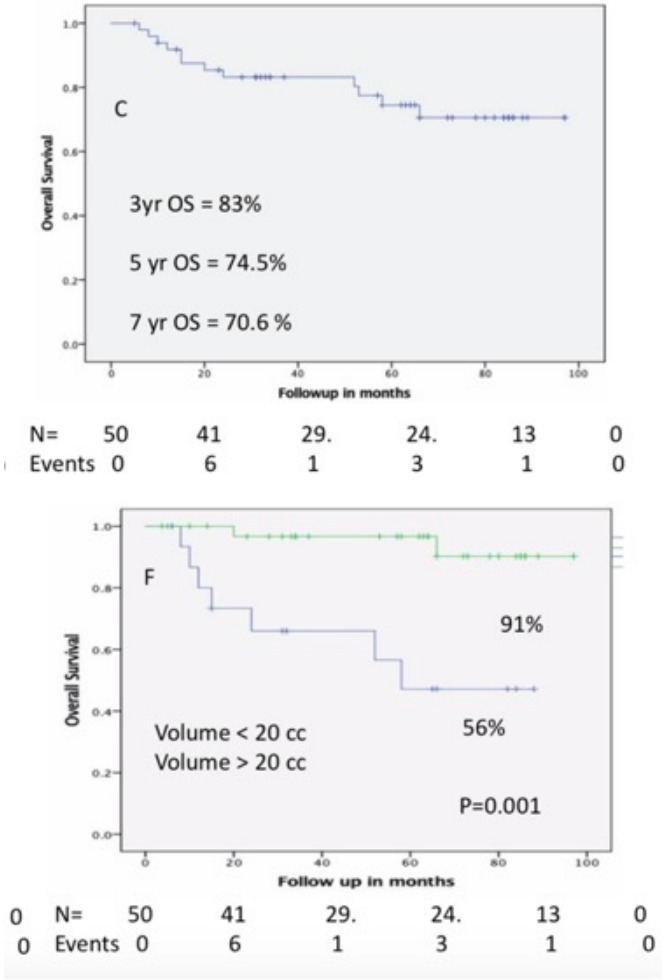
ROI	Single Channel Cylinder	Rotte- Y Applicator	Venezia with Parallel and Oblique Needles
GTV D98	63 $Gy_{4.5}$	67.7 $Gy_{4.5}$	71.9 $Gy_{4.5}$
CTV D90	50.6 $Gy_{4.5}$	67 $Gy_{4.5}$	72.8 $Gy_{4.5}$
BLADDER D2cc	87.6 Gy_{3}	79.5 Gy_{10}	79.5 Gy_{10}
RECTUM D2cc	63 Gy_{3}	58.3 Gy_{10}	64.7 Gy_{10}
SIGMOID D2cc	59.8 Gy_{3}	64 Gy_{10}	68.3 Gy_{10}
BOWEL D2cc	69.2 Gy_{3}	75 Gy_{10}	67.4 Gy_{10}

Post Surgery Recurrent Endometrial Cancer (Vaginal)

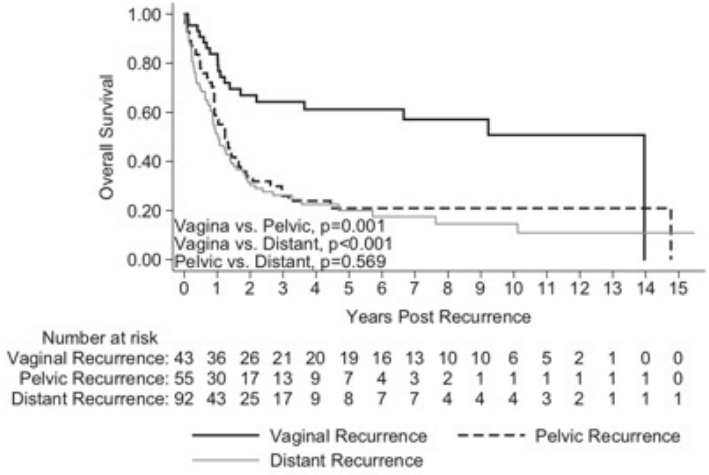




Outcomes of Patients with Vaginal Recurrences



Recurrences, Cervix Cancer, Chopra IJROBP, 2019



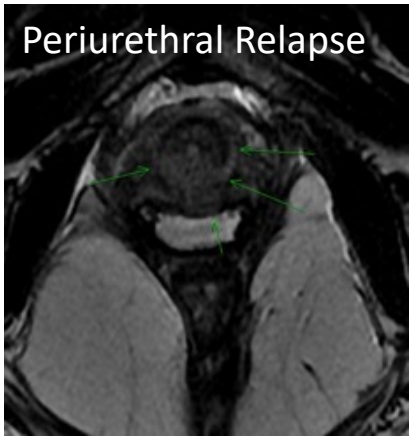
Recurrences, Endometrial cancers

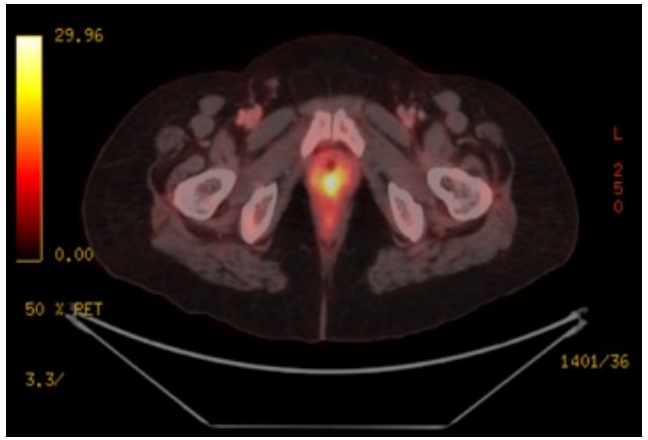
Francis S, Gynec Oncology 2019

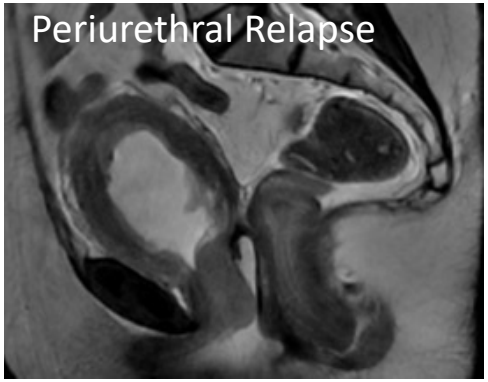
Median Survival >10 years

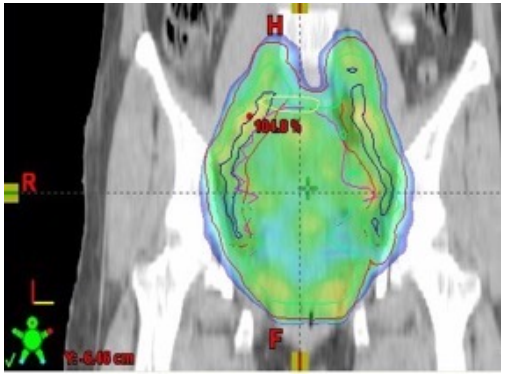
Post RT recurrences in Endometrial Cancer: Reirradiation

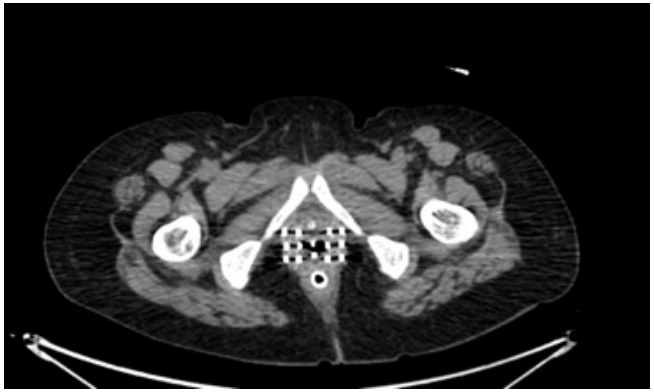
- 22/249 (8.8% pelvic Recurrences) : Early Endometrial Cancer
- High risk Endometrial cancer
- Post RT recurrences : Periurethral, vaginal apex, nodal







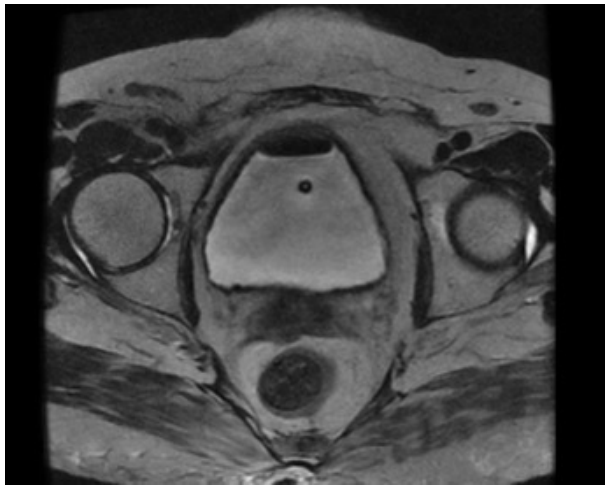


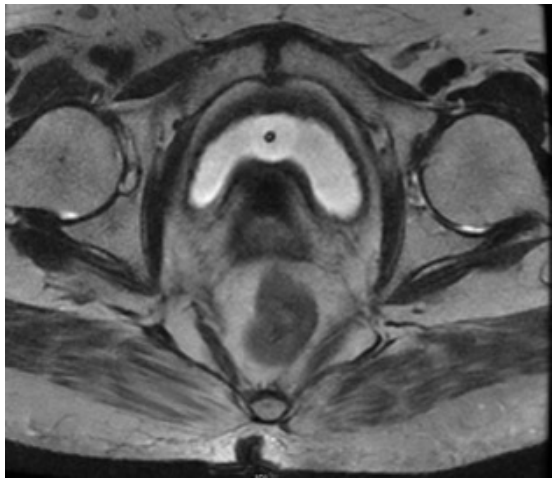


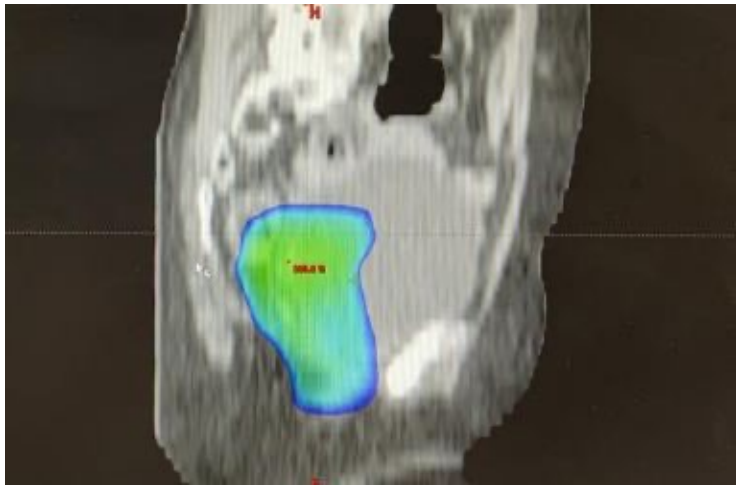
VBT, PERIURETHRAL RELAPSE 7 YEAR DFI.

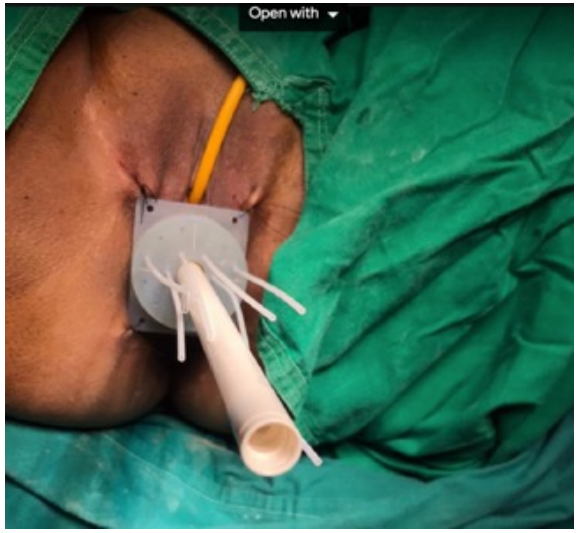
EBRT+INTERSTITIAL BT 65-70 GY

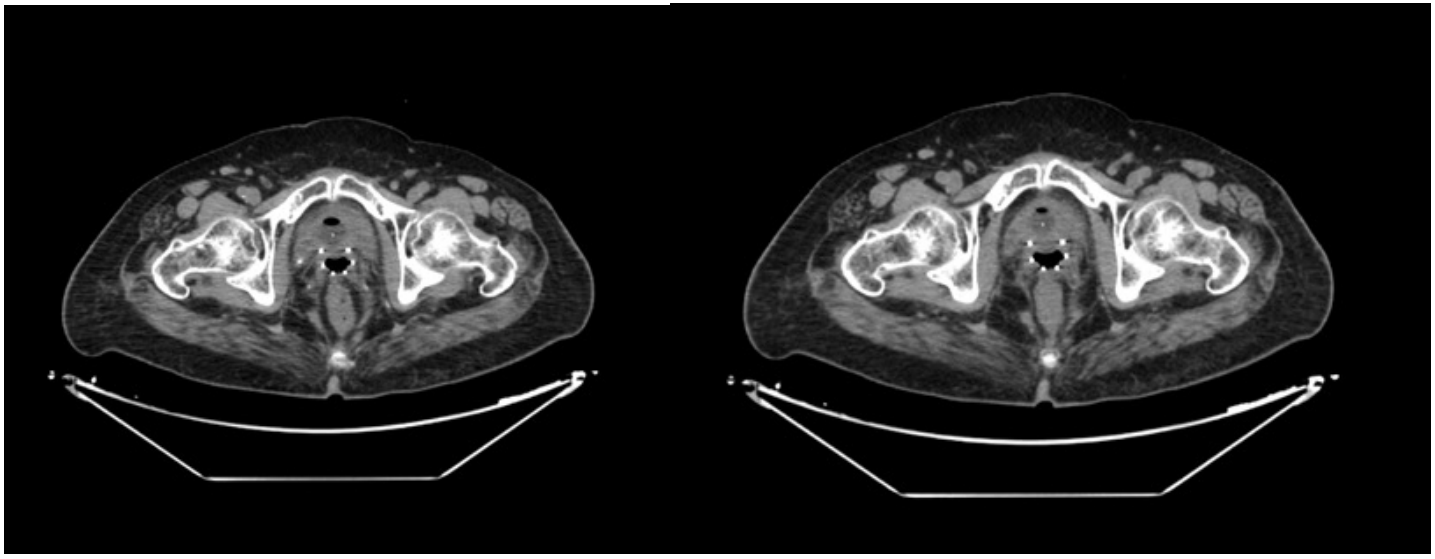
Post RT Vaginal recurrences in Endometrial Cancer











Conclusions

- Early stage Endometrial Cancer is a heterogenous disease. Most current trials based on ”pathological risk factors”
- “Molecular risk factors and classification” may greatly improve treatment selection, response prediction and treatment efficacy
- First clinical trials of adjuvant molecular-based treatment
- Brachytherapy for Medically Inoperable and Recurrent Cervical Cancer individualized approach.