Impatto degli studio PORTEC nella terapia adiuvante del tumore endometriale Early

A. Galuppi

Dept. of Experimental, Diagnostic and Specialty Medicine,University of Bologna, S.Orsola-Malpighi Hospital

Carcinoma dell'endometrio

- 8-10% delle neoplasie femminili nei Paesi industrializzati con circa 288.000 nuovi casi e 74.000 morti per anno.

- Quarto posto tra i tumori del sesso femminile dopo il carcinoma della mammella, del colon e del polmone.

Ferlay J, Shin HR et al. GLOBOCAN 2008, Cancer Incidence and Mortality Worldwide: IARC CancerBase No. 10 [Internet]. Lyon, France: International Agency for Research on Cancer; 2010; http://globocan.iarc.fr

Report 2014

Pool of Italian Cancer Registries - 1 January 2010

ENDOMETRIO
CORPUS UTERI
(ICD-10 C54)

COMPLETE PREVALENCE BY YEARS SINCE DIAGNOSIS

YEARS →	≤ 2	(2 - 5]	(5 - 10]	(10 - 15]	(15 - 20]	> 20
No. →	13 360	17 584	22 836	17 374	11 979	18 954
% →	13%	17%	22%	17%	12%	19%
PROPORTION → PER 100 000	44	59	76	59	40	65

2 587 347 CANCER SURVIVORS

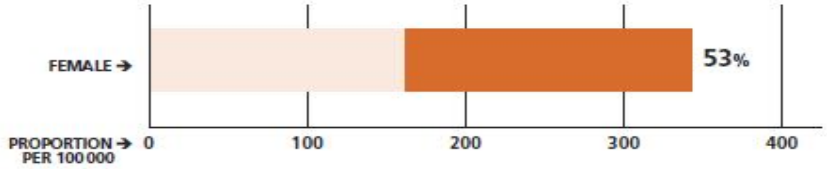
102 088
CORPUS UTERI
CANCER SURVIVORS

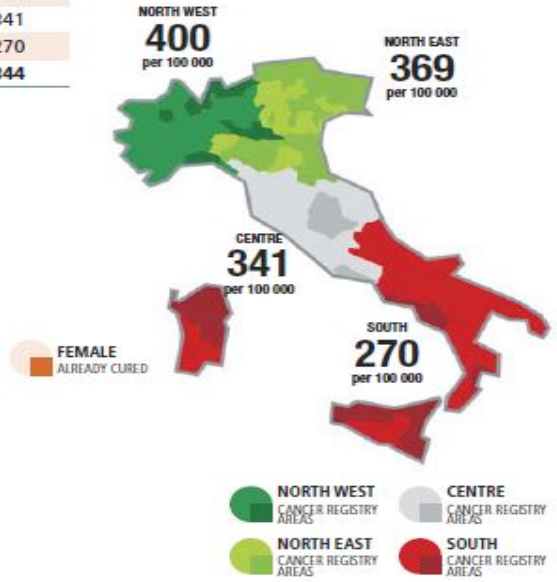
ALREADY CURED
at 1 JANUARY 2010
53 873 (53%)

COMPLETE PREVALENCE BY SEX, MACRO-AREA, AND AGE
(PROPORTION PER 100 000)

AGE CLASS →	0-44	45-59	60-74	75+	ALL AGES
FEMALE					
NORTH WEST	11	220	940	1 215	400
NORTH EAST	9	223	932	1 182	369
CENTRE	11	207	886	1 127	341
SOUTH	9	215	788	996	270
POOL	9	219	889	1 139	344

COMPLETE PREVALENCE AND PROPORTION OF ALREADY CURED SURVIVORS BY SEX





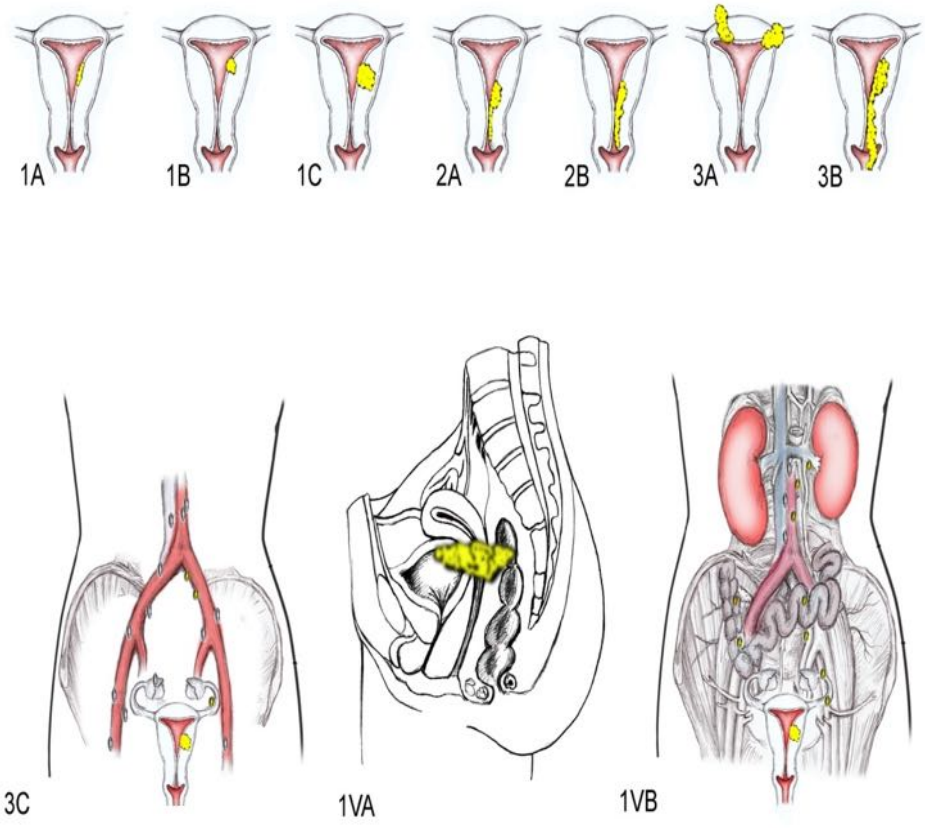
http://www.registri-tumori.it/cms/

Fattori di rischio

Factors Influencing Risk	Estimated Relative Risk*
Older age	2–3
Residency in North America or Northern Europe	3–18
Higher level of education or income	1.5–2
White race	2
Nulliparity	3
History of infertility	2–3
Menstrual irregularities	1.5
Late age at natural menopause	2–3
Early age at menarche	1.5–2
Long-term use of unopposed estrogen	10–20
Tamoxifen use	2–3†
Obesity	2–5
Estrogen-producing tumor	>5
History of type 2 diabetes, hypertension, gallbladder disease, or thyroid disease	1.3–3
Lynch syndrome	6–20‡

Uterine Cancer Staging System
FIGO 1988

Stadio I		**Tumore limitato al corpo dell'utero**
	IA	Limitato all'endometrio
	IB	Infiltrazione < 1/2 del miometrio
	IC	Infiltrazione > 1/2 del miometrio
Stadio II		**Tumore esteso alla cervice uterina**
	IIA	Infiltrazione delle ghiandole, ma non dello stroma
	IIB	Infiltrazione dello stroma cervicale
Stadio III		**Tumore esteso al di fuori dell'utero, entro la pelvi o ai linfonodi**
	IIIA	Estensione alla sierosa, o alle ovaie, o *washing* positivo
	IIIB	Estensione alla vagina
	IIIC	Estensione ai linfonodi pelvici o lombo-aortici
Stadio IV		**Estensione extrapelvica o alla mucosa vescicale o intestinale**
	IVA	Estensione agli organi adiacenti
	IVB	Metastasi a distanza o ai linfonodi inguinali



Int J Gynecol Obstet 28, 169-190, 1989.

FIGO 2010

Stage I: 75-90%

A G123, invasion < 50% myometrium: 88%

B G123, invasion > 50% myometrium: 75%

Stage II: 70%

G123, endocervix stroma

Stage III: 45-60%

A G123, (+) serosa/ adnexa: 58%

B G123, (+) vagina/parametrium: 50%

C G123, (+) nodes: 47%

IIIC1: (+) pelvic nodes

IIIC2: (+) PAN nodes

Stage IV: 15-20%

A G123, (+) GI, GU mucosa: 17%

B G123, distant mets, + groin nodes: 15%

Pecorelli S, Int J Gynecol Obstet 2009; 103-104

ENDOMETRIAL CANCER
risk of recurrence (FIGO 1998)

<table>
<tr><th></th><th>G1</th><th>G2</th><th>G3</th></tr>
<tr><td>St. IA</td><td colspan="2" rowspan="2">low (2 – 4 % >local)</td><td rowspan="2"></td></tr>
<tr><td>St. IB</td></tr>
<tr><td>St. IC</td><td colspan="2" rowspan="2">intermediate (5 – 20 %)</td><td rowspan="2"></td></tr>
<tr><td>St. IIA</td></tr>
<tr><td>St. IIB</td><td colspan="3" rowspan="2">high (> 20 % > distant)</td></tr>
<tr><td>St. III</td></tr>
</table>

Lukka H et al, Gynecol Oncol 102:361, 2006 (modif).

Adenocarcinoma endometriode corpus uteri
Rischio di recidiva

<table>
<tr><th>Stadio</th><th>G1</th><th>G2</th><th>G3</th></tr>
<tr><td>IA</td><td colspan="2">Basso 2 – 4% (> locali)</td><td></td></tr>
<tr><td>IB</td><td colspan="2">Intermedio 4-20 % (locale ± regionale)</td><td rowspan="5"></td></tr>
<tr><td>II</td><td colspan="2" rowspan="4">Elevato > 20 % (loco-regionale ± distanza)</td></tr>
<tr><td>IIIA</td></tr>
<tr><td>IIIB</td></tr>
<tr><td>IIIC</td></tr>
</table>

Lukka H et al - Gynecol Oncol 102: 361, 2006 (mod)

Q1: Current best definition of risk groups?

➢ FIGO 2009 staging used

Risk Group	Description	LoE
Low	• Stage IA Endometrioid + grade 1-2 + LVSI negative	1
Intermediate	• Stage IB Endometrioid + grade 1-2 + LVSI negative	1
High Intermediate	• Stage IA Endometrioid + grade 3, regardless of LVSI status • Stage I Endometrioid + grade 1-2 + LVSI unequivocally positive, regardless of depth of invasion	1 2
High	• Stage IB Endometrioid + grade 3, regardless of LVSI status • Stage II & stage III with no residual disease • Non endometrioid (serous, clear cell, undifferentiated carcinoma, carcinosarcoma, mixed >10%)	1 1 1
Advanced Metastatic	• Stage III with residual disease & IVA • Stage IVB	1 1

TRATTAMENTO ADIUVANTE: domande aperte?

- **Quale ruolo della RT adiuvante nel Rischio Intermedio?**
- **Quando scegliere EBRT o BRT nel Rischio Intermedio?**
- **Potrebbe l'associazione di RT e CT aggiungere dei benefici nel Rischio Intermedio e Alto Rischio?**

RT post-operatoria – Stadio I e II

- **5 studi randomizzati sono stati condotti per valutare il ruolo della RT adiuvante negli stadi iniziali delle neoplasie endometriali:**

  - Norwegian
  - PORTEC -1
  - GOG -99
  - ASTEC/EN 5
  - PORTEC -2

Norwegian Trial

540 Pazienti Stadio I

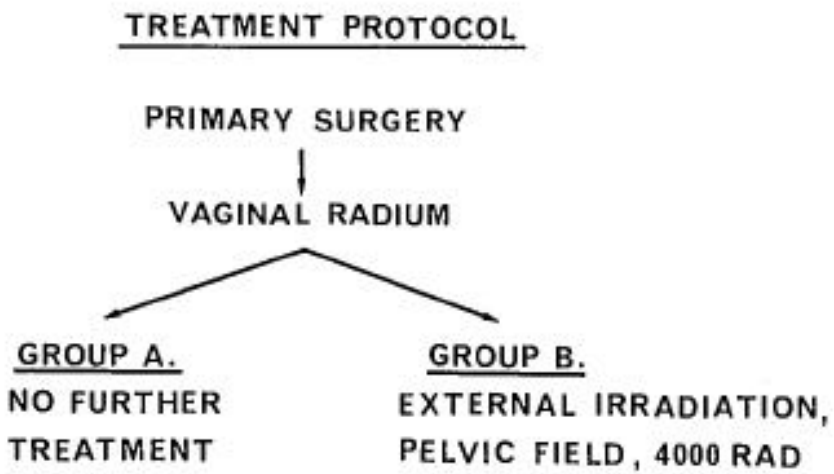


Figure 1. Treatment protocol in stage I carcinoma of the corpus uteri.

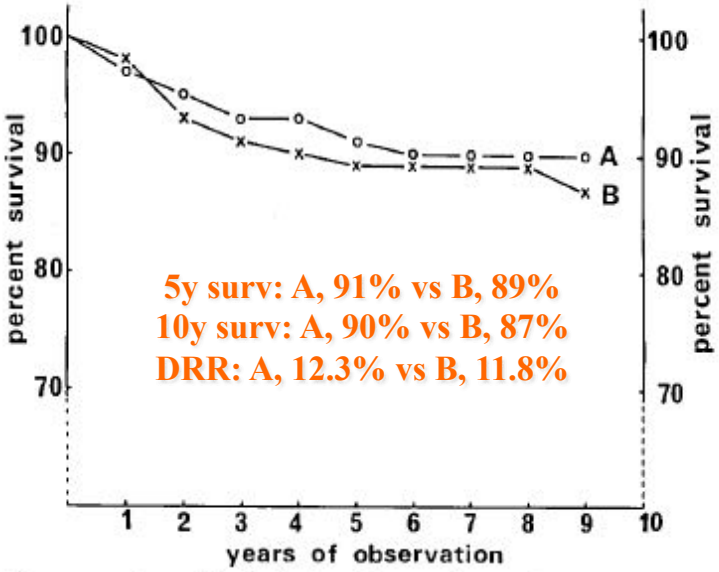


Figure 2. Actuarial calculation of survival rates. Group A received vaginal radium only, whereas group B also received high-voltage irradiation to the pelvis. Open circles = group A, controls (277); crosses = group B, additional irradiation (263).

Aalders J et al. Obstet Gynecol, 1980; 56: 419

Conclusioni del Norwegian Trial

- **Indicazioni alla radioterapia esterna:**
  - **G3 M2**
  - **INVASIONE LINFOVASCOLARE**

Brachiterapia per tutti gli altri casi

Aalders J et al. Obstet Gynecol, 1980; 56: 419

GOG 99

- Stadio I-II (392 pz)
- LIAB + Linfoadenectomia
- Linfonodi -

RANDOM

Nessun trattamento
202 pz

RT pelvica
190 pz

GOG 99
gruppo alto-medio rischio

- **33% delle pazienti dello studio GOG 99**

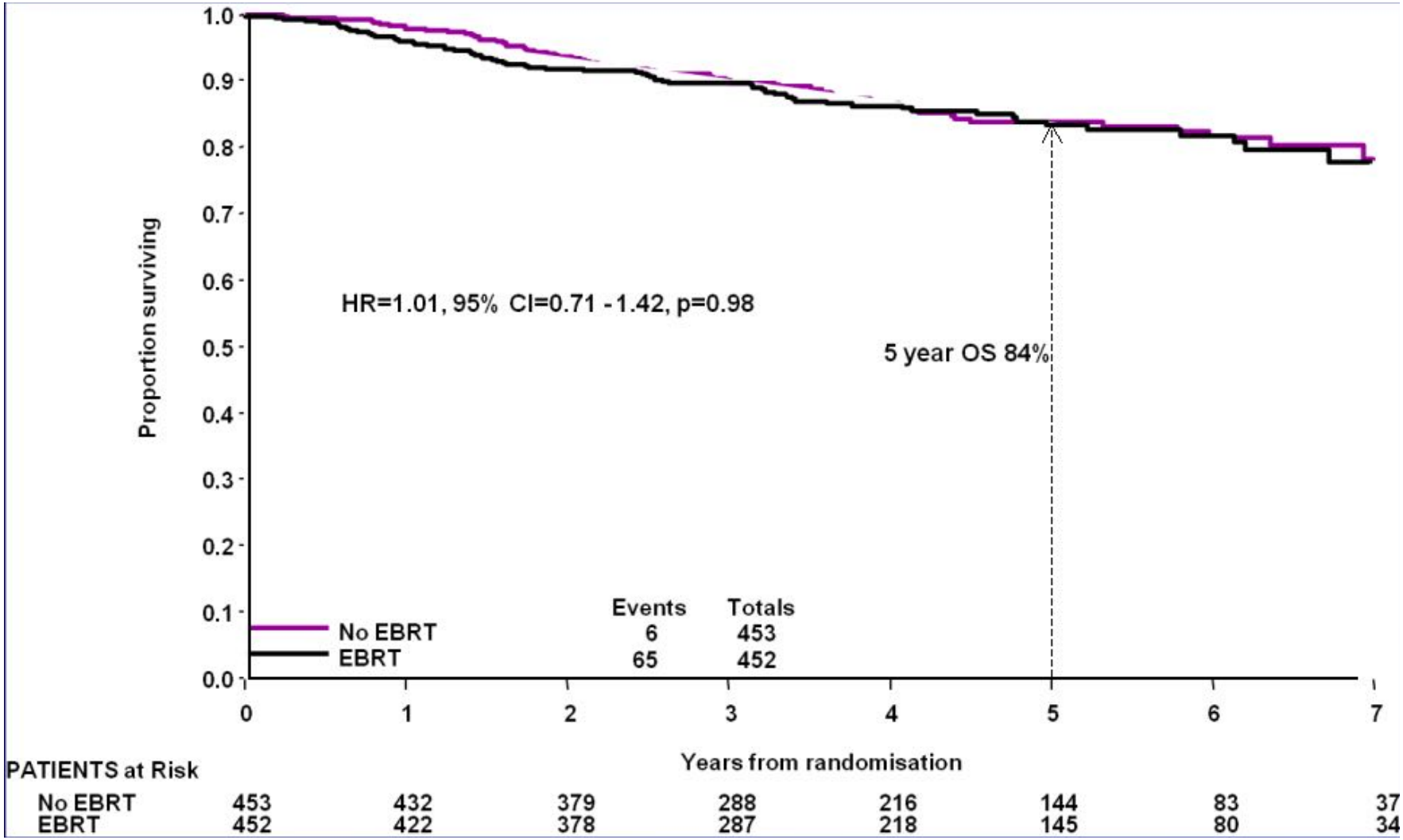
- **Ogni età con:**
  - **G2 o G3**
  - **Invavione del terzo esterno del miometrio**
  - **Invasione linfo-vascolare**
- **Età > 70 anni più un fattore di rischio**
- **Età > 50 anni più due fattori di rischio**

Trial ASTEC e EN 5

- Isteroannessiectomia e 30% linfadenectomia
- Randomizzazione per pazienti ad alto rischio
- Randomizzazione:
  - Osservazione n=453
  - Radioterapia pelvica n=452
- BRT permessa

- 53% di BRT nel gruppo osservazionale

Trial ASTEC e EN 5



PORTEC-1

- 715 Pz
- LIAB no linfoadenect.

RANDOM

- **osservazione**
- **EBRT 46 Gy**

Stage
- IB G2-3
- IC G1-2

Creutzberg et al, Lancet 2000; 355: 1404-1411

Surgery and postoperative radiotherapy versus surgery alone for patients with stage-1 endometrial carcinoma: multicentre randomised trial

2000

Characteristic	Radiotherapy (n=354)	Control (n=360)	Total (n=714)
Age (years)			
<60	93 (26)	108 (30)	201 (28)
60–70	136 (38)	134 (37)	270 (38)
>70	125 (35)	118 (33)	243 (34)
Mean (SD)	66·3 (9)	65·7 (9)	66·0 (9)
Range	41–85	43–90	41–90
Nulliparous	71 (20)	86 (24)	157 (22)
Diabetes	42 (12)	47 (13)	89 (12)
Hypertension	92 (26)	84 (23)	176 (25)
Histological diagnosis			
Adenocarcinoma	321 (91)	341 (95)	662 (93)
Adenoacanthoma	17 (5)	7 (2)	24 (3)
Adenosquam.carc.	8 (2)	4 (1)	12 (2)
Papillary serous ca.	1 (<1)	0 (0)	1 (<1)
Clear cell carc.	2 (<1)	2 (<1)	4 (<1)
Other	5 (1)	6 (2)	11 (2)
Myometrial invasion			
<50%	138 (39)	156 (43)	294 (41)
≥50%	216 (61)	204 (57)	420 (59)
Histological grade			
1	74 (21)	68 (19)	142 (41)
2	245 (69)	253 (70)	498 (70)
3	35 (10)	39 (11)	74 (10)
FIGO stage			
IB grade 2	104 (29)	117 (32)	221 (31)
IB grade 3	34(10)	39 (11)	73 (10)
IC grade 1	74 (21)	68 (19)	142 (20)
IC grade 2	141 (40)	136 (38)	277 (39)
IC grade 3	1 (<1)		1 (<1)
Vascular space invasion	22 (6)	19 (5)	41 (6)

5-year (RT vs control arm):

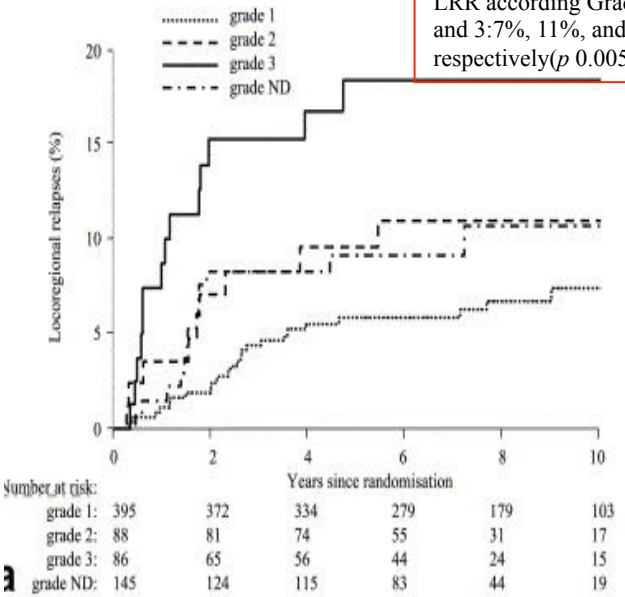
LRR: 4% vs 14% (p<0.001).
OS: 81% vs 85% (p=0.31).

Creutzberg et al. *Lancet* 2000; 355: 1404–11

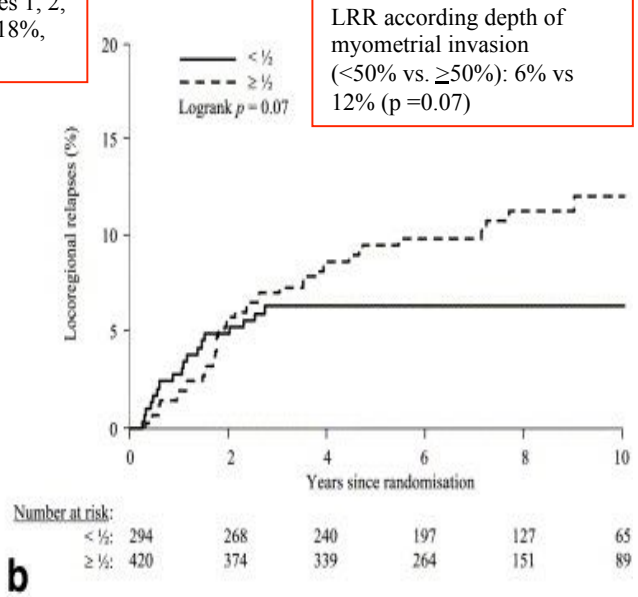
Postoperative radiotherapy for Stage 1 endometrial carcinoma: Long-term outcome of the randomized PORTEC trial with central pathology review

2005

LRR according Grades 1, 2, and 3:7%, 11%, and 18%, respectively(p 0.005)

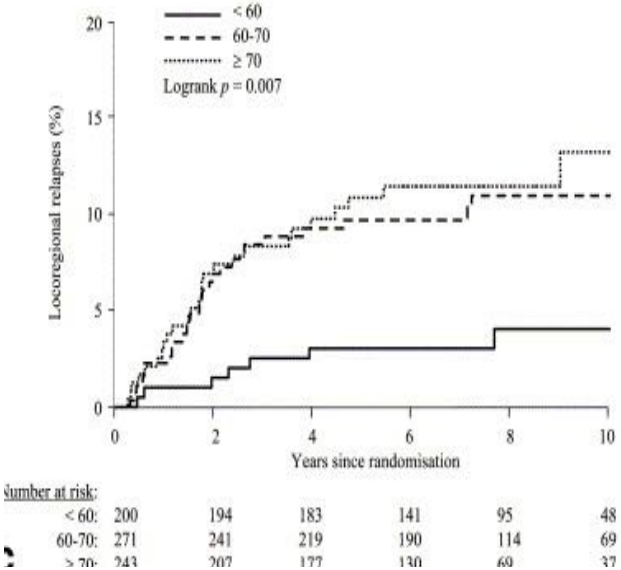


LRR according depth of myometrial invasion (<50% vs. ≥50%): 6% vs 12% (p =0.07)



mediana FU 97 mesi

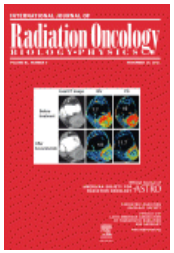
10 year (RT arm vs Control arm)
LRR: 5% vs 14% ($p < 0.0001$).
OS: 66% vs 73%($p = 0.09$).



LRR according aged (60,60–70, and 70 years were 4%, 11%, and 13%, respectively (p 0.007)

Scholten et al. 63 (3),834–838

Fifteen-year radiotherapy outcomes of the randomized PORTEC-1 trial for endometrial carcinoma



2011

Conclusions:

The 15-year outcomes of PORTEC-1 confirm the relevance of HIR criteria for treatment selection, and a trend for long-term risk of second cancers. EBRT should be avoided in patients with low- and intermediate-risk EC

Creutzberg et al. Int J Radiat Oncol Biol Phys. 2011,81(4):e631-8

Conclusioni PORTEC-1

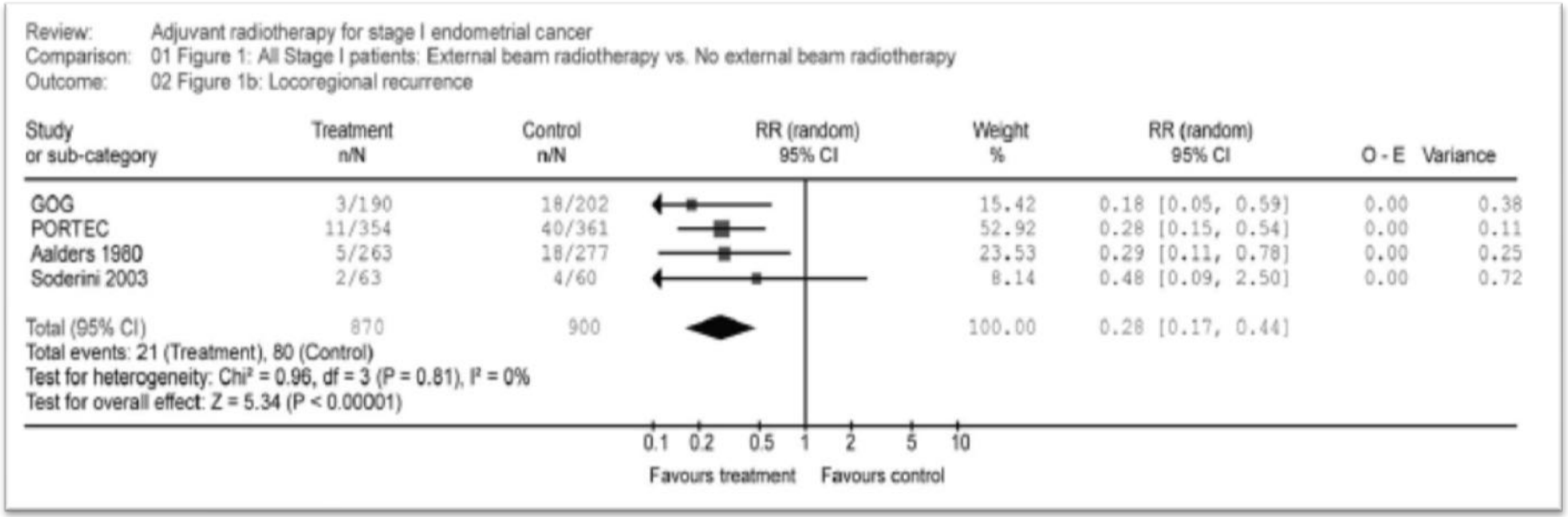
- **3 fattori di rischio principali:**
  - **G3**
  - **M2**
  - **Età >60 anni**
- **Radioterapia indicata se 2 o più fattori di rischio**
- **Riduzione delle indicazioni alla radioterapia in più del 50% dei casi**

Meta-analysis on all stage I endometrial cancer patients who had adjuvant radiotherapy versus no radiotherapy

Study	Methods	Participants	Interventions	Outcomes	Notes	Allocation concealment
Aalders 1980	Methods of randomisation not specified. Attrition rate and application of intention-to-treat analysis were not mentioned	Patients with stage 1 endometrial cancer following TAH and BSO. Also included patients with stage 1b and grade 1 tumour	All had intravaginal radium. Intervention group received further pelvic RT but not the control group. Follow-up was 3–10 years	Pelvic RT reduced vaginal and pelvic recurrences (1.9% versus 6.9%, $P < 0.001$) but not overall survival rate	Only patients with grade 3 and stage 1c tumour might have benefited from pelvic RT	B
GOG study	A balanced block randomisation scheme was used. Fifty-six women were excluded from the intention-to-treat analysis on the basis that they were ineligible either because of inadequate staging or because of histology or FIGO stage	Patients with stage 1b and Ic, also IIa (occult) and IIb (occult) and had TAH and BSO and selective bilateral pelvic, and paraaortic lymphadenectomy with removal of any enlarged or suspicious nodes	Patients were randomised to either whole pelvic RT or no additional therapy. Median follow-up was 56 months with 9% followed for <2 years	Pelvic RT reduced pelvic and vaginal recurrences but not the overall survival as pelvic recurrences were often effectively treated with second-line therapy		A
PORTEC	Multicentre RCT. Centre-blocked randomisation by telephone was done at the trial office with variable block sizes and was stratified by radiation oncology centre and depth of myometrial invasion. Intention-to-treat analysis was used	Patients with stage 1 endometrial carcinoma (grade 1 with deep myometrial invasion, grade 2 with any invasion or grade 3 with superficial invasion). All had TAH and BSO without lymphadenectomy	Patients were randomised to pelvic RT or no further treatment. Intravaginal brachytherapy was not given. Follow-up was 5–7 years	Pelvic RT reduced locoregional recurrence (4% versus 14%, $P < 0.001$) but not overall survival or endometrial cancer-related death. Treatment-related complications occurred in 25% of RT patients and in 6% of the control group		A
Soderini 2003	Only an abstract. Methods of randomisation not specified. Attrition rate and application of intention-to-treat analysis were not mentioned	Patients with intermediate risk (1b grades 2–3 to 1c) endometriod endometrium carcinoma. All patients had TAH-BSO, pelvic–paraaortic lymphadenectomy and peritoneal washings	Patients were randomised to pelvic RT 50 Gy or no RT	Recurrence rate was lower in RT arm although not statistically significant	Only an abstract is available	B

Kong, A. et al. Ann Oncol 2007 18:1595-1604

Meta-analysis on all stage I endometrial cancer patients who had adjuvant radiotherapy versus no radiotherapy



- **1770 pts**
- **RTE riduce le recidive loco-regionali (RR 0.28 - p< 0.0001), con una riduzione assoluta del rischio del 6%**
  - **Nessuna variazione della OS o di metastasi a distanza**
  - **EBRT dovrebbe essere utilizzata in pazienti con multipli fattori di rischio**

Kong, A. et al. Ann Oncol 2007 18:1595-1604

Vaginali brachytherapy versus pelvic external beam radiotherapy for patients with endometrial cancer of high-intermediate risk (PORTEC-2): an open-label, non-inferiority, randomised trial

- 427 PTS
- LIAB no linfadenect.

RANDOM

VBT
21 Gy/3 fr

EBRT
46 Gy/23 fr

Stage

- ICG1-2 IB G3 > 60 y
- IIA G1-2, G3 M1

Nout et al. Lancet. 2010;375(9717):816-23

Vaginali brachytherapy versus pelvic external beam radiotherapy for patients with endometrial cancer of high-intermediate risk (PORTEC-2): an open-label, non-inferiority, randomised trial

	EBRT (n=214)	VBT (n=213)
Age (years)		
<60	8 (3·7%)	8 (3·8%)
60–70	109 (50·9%)	99 (46·5%)
>70	97 (45·3%)	106 (49·8%)
Median (SD)	69 (7)	70 (7)
KPS		
0	157 (73·4%)	141 (66·5%)
1	56 (26·2%)	66 (31·1%)
2	1 (0·5%)	5 (2·4%)
Comorbidity		
IBD	4 (1·9%)	2 (0·9%)
Diabetes	28 (13·1%)	34 (16·0%)
Hypertension	75 (35·0%)	75 (35·2%)
Cardiovascular	47 (22·0%)	51 (24·0%)
Other	33 (15·4%)	33 (15·5%)
FIGO stage		
IB	19 (8·9%)	16 (7·5%)
IC	172 (80·4%)	171 (80·3%)
IIA	23 (10·7%)	26 (12·2%)
Grade		
1	99 (46·3%)	103 (48·4%)
2	97 (45·3%)	94 (44·1%)
3	18 (8·4%)	16 (7·5%)
LVSI		
Present	25 (11·7%)	21 (9·9%)
Absent	189 (88·3%)	191 (90·1%)
Distance to serosa (mm)		
0–1	17 (14·2%)	23 (16·9%)
2–3	46 (38·3%)	43 (31·6%)
4–5	35 (29·2%)	36 (26·5%)
≥6	22 (18·3%)	34 (25·0%)
Not recorded	94 (43·9%)	77 (36·2%)
Median (SD)	3·8 (2·5)	4·3 (3·2)

Data are number (%) unless otherwise indicated. EBRT=external beam radiotherapy. VBT=vaginal brachytherapy. KPS=Karnofsky performance score. IBD=irritable bowel disease. FIGO=International Federation of Gynecology and Obstetrics. LVSI=lymph vascular space invasion.

	EBRT (n=214)	VBT (n=213)
Time between surgery and radiotherapy (days)	43·4 (0·8)	42·5 (0·8)
Duration of radiotherapy (days)	30·9 (0·2)	12·9 (0·4)
Dose (Gy)		
EBRT	46·0 (0·9)	..
VBT: HDR*	..	21·1 (0·1)
VBT: MDR*	..	28·5 (0·5)
VBT: LDR*	..	29·0 (0·3)
Median VBT cylinder diameter (mm [range])	..	30 (20–40)
VBT length of 100% isodose (mm)	..	46·5 (0·7)

Data are mean (SE) unless otherwise indicated. EBRT=external beam radiotherapy. VBT=vaginal brachytherapy. HDR=high-dose rate. MDR=medium-dose rate. LDR=low-dose rate. *VBT was delivered with HDR in 182 (85·4%) patients, with LDR in 19 (8·9%) patients, and with MDR in eight (3·8%) patients.

Nout et al. Lancet. 2010;375(9717):816-23

PORTEC 2

	Events/total	Estimated 5-year (%; 95% CI)	Hazard ratio (95% CI)*	Log-rank p value*
Vaginal recurrence				
EBRT	4/183	1·9% (0·6–5·8)	1·00	0·39
VBT	2/183	1·5% (0·4–6·5)	0·48 (0·09–2·64)	
Pelvic recurrence				
EBRT	1/183	0·6% (0·1–4·0)	1·00	0·06
VBT	6/183	3·3% (1·5–7·3)	6·10 (0·73–50·7)	
Locoregional recurrence				
EBRT	5/183	2·4% (0·9–6·5)	1·00	0·42
VBT	8/183	4·8% (2·4–9·7)	1·58 (0·52–4·86)	
Distant metastases				
EBRT	10/183	5·0% (2·6–9·4)	1·00	0·79
VBT	11/183	6·4% (3·6–11·5)	1·12 (0·48–2·64)	
Disease-free survival				
EBRT	24/183	80·2% (71·4–89·0)	1·00	0·89
VBT	25/183	84·5% (78·6–90·4)	1·04 (0·59–1·82)	
Overall survival				
EBRT	19/183	82·1% (73·5–90·7)	1·00	0·66
VBT	22/183	86·2% (80·5–91·9)	1·15 (0·62–2·13)	

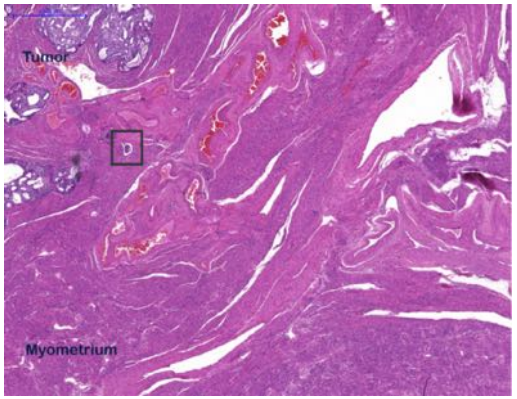
EBRT=external beam radiotherapy. VBT=vaginal brachytherapy. *Both log-rank tests and Cox proportional hazards models are stratified for FIGO (International Federation of Gynecology and Obstetrics) stage.

Nout et al. Lancet. 2010;375(9717):816-23

Substantial lymph-vascular space invasion (LVSI) is a significant risk factor for recurrence in endometrial cancer – A pooled analysis of PORTEC 1 and 2 trials

2015

A



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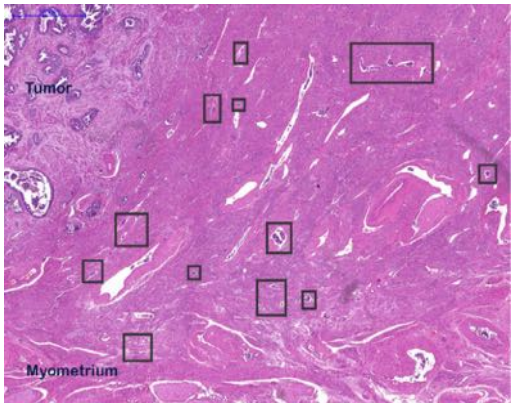


Focal (A) and substantial (B) Lymph-vascular space invasion (LVSI)

Substantial LVSI, in contrast to focal or no LVSI, was the strongest independent prognostic factor for pelvic regional recurrence, distant metastasis and overall survival. Therapeutic decisions should be based on the presence of substantial, not 'any' LVSI. Adjuvant EBRT and/or chemotherapy should be considered for stage I EC with substantial LVSI

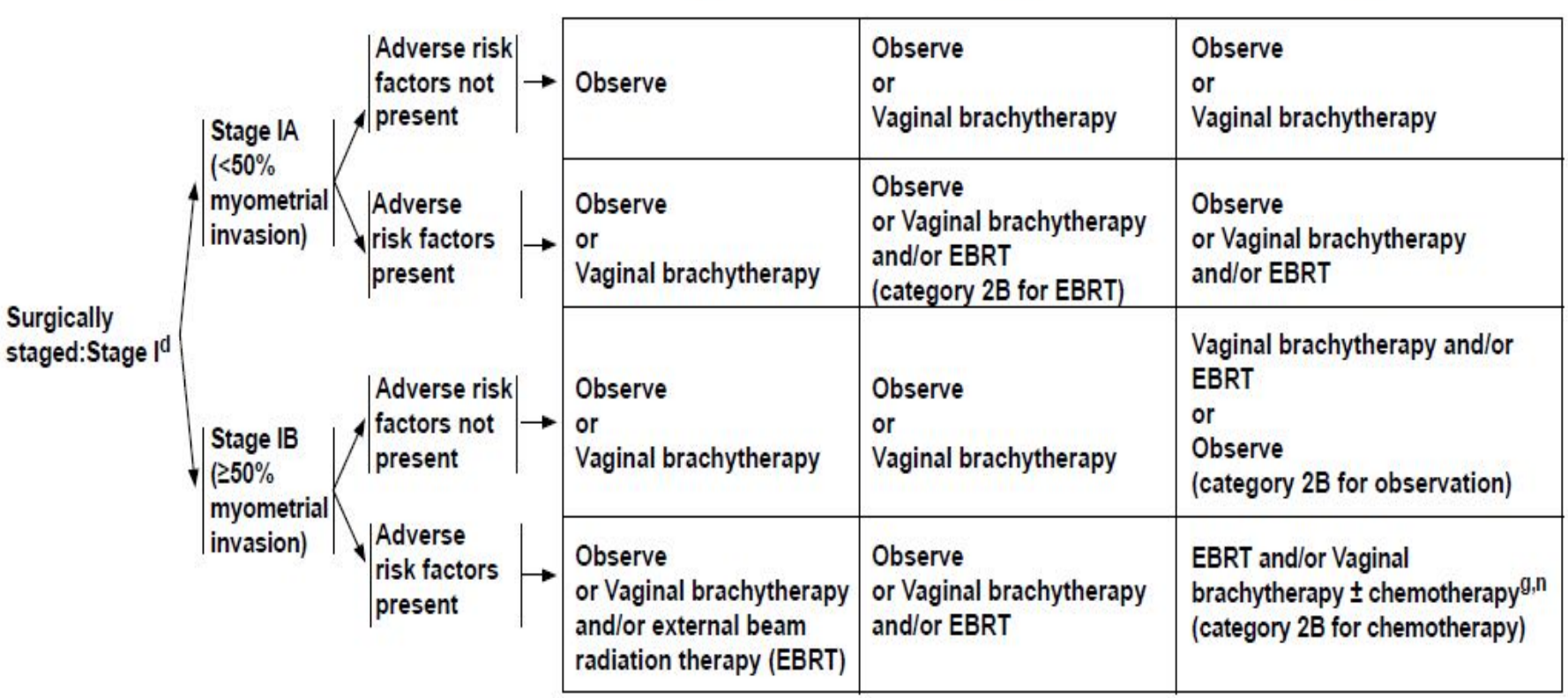
Bosse T, Peters EE, Creutzberg CL et al. 51, 2015:1742-1750

National Comprehensive Cancer Network®

NCCN Guidelines Version 1.2016
Endometrial Carcinoma

NCCN Guidelines Index
Uterine Neoplasms TOC
Discussion

All staging in guideline is based on updated 2010 FIGO staging. (See ST-1)

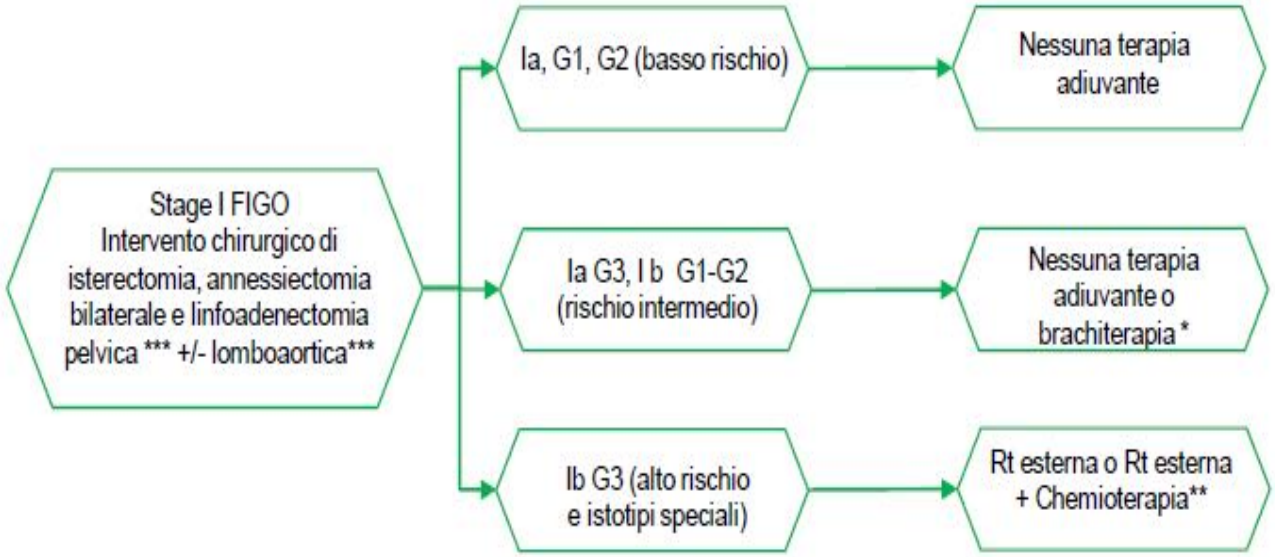


Linee guida

NEOPLASIE DELL'UTERO: ENDOMETRIO E CERVICE

2014

TRATTAMENTO: STADIO I



*in particolare la brachiterapia viene proposta in presenza di eta'> 60 anni, infiltrazione miometriale >50% e G3 (rischio intermedio-alto);

** Impiego adiuvante della chemioterapia con carboplatino e taxolo in aggiunta alla radioterapia con livello di evidenza positivo debole; forza della raccomandazione C; negli istotipi speciali anche in assenza di definitive evidenze la chemioterapia è consigliata

*** solo nell'alto rischio

http://www.aiom.it/

JOURNAL OF CLINICAL ONCOLOGY

Postoperative Radiation Therapy for Endometrial Cancer: ASCO Clinical Practice Guideline Endorsement of the ASTRO Evidence-Based Guideline

2015

Which patients with endometrioid endometrial cancer should receive vaginal cuff radiation?

G1,2 with ≥50% myometrial invasion or G3 with <50% myometrial invasion.

Postoperative Radiation Therapy for Endometrial Cancer:

ASCO Clinical Practice Guideline Endorsement of the ASTRO Evidence-Based Guideline

2015

Which women should receive postoperative external beam radiation?

- *G3 with ≥50% myometrial invasion or cervical stroma invasion*
- *G1,2 with ≥50% myometrial invasion + age >60 years and/or LVSI.*
- *Vaginal brachytherapy may be a better option for patients with these features, especially if surgical staging was adequate and nodes were negative.*

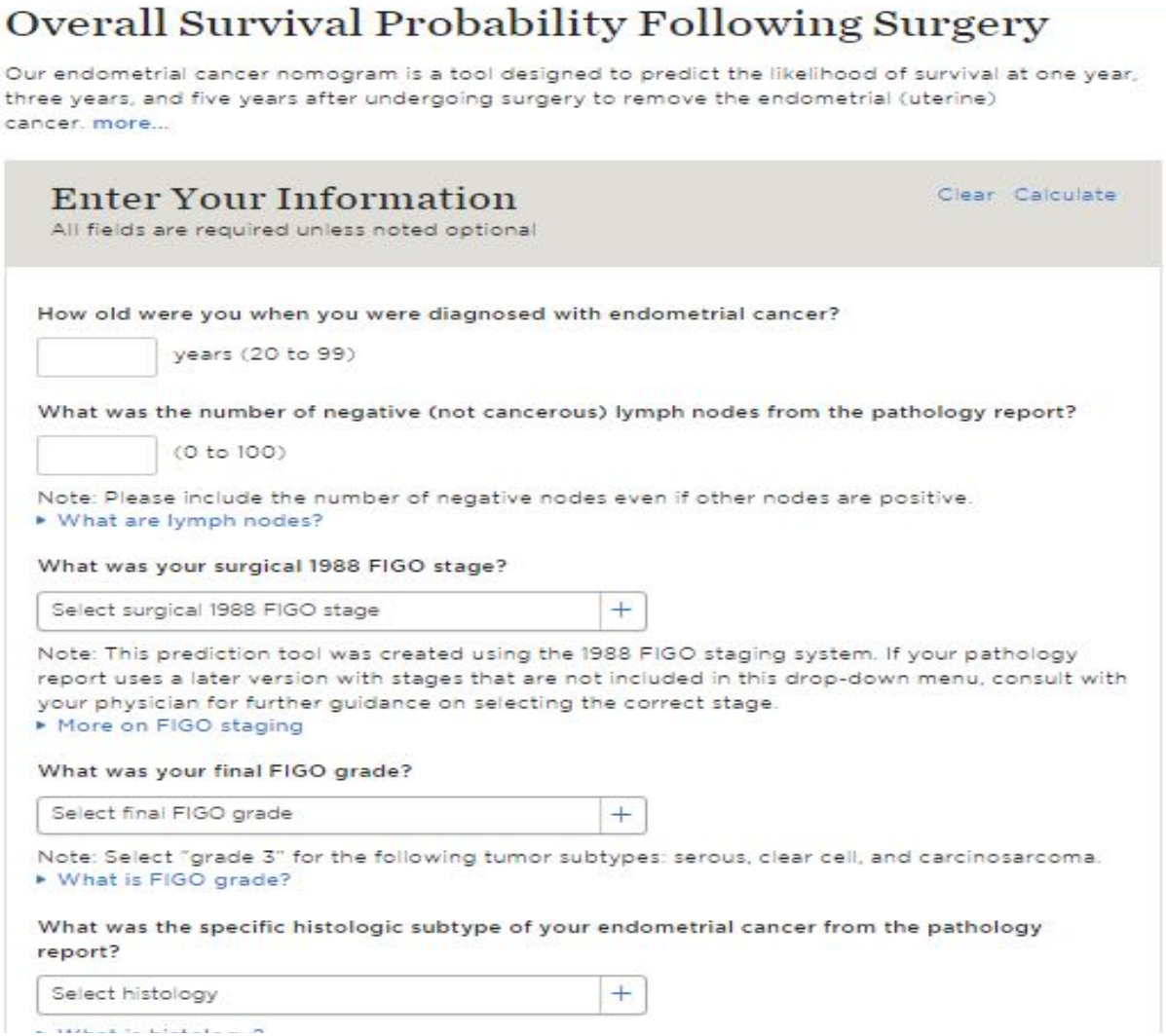
A. Meyer et al. J Clin Oncol 33.

When should brachytherapy be used in addition to external beam radiation?

Use of vaginal brachytherapy in patients also undergoing pelvic external beam radiation is not generally warranted, unless risk factors for vaginal recurrence are present.

Nomogrammi

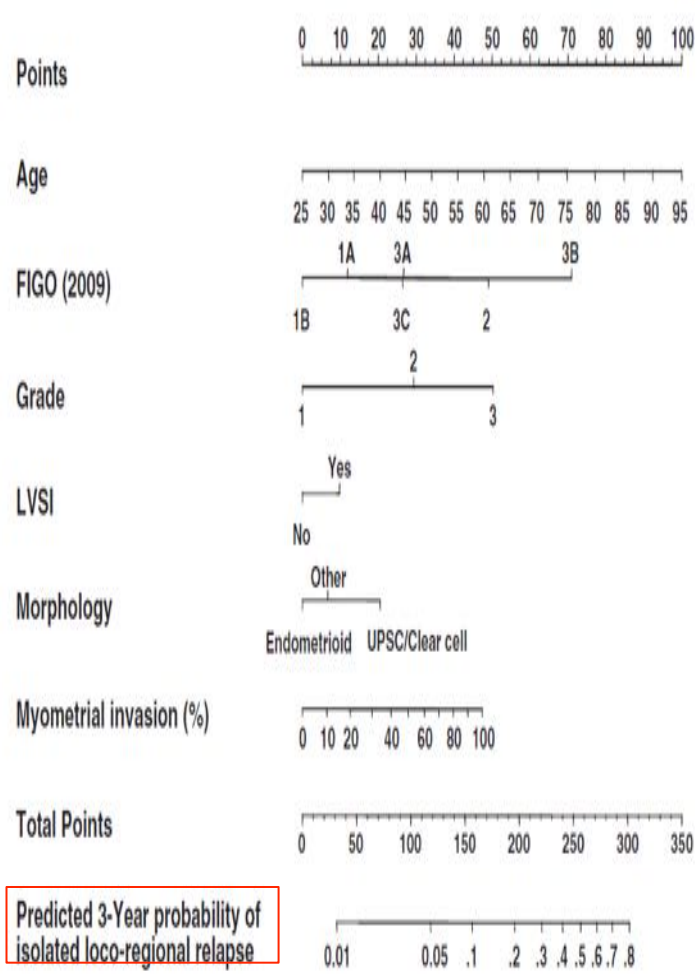
Memorial Sloan Kettering Cancer Center

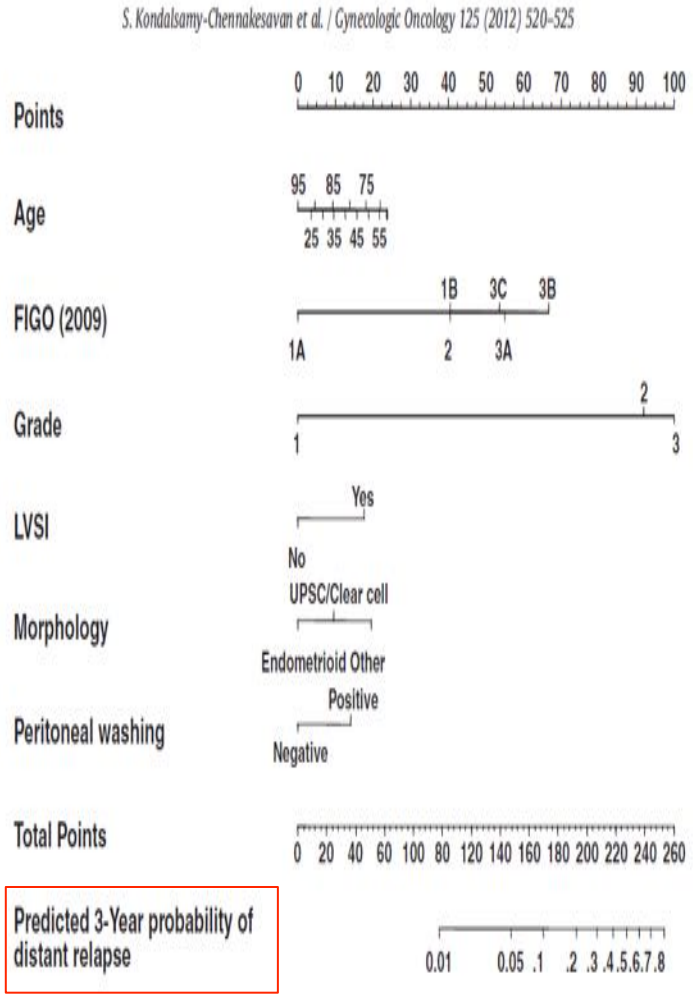


- Età
- Nr. dei LNF negativi
- Stadio FIGO 1988
- Grade
- Istologia

https://www.mskcc.org/nomograms/endometrial/post-op

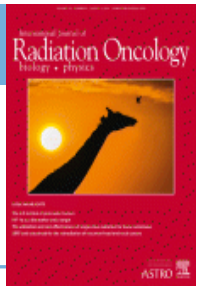
Nomograms to predict isolated loco-regional or distant recurrence among women with uterine cancer





Kondalsamy-Chennakesavan et al.Gynecologic Oncology 125 (2012) 520–525

Nomograms for Prediction of Outcome With or Without Adjuvant Radiation Therapy for Patients With Endometrial Cancer: A Pooled Analysis of PORTEC-1 and PORTEC-2 Trials



2015

Table 2 Patient characteristics of the initial and final pooled trial cohort and the validation sets

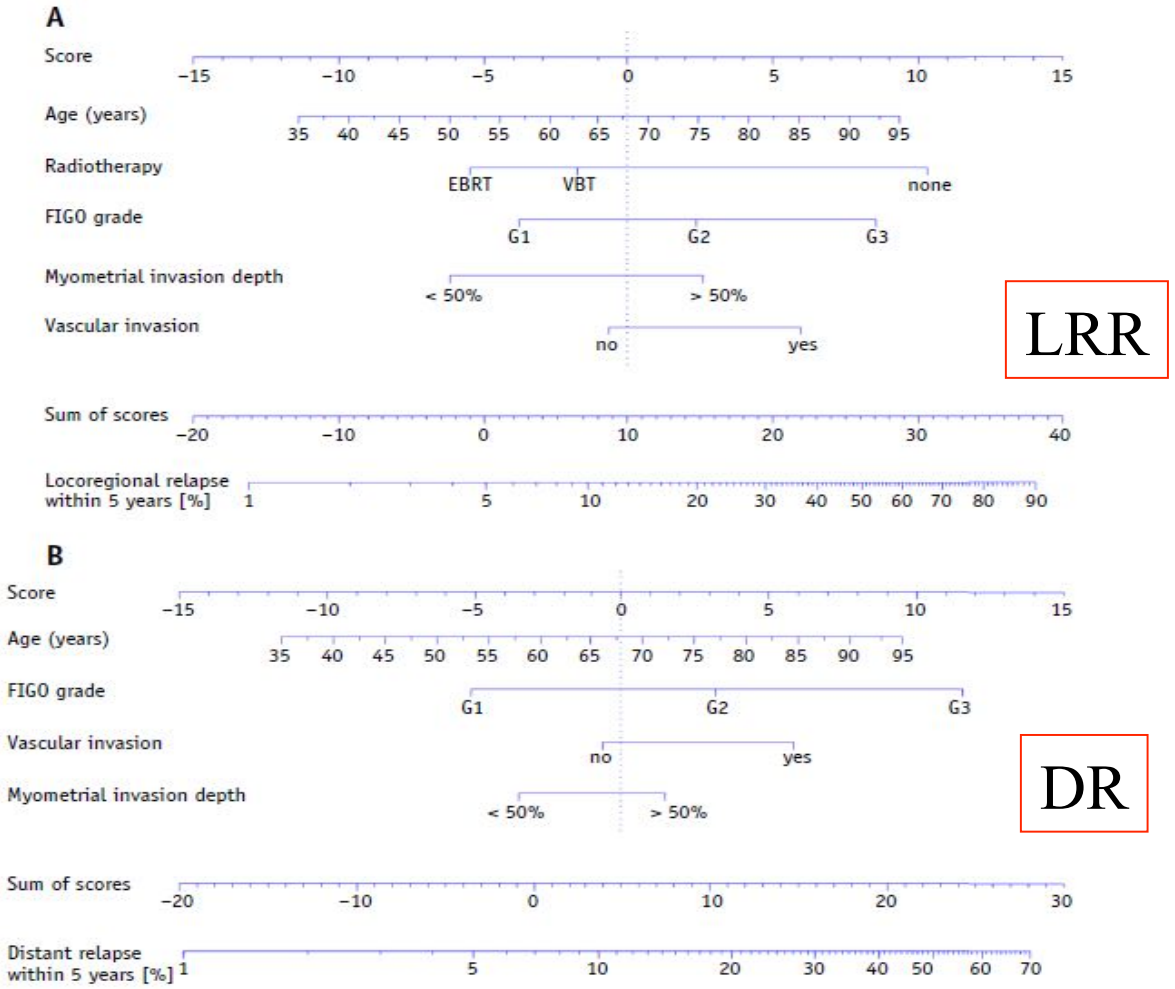
	Initial pooled trial cohort*	Final trial cohort*	Validation Maastro	Validation Enschede
Characteristic	N (%)	n (%)	n (%)	n (%)
Total	1240	1240	244	291
Age (y)				
Median	68.0	68.0	65.8	68.0
Range	35.2-92.2	35.2-92.2	19.5-86.8	44.0-92.0
FIGO histological grade				
1	344 (27.7)	730 (58.9)	93 (38.1)	96 (33.0)
2	689 (55.6)	256 (20.6)	124 (50.8)	98 (33.7)
3	207 (16.7)	254 (20.5)	20 (8.2)	91 (31.3)
Unknown	0 (0)	0 (0)	7 (2.9)	6 (2.1)
Myometrial invasion				
<50%	352 (28.4)	368 (29.7)	110 (45.1)	77 (26.5)
>50%	888 (71.6)	872 (70.3)	131 (53.7)	214 (73.5)
Unknown	0 (0)	0 (0)	3 (1.2)	0 (0)
Invasion of cornuae				
No	865 (69.8)	886 (71.5)	176 (72.1)	291 (100)
Yes	333 (26.9)	324 (26.1)	41 (16.8)	0 (0)
Unknown	42 (3.4)	30 (2.4)	27 (11.1)	0 (0)
Vascular invasion				
No	1046 (84.4)	1106 (89.2)	192 (78.7)	246 (84.5)
Yes	111 (9.0)	117 (9.4)	52 (21.3)	45 (15.5)
Unknown	83 (6.7)	17 (1.4)	0 (0)	0 (0)
Radiation therapy				
None	378 (30.5)	378 (30.5)	0 (0)	0 (0)
EBRT	648 (52.3)	648 (52.3)	150 (61.5)	203 (69.8)
VBT	214 (17.3)	214 (17.3)	94 (38.5)	88 (30.2)

Pooled for analysis:1240 pts

Creutzberg CL et al. Int J Radiat Oncol Biol Phys. ;91(3):530-9.

Nomograms for Prediction of Outcome With or Without Adjuvant Radiation Therapy for Patients With Endometrial Cancer: A Pooled Analysis of PORTEC-1 and PORTEC-2 Trials

2015

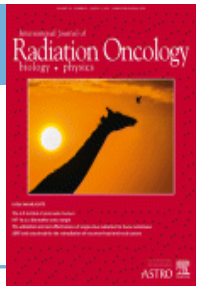


LRR

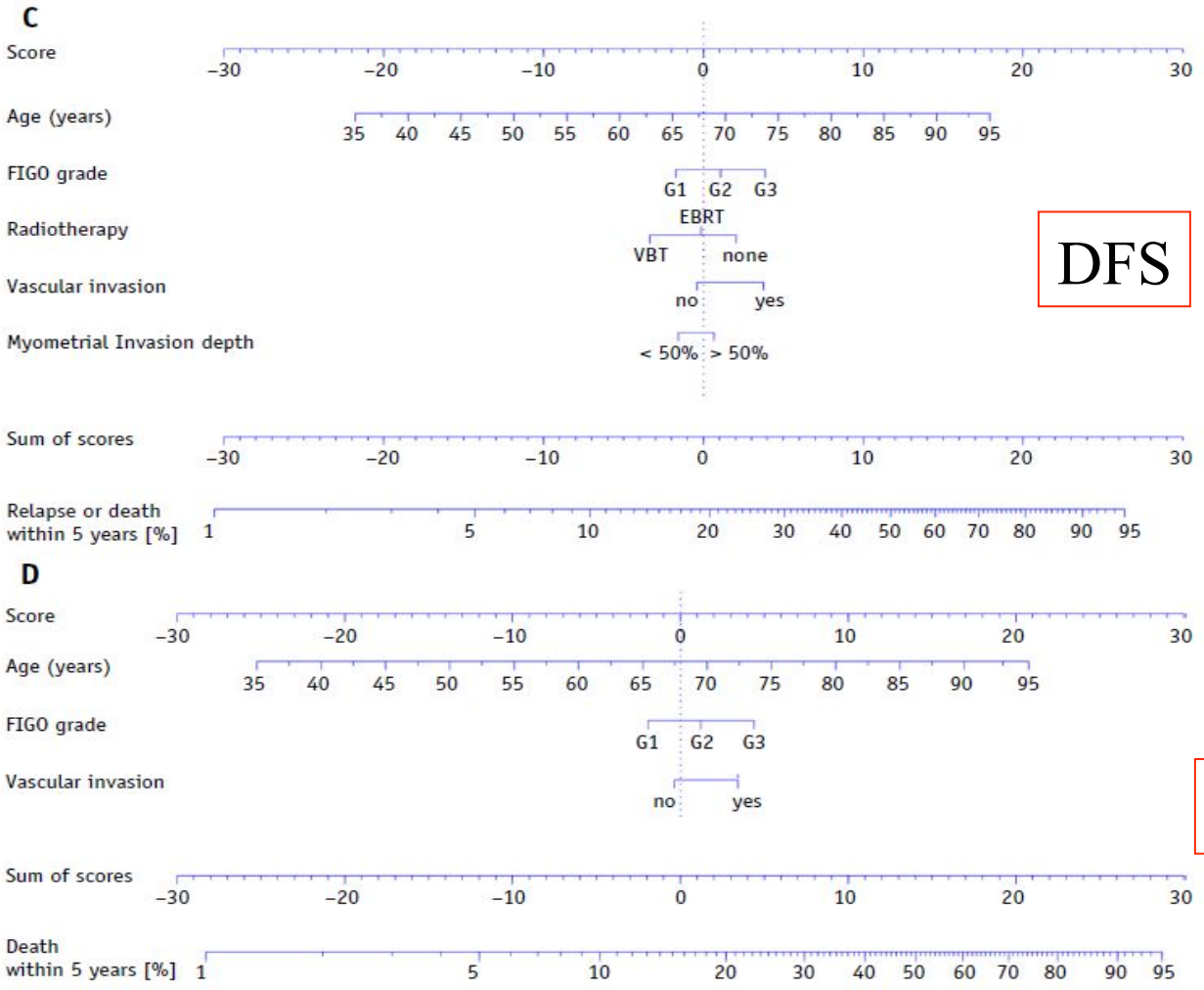
DR

Creutzberg CL et al. Int J Radiat Oncol Biol Phys. ;91(3):530-9.

Nomograms for Prediction of Outcome With or Without Adjuvant Radiation Therapy for Patients With Endometrial Cancer: A Pooled Analysis of PORTEC-1 and PORTEC-2 Trials



2015



DFS

OS

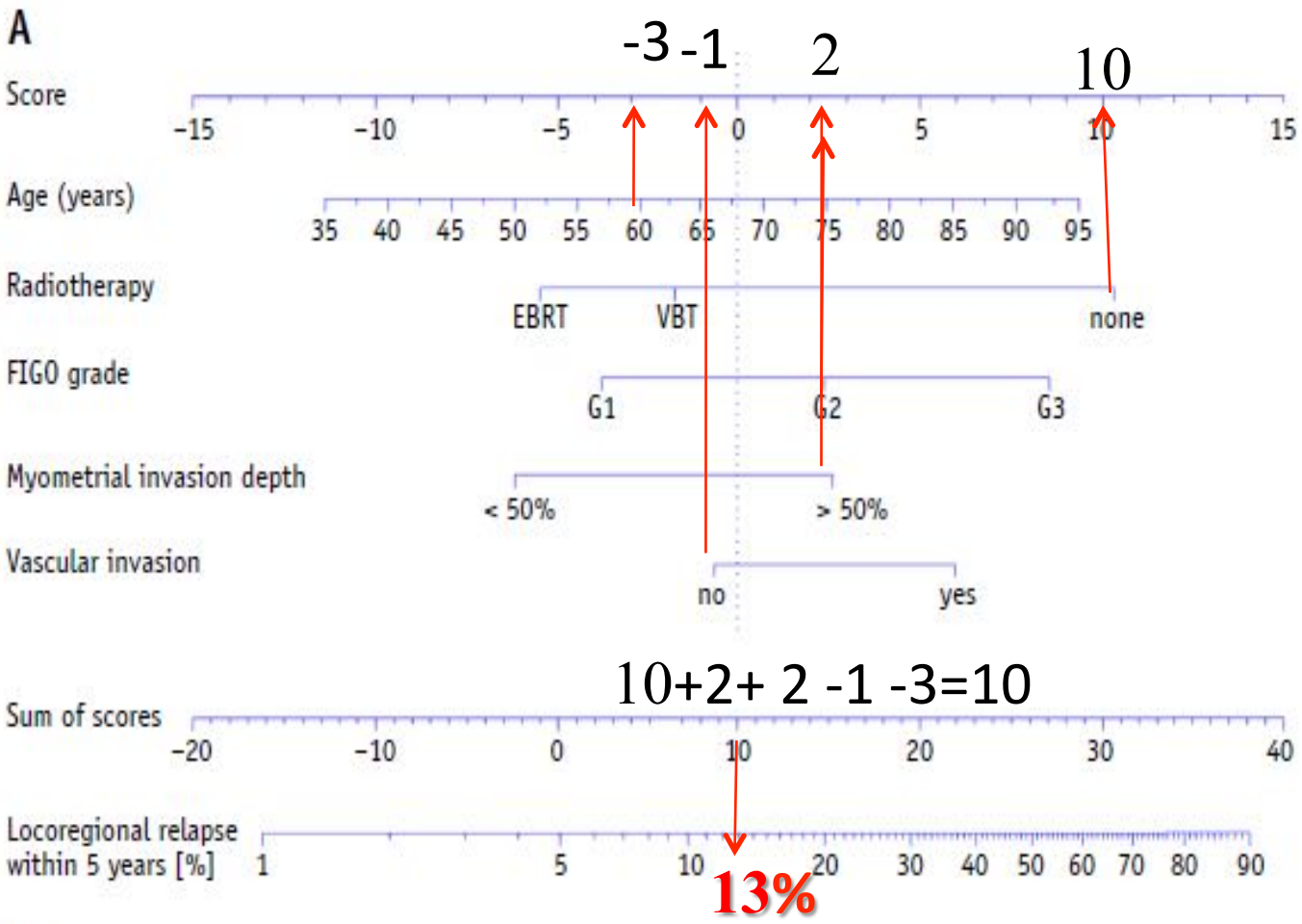
Creutzberg CL et al. Int J Radiat Oncol Biol Phys. ;91(3):530-9.

Caso clinico

Età 60 aa
IAB + linfoadectomia pelvica:adenocarcinoma endometroide, G3,
LVI -,pT1BpN0
LRR a 5 anni ?

LRR

)15



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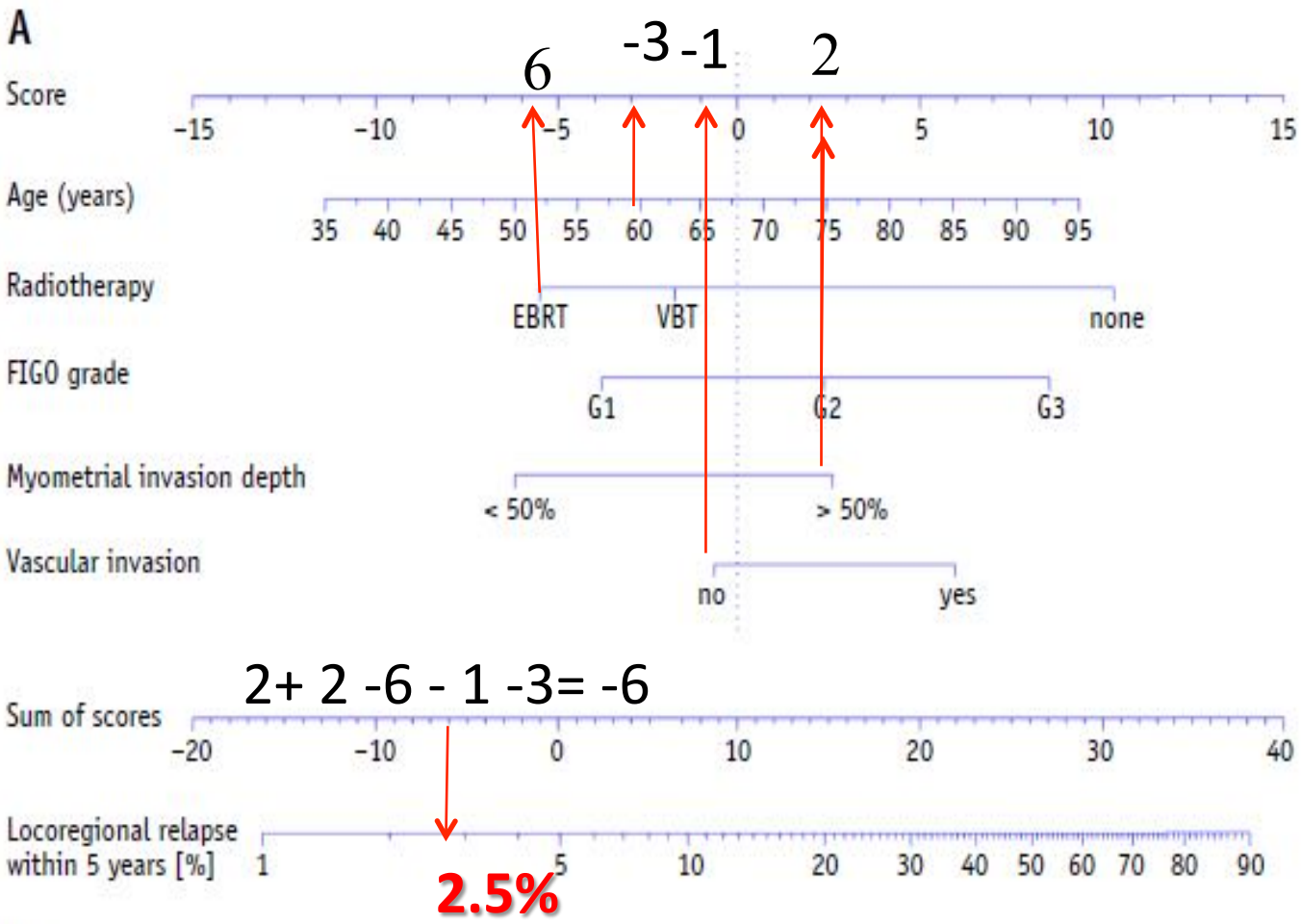
LRR

)15



Creutzberg CL et al. Int J Radiat Oncol Biol Phys. ;91(3):530-9.

Caso clinico

Età 66 aa
Luglio 2015: IAB+ linfoadectomia pelvica:adenocarcinoma endometroide, G3, LVI +,pT1BpN0 (0/12)
OS a 5 anni ?

Overall Survival Probability Following Surgery

Memorial Sloan Kettering Cancer Center

Our endometrial cancer nomogram is a tool designed to predict the likelihood of survival at one year, three years, and five years after undergoing surgery to remove the endometrial (uterine) cancer. more...

Enter Your Information

Clear Calculate

All fields are required unless noted optional

How old were you when you were diagnosed with endometrial cancer?

66 years (20 to 99)

What was the number of negative (not cancerous) lymph nodes from the pathology report?

12 (0 to 100)

Note: Please include the number of negative nodes even if other nodes are positive.

▸ What are lymph nodes?

What was your surgical 1988 FIGO stage?

IC +

Note: This prediction tool was created using the 1988 FIGO staging system. If your pathology report uses a later version with stages that are not included in this drop-down menu, consult with your physician for further guidance on selecting the correct stage.

▸ More on FIGO staging

What was your final FIGO grade?

Grade 3 +

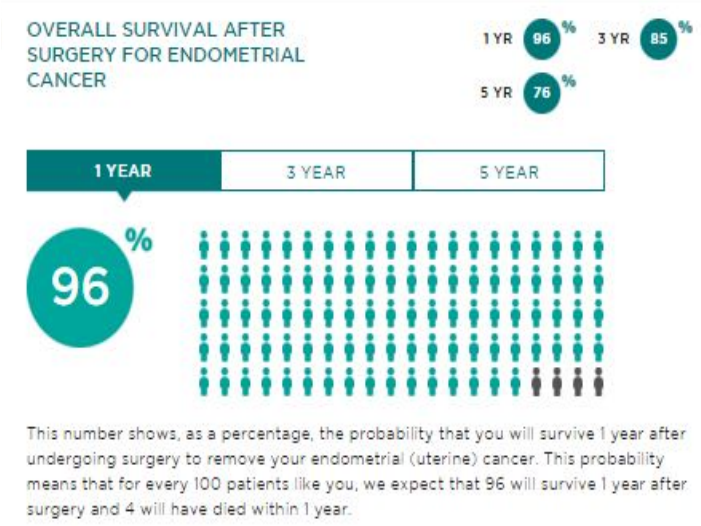
Note: Select "grade 3" for the following tumor subtypes: serous, clear cell, and carcinosarcoma.

▸ What is FIGO grade?

What was the specific histologic subtype of your endometrial cancer from the pathology report?

Endometrioid +

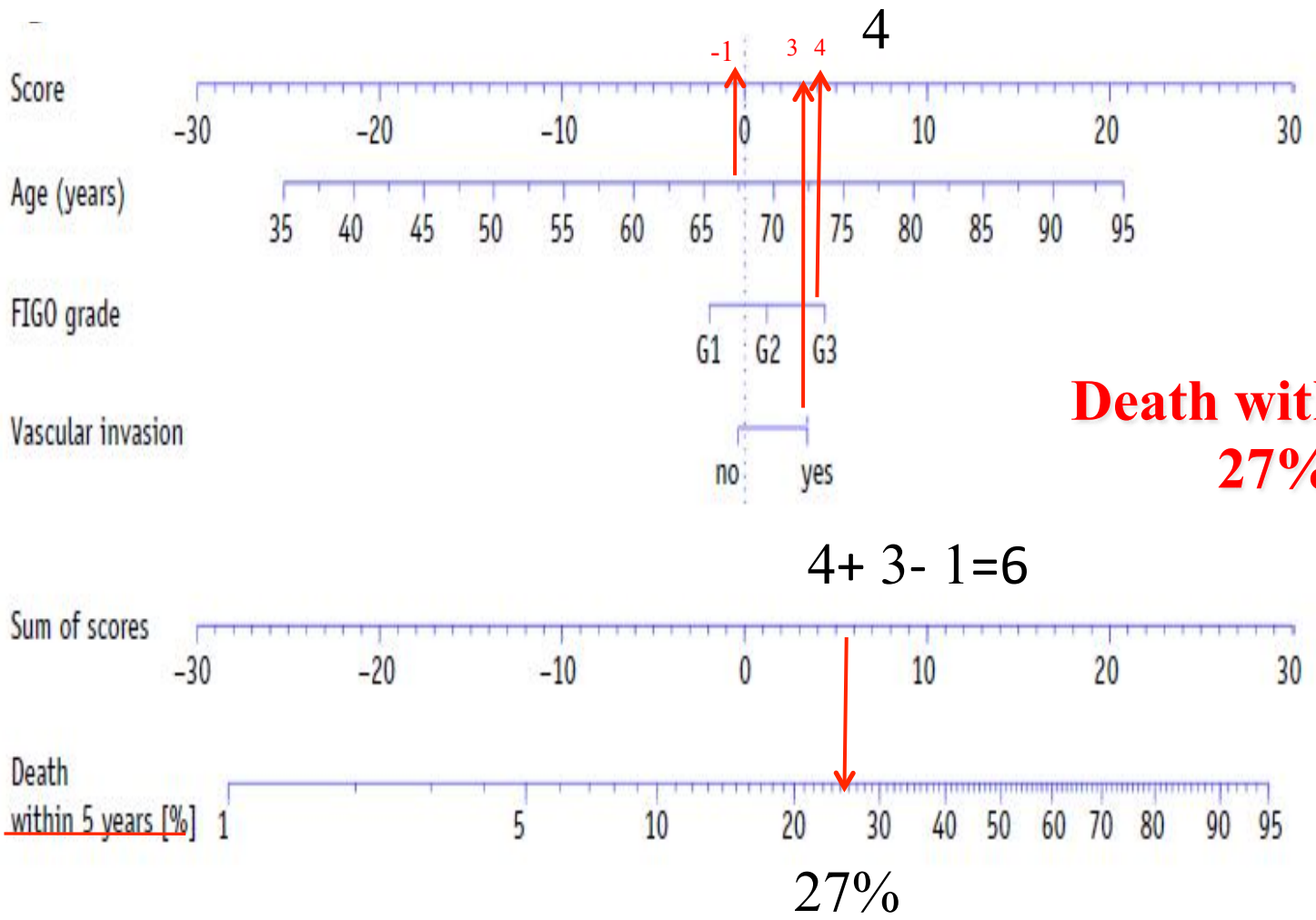
▸ What is histology?



5 y OS: 76%

https://www.mskcc.org/nomograms/endometrial/post-op

Nomograms for Prediction of Outcome With or Without Adjuvant Radiation Therapy for Patients With Endometrial Cancer: A Pooled Analysis of PORTEC-1 and PORTEC-2 Trials



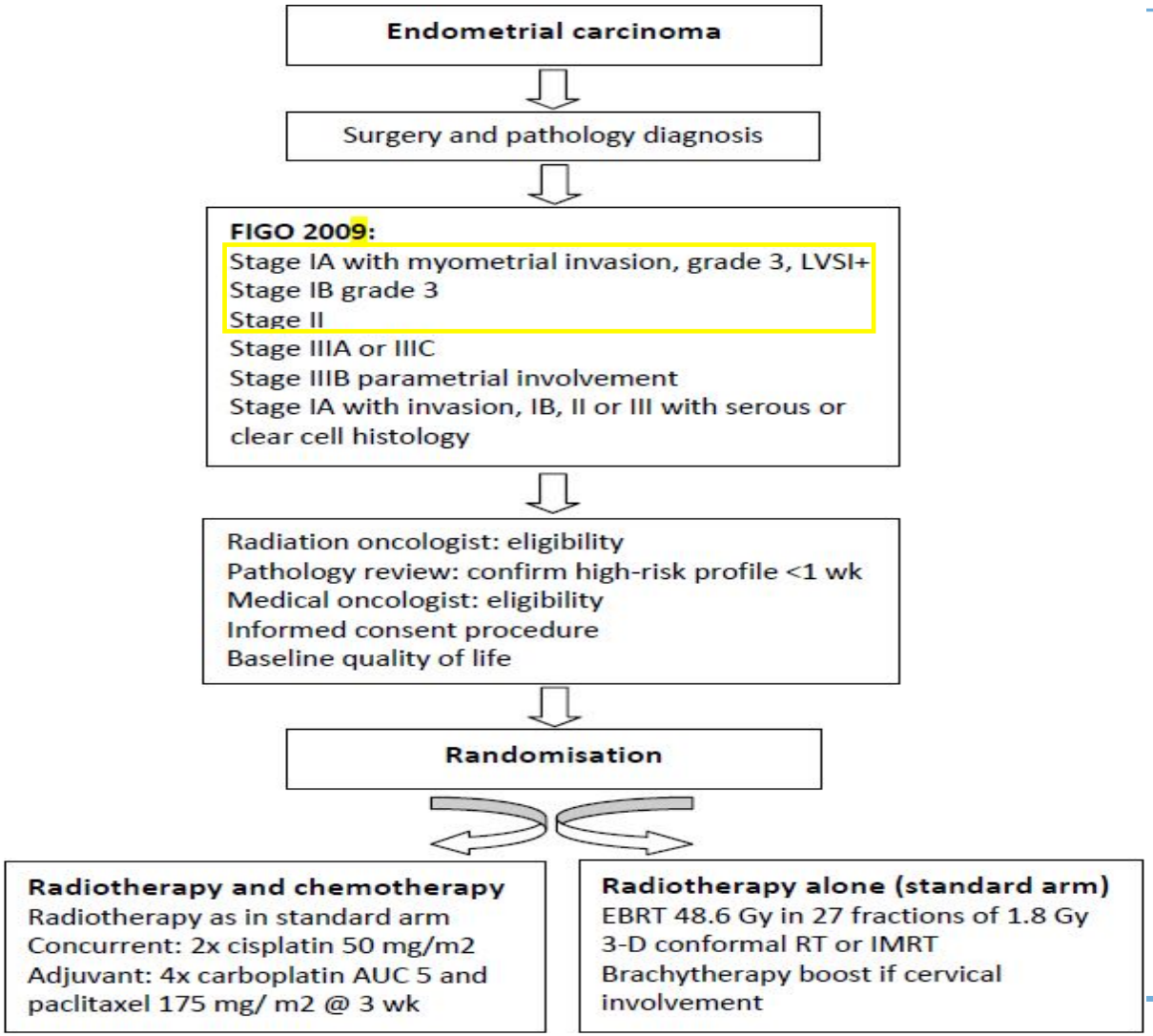
2015

Death within 5 y 27%

OS

Creutzberg CL et al. Int J Radiat Oncol Biol Phys. ;91(3):530-9.

Randomized Phase III Trial Comparing Concurrent Chemoradiation and Adjuvant Chemotherapy with Pelvic Radiation Alone in High Risk and Advanced Stage Endometrial Carcinoma: **PORTEC-3**



Primary endpoint:
OS

Second primary endpoint:
Failure-free survival

Secondary endpoint:
Pelvic and distant recurrence, severe (grades 3 and 4) treatment-related toxicity, and quality of life.

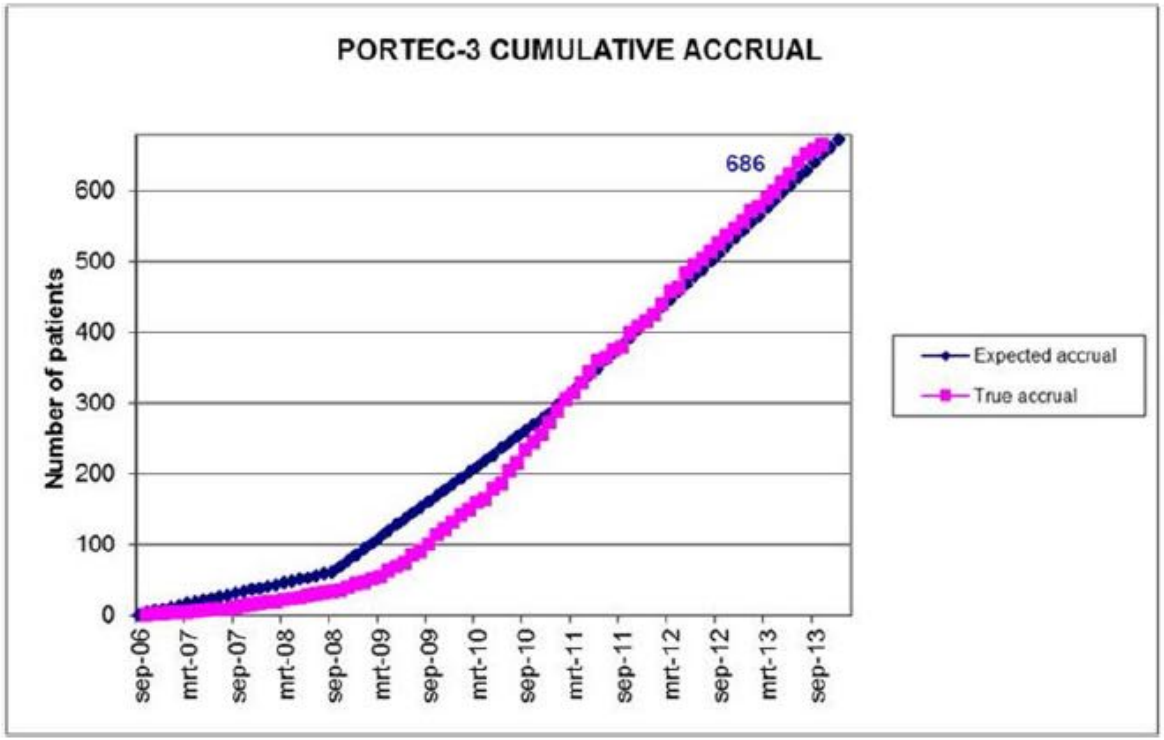
CLOSED

www.clinicalresearch.nl/portec3

PORTEC-3 Newsletter no 10 14 March 2014

PORTEC-3 has closed on 20-12-2013 after achieving full accrual !

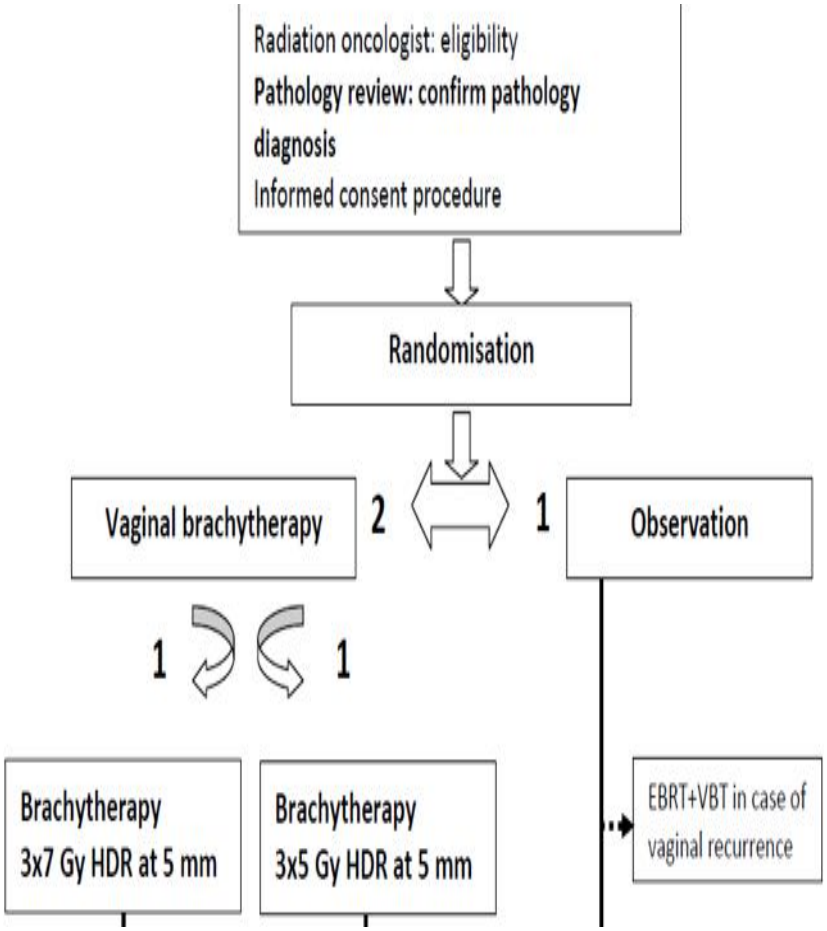
Accrual to PORTEC3 has reached and exceeded the target number of 670 patients, for a **final total of 686 patients included**.



www.clinicalresearch.nl/portec3

Randomised Phase III Trial Comparing Vaginal Brachytherapy (two doses schedules: 21 or 15 Gy HDR in 3 fractions) and Observation after Surgery in patients with Endometrial Carcinoma with High-Intermediate Risk Features

PORTEC-4



Inclusion Criteria:

Histologically confirmed endometrioid type endometrial carcinoma, FIGO 2009 stage I, with one of the following combinations of substage, age, and grade:

- Stage IA, any age and grade 3 without lymph-vascular space invasion (LVSI)
- Stage IB, age 60 years or older and grade 1 or 2
- Stage IB, any age, grade 1-2 with documented LVSI

Primary endpoint: vaginal recurrence

Second primary endpoint: 5-year vaginal control including treatment for relapse

Secondary endpoints: vaginal toxicity, quality of life, pelvic recurrence, and overall and failure-free survival.

www.msbi.nl/portec4

Conclusioni

1)Le recenti analisi degli studi randomizzati (PORTEC) hanno dato nuovi strumenti di riflessione sul ruolo della RT adiuvante nel gruppo di rischio intermedio/alto.

2)Questo informazioni ci possono guidare nella elaborazione di terapie sempre più personalizzate per ogni paziente operata per ca endometriale.

3)L'utilizzo di quest'ultimo nomogramma ci può dare informazioni sul profilo di rischio individuale, sull'outcome con o senza RT (RTE oVBT).

4)La possibilità di valutare rischi e benefici della terapia adiuvante.

Grazie per l'attenzione