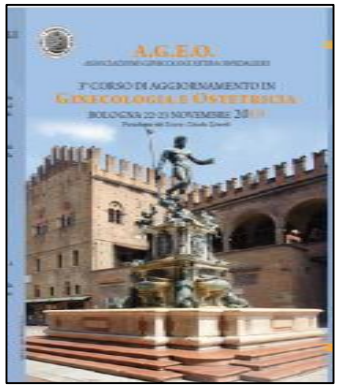


Oncologia ginecologica: cosa deve sapere lo specialista ambulatoriale?

P. De Iaco
Ginecologia Oncologica
Policlinico S.Orsola-Malpighi, Bologna

- **CERVIX**
- ENDOMETRIUM
- OVARY

VACCINAZIONE CONTRO IL PAPILLOMA VIRUS (HPV)
Giovani donne (18-26 anni)
Donne trattate per lesioni HPV correlate

CHE COSA OFFRE IL SERVIZIO SANITARIO REGIONALE ALLE DONNE ADULTE?

Il vaccino attualmente utilizzato in Emilia-Romagna è efficace nei confronti di 9 tipi di papilloma virus umano (i sierotipi 6, 11, 16, 18, 31, 33, 45, 52, 58) e protegge da quasi il 90% dei tumori del collo dell'utero, intorno all'80% degli altri tipi di tumori HPV correlati e da quasi il 100% dei condilomi.

La vaccinazione viene offerta gratuitamente:

- **fino al compimento dei 26 anni a tutte le giovani donne non ancora vaccinate per HPV;** a partire dal 2019 le ragazze di 25 anni riceveranno l'invito alla vaccinazione gratuita.
- **a tutte le donne, fino ai 65 anni di età, con storia documentata di trattamento per lesioni cervicali** di grado elevato (CIN2+) negli ultimi 12 mesi.

Per tutte le persone adulte, al di fuori dell'offerta gratuita, è comunque possibile effettuare la vaccinazione presso gli ambulatori vaccinali delle Aziende Usl, con pagamento di un prezzo agevolato.
Il costo a carico degli utenti è significativamente inferiore a quello praticato privatamente e corrisponde al puro costo del vaccino per l'Azienda Usl, più il costo della vaccinazione secondo il tariffario regionale.

SI PUÒ ESEGUIRE LA VACCINAZIONE IN GRAVIDANZA?

Il vaccino non deve essere somministrato alle donne in gravidanza. Se una ragazza scopre di essere incinta dopo aver iniziato il ciclo vaccinale deve aspettare la fine della gravidanza prima di completarlo. Gli studi clinici effettuati finora non hanno dimostrato particolari problemi per la donna o per il feto. Sono comunque in corso ulteriori approfondimenti.

ESTRO
European Society for
RADIOTHERAPY
& ONCOLOGY

ESGO
European Society of
Gynaecological Oncology

European
Society of
Pathology

CERVICAL CANCER

GUIDELINES

5.4 Management of stages T1b1/T2a1

5.4.1 General recommendation

B	Treatment strategy should aim for the avoidance of combining radical surgery and radiotherapy because of the highest morbidity after combined treatment.

5.4.2 Negative lymph nodes on radiological staging

5.4.2.1 Surgical treatment

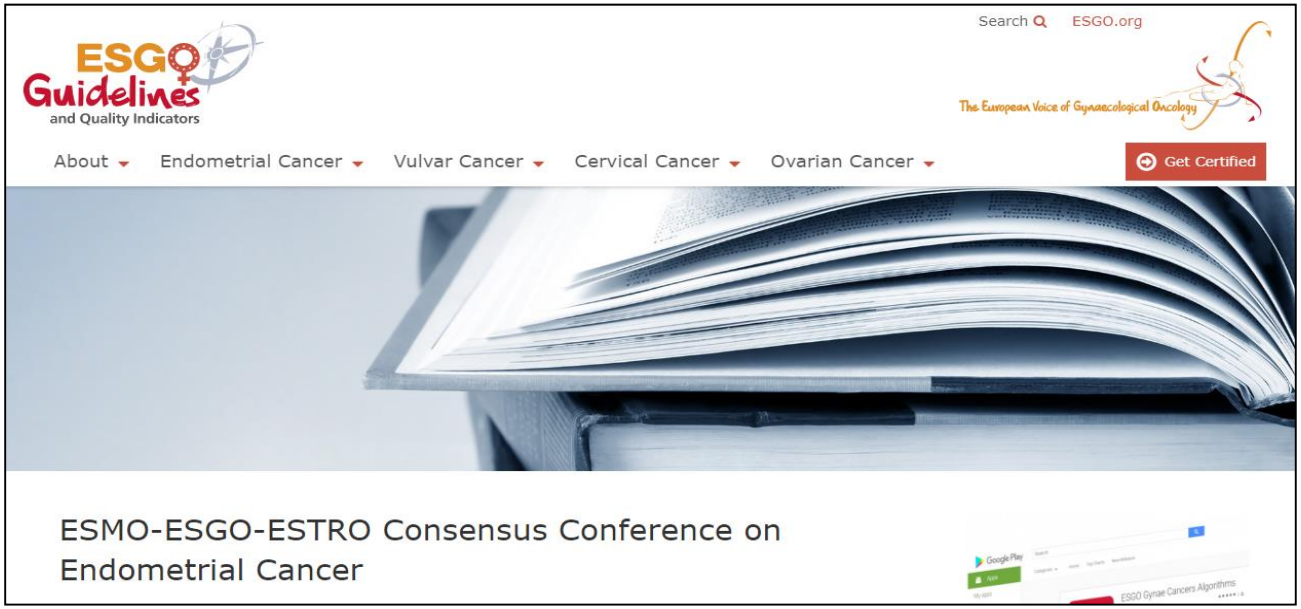
B	Radical surgery by a gynecologic oncologist is the preferred treatment modality. Minimally invasive approach is favored.
B	The standard LN staging procedure is systematic pelvic lymphadenectomy. SN biopsy before pelvic lymphadenectomy is strongly recommended. Combination of blue dye with radiocolloid or use of indocyanine green alone is the recommended technique.

5.7 Management of locally advanced cervical cancer

5.7.1 Stage T1b2/T2a2 and negative lymph nodes on radiological staging

B	Treatment strategy should aim for avoiding the combination of radical surgery and postoperative external radiotherapy because of the significant increase in morbidity and no evident impact on survival.
A	Definitive platinum-based chemoradiotherapy and brachytherapy are the preferred treatment (see Principles of radiotherapy).
C	PALN dissection, at least up to inferior mesenteric artery, may be considered before chemoradiotherapy and brachytherapy. PLN dissection is not required.

- CERVIX
- **ENDOMETRIUM**
- OVARY



Radiotherapy and Oncology 117 (2015) 559–581

Contents lists available at ScienceDirect

Radiotherapy and Oncology

journal homepage: www.thegreenjournal.com

ESMO-ESGO-ESTRO Consensus guidelines

ESMO–ESGO–ESTRO consensus conference on endometrial cancer: Diagnosis, treatment and follow-up ☆

Nicoletta Colombo [a,*], Carien Creutzberg [b], Frederic Amant [c,d], Tjalling Bosse [e], Antonio González-Martín [f,g], Jonathan Ledermann [h], Christian Marth [i], Remi Nout [j], Denis Querleu [k,l], Mansoor Raza Mirza [m], Cristiana Sessa [n], The ESMO–ESGO–ESTRO Endometrial Consensus Conference Working Group [1]

Pre-operative work up (1)

- Mandatory work-up must include
  - **Family history**;
  - General assessment and inventory of commorbidities;
  - **Geriatric assessment**, if appropriate;
  - **Clinical examination**;
  - Including pelvic examination;
  - Transvaginal or trans rectal ultrasound; and
  - Complete pathology assessment (histotype and grade) of an endometrial biopsy or curettage

Colombo N et al. ESMO-ESGO-ESTRO consensus conference on endometrial cancer: Radiother Oncol. 2015

Surgical management of apparent stage I endometrial cancer

- Standard surgery is total hysterectomy with bilateral salpingoovariectomy without vaginal cuff
- **Minimally invasive surgery** is recommended in the surgical management of low-and intermediate-risk endometrial cancer
- **Ovarian preservation can be considered in patients younger than 45** years old with grade 1 endometrioid endometrial cancer with myometrial invasion < 50% and no obvious ovarian or other extrauterine disease.
- In cases of ovarian preservation, salpingectomy is recommended
- **Ovarian preservation is not recommended for patients with cancer family history involving ovarian cancer risk** (eg BRCA mutation, Lynch syndrome, etc). **Genetic counselling/ testing should be offered**.

Colombo N et al. ESMO-ESGO-ESTRO consensus conference on endometrial cancer: Radiother Oncol. 2015

National Comprehensive Cancer Network®

NCCN Guidelines Version 4.2019
Endometrial Carcinoma

NCCN Guidelines Index
Table of Contents
Discussion

PRINCIPLES OF EVALUATION AND SURGICAL STAGING

Principles of Surgical Staging for Endometrial Cancer[1-15]

- TH/BSO,and lymph node assessment is the primary treatment of apparent uterine-confined endometrial carcinoma, unless patients desire (and are candidates for) fertility-sparing options (See ENDO-8).[1-3] Select patients with metastatic endometrial carcinoma are also candidates for hysterectomy. (See Principles of Pathology [ENDO-A])

Sentinel lymph node (SLN) mapping may be considered

a Cochrane Database Systematic Review, and population-based surgical studies support that minimally invasive techniques are preferred in this setting due to a lower rate of surgical site infection, transfusion, venous thromboembolism, decreased hospital stay, and lower cost of care, without compromise in oncologic outcome.[4-9]

- The lymph node assessment includes evaluation of the nodal basins that drain the uterus, and often comprises a pelvic nodal dissection with or without para-aortic nodal dissection. This continues to be an important aspect of surgical staging in women with uterine-confined endometrial carcinoma, as the procedure provides important prognostic information that may alter treatment decisions.
- Pelvic lymph nodes from the external iliac, internal iliac, obturator, and common iliac nodes are frequently removed for staging purposes.
- Para-aortic nodal evaluation from the inframesenteric and infrarenal regions may also be utilized for staging in women with high-risk tumors such as deeply invasive lesions, high-grade histology, and tumors of serous carcinoma, clear cell carcinoma, or carcinosarcoma.
- Sentinel lymph node (SLN) mapping may be considered. (See pages 2–6 of ENDO-C)[15]
- Excision of suspicious or enlarged lymph nodes in the pelvic or aortic regions is important to exclude nodal metastasis.
- Some patients may not be candidates for lymph node dissection.
- Visual evaluation of the peritoneal, diaphragmatic, and serosal surfaces with biopsy of any suspicious lesions is important to exclude extrauterine disease.
- While peritoneal cytology does not impact staging, FIGO and AJCC nonetheless recommend that surgeons continue to obtain this during the TH/BSO.
- Omental biopsy is commonly performed in those with serous carcinoma, clear cell carcinoma, or carcinosarcoma histologies.

PRINCIPLES OF EVALUATION AND SURGICAL STAGING WHEN SLN MAPPING IS USED

Figure 1: Common cervical injection sites for mapping uterine cancer†

Figure 2: Most common location of SLNs (blue, arrow) following a cervical injection†

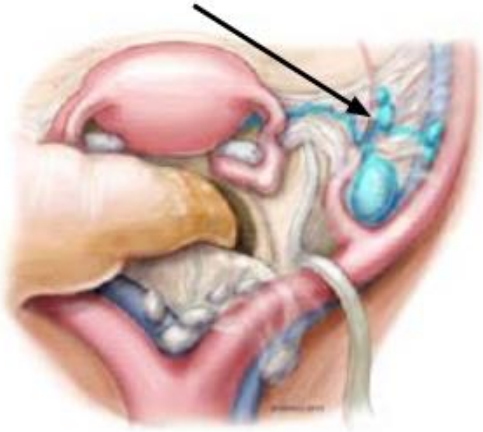
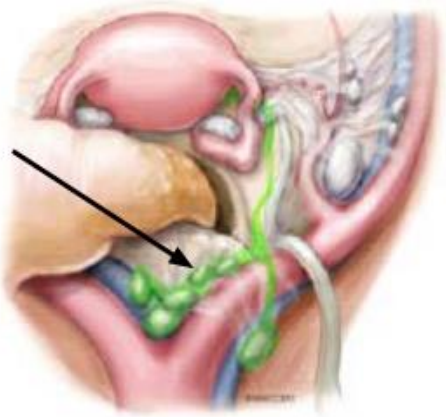
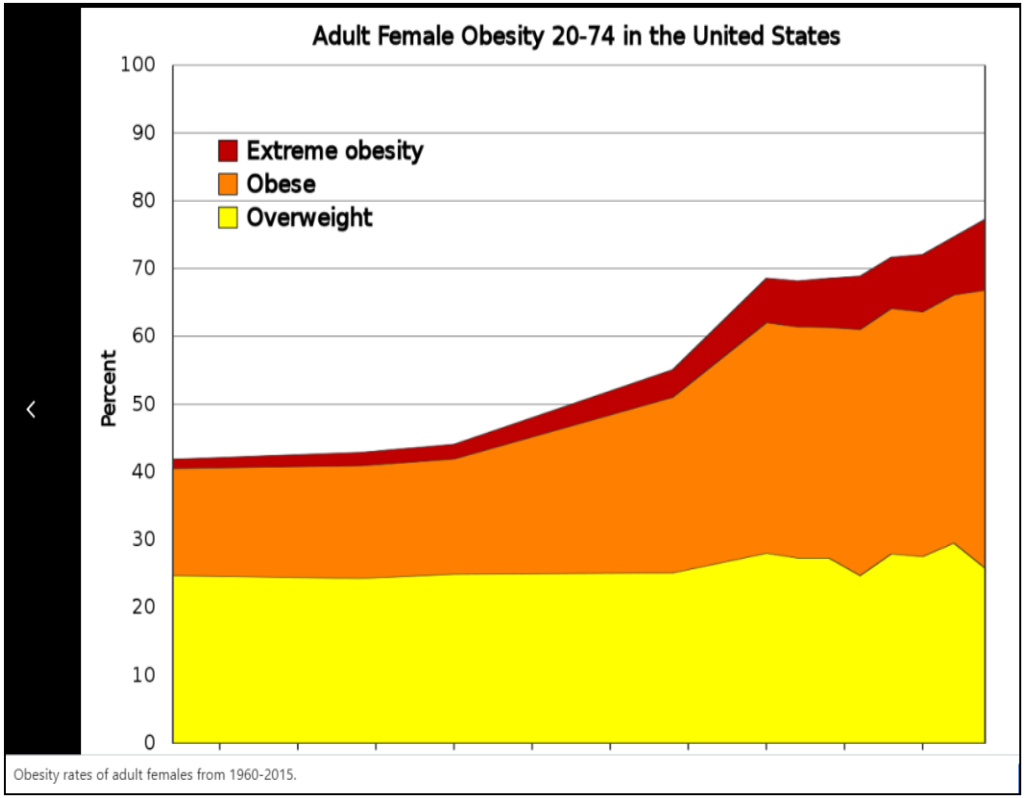


Figure 3: Less common location of SLNs (green, arrow) usually seen when lymphatic trunks are not crossing over the umbilical ligament but following the mesoureter cephalad to common iliac and presacral region†



Obesità e carcinoma endometriale

- Obesità fattore di rischio del ca. endometriale (tipo I)
- Aumento dell'incidenza dell'obesità nelle popolazioni occidentali
- Necessità di considerare il trattamento chirurgico del carcinoma endometriale nel grande obeso



CHIRURGIA ROBOTICA E CARCINOMA ENDOMETRIALE IN PAZIENTI OBESE

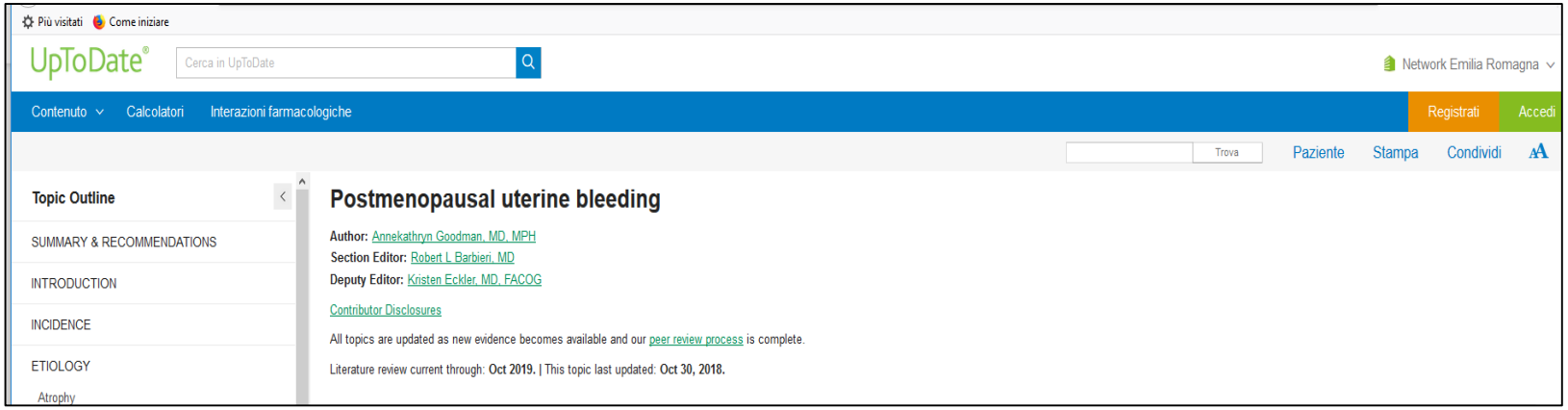
CHIRURGIA ROBOTICA – CARCINOMA ENDOMETRIALE E OBESITA'
Esperienza di Bologna
2016-2018

Totale pazienti	64
BMI (media)	35,7 (DS 4,7)
BMI > 30	33 pazienti
Età (media)	61 (DS 9)
Pregresso taglio cesareo	6 (18%)
Grading	
G1	30 (90%)
G2	3 (9%)
Neg	1 (1%)

CHIRURGIA ROBOTICA – CARCINOMA ENDOMETRIALE E OBESITA'
Esperienza di Bologna
2016-2018

Totale pazienti	33
Recovery Room	18 (55%)
Complicanze (sec Dindo Clavier)	
Grado 1	18 (55%)
Grado 2	1 (3%)
Grado 3	2 (6%)
Grado 4	0
Ricovero ospedaliero (Media±DS) gg	4,5 (±4,5)
Radioterapia post-operatoria	6 (18%)
Follow-up	100% vive - NED

ABNORMAL UTERINE BLEEDING



- Atrophy
- Polyps
- Postmenopausal hormone therapy
- Endometrial hyperplasia
- Leiomyomata uteri
- Adenomyosis
- Disease in adjacent organs
- Post radiation therapy
- Anticoagulant therapy
- Herbal and dietary supplements
- Infection

ABNORMAL UTERINE BLEEDING

- Cancer
  - endometrial
  - sarcoma
  - fallopian tube
  - ovarian
  - cervical
  - vaginal
  - vulvar
  - vaginal
  - choriocarcinoma

ABNORMAL UTERINE BLEEDING

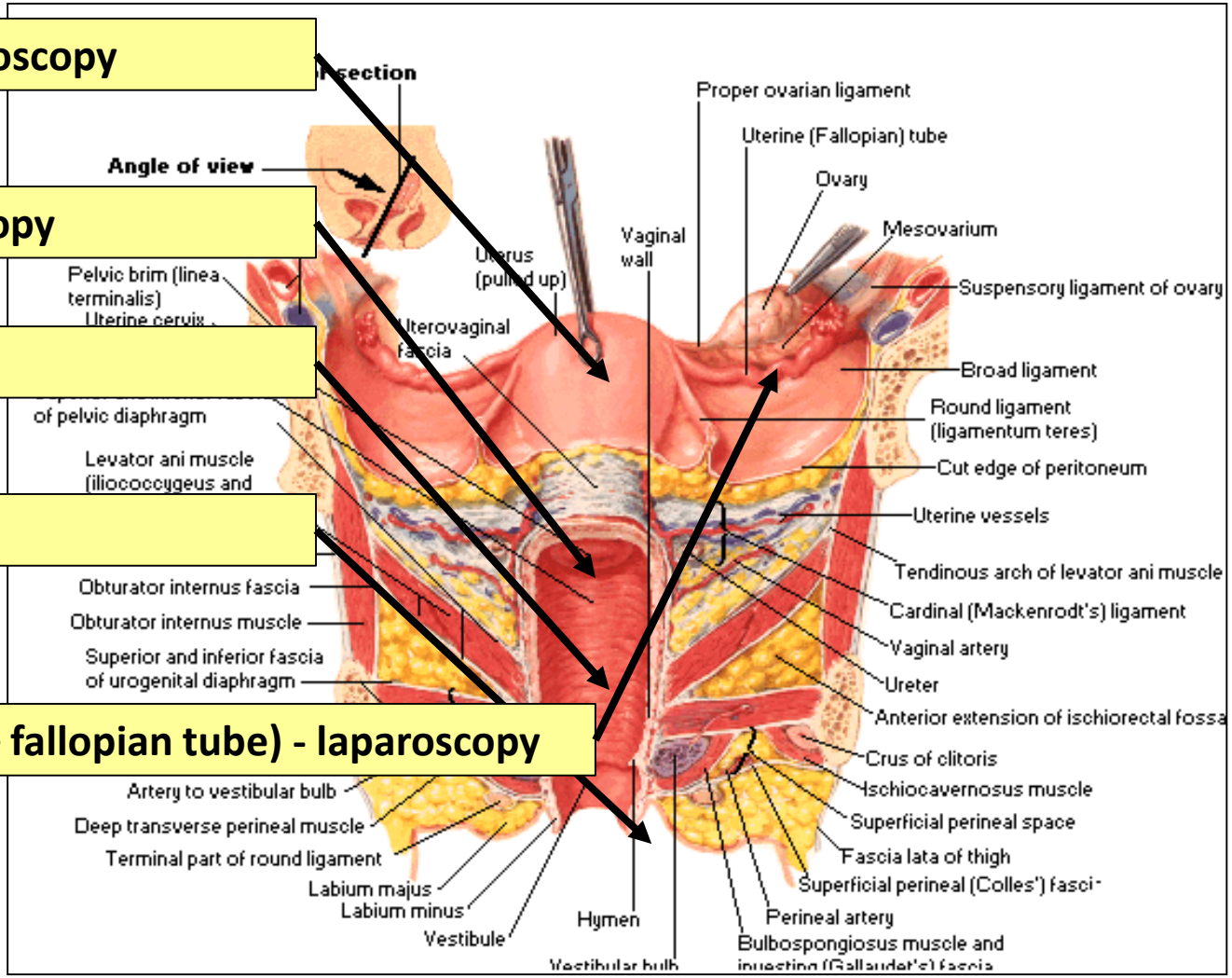
Sonography - hysteroscopy

Pap smear - colposcopy

Observation

Observation

Sonography (ovary – fallopian tube) - laparoscopy



ABNORMAL UTERINE BLEEDING

Polyps: in absence of abnormal uterine bleeding the risk of malignancy is 0,1%

Ferrazzi 2009

Operative hysteroscopy/curettage procedures in asymptomatic patients with ultrasonographically diagnosed endometrial polyps or thick endometrium are rarely indicated. It is reasonable to reserve these procedures for patients whose ultrasonographic findings demonstrate significant change over time.

Gemer O, 2018

ABNORMAL UTERINE BLEEDING

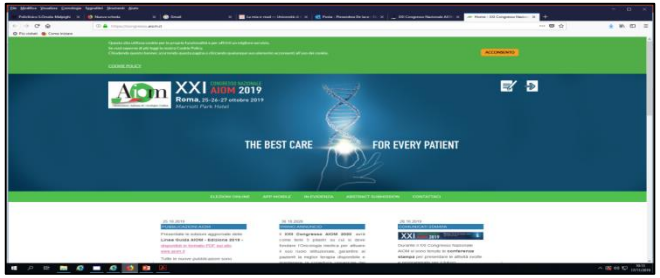
Women with type II endometrial cancer had a **thin/indistinct endometrial stripe on TVUS in approximately 25% of cases**.

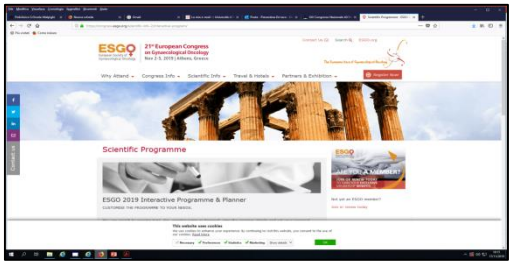
Lack of any ultrasound abnormality, including a thickened EMS, was noted in approximately 10% of patients.

The use of TVUS, which has been of value in type I cancer, is limited in type II endometrial cancer.

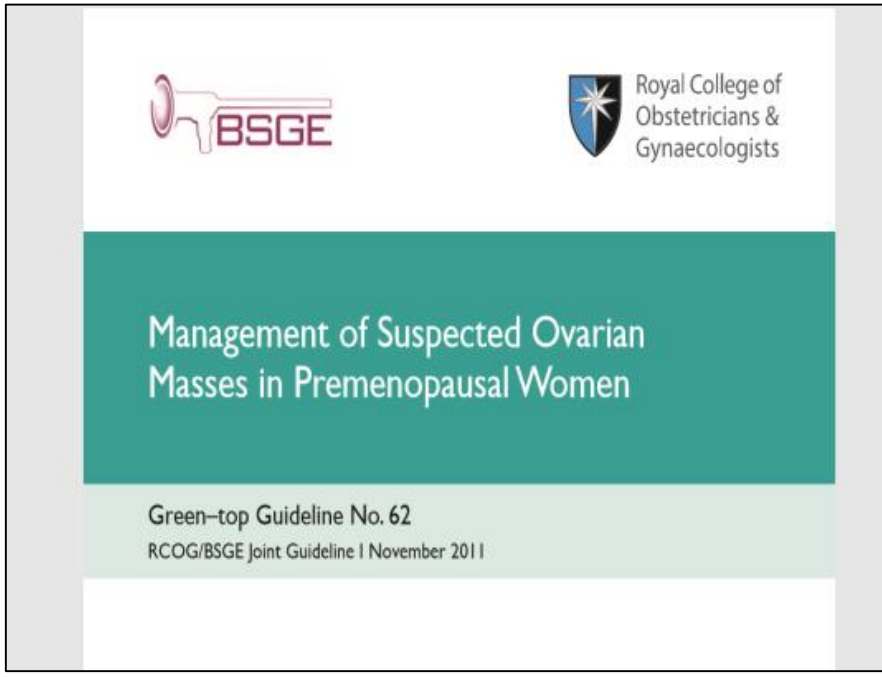
Therefore, **endometrial sampling should be included in the evaluation of all women with postmenopausal bleeding**, regardless of EMS thickness

Billingsley 2005





- CERVIX
- ENDOMETRIUM
- **OVARY**



REGIONE EMILIA-ROMAGNA

E-R Salute

PERCORSO REGIONALE: IL CORRETTO APPROCCIO CHIRURGICO DELLA PAZIENTE CON CARCINOMA OVARICO

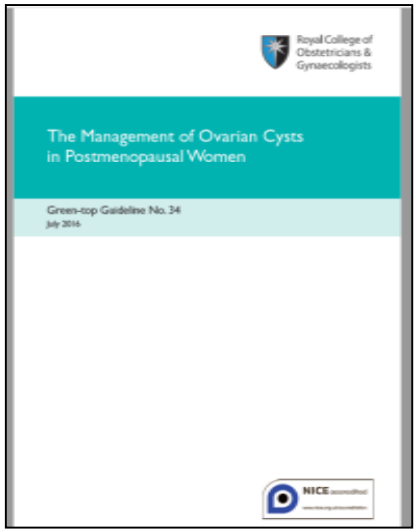
Questo Percorso Regionale ha lo scopo di garantire una corretta gestione chirurgica del paziente con tumore maligno dell'ovaio in modo da offrire a tutte le donne della Regione la migliore sopravvivenza, considerato che la chirurgia riveste oggi un ruolo fondamentale per la prognosi delle pazienti.

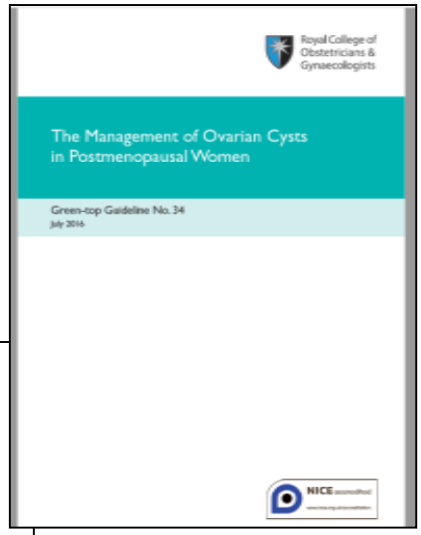
• Ovarian cysts are diagnosed with **increasing frequency in postmenopausal women** as more patients are undergoing imaging in connection with medical care.

• An ovarian cyst inevitably raises the question of its relevance to the woman's symptoms and concerns for the possibility of ovarian cancer

• The large numbers of ovarian cysts now being discovered by ultrasound and the low risk of malignancy of many of these cysts suggest that **they need not all be managed surgically.**

• The **further investigation and management** of these women has **implications for morbidity, mortality, resource allocation and tertiary referral patterns**.





The morbidity and outcomes can be improved by:

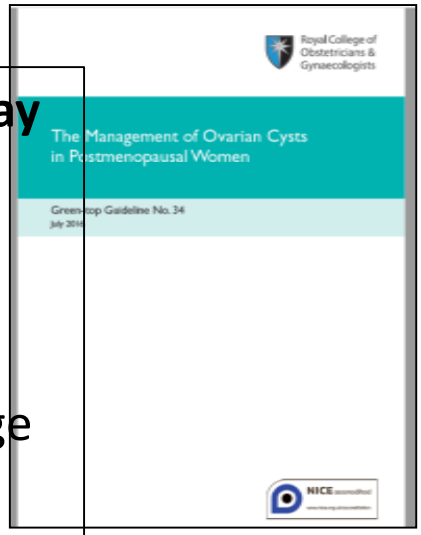
- using **conservative management** where possible
- the use of **laparoscopic techniques where appropriate**, thus avoiding laparotomy where possible
- **referral to a gynaecological oncologist** when appropriate.

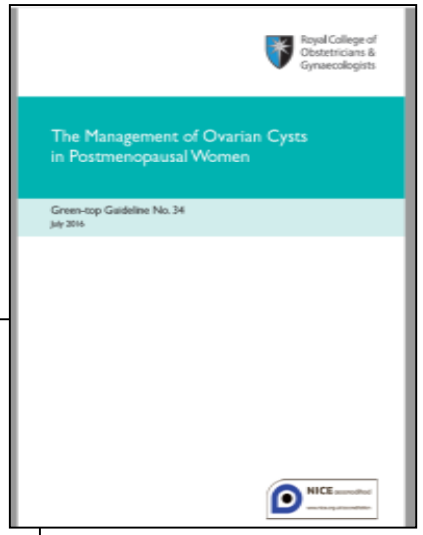
A **transvaginal pelvic ultrasound is the single most effective way** of evaluating ovarian cysts in postmenopausal women.

Transabdominal ultrasound should not be used in isolation. It should be used to provide supplementary information to transvaginal ultrasound particularly when an ovarian cyst is large or beyond the field of view of transvaginal ultrasound.

On transvaginal scanning, the **morphological description** and subjective assessment of the ultrasound features should be **clearly documented** to allow calculation of the **risk of malignancy**.

Transvaginal ultrasound scans should be performed using multifrequency probes by **trained clinicians** with expertise in gynaecological imaging.



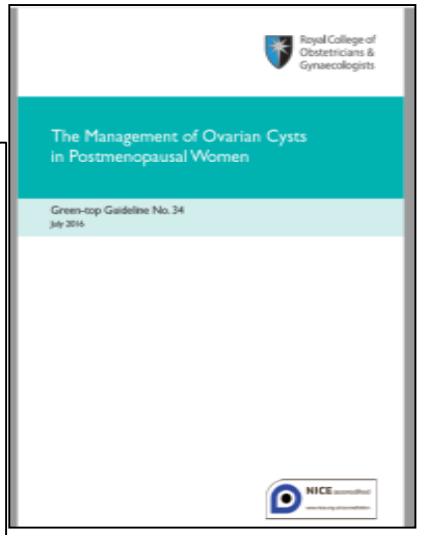


MRI should be used as the **second-line imaging modality** for the characterisation of indeterminate ovarian cysts when ultrasound is inconclusive**.**

While assessment with MRI can improve overall sensitivity and specificity of ovarian cyst characterisation, there are **inherent limitations** to the more widespread use of MRI, which **preclude its routine use** over transvaginal ultrasonography

Asymptomatic, **simple, unilateral, unilocular ovarian cysts, less than 5 cm in diameter**, have a low risk of malignancy. In the presence of normal serum CA125 levels, these cysts **can be managed conservatively, with a repeat evaluation in 4–6 months**.

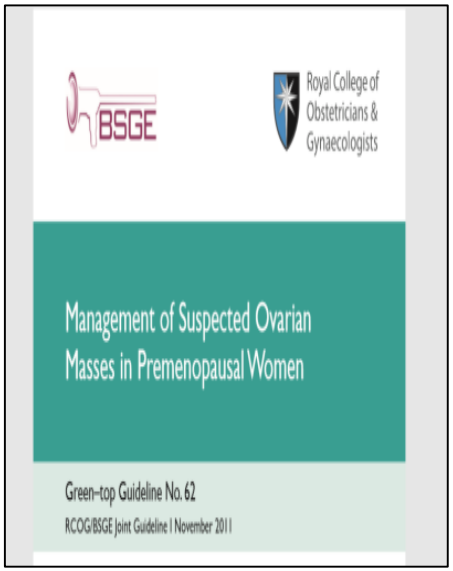
It is reasonable to discharge these women from follow-up after 1 year if the cyst remains unchanged or reduces in size, with normal CA125, **taking into consideration a woman's wishes and surgical fitness**.



Ovarian cysts that persist or **increase in size** are unlikely to be functional and may warrant surgical management.

There is no evidence-based consensus on the size above which surgical management should be considered. Most studies have used an arbitrary maximum diameter of **50–60 mm** among their inclusion criteria to offer **conservative management.**

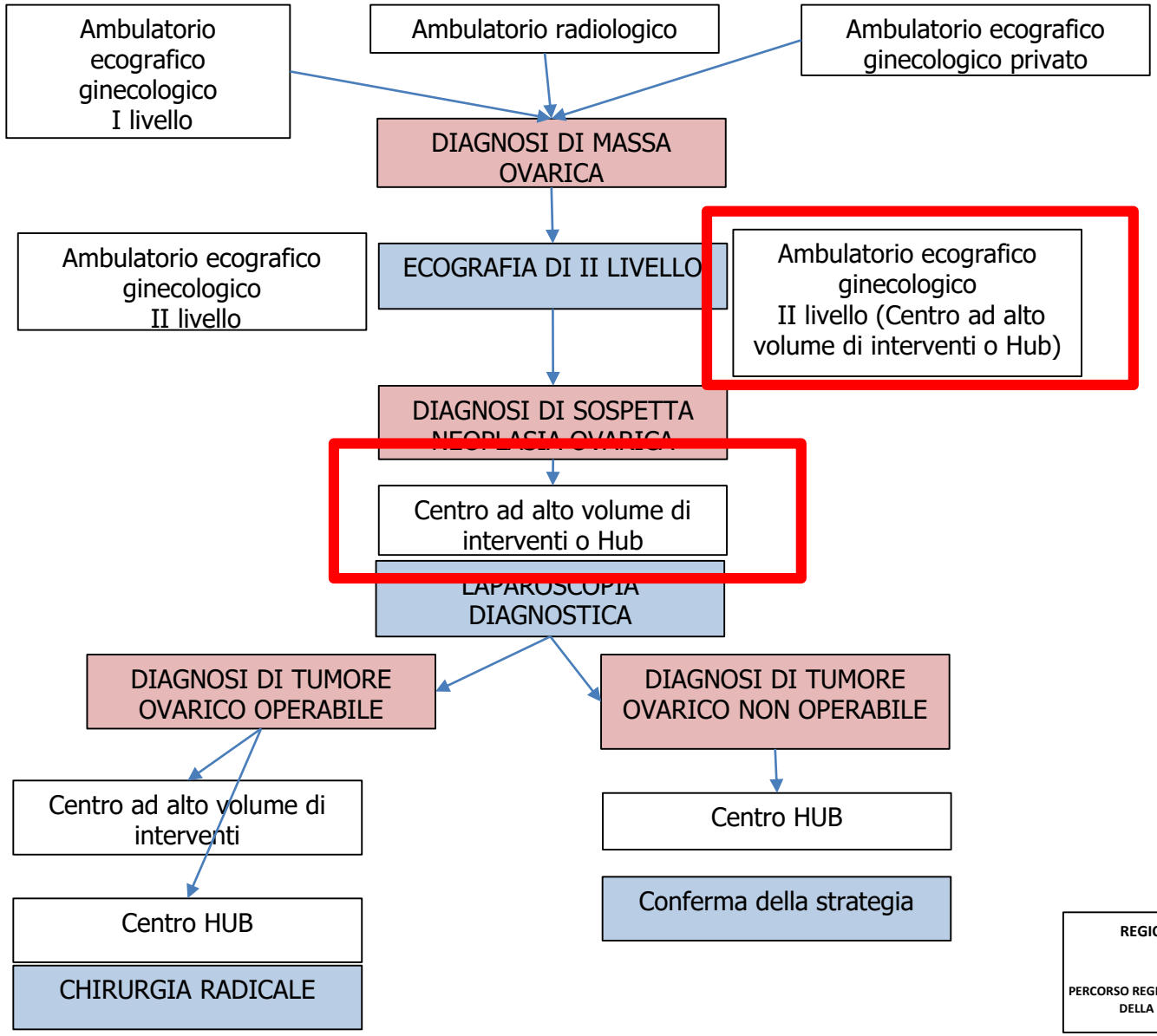
The use of the combined oral contraceptive pill does not promote the resolution of functional ovarian cysts.



PERCORSO REGIONALE DI GESTIONE DEL TUMORE OVARICO

• Le masse annessiali con l'applicazione delle simple rules possono essere classificate in: **benigne, maligne e inconclusive**. La massa classificata come benigna potrà essere gestita in maniera conservativa o chirurgica da qualunque struttura ed esula da questo percorso. **Le masse con caratteristiche di malignità dovranno essere inviate ad un centro di riferimento per le cure del caso**. Le masse con esito inconclusivo alla valutazione con le SR dovranno essere inviate ad una valutazione ecografica di II livello che ne stabilirà la categoria di rischio.

PERCORSO CENTRALIZZAZIONE CHIRURGICA TUMORE OVAIO REGIONE EMILIA ROMAGNA



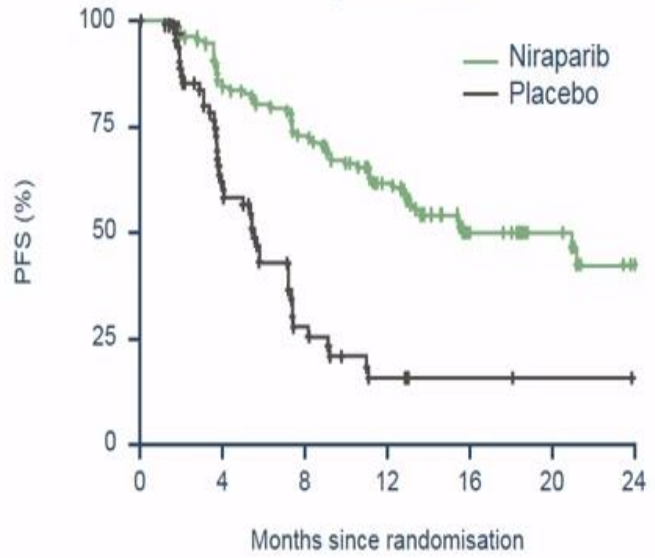
REGIONE EMILIA-ROMAGNA

PERCORSO REGIONALE: IL CORRETTO APPROCCIO CHIRURGICO DELLA PAZIENTE CON CARCINOMA OVARICO

Niraparib maintenance therapy improved PFS

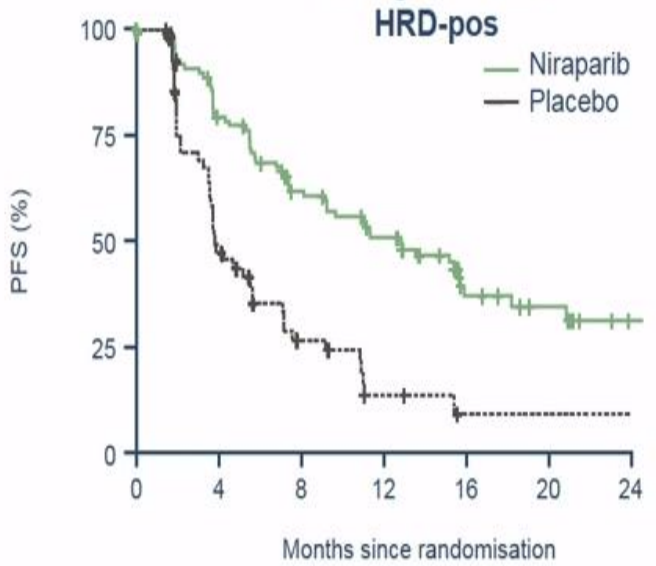
TESARO
ESGO 2017
SATELLITE SYMPOSIUM

g*BRCA*mut



Treatment	Median PFS, mo (95% CI)	HR (95% CI) *P* Value	Patients without progression or death, %		
			12 mo	18 mo	24 mo
Niraparib (N=138)	**21.0** (12.9, NR)	0.27 (0.173, 0.410) <0.001	62	50	**42**
Placebo (N=65)	**5.5** (3.8, 7.2)		16	16	**16**

Non-g*BRCA*mut HRD-pos

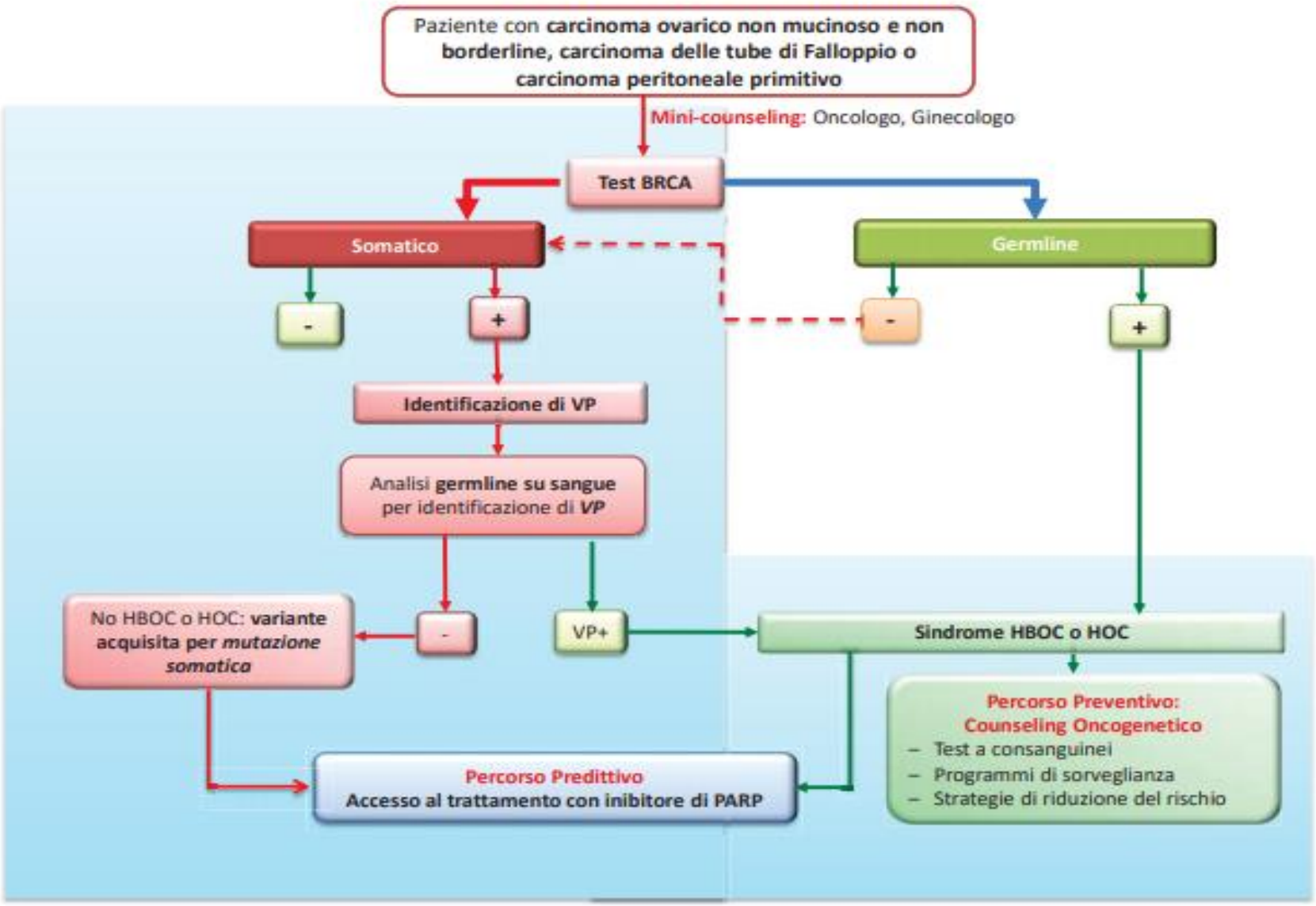


Treatment	Median PFS, mo (95% CI)	HR (95% CI) *P* Value	Patients without progression or death, %		
			12 mo	18 mo	24 mo
Niraparib (N=106)	**12.9** (8.1, 15.9)	0.38 (0.243, 0.586) <0.001	51	37	**31**
Placebo (N=56)	**3.8** (3.5, 5.7)		13	9	**9**

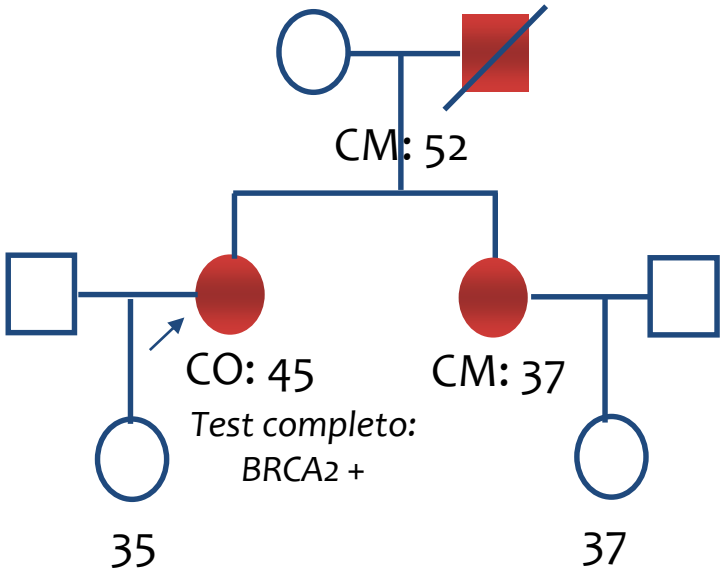
CI, confidence interval; g*BRCA*mut, germline breast cancer susceptibility gene mutation; HR, hazard ratio; HRD, homologous recombination deficiency; Mo, months; NR, not reported; PFS, progression-free survival; pos, positive.

Mirza MR et al. *N Engl J Med*. 2016;375:2154–2164;
TESARO Inc., Data on File.

TESARO


Paziente con carcinoma ovarico non mucinoso e non borderline, carcinoma delle tube di Falloppio o carcinoma peritoneale primitivo
Mini-counseling: Oncologo, Ginecologo
Test BRCA
Somatico
Germline
-
+
-
+
Identificazione di VP
Analisi germline su sangue per identificazione di VP
No HBOC o HOC: variante acquisita per mutazione somatica
-
VP+
Sindrome HBOC o HOC
Percorso Preventivo:
Counseling Oncogenetico
– Test a consanguinei
– Programmi di sorveglianza
– Strategie di riduzione del rischio
Percorso Predittivo
Accesso al trattamento con inibitore di PARP

Il test BRCA germinale: come procedere?

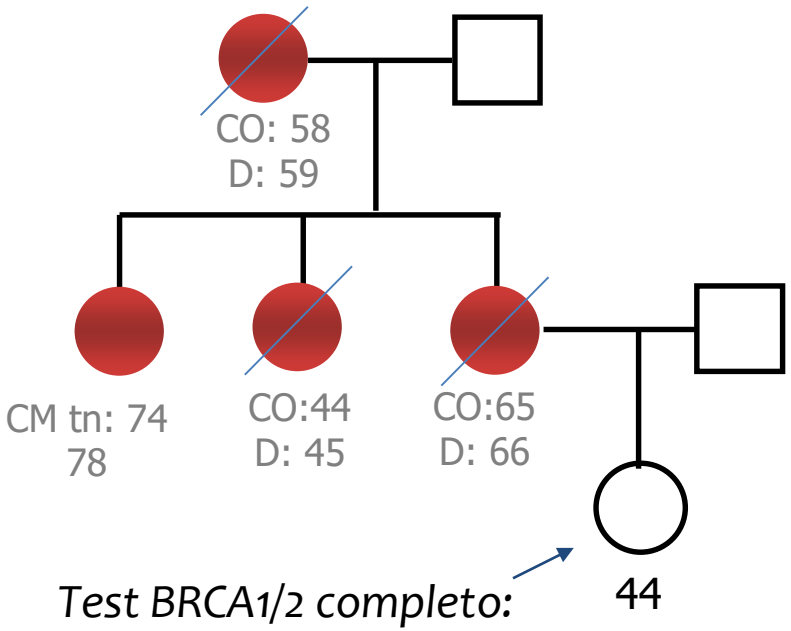


BRCA2 mut -

Rischio geneRico

BRCA2 mut +

Rischio geneTico



Test BRCA1/2 completo:
Nessuna mutazione

Vero negativo?
O mutazione predisponente non identificabile?

- Rischio non calcolabile
- Falsa rassicurazione

RegioneEmiliaRomagna

PREVENZIONE NEI LUOGHI DI VITA E DI LAVORO

contributi

83

Protocollo assistenziale nelle donne a rischio ereditario di tumore della mammella e/o ovaio

Regione Emilia-Romagna
I edizione
Anno 2014

1. **Breast Ovarian Cancer (BOC): Pazienti affette da tumore sia mammario che ovarico**
2. Hereditary Ovarian Cancer (HOC): 2 o più pazienti affetti da neoplasia ovarica
3. **Hereditary Breast and Ovarian Cancer (HBOC): Famiglie con ≥ 1 caso carcinoma ovarico associato a ≥ 2 carcinomi mammari di cui uno ≤ 40 anni** o bilaterale e parentela di I grado tra i 3 individui
4. Carcinoma mammario e ovarico sospetto ereditario (SHBOC): 3 o più pazienti affetti da carcinoma mammario/ovarico con parentela di I grado senza giovane età o bilateralità, oppure con giovane età o bilateralità ma senza parentela di I grado
5. Hereditary Breast Cancer (HBC): 3 o più pazienti affette da carcinoma mammario, di cui uno entro i 40 anni o bilaterale e parentela di I grado tra i 3 individui.
6. Carcinoma mammario e ovarico fortemente sospetto per familiarità (SFBOC+): 1 paziente affetta da carcinoma mammario e 1 da carcinoma ovarico con familiarità di I grado e ≤40 anni o bilateralità.
7. Early Onset Breast Cancer (EOBC): Pazienti affette in età ≤35 anni senza familiarità:
8. Male Breast Cancer (MBC): Paziente affetto da carcinoma mammario maschile
9. Familiare per carcinoma mammario ed ovarico (FBOC): 3 pazienti affetti da carcinoma mammario ed ovarico senza essere HBOC o SHBOC
10. Fortemente sospette per familiarità per carcinoma mammario (SFBC+):2 casi parenti di I grado, di cui 1 con età ≤ 40 anni o bilaterale
11. Carcinoma mammario duttale infiltrante G3I “triplo negativo” (RE=negativo; RPg=negativo, c-Erb=negativo), in età ≤40 anni

ESGO
European Society of Gynaecological Oncology

Certificate of Accreditation

Sant'Orsola-Malpighi Hospital

Gynecologic Oncology Unit, Bologna, Italy

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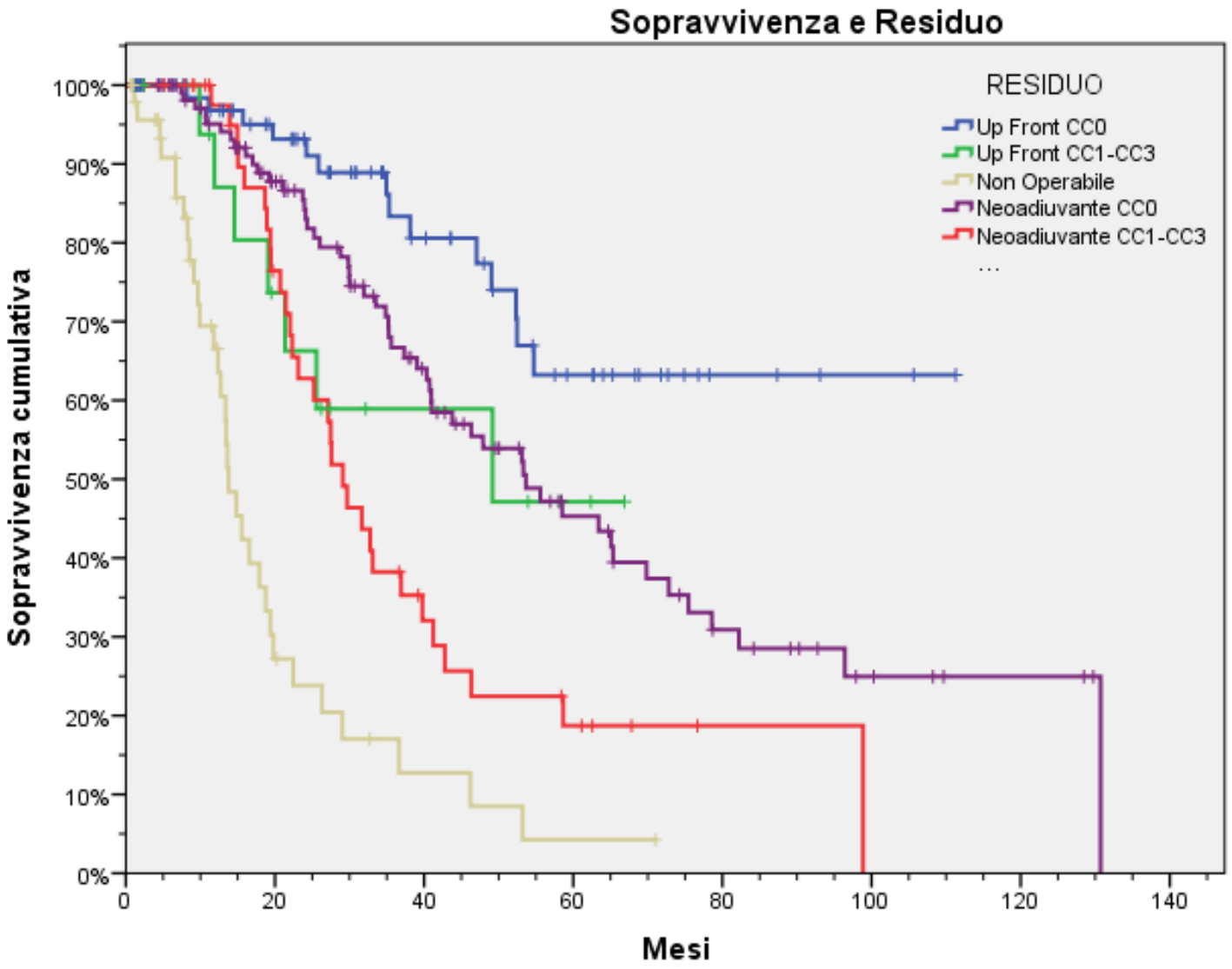
For a time period of 5 years

Prof. David Cibula
President ESGO

Ass. Prof. Dimitrios Haidopoulos
Chair, ESGO Fellowships and accreditations committee

Prague,
May 12, 2017

The European Voice of Gynaecological Oncology


Sopravvivenza e Residuo
RESIDUO
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Sopravvivenza cumulativa
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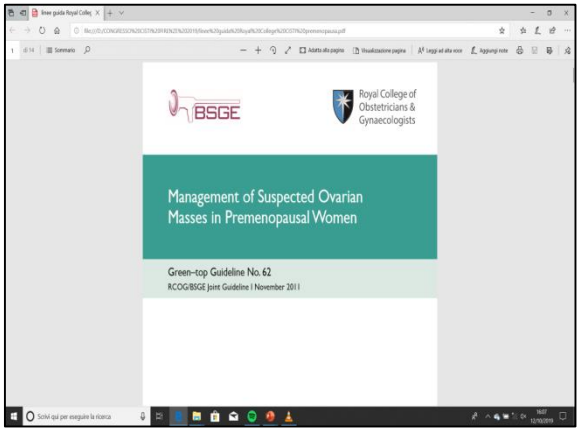
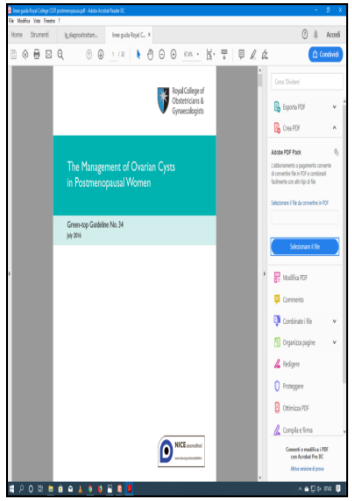
Mesi

PROTOCOLLO DIAGNOSTICO

‘**Pattern recognition**’ of specific ultrasound findings can produce sensitivity and specificity equivalent to logistic regression models, especially when performed by more experienced clinicians specialising in women’s imaging.

Repeating ultrasound assessment in the postmenstrual phase may be helpful in cases of doubt and endometrial views may contribute to diagnosis in cases of estrogen-secreting tumours of the ovary.





it is reasonable to manage these simple cysts conservatively: with a follow-up assessment of serum CA125 and a repeat ultrasound scan.

The ideal frequency of repeat imaging is yet to be determined. A reasonable proposed interval is 4–6 months.

This, of course, depends upon the views and symptoms of the woman, her surgical fitness and on the clinical assessment.

It is reasonable to discharge these women from follow-up after 1 year if the cyst remains unchanged or reduces in size, with normal CA125