Dr.ssa Laura Masini

Radioterapia nelle forme localizzate o localmente avanzate

3°Edizione

I tumori femminili

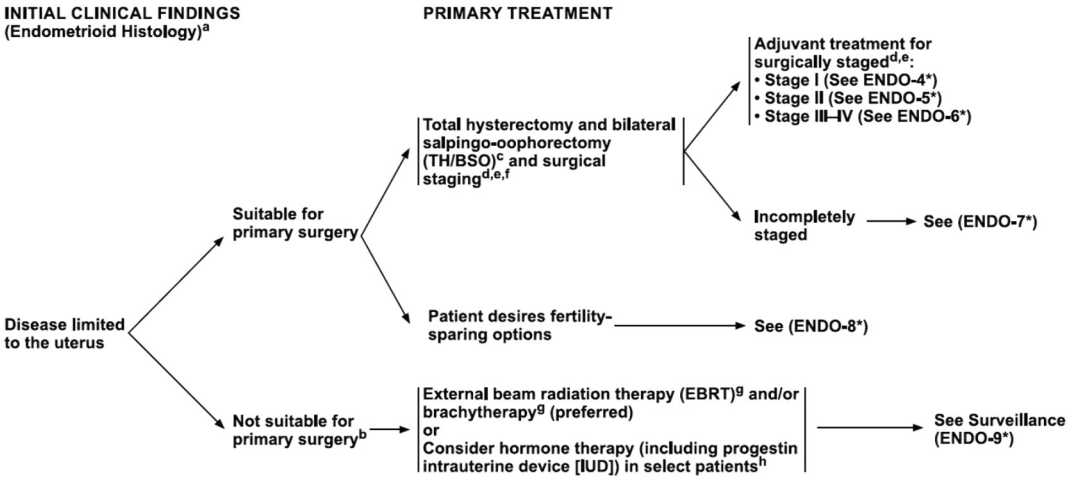
Dal gene profiling alla terapia personalizzata

22-23 Novembre 2023

Casale Monferrato, AL

Hotel Candiani

Endometrial Carcinoma



[a] See (UN-1*) for classification of uterine neoplasms.
[b] Patient declines surgery or is not suitable for surgery based on comorbidities.
[c] See Principles of Pathology and Molecular Analysis (ENDO-A).
[d] Minimally invasive surgery (MIS) is the preferred approach when technically feasible. See Principles of Evaluation and Surgical Staging (ENDO-C).
[e] The degree of surgical staging to assess disease status depends on preoperative and intraoperative findings. Multidisciplinary expertise is recommended. See Principles of Evaluation and Surgical Staging (ENDO-C).
[f] Ovarian preservation may be safe in select premenopausal patients with early-stage endometrioid cancer, normal-appearing ovaries, and no family history of breast/ovarian cancer or Lynch syndrome. Salpingectomy is recommended.
[g] See Principles of Radiation Therapy for Uterine Neoplasms (UN-A*).
[h] See Systemic Therapy for Endometrial Carcinoma (ENDO-D).

*Available online, in these guidelines, at NCCN.org.

Table 2. Staging of endometrial cancer (FIGO: 2009). Reprinted from [5], with permission from Elsevier B.V.

Stage I	Tumour confined to the corpus uteri
I A	NO or less than half myometrial invasion
I B	Invasion equal to or more than half of the myometrium
Stage II	Tumour invades cervical stroma, but does not extend beyond the uterus
Stage III	Local and/or regional spread of the tumour
III A	Tumour invades the serosa of the corpus uteri and/or adnexae
III B	Vaginal and/or parametrial involvement
III C	Metastasis to pelvic and/or para-aortic lymph nodes
III C1	Positive pelvic nodes
III C2	Positive para-aortic lymph nodes with or without positive pelvic lymph nodes
Stage IV	Tumour invades bladder and/or bowel mucosa, and/or distant metastases
IV A	Tumour invasion of bladder and/or bowel mucosa
IV B	Distant metastases, including intra-abdominal metastases and/or inguinal lymph nodes

Multiple factors have been identified for high risk of recurrence in apparent early-stage disease: histological subtype, grade 3 histology, myometrial invasion ≥50%, lymphovascular space invasion (LVSI), lymph node metastases and tumour diameter >2 cm.

In this regard, stage I can be subdivided into three risk categories (reprinted from [5] with permission from Elsevier B.V.):

Low risk:	Stage IA (G1 and G2) with endometrioid type
Intermediate risk:	Stage IA G3 with endometrioid type Stage IB (G1 and G2) with endometrioid type
High risk:	Stage IB G3 with endometrioid type all stages with non-endometrioid type

clinical practice guidelines

Annals of Oncology 24 (Supplement 6): vi33–vi38, 2013
doi:10.1093/annonc/mdt353

Endometrial cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up†

N. Colombo[1], E. Preti[1], F. Landoni[1], S. Carinelli[2], A. Colombo[3], C. Marini[4] & C. Sessa[5], on behalf of the ESMO Guidelines Working Group*

[1]Division of Gynecologic Oncology, European Institute of Oncology, Milan; [2]Department of Pathology, European Institute of Oncology, Milan; [3]Department of Radiotherapy, Manzoni Hospital, Lecco, Italy; [4]Department of Medical Oncology, Oncology Institute of Southern Switzerland, Lugano; [5]Oncology Institute of Southern Switzerland, Bellinzona, Switzerland

Table 4. Adjuvant treatment

Stage I	I A G1–G2	Observation
	IA G3	Observation or vaginal BT - If negative prognostic factor pelvic RT and/or adjunctive chemotherapy could be considered
	I B G1 G2	Observation or vaginal BT - If negative prognostic factor pelvic RT and/or adjunctive chemotherapy could be considered
	IB G3	Pelvic RT - If negative prognostic factor: combination of radiation and chemotherapy could be considered
Stage II	Pelvic RT and vaginal BT - If grade 1–2 tumour, myometrial invasion <50%, negative LVSI and complete surgical staging: brachytherapy alone - If negative prognostic factor: chemotherapy ± radiation	
Stage III–IV	Chemotherapy If positive nodes: sequential radiotherapy If metastatic disease: chemotherapy – RT for palliative treatment	

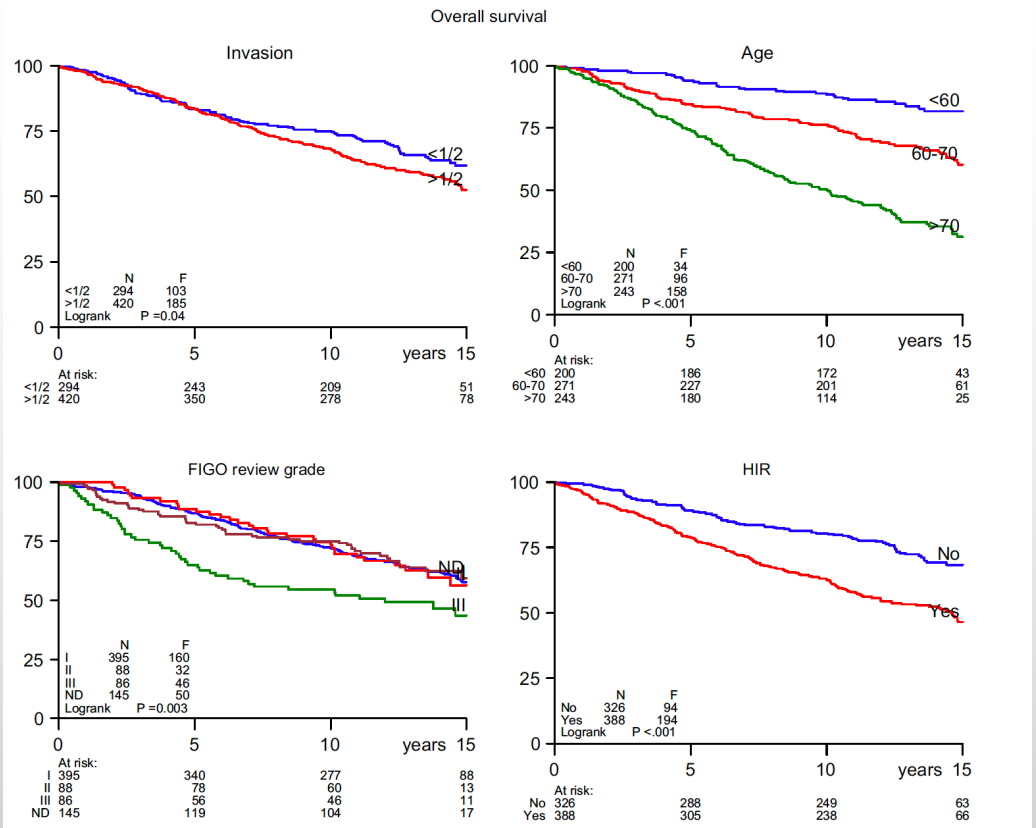


Fig. 3. Probability of overall survival according to prognostic factors: depth of myometrial invasion (<50% vs. ≥50%, top left), patient age (<60 vs. 60–70 vs. >70 years, top right), revised International Federation of Gynecology and Obstetrics (FIGO) Grade (1 vs. 2 vs. 3 vs. ND grade, bottom left), and presence vs. absence of high-intermediate-risk (HIR) features (bottom right).

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0360-3016/$ - see fr
ELSEVIER
doi:10.1016/j.ijrobp.2011.04.013

CLINICAL INVESTIGATION Endome

FIFTEEN-YEAR RADIOTHERAPY OUTCOMES OF THE RANDOMIZED PORTEC TRIAL FOR ENDOMETRIAL CARCINOMA

Carien L. Creutzberg, M.D., Ph.D.,* Remi A. Nout, M.D.,* Marnix L. M. Lybeert, M.D.,†
Carla C. Wárlám-Rodenhuis, M.D.,‡ Jan J. Jobsen, M.D., Ph.D.,§ Jan-Willem M. Mens, M.D
Ludy C. H. W. Lutgens, M.D., Ph.D.,** Elisabeth Pras, M.D., Ph.D.,††
Lonneke V. van de Poll-Franse, Ph.D.,‡‡ and Wim L. J. van Putten, M.Sc.‖
for the PORTEC Study Group

The 15-year results of the PORTEC-1 trial have confirmed the highly significant improvement of local control obtained by EBRT but an absence of survival benefit.

HIR features were shown to be useful for selection for RT (currently VBT).

EBRT should be avoided in patients with low- and intermediate-risk ec.

BJC British Journal of Cancer www.nature.com/bjc

ARTICLE
Clinical Study

Ten-year results of the PORTEC-2 trial for high-intermediate risk endometrial carcinoma: improving patient selection for adjuvant therapy

B. G. Wortman[1], C. L. Creutzberg[1], H. Putter[2], I. M. Jürgenliemk-Schulz[3], J. J. Jobsen[4], L. C. H. W. Lutgens[5], E. M. van der Steen-Banasik[6], J. W. M. Mens[7], A. Slot[8], M. C. Stenfert Kroese[9], B. van Triest[10], H. W. Nijman[11], E. Stelloo[12], T. Bosse[12], S. M. de Boer[1], W. L. J. van Putten[13], V. T. H. B. M Smit[12] and R. A. Nout[1] for the PORTEC Study Group

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

R A Nout, V T H B M Smit, H Putter, I M Jürgenliemk-Schulz, J J Jobsen, L C H W Lutgens, E M van der Steen-Banasik, J W M Mens, A Slot, M C Stenfert Kroese, B N F M van Bunningen, A C Ansink, W L J van Putten, C L Creutzberg, for the PORTEC Study Group

ELSEVIER

Int. J. Radiation Oncology Biol. Phys., Vol. 82, No. 3, pp. 1249–1255, 2012

0360-3016/$ - see front matter

doi:10.1016/j.ijrobp.2011.04.014

CLINICAL INVESTIGATION **Gynecologic Cancer**

EXTERNAL PELVIC AND VAGINAL IRRADIATION VERSUS VAGINAL IRRADIATION ALONE AS POSTOPERATIVE THERAPY IN MEDIUM-RISK ENDOMETRIAL CARCINOMA—A PROSPECTIVE RANDOMIZED STUDY

BENGT SORBE, M.D., PH.D.,* GYÖRGY HORVATH, M.D., PH.D.,† HÅKAN ANDERSSON, M.D., PH.D.,† KARIN BOMAN, M.D., PH.D.,‡ CAROLINE LUNDGREN, M.D., PH.D.,¶ AND BIRGITTA PETTERSSON, M.D., PH.D.§

- Despite a significant locoregional control benefit with combined radiotherapy, no survival improvement was recorded, but increased late toxicity was noted in the intestine, bladder, and vagina.
- Combined RT should probably be reserved for high-risk cases with two or more high-risk factors.
- VBT alone should be the adjuvant treatment option for purely medium-risk cases.

External beam radiotherapy versus vaginal brachytherapy in patients with stage II endometrial cancer: a systematic review and meta-analysis

Narasimhulu DM, et al. Int J Gynecol Cancer 2020;30:797–805.

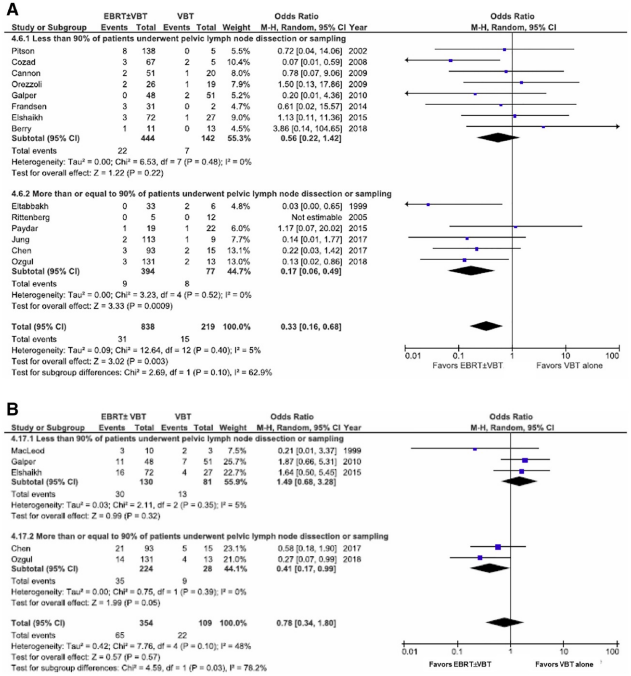


Figure 2 (A) Locoregional recurrence. Patients had stage II endometrial cancer and were treated with external beam radiotherapy with or without vaginal brachytherapy or vaginal brachytherapy. (B). Five year overall survival. Patients had stage II endometrial cancer and were treated with external beam radiotherapy with or without vaginal brachytherapy or vaginal brachytherapy. EBRT, external beam radiotherapy; M-H, Mantel–Haenszel test; VBT, vaginal brachytherapy.

External beam radiotherapy with or without vaginal brachytherapy improved locoregional control of stage II endometrial cancer, regardless of whether pelvic lymph node assessment was performed.

Most women who had recurrence locoregionally had at least one high risk factor (grade 3 tumor, myometrial invasion >50%, or lymphovascular invasion).

Vaginal brachytherapy alone may be sufficient therapy for node negative stage II endometrial cancer without uterine risk factors, while those with uterine riskfactors may be considered for external beam radiotherapy with or without vaginal brachytherapy to improve locoregional control.

VOLUME 33 · NUMBER 26 · SEPTEMBER 10 2015

JOURNAL OF CLINICAL ONCOLOGY

ASCO SPECIAL ARTICLE

Check for updates

Postoperative Radiation Therapy for Endometrial Cancer: American Society of Clinical Oncology Clinical Practice Guideline Endorsement of the American Society for Radiation Oncology Evidence-Based Guideline

G1or G2 grade cancer and < 50% myometrial invasion, when no other high-risk features are present, such as age > 60 and/or LVSI, surveillance without adjuvant radiation therapy is a reasonable option

G1or G2 cancer and ≥ 50% myometrial invasion or G3 cancer and < 50% myometrial invasion, Vaginal brachytherapy is as effective as pelvic radiation therapy at preventing vaginal recurrence and **is preferred.**

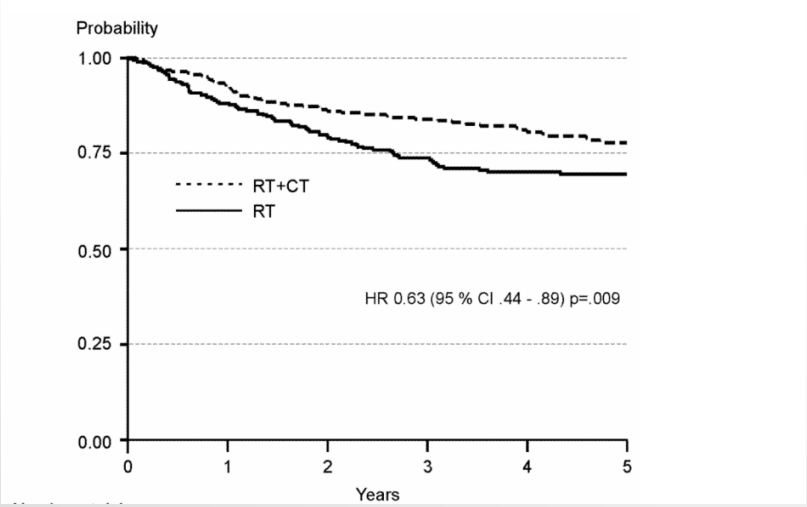
G3 cancer and 50% myometrial invasion or cervical stroma invasion may benefit from pelvic radiation to prevent pelvic recurrence.

High-risk early-stage disease and advanced disease, the ASCO e ASTRO recommend chemotherapy (with or without radiation therapy).

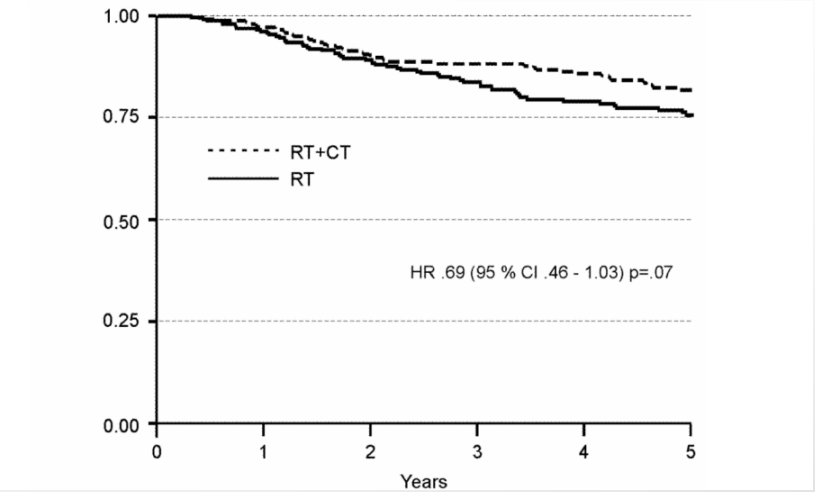
Eur J Cancer. 2010 September ; 46(13): 2422–2431. doi:10.1016/j.ejca.2010.06.002.

NSGO9501/EORTC55991 and MANGO ILIADE-III

Sequential adjuvant chemotherapy and radiotherapy in endometrial cancer - results from two randomised studies



PFR: p=0.009 HR 0.63



OS: p=0.07 HR 0.69

Addition of adjuvant chemotherapy to radiation improves progression-free survival in operated endometrial cancer patients with no residual tumour and high risk profil

Adjuvant chemoradiotherapy versus radiotherapy alone for women with high-risk endometrial cancer (PORTEC-3): final results of an international, open-label, multicentre, randomised, phase 3 trial

*Stephanie M de Boer, Melanie E Powell, Linda Mileshkin, Dionyssios Katsaros, Paul Bessette, Christine Haie-Meder, Petronella B Ottevanger, Jonathan A Ledermann, Pearly Khaw, Alessandro Colombo, Anthony Fyles, Marie-Helene Baron, Ina M Jürgenliemk-Schulz, Henry C Kitchener, Hans W Nijman, Godfrey Wilson, Susan Brooks, Silvestro Carinelli, Diane Provencher, Chantal Hanzen, Ludy C H W Lutgens, Vincent T H B M Smit, Naveena Singh, Viet Do, Romerai D'Amico, Remi A Nout, Amanda Feeney, Karen W Verhoeven-Adema, Hein Putter, Carien L Creutzberg, on behalf of the PORTEC study group**

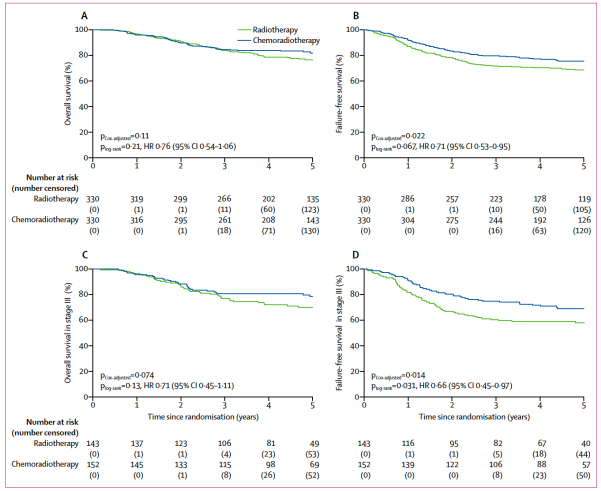


Figure 2: Overall survival and failure-free survival
Kaplan-Meier survival curves for overall survival (A) and failure-free survival (B) in all patients, and for overall survival (C) and failure-free survival (D) of patients with stage III endometrial cancer. $P_{log\text{-}rank}$=unadjusted log-rank p value. $P_{cox\ adjusted}$=p value adjusted for stratification factors. HR=hazard ratio.

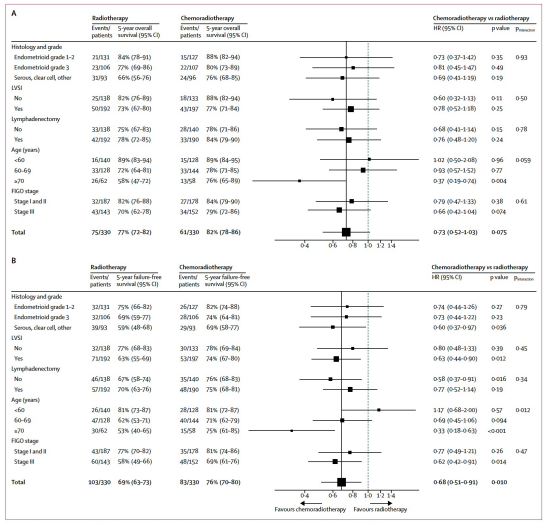


Figure 3: Forest plot of multivariable analysis (treatment by covariate interaction) of overall survival (A) and failure-free survival (B)
For the multivariable analysis the stratification factors (participating group, lymphadenectomy, stage of cancer, and histological type), lymphovascular space invasion, and age were used. HR=hazard ratio. LVSI=lymphovascular space invasion. FIGO=International Federation of Gynecology and Obstetrics.

Chemoradiotherapy significantly improved 5-year failure-free survival for patients with high-risk endometrial cancer compared with radiotherapy alone, but there was no significant difference in overall survival.

For stage III endometrial cancer, a significant improvement in failure free survival was found.

Table 3 Trials of adjuvant radiotherapy and chemotherapy in endometrial cancer

Trial	Enrollment	No. of patients	Eligibility	Randomization	5-Year overall survival	5-Year progression-free survival
Italian[15]	1990–1997	345	Stage I–II with grade 3 tumor; stage III	Pelvic RT vs 5 x CAP	69% vs 66% (NS)	63% vs 63% (NS)
GOG-122[14]	1992–2000	396	Stage III and IV, up to 2 cm residual disease after surgery allowed	Whole abdomen irradiation vs 8 x AP	42% vs 55% (p<0.01)	38% vs 50% (p<0.01)
Japanese[16]	1994–2000	385	Stage I–II with >50% myometrial invasion	Pelvic RT vs 3 x CAP	85% vs 87% (NS)	84% vs 82% (NS)
NSGO/EORTC pooled with Iliade-III[17]	1996–2007	534, NSGO/EORTC 378 and Iliade 156	NSGO/EORTC stage I–III; Iliade stage II–III	Pelvic RT vs pelvic RT and 4 x AP or TAP or TC or TEP	75% vs 82% (p=0.07)	69% vs 78% (p=0.02)
PORTEC-3[20]	2006–2013	686	Stage I–II with high-risk factors, stage III	Pelvic RT vs pelvic RT with 2 x CP followed by 4 x TC	76% vs 81% (p=0.034) Stage III 69% vs 79% Serous EC 53% vs 71%	69% vs 77% (p=0.016) Stage III 58% vs 71% Serous EC 47% vs 60%
GOG-249[18]	2009–2013	601	Stage I–II with high-intermediate or high-risk factors	Pelvic RT vs VBT and 3 x TC	87% vs 85% (NS)	76% vs 76% (NS)
GOG-258[21]	2009–2014	736	Stage III and IVa without residual disease up to 2 cm	Pelvic RT with 2 x CP followed by 4 x TC vs 6 x TC	70% vs 73% (NS)	59% vs 58% (NS)

La radiochemioterapia è stata associata ad una minore incidenza di recidiva vaginale e di recidiva linfonodale pelvica e para-aortica rispetto alla sola chemioterapia, ma con una maggiore incidenza di metastasi a distanza.

Sulla base di questi dati, sembra che la sequenza di radioterapia e chemioterapia debba essere determinata caso per caso e dipenda da criteri istologici e prognostici.

Quando il rischio è principalmente metastatico, può essere preferibile iniziare con la chemioterapia.

Quando è prevalentemente locoregionale (es: stadio IIIB a basso grado), sembra preferibile iniziare un trattamento adiuvante di chemioradioterapia concomitante (regime PORTEC-3)

Improvement in Patient-Reported Outcomes With Intensity-Modulated Radiotherapy (RT) Compared With Standard RT: A Report From the NRG Oncology RTOG 1203 Study

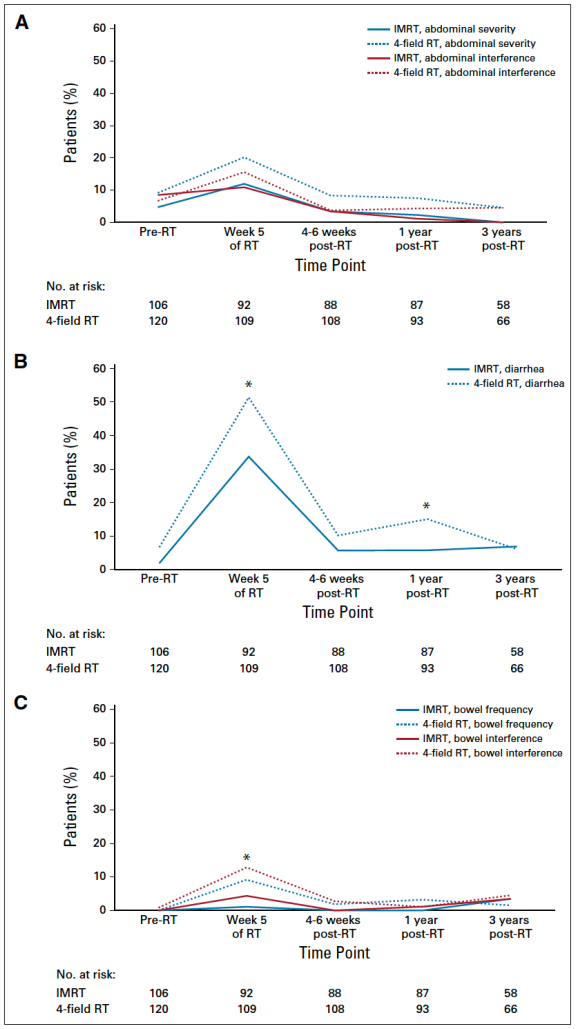


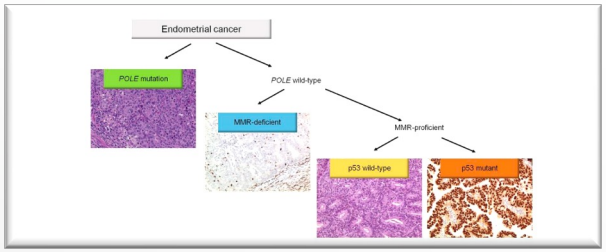
FIG 3. (A) Percentage of patients with high-grade (score ≥ 3) abdominal pain severity and interference by arm. (B) Percentage of patients with high-grade diarrhea frequency by arm. (C) Percentage of patients with high-grade fecal incontinence frequency and interference by arm. IMRT, intensity-modulated radiotherapy; RT, radiotherapy. (*) $P < .05$.

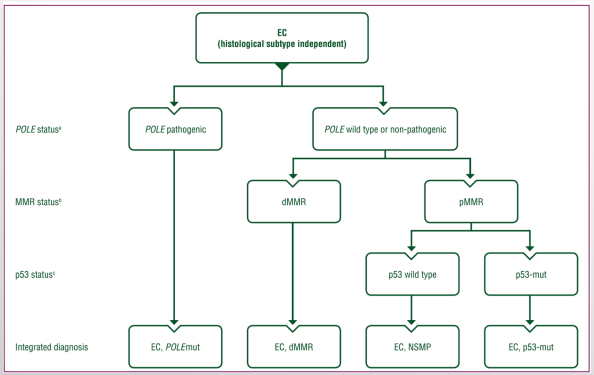
Patients who received IMRT experienced fewer GI AEs than patients who received 4-field pelvic RT:

- frequency of diarrhea (18.2% difference; p = .01)
- frequency of fecal incontinence (8.2% difference; p = .01)
- interference of fecal incontinence (8.5% difference; p = .04).

J Clin Oncol 2020 38:1685-1692

TCGA ha identificato quattro sottogruppi molecolari di EC con differenze prognostiche significative tra loro





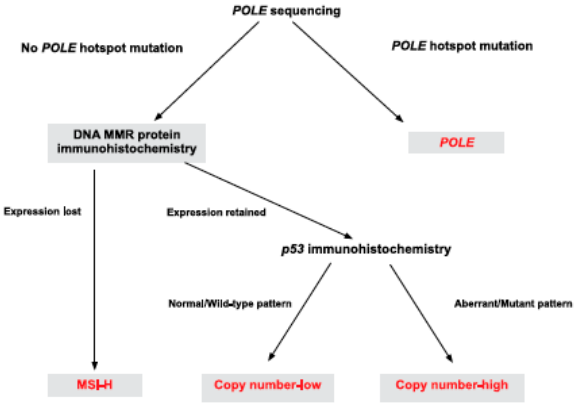
NCCN GUIDELINES®

Uterine Neoplasms, Version 1.2023

Endometrial Carcinoma

PRINCIPLES OF MOLECULAR ANALYSIS

FIGURE 1: PATHOLOGY AND GENOMICS IN ENDOMETRIAL CARCINOMA
(The decision to use molecular testing/classification depends on the availability of resources and the multidisciplinary team of each center)[f,g]



[f] Adapted with permission from Murali R, Delair DF, Bean SM, et al. Evolving roles of histologic evaluation and molecular/genomic profiling in the management of endometrial cancer. J Nat Compr Canc Netw 2018;16:201-209.
[g] Diagnostic algorithm for integrated genomic-pathologic classification of endometrial carcinomas.

	Low risk	Intermediate risk	High-intermediate risk	High risk	Advanced or metastatic
Molecular classification unknown	Stage IA, endometrioid, low-grade, with negative or focal LVSI	Stage IB, endometrioid, low-grade, with negative or focal LVSI Stage IA, endometrioid high-grade, with negative or focal LVSI Stage IA non-endometrioid (serous, clear cell, undifferentiated carcinoma, carcinosarcoma, or mixed) without myometrial invasion	Stage I endometrioid with substantial LVSI, regardless of grade or depth of invasion Stage IB, endometrioid high-grade, regardless of LVSI Stage II endometrioid	Stage III–IVA endometrioid with no residual disease Stage I–IVA non-endometrioid (serous, clear cell, undifferentiated carcinoma, carcinosarcoma, or mixed) with myometrial invasion and no residual disease	Stage II–IVA with residual disease Stage IVB
Molecular classification known*	Stage I–II *POLE*-mutant no residual disease Stage IA, MMRd or NSMP, endometrioid, low-grade, with negative or focal LVSI	Stage IB, MMRd or NSMP, endometrioid, low-grade, with negative or focal LVSI Stage IA, MMRd or NSMP, endometrioid, high-grade, with negative or focal LVSI Stage IA, p53-abnormal, or non-endometroid (serous, clear cell, undifferentiated carcinoma, carcinosarcoma, or mixed), or any combination thereof, without myometrial invasion	Stage I, MMRd or NSMP, endometrioid with substantial LVSI, regardless of grade or depth of invasion Stage IB, MMRd or NSMP, endometrioid high-grade regardless of LVSI Stage II, MMRd or NSMP, endometrioid	Stage III–IVA, MMRd or NSMP, endometrioid with no residual disease Stage I–IVA, MMRd or NSMP, serous, undifferentiated carcinoma, or carcinosarcoma with myometrial invasion and no residual disease Stage I–IVA, p53-abnormal, with myometrial invasion and no residual disease	Stage III–IVA with residual disease of any molecular type Stage IVB of any molecular type

ESGO=European Society of Gynaecological Oncology. ESP=European Society of Pathology. ESTRO=European Society for Radiotherapy and Oncology. LVSI=lymphovascular space invasion. MMRd=mismatch repair deficient. NSMP=non-specific molecular profile. *POLE*=polymerase epsilon. *Insufficient data are available for stage III–IVA *POLE*-mutated endometrial carcinoma and stage I–IVA MMRd or NSMP clear cell carcinoma with myometrial invasion to enable allocation of these patients to a prognostic risk group in the molecular classification. Prospective registries are recommended for these categories.

Table 2: **ESGO–ESP–ESTRO prognostic risk groups defined with and without molecular classification**[53]

Il comitato ESGO/ESTRO/ESP ha recentemente proposto un nuovo sistema di stratificazione del rischio per le pazienti con cancro dell'endometrio che incorpora caratteristiche clinico-patologiche e molecolari per superare i limiti delle classificazione precedentemente adottate.

Crosbie EJ et al Lancet 2022

ESMO GOOD SCIENCE BETTER MEDICINE BEST PRACTICE

ANNALS OF ONCOLOGY driving innovation in oncology

SPECIAL ARTICLE

Endometrial cancer: ESMO Clinical Practice Guideline for diagnosis, treatment and follow-up☆

A. Oaknin[1], T. J. Bosse[2], C. L. Creutzberg[3], G. Giornelli[4], P. Harter[5], F. Joly[6,7], D. Lorusso[8,9], C. Marth[10], V. Makker[11,12], M. R. Mirza[13], J. A. Ledermann[14,15] & N. Colombo[16,17], on behalf of the ESMO Guidelines Committee*

Table 2. EC risk groups

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

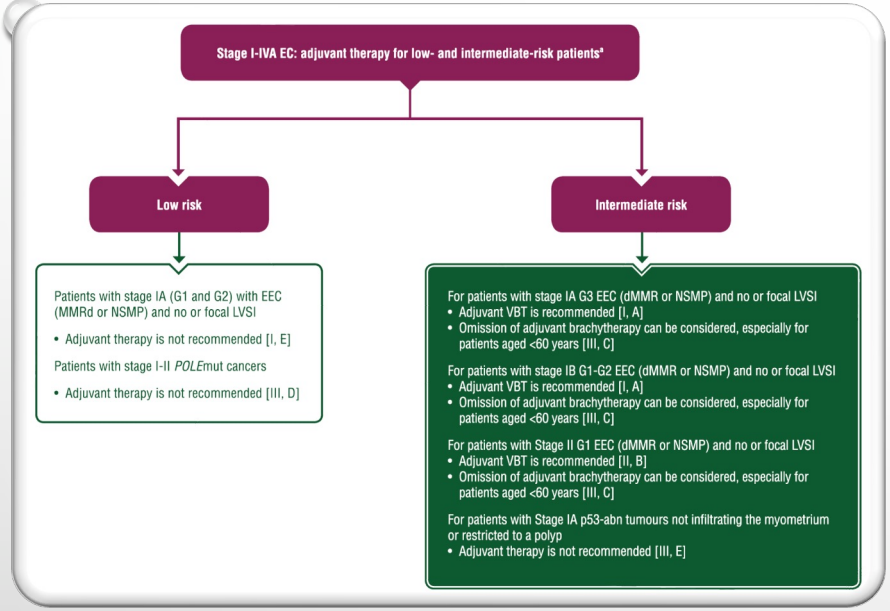
ESMO GOOD SCIENCE BETTER MEDICINE BEST PRACTICE

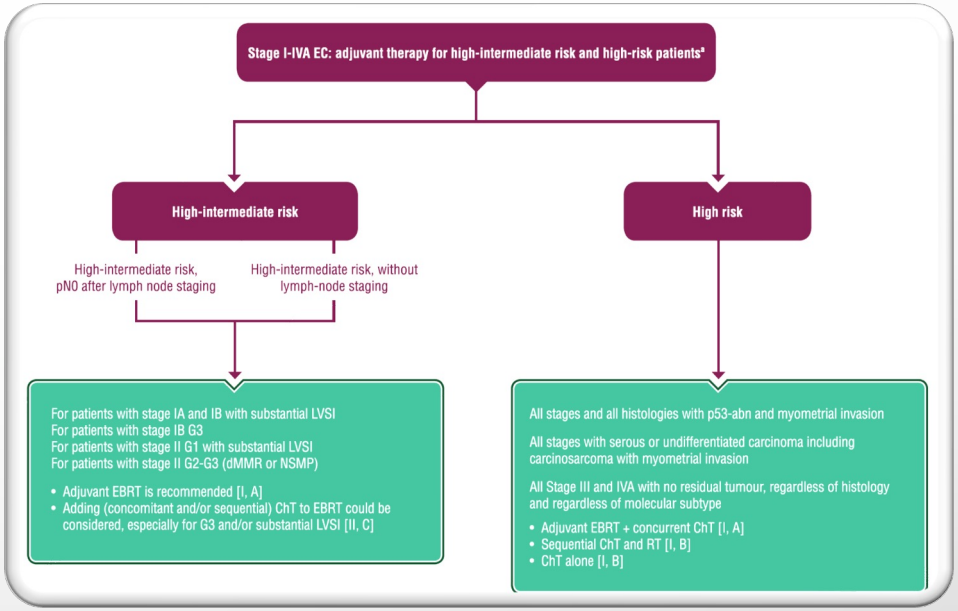
ANNALS OF ONCOLOGY driving innovation in oncology

SPECIAL ARTICLE

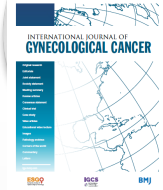
Endometrial cancer: ESMO Clinical Practice Guideline for diagnosis, treatment and follow-up☆

A. Oaknin[1], T. J. Bosse[2], C. L. Creutzberg[3], G. Giornelli[4], P. Harter[5], F. Joly[6,7], D. Lorusso[8,9], C. Marth[10], V. Makker[11,12], M. R. Mirza[13], J. A. Ledermann[14,15] & N. Colombo[16,17], on behalf of the ESMO Guidelines Committee*





L'assegnazione alla corretta classe di rischio ha valore prognostico e può influenzare l'appropriata gestione postoperatoria dei pazienti e la scelta del corretto trattamento adiuvante



Adjuvant therapy for endometrial cancer in the era of molecular classification: radiotherapy, chemoradiation and novel targets for therapy

Table 2 Adjuvant radiotherapy in stage I–II endometrial cancer

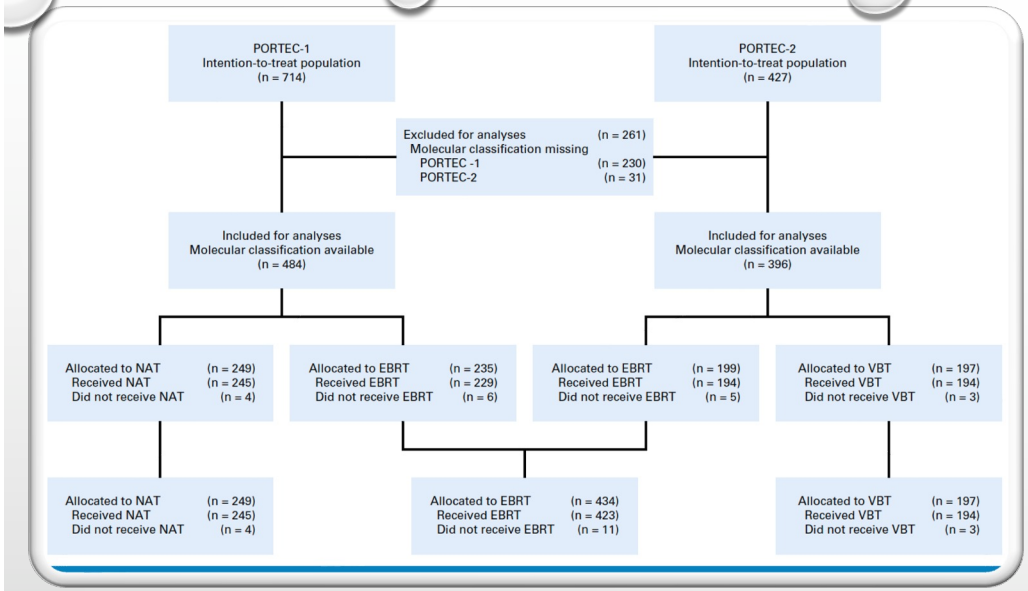
Trial	Enrollment	No. of patients	Surgery	Eligibility	Randomization	Loco-regional recurrence	Survival
GOG-99[4]	1987–1995	392	TH-BSO+LND	Stages IB/C; stage II (occult)	EBRT vs NAT	2 years: 3% vs 12% (p=0.007)	4 years: 86% vs 92% (p=0.0557)
PORTEC-1[5]	1990–1997	714	TH-BSO	Stages IB G2-3; stages IC G1-2	EBRT vs NAT	5 years: 4% vs 14% (p<0.001)	5 years: 85% vs 81% (p=0.31)
Swedish[7]	1997–2008	527	TH-BSO	Stage I intermediate risk	VBT vs VBT+EBRT	5 years: 5% vs 1.5% (p=0.013)	5 years: 90% vs 89% (p=0.55)
ASTEC/EN.5[6]	1996–2008	905	TH-BSO±LND	Stages IA/B G3; IC; stage II; serous/CC	EBRT vs NAT	5 years: 6% vs 3% (p=0.02)	5 years: 84% vs 84% (p=0.98)
PORTEC-2[8]	2002–2006	427	TH-BSO	Age >60 and stage IB G3 or stages IC G1-2; stage IIA	EBRT vs VBT	5 years: 5% vs 2% (p=0.17)	5 years: 85% vs 80% (p=0.57)

Table 3 Trials of adjuvant radiotherapy and chemotherapy in endometrial cancer

Trial	Enrollment	No. of patients	Eligibility	Randomization	5-Year overall survival	5-Year progression-free survival
Italian[15]	1990–1997	345	Stage I–II with grade 3 tumor; stage III	Pelvic RT vs 5 x CAP	69% vs 66% (NS)	63% vs 63% (NS)
GOG-122[14]	1992–2000	396	Stage III and IV, up to 2 cm residual disease after surgery allowed	Whole abdomen irradiation vs 8 x AP	42% vs 55% (p<0.01)	38% vs 50% (p<0.01)
Japanese[16]	1994–2000	385	Stage I–II with >50% myometrial invasion	Pelvic RT vs 3 x CAP	85% vs 87% (NS)	84% vs 82% (NS)
NSGO/EORTC pooled with Iliade-III[17]	1996–2007	534, NSGO/EORTC 378 and Iliade 156	NSGO/EORTC stage I–III; Iliade stage II–III	Pelvic RT vs pelvic RT and 4 x AP or TAP or TC or TEP	75% vs 82% (p=0.07)	69% vs 78% (p=0.02)
PORTEC-3[20]	2006–2013	686	Stage I–II with high-risk factors, stage III	Pelvic RT vs pelvic RT with 2 x CP followed by 4 x TC	76% vs 81% (p=0.034) Stage III 69% vs 79% Serous EC 53% vs 71%	69% vs 77% (p=0.016) Stage III 58% vs 71% Serous EC 47% vs 60%
GOG-249[18]	2009–2013	601	Stage I–II with high-intermediate or high-risk factors	Pelvic RT vs VBT and 3 x TC	87% vs 85% (NS)	76% vs 76% (NS)
GOG-258[21]	2009–2014	736	Stage III and IVa without residual disease up to 2 cm	Pelvic RT with 2 x CP followed by 4 x TC vs 6 x TC	70% vs 73% (NS)	59% vs 58% (NS)

Significant benefit of added adjuvant chemotherapy to RT in patients with p53 mutational expression, whereas those with POLE mutation had almost 100% recurrence-free survival in both arms.

Mismatch repair deficiency cancers do not seem to benefit from added chemotherapy, whereas those with no specific molecular profile had slightly higher relapse-free survival with chemoradiation, comparable to the overall PORTEC-3 trial outcomes



Original Reports | Gynecologic Cancer

Check for updates

Molecular Classification Predicts Response to Radiotherapy in the Randomized PORTEC-1 and PORTEC-2 Trials for Early-Stage Endometrioid Endometrial Cancer

Nanda Horeweg, MD, PhD[1]; Remi A. Nout, MD, PhD[1,2]; Ina M. Jürgenliemk-Schulz, MD, PhD[3]; Ludy C.H.W. Lutgens, MD, PhD[4]; Jan J. Jobsen, MD, PhD[5]; Marie A.D. Haverkort, MD[6]; Jan Willem M. Mens, MD[2]; Annerie Slot, MD[7]; Bastiaan G. Wortman, MD, PhD[1,8]; Stephanie M. de Boer, MD, PhD[1]; Ellen Stelloo, PhD, MSc[9]; Karen W. Verhoeven-Adema, PhD[10]; Hein Putter, PhD[11]; Vincent T.H.B.M. Smit, MD, PhD[9]; Tjalling Bosse, MD, PhD[9]; and Carien L. Creutzberg, MD, PhD[1]; for the PORTEC Study Group

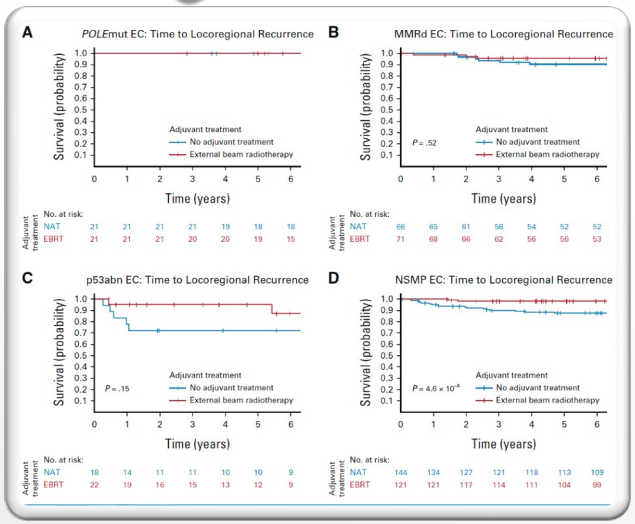
J Clin Oncol 00:1-12, 2023

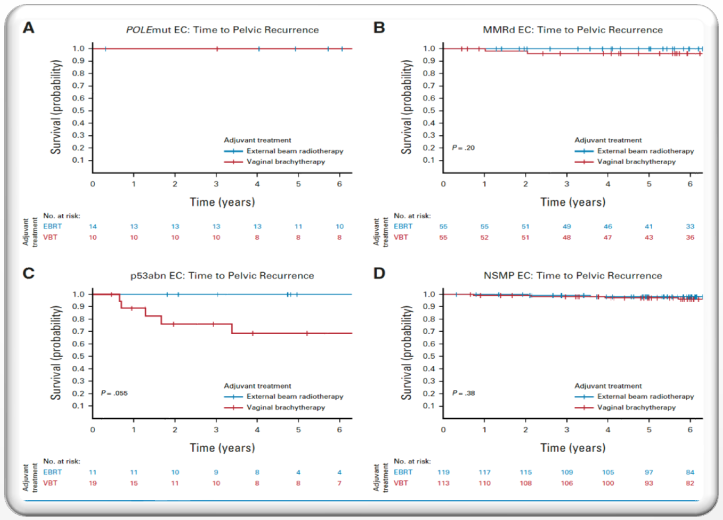
The majority were FIGO-2009 stageData of the randomized PORTEC-1 trial (n 714) comparing pelvic EBRT with no adjuvant therapy in early-stage intermediate-risk EC and the PORTEC-2 trial (n 427) comparing VBT with EBRT in early-stage high-intermediate-risk EC were used.

Locoregional (including vaginal and pelvic) recurrence-free survival was compared between treatment groups across the four molecular classes

Stage I EEC (97.2%)

The median follow-up11.3 years



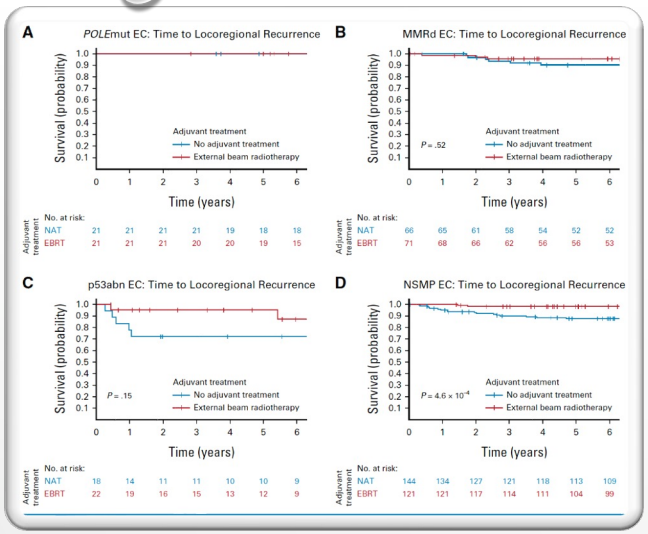


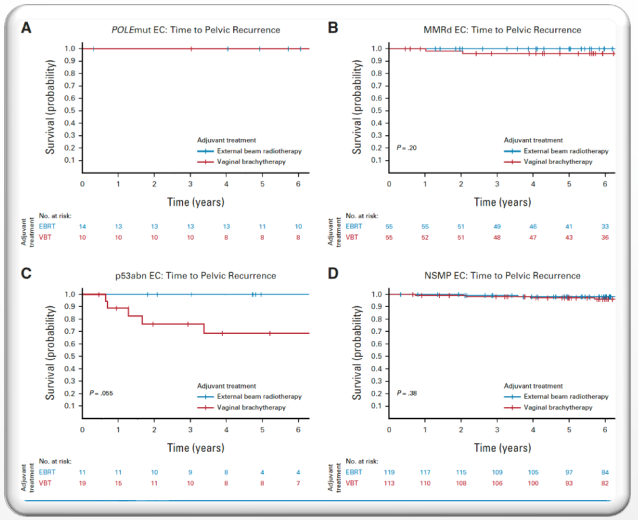
No locoregional recurrences were observed in POLEmut EC

In MMRd) EC, LRRFS locoregional recurrence-free survival was similar after EBRT (94.2%), VBT (94.2%), and no adjuvant therapy (90.3%).

In EC with a p53 abnormality, EBRT (96.9%) had a substantial benefit over VBT (64.3%) and no adjuvant therapy (72.2%).

In EC with no specific molecular profile (NSMP EC), both EBRT (98.3%) and VBT (96.2%) yielded better locoregional control than no adjuvant therapy (87.7%; P < .0001).





The molecular classification of EC predicts response to radiotherapy in stage I EEC and may guide adjuvant treatment decisions.

Omitting radiotherapy seems to be safe in POLEmut EC

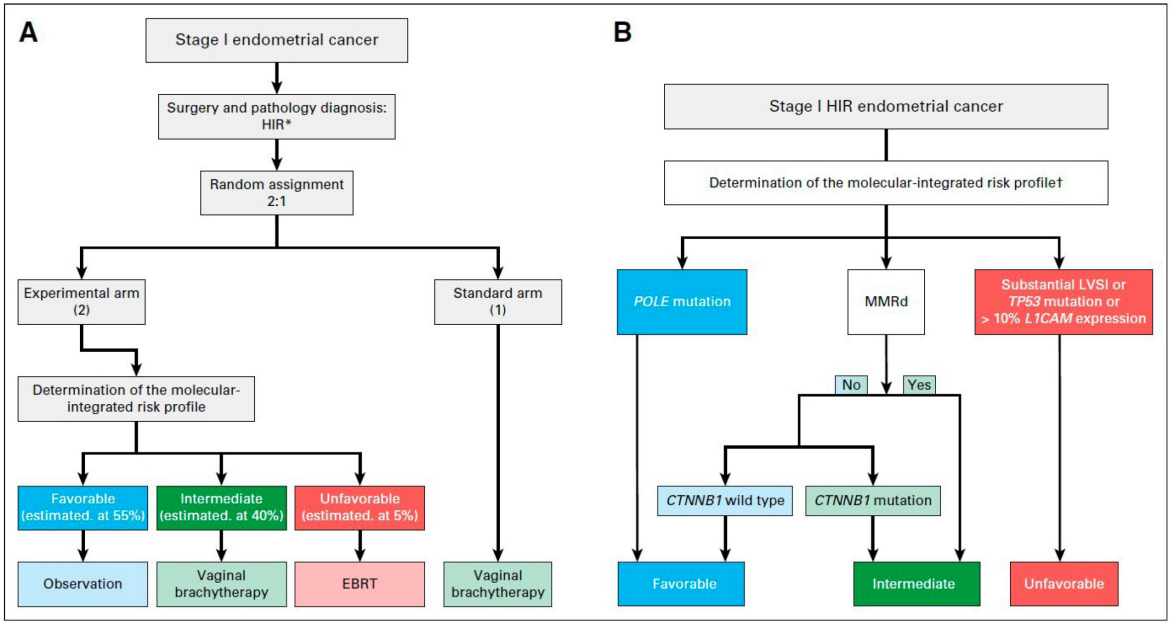
The benefit of radiotherapy seems to be limited in MMRd EC

EBRT yields a significantly better locoregional recurrence-free survival than VBT or no adjuvant therapy in p53abn EC

VBT is the treatment of choice for NSMP EC as it is as effective as EBRT and significantly better than no adjuvant therapy for locoregional tumor control

Clinical trial

PORTEC-4a: international randomized trial of molecular profile-based adjuvant treatment for women with high-intermediate risk endometrial cancer



The primary endpoint is vaginal recurrence.

Randomization between standard or individualized treatment based on the molecular risk profile.

PORTEC-4a will show if omitting treatment in cases of favorable molecular profiles is safe and cost-effective

ELSEVIER

International Journal of Radiation Oncology*Biology*Physics

Volume 109, Issue 2, 1 February 2021, Pages 396-412

Clinical Investigation

Current Status of Clinical Trials for Cervical and Uterine Cancer Using Immunotherapy Combined With Radiation

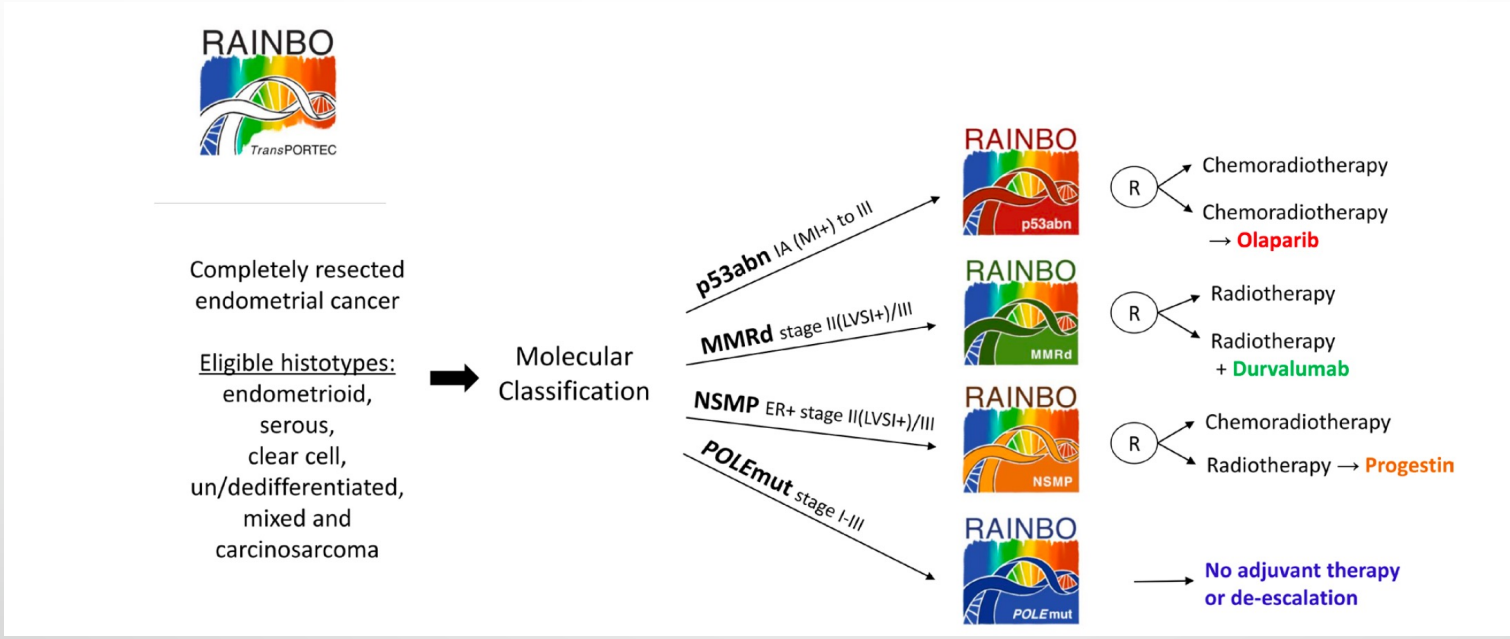
Brandon A. Dyer MD *, Christine H. Feng MD †, Ramez Eskander MD ‡, Andrew B. Sharabi MD, PhD †, Loren K. Mell MD †, Michael McHale MD ‡, Jyoti S. Mayadev MD †

- Multiple clinical trials both published and underway investigate the role of IO and RT in gynecologic cancers.
- Combination IO and RT can promote an enhanced immunogenic environment through increased antigen presentation, phagocytosis, cell death, and immune-mediated tumor surveillance.
- In an effort to promote systemic antitumor immune responses ablative RT doses can be used to enhance T cell activation and antigen presentation.
- With an improved understanding of tumor biology, checkpoint biology, and immune evasion we will be able to time and deliver therapy to maximize tumor outcomes, promote in situ antitumor immune responses, and enhance patient outcomes

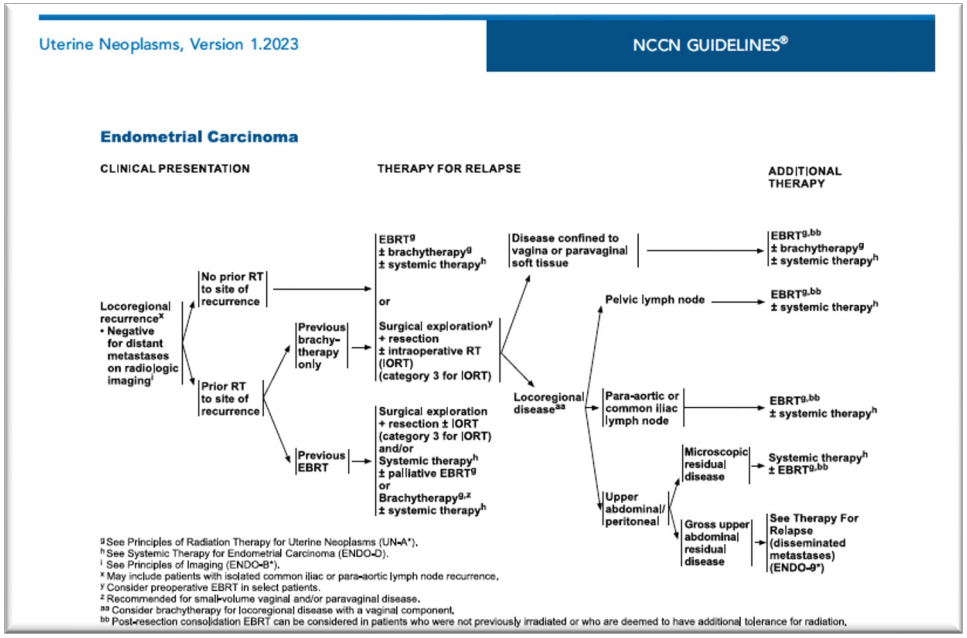
Clinical trial

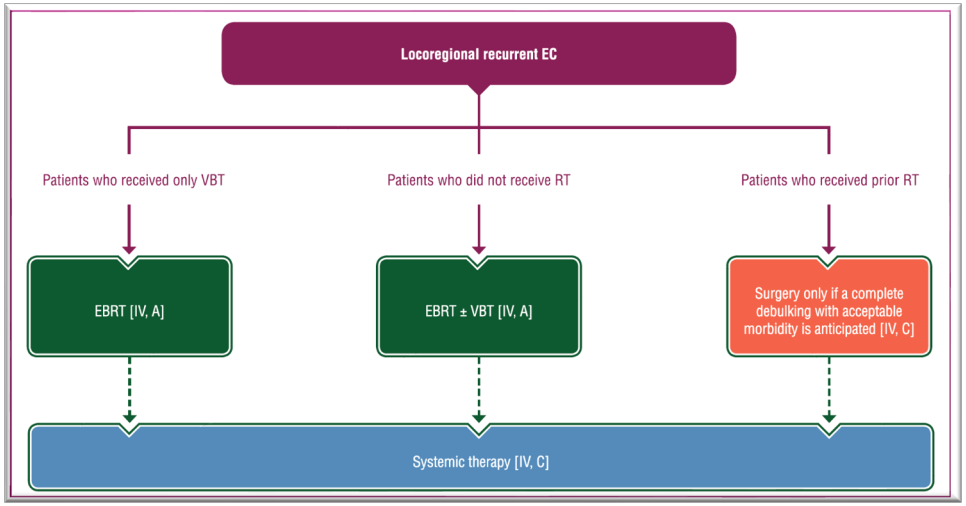
Refining adjuvant treatment in endometrial cancer based on molecular features: the RAINBO clinical trial program

RAINBO Research Consortium



The four clinical trials will have different completion dates; main results are expected from 2028.


Uterine Neoplasms, Version 1.2023
NCCN GUIDELINES®
Endometrial Carcinoma
CLINICAL PRESENTATION
THERAPY FOR RELAPSE
ADDITIONAL THERAPY
Locoregional recurrence[x] • Negative for distant metastases on radiologic imaging[i]
No prior RT to site of recurrence
Prior RT to site of recurrence
Previous brachy-therapy only
Previous EBRT
EBRT[g] ± brachytherapy[g] ± systemic therapy[h]
or
Surgical exploration[y] + resection ± intraoperative RT (IORT) (category 3 for IORT)
Surgical exploration + resection ± IORT (category 3 for IORT) and/or Systemic therapy[h] ± palliative EBRT[g] or Brachytherapy[g,z] ± systemic therapy[h]
Disease confined to vagina or paravaginal soft tissue
Locoregional disease[aa]
Pelvic lymph node
Para-aortic or common iliac lymph node
Upper abdominal/ peritoneal
Microscopic residual disease
Gross upper abdominal residual disease
EBRT[g,bb] ± brachytherapy[g] ± systemic therapy[h]
EBRT[g,bb] ± systemic therapy[h]
EBRT[g,bb] ± systemic therapy[h]
Systemic therapy[h] ± EBRT[g,bb]
See Therapy For Relapse (disseminated metastases) (ENDO-9*)
[g] See Principles of Radiation Therapy for Uterine Neoplasms (UN-A*).
[h] See Systemic Therapy for Endometrial Carcinoma (ENDO-D).
[i] See Principles of Imaging (ENDO-B*).
[x] May include patients with isolated common iliac or para-aortic lymph node recurrence.
[y] Consider preoperative EBRT in select patients.
[z] Recommended for small-volume vaginal and/or paravaginal disease.
[aa] Consider brachytherapy for locoregional disease with a vaginal component.
[bb] Post-resection consolidation EBRT can be considered in patients who were not previously irradiated or who are deemed to have additional tolerance for radiation.


Locoregional recurrent EC
Patients who received only VBT
Patients who did not receive RT
Patients who received prior RT
EBRT [IV, A]
EBRT ± VBT [IV, A]
Surgery only if a complete debulking with acceptable morbidity is anticipated [IV, C]
Systemic therapy [IV, C]

cancers

MDPI

Article

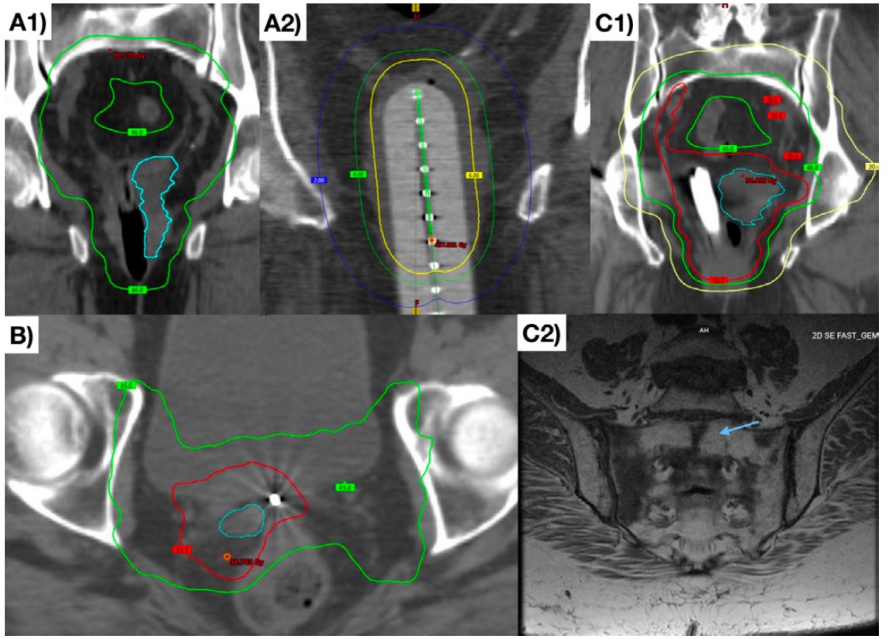
Stages I–III Inoperable Endometrial Carcinoma: A Retrospective Analysis by the Gynaecological Cancer GEC-ESTRO Working Group of Patients Treated with External Beam Irradiation and 3D-Image Guided Brachytherapy †

Ángeles Rovirosa [1,2,*], Yaowen Zhang [3], Kari Tanderup [4], Carlos Ascaso [1,2], Cyrus Chargari [5], Elzbieta Van der Steen-Banasik [6], Piotr Wojcieszek [7], Magdalena Stankiewicz [7], Dina Najjari-Jamal [8], Peter Hoskin [9], Kathy Han [10], Barbara Segedin [11], Richard Potter [12] and Erik Van Limbergen [13] on behalf of the Endometrial Task Group

Original research

Outcomes and toxicity after salvage radiotherapy for vaginal relapse of endometrial cancer

Lucas Gomes Sapienza ,[1,2] Matthew S Ning,[3] Rosinda de la Pena,[4] Laura Kollar McNew,[5] Anuja Jhingran ,[3] Larissa Georgeon,[6] Nabila Rasool,[4] Maria José Leite Gomes,[7] Eyad Abu-Isa,[5] Glauco Baiocchi [8]



Salvage radiotherapy imparts excellent loco-regional control for vaginal relapses of endometrial cancer and should entail combination external-beam radiotherapy and vaginal brachytherapy

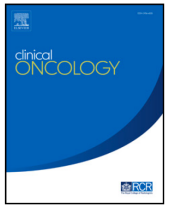
Local control is typically in the 80% to 90% range

Clinical Oncology 30 (2018) 110–115

Contents lists available at ScienceDirect

Clinical Oncology

journal homepage: www.clinicaloncologyonline.net



Overview

Re-irradiation in Gynaecological Malignancies: A Review

A.H. Sadozye

Beatson West of Scotland Cancer Centre, Gartnavel General Hospital, Glasgow, UK

Abstract

Re-irradiation in gynaecological malignancies has become an increasingly frequent consideration. This can be delivered in multiple settings, with the most common being a patient with a history of cervical cancer developing a new vaginal cancer or endometrial cancer with local recurrence after hysterectomy and adjuvant pelvic radiation. A systematic review of the literature has unearthed a handful of reports, most delivering brachytherapy, with a small number on both external beam radiotherapy and stereotactic ablative radiotherapy. A detailed review of these papers suggests that it is not possible to draw any firm conclusions or put forward guidelines for this challenging area of gynaecological oncology. Here the author has provided a brief account of each paper, followed by a discussion of the literature, aiming to outline some very broad principles for management. It is recommended that such patients be referred to centres that treat high volumes of gynaecological malignancies, as the experience of the treating oncologist may be the most important factor in the management of these patients.

Clinical Oncology 29 (2017) 378–384

Contents lists available at ScienceDirect

Clinical Oncology

journal homepage: www.clinicaloncologyonline.net

Original Article

The Role of Stereotactic Ablative Body Radiotherapy in Gynaecological Cancers: A Systematic Review

L.C. Mendez, E. Leung, P. Cheung, L. Barbera

Department of Radiation Oncology, Sunnybrook Health Science Centre, University of Toronto, Toronto, Ontario, Canada

Table 1
Summary of studies, dose and local control of stereotactic ablative body radiotherapy (SABR) in different clinical scenarios (the five patients with vaginal or vulvar cancers are not reported)

Reference	Design	Number of patients	Total number of patients	EBRT	Number of patients with respective BED (α/β=10)	Median SABR BED	PTV (cm^3)	Follow-up (months)	Local control % (no. patients)	Combined local control
(A) SABR as a cervical boost										
[11]	Retrospective	11	34	Yes	11 48 Gy	39.1 Gy	31–68	6	100 (11)	91%
[12]	Retrospective	9		Yes	1 19.2 Gy, 1 19.5 Gy, 2 28 Gy, 1 33.6 Gy, 3 39.1 Gy, 1 51.3 Gy		NR	NR	77.8 (7)	
[13]	Retrospective	6		Yes	5 28 Gy, 1 32.1 Gy		NR	14	100 (6)	
[14]	Retrospective	4		Yes	1 7.5 Gy, 1 22.5 Gy, 1 35.5 Gy, 1 37.5 Gy		11–174‖	4	100 (4)	
[15]	Retrospective	2		Yes	2 28 Gy		NR	12	100 (2)	
[16]	Case report	1		Yes	1 33.6 Gy		NR	22	100 (1)	
[17]	Retrospective	1		Yes	1 22.5 Gy		258	13	0 (0)	
(B) SABR as an endometrial boost										
[18]	Retrospective	11	13	Yes	9 45 Gy, 1 38,4 Gy, 1 30 Gy	45 Gy	NR	18	55 (6)	53%
[14]	Retrospective	1		Yes	1 31.2 Gy		45.8‖	4	100 (1)	
[17]	Retrospective	1		Yes	1 22.5 Gy		180	15	0% (0)	
(C) SABR for pelvic or para-aortic lymph node metastases										
[19]	Retrospective	83#	83*	43 patients§	44 89.7 Gy; 19 100–137 Gy; 33 51–79 Gy	89.7 Gy	NR	20.4	80 (67)	83%
[20]	Retrospective	52		12 patients	Not possible to define		NPD	31	92 (48)	
[21]	Retrospective	30		4 patients	5 69.3 Gy; 1 29.9 Gy; 2 60 Gy; 5 79 Gy; 3 84.3 Gy; 11 89 Gy; 2 100 Gy; 1 112 Gy		1.3–57.3	19	67 (20)	
[22]	Retrospective	13		NR	Not possible to define		NR	4.6	100 (13)	
[23]	Phase I	6		NPD	Not possible to define		NPD	15.5	NPD	
[24]	Retrospective	5		4 patients	1 28 Gy, 4 45 Gy		NPD	16	80 (4)	
(D) Adjuvant SABR										
[25]	Retrospective	26	38†	Yes	26 23.8 Gy	23.8 Gy	NR	47	92 (24)	92%
[26]	Retrospective	23		NR	23 28.8 Gy		NR	132	NPD	
[15]	Retrospective	12		Yes	12 23.8 Gy		NR	12.6	92(11)	
(E) Salvage SABR to pelvic recurrences (non-nodal)										
[27]	Retrospective	19	57‡	Yes	12 22.5 Gy; 2 60 Gy; 2 15 Gy; 1 47.6 Gy;1 30 Gy; 1 12 Gy	22.5 Gy	37–619	22	81 (16)	86%
[28]	Retrospective	16		Yes, 15/16	Not possible to define. 15–40 Gy in 3–5		25–310¶	12	93.7 (15)	
[17]	Retrospective	9		Yes	9 22.5 Gy		55–619	20	77 (7)	
[29]	Retrospective	8		Yes	Not possible to define		Not possible to define			
[30]	Retrospective	5		Yes	5 57.6 Gy		NR	10.6	NPD	
[31]	Retrospective	5		Yes	1 32 Gy, 1 36 Gy, 1 46 Gy, 1 57.6 Gy and 1 61.7 Gy		20–217	9	80 (4)	
[14]	Retrospective	4		Yes	3 37.5 Gy, 1 42.6 Gy		98–348‖	4	75 (3)	

The current literature suggests that SABR is an effective safe modality for nodal relapses.

Local control in non-operable endometrial tumours receiving SABR was 53%.

In recurrent pelvic tumours, however, SABR seems to be associated with high rates of gastrointestinal toxicity.

Dr.ssa Laura Masini

3°Edizione

I tumori femminili

Dal gene profiling alla terapia personalizzata

22-23 Novembre 2023

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