

Radio-chemioterapia **neoadiuvante** negli stadi avanzati del carcinoma della cervice uterina

XXIII CONGRESSO
AIRO

Giardini Naxos - Taormina, 26 - 29 ottobre



Regione Siciliana - Assessorato Regionale del Beni Culturali e dell'Identità Siciliana
Organizzato da Beni Culturali e del Turismo Siciliana
Servizi Musei Interdipartimenti Regionali "3" - Pagine 17/2000

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Rubens, *Daniele nella fossa dei leoni*, (1615)

National Gallery of Art (Washington).

Presunta maggiore tossicità
(trattamento trimodale)

Bassi livelli di
evidenza su reale
efficacia/necessità

Interdisciplinarietà



Stage IB2
and Stage IIA2

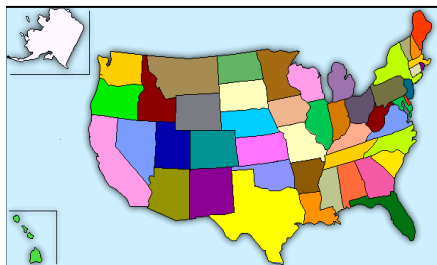
Pelvic RT^f
+ concurrent cisplatin-containing chemotherapy^h
+ brachytherapy (total point A dose ≥ 85 Gy)^g
(category 1)

or

Radical hysterectomy
+ pelvic lymph node dissection
 \pm para-aortic lymph node sampling
(category 2B)

or

Pelvic RT^f
+ concurrent cisplatin-containing chemotherapy^h
+ brachytherapy (total point A dose 75-80 Gy)^g
+ adjuvant hysterectomy
(category 3)



Vantaggi potenziali

➤ **Rimozione di eventuali focolai neoplastici chemio/radio resistenti**

- Una CT-RT sebbene ottimale non riesce a sterilizzare lfn pelvici in circa il 16% dei casi

Moyses Am J Clin Oncol 1996; Houvenaghel Gyn Onc 2006

➤ **Valutazione della risposta patologica**

- Valore prognostico

Keys Gyn Onc 2003

➤ **Patterns differenti di tossicità/complicazioni**

Ferrandina G Ann Surg Onc 2013

➤ **Istotipi differenti**

Shibata K 2009

➤ **Impatto psicologico del "sentirsi libera da malattia"**

- Es. Gineco chiuso per mancato reclutamento

Studi fase II pubblicati

No. Studi (1994-2013)	20
No. pazienti	1341 (15% stadio IIIa-IVa)
Chemioterapia	Regimi a base di CDDP
Dose mediana cumulativa (range)	50 (40-80), \pm BRT
5-yr DFS (range)	57-85 %
5-yr OS (range)	64-90 %

Studi randomizzati

CISPLATIN, RADIATION, AND ADJUVANT HYSTERECTOMY COMPARED WITH RADIATION AND ADJUVANT HYSTERECTOMY FOR BULKY STAGE IB CERVICAL CARCINOMA

HENRY M. KEYS, M.D., BRIAN N. BUNDY, PH.D., FREDERICK B. STEHMAN, M.D., LAILA I. MUDERSPACH, M.D., WELDON E. CHAFE, M.D., CHARLES L. SUGGS III, M.D., JOAN L. WALKER, M.D., AND DEBORAH GERSELL, M.D.

N Engl J Med 1999;340:1154-61



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Gynecologic Oncology 89 (2003) 343–353

Gynecologic
Oncology

www.elsevier.com/locate/ygyno

Radiation therapy with and without extrafascial hysterectomy for bulky stage IB cervical carcinoma: a randomized trial of the Gynecologic Oncology Group[☆]

Henry M. Keys, M.D.,^{a,*} Brian N. Bundy, Ph.D.,^b Frederick B. Stehman, M.D.,^c Takashi Okagaki, M.D., Ph.D., M.P.H.,^d Donald G. Gallup, M.D.,^e Alexander F. Burnett, M.D.,^f Marvin Z. Rotman, M.D.,^g and Wesley C. Fowler, Jr., M.D.^h

The
Oncologist®

Gynecologic Oncology

Results of the GYNECO 02 Study, an FNCLCC Phase III Trial Comparing Hysterectomy with No Hysterectomy in Patients with a (Clinical and Radiological) Complete Response After Chemoradiation Therapy for Stage IB2 or II Cervical Cancer

PHILIPPE MORICE,^{a,*} PHILIPPE ROUANET,^d ANNIE REY,^b PASCALE ROMESTAING,^c GILLES HOUVENAEGHEL,^f JEAN CHARLES BOULANGER,^g JEAN LEVEQUE,^h DIDIER COWEN,ⁱ PATRICE MATHEVET,^j JEAN PIERRE MALHAIRE,^k GUILLAUME MAGNIN,^l ERIC FONDRINIER,^m JOCELYNE BERILLE,ⁿ CHRISTINE HAIE-MEDER^c

The Oncologist 2012;17:64–71 www.TheOncologist.com

Annals of Oncology Advance Access published April 21, 2013

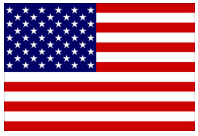
original article

Annals of Oncology 00: 1–5, 2013
doi:10.1093/annonc/ndt142

Brachytherapy versus radical hysterectomy after external beam chemoradiation with gemcitabine plus cisplatin: a randomized, phase III study in IB2–IIB cervical cancer patients

L. Cetina¹, A. González-Enciso², D. Cantú¹, J. Coronel¹, D. Pérez-Montiel³, J. Hinojosa⁴, A. Serrano¹, L. Rivera⁴, A. Poitevin⁴, A. Mota⁴, E. Trejo⁴, G. Montalvo², D. Muñoz², J. Robles-Flores², J. de la Garza¹, J. Chanona², R. Jiménez-Lima¹, T. Wegman¹ & A. Dueñas-González^{5*}

¹Division of Clinical Research; Departments of ²Gynecology; ³Pathology; ⁴Radiotherapy, National Cancer Institute, Mexico; ⁵Unit of Biomedical Research on Cancer, Institute of Biomedical Research, National Autonomous University of Mexico/National Cancer Institute, Mexico City, Mexico



Studi randomizzati

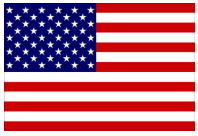
GOG 71 Keys Gyn Onc 2003

- ERT+ BRT (124)

No CRT

256 IB bulky \geq 4 cm

- ERT+ isterectomia extrafasciale (132)
- no differenze in termini OS
- lieve vantaggio PFS (- fallimenti pelvici nel braccio sperimentale)
- risposta patologica correla con DFS e OS
- tumori < 7 cm > OS se chirurgia (dato in controtendenza)



Studi randomizzati

GOG 123 Keys NEJM 1999

369 IB bulky \geq 4 cm

- ERT+ BRT + isterectomia extrafasciale (186)
- CRT + BRT + isterectomia extrafasciale (183)

CRT con platino + isterectomia riduce significativamente il rischio di recidiva e di morte nel IB2



Studi randomizzati

GYNECO 02 Morice P. The Gynecologist 2012



25 centri
2003–2006

61 IB2-II CRT + BRT

Se risposta clinica
e radiologica
completa

- isterectomia extrafasciale o radicale (31)
- No ulteriori trattamenti (30)

chiusura dello studio per mancato reclutamento pazienti:
campione statistico insufficiente

**Isterectomia di completamento non impatta su DFS e OS nelle
pz con risposta completa dopo CRT, ma la conclusione è
limitata dalla mancata potenza dello studio**



Studi randomizzati

Cetina L. Annals of Oncology 2013

211 IB2-IIB

CRT 50 Gy
CDDP+Gem

- BRT (100)
- CH (isterectomia radicale-PIVER III) (111)

FUP mediano 36 mesi (3-80)

Fallimenti

- BRT 15%

- CH 11.7%

- 10% locali
- 5% sistemici



P=0. 918

- 7% locali
- 5.4% sistemici



Tossicità tardiva

Event	BCT arm (100)		RH arm (111)		<i>p-value</i>
	G1	G2	G1	G2	
Proctitis	22	36	2	8	0.0750
Cystitis	11	36	3	2	
Hydronephrosis	4	32	2	5	
Grade	G3	G4	G3	G4	<i>p-value</i>
Proctitis	2	2	2	0	0.5303
Cystitis	1	2	0	0	
Hydronephrosis	0	0	0	0	

BRT

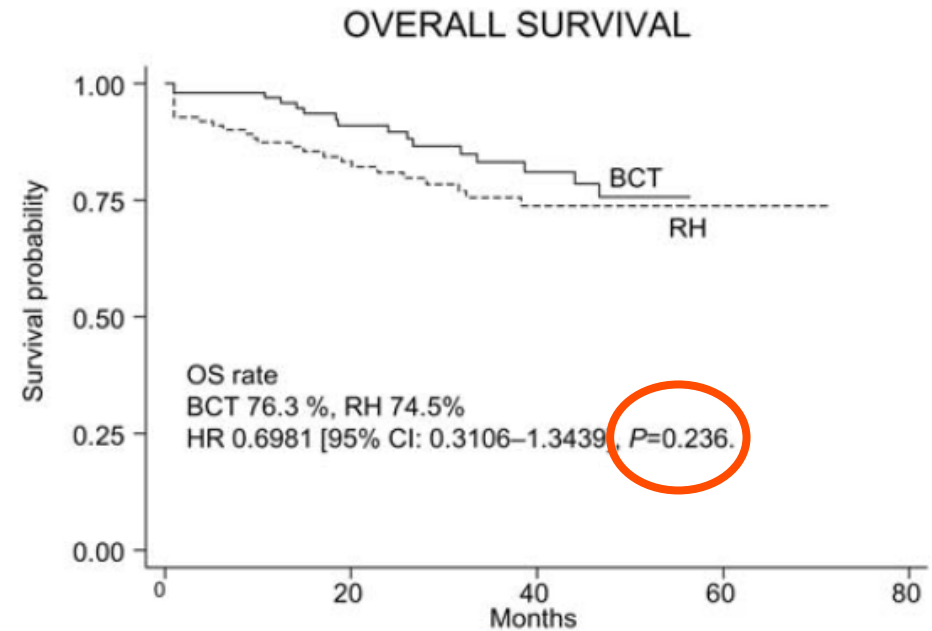
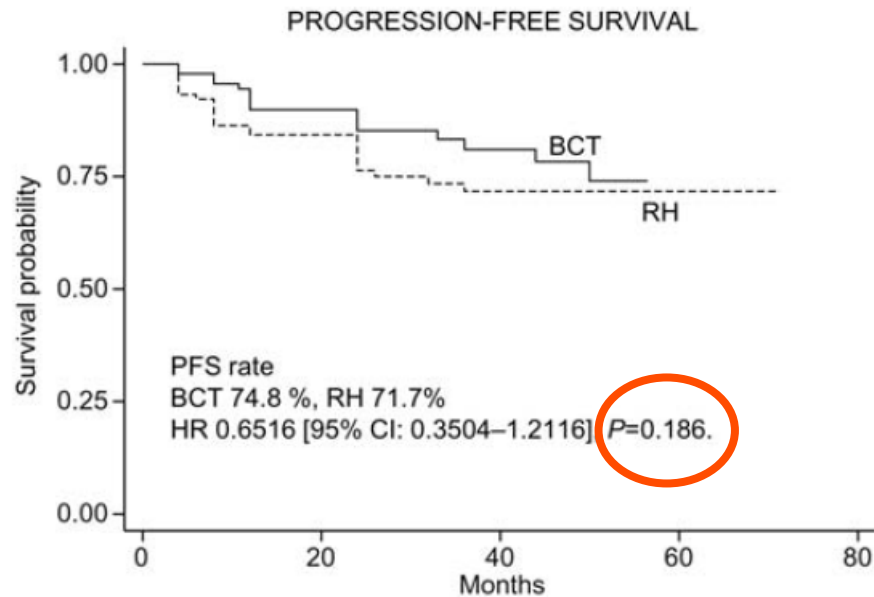
- 50% pz G1-2 proctite e cistite
- 2% pz G3
- 2% pz G4

CH

- 3.4% chirurgia per linfoceli
- 2.3% chirurgia fistole ureterocut.



Studi randomizzati



- CH dopo CRT **NON** è superiore allo standard (BRT)

MA

- isterectomia radicale dopo CRT: fattibile e sicura
- CH invece di BRT dopo CRT **NON** compromette OS
- particolare rilevanza in contesti con risorse BRT limitate o assenti

RTCT neoadiuvante in stadi avanzati del cervicocarcinoma

Staging

Response

RADIOCHEMOTHERAPY

CDDP 20 mg/mq/day iv

5-FU 1 g/mq/day iv
for 96 hrs

**S
U
R
G
E
R
Y**

ERT
40-45 Gy

Weeks

I

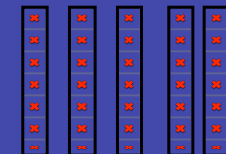
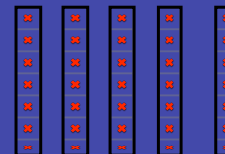
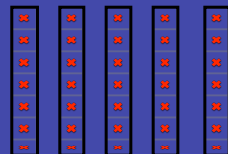
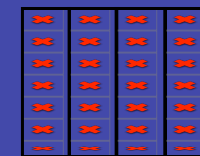
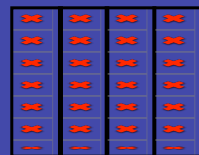
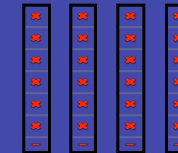
II

III

IV

V

XI-XII



Punti in Discussione

1. **Outcomes** rispetto a trattamento standard
2. **Fattibilità** negli **stadi avanzati**
3. **Sicurezza** della **chirurgia radicale** dopo RT/CT preoperatoria
4. **Complicanze tardive e QoL** dopo trattamento RT/CT + chirurgia radicale
5. **Prospettive future**

Punti in Discussione

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4. **Complicanze tardive e QoL** dopo trattamento RT/CT + **chirurgia radicale**
5. **Prospettive future**

- **Tassi molto favorevoli di controllo locale** [Resbeut M Gynecol Oncol. 1994, Jurado M Gynecol Oncol. 1999, Classe JM Gynecol Oncol 2006, Ferrandina Gynecol Oncol 2007]

73.0% risposte patologiche complete/parziali micro

- **Risultati promettenti in termini di outcome clinico a lungo termine** [Distefano M Gynecol Oncol 2005, Houvenaeghel G Gynecol Oncol 2006]

5-years DFS: 83%; 5-years OS: 90%

RTCT neoadiuvante in stadi avanzati del cervicocarcinoma

Autore	Stadio	DFS	OS	note
Jurado M <i>Gyn Onc 1999</i>	IB2-IVA	81% 9aa	85% 9aa	
Shibata K <i>Eur J Surg Oncol. 2009</i>	IB2-IVB	84% 5aa	76% 5aa	adk
Huguet F <i>IJROBP 2008</i>	IB2-IIB	72.2% 5 aa		
Ferrandina G. <i>Gyn Onc 2007</i>	IB2-IVA	83% 5aa	90% 5aa	
Bernard A <i>Cancer Radiother 2002</i>	IB2-II	76% 5aa	79% 5aa	
Classe JM <i>Gyn Onc 2006</i>	IB2-IVA	66% 5aa	89% (PCR) 90%(PMIC) 54% (PMAC)	
Reusbet M <i>Gyn Onc 1994</i>	IB2-IIB III-IVA	61% 65%	66% 77%	
Houvenaghel G <i>Eur J Surg Oncol 2007</i>	IB2-IVA	50.8%	55.6%	

OS per stadio

Stadio FIGO	5y OS RTCT	5y OS CRT + CH
Ia-b1	92%	/
Ib2	79%	55-90%
IIa	76%	
IIb	73%	
IIIa	51%	
IIIb	46%	
IVa	25%	

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1. Outcomes rispetto a trattamento standard
- 2. Fattibilità negli stadi avanzati**
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5. Prospettive future

Neoadjuvant Chemoradiation Followed by Radical Hysterectomy in FIGO Stage **IIIB** Cervical Cancer

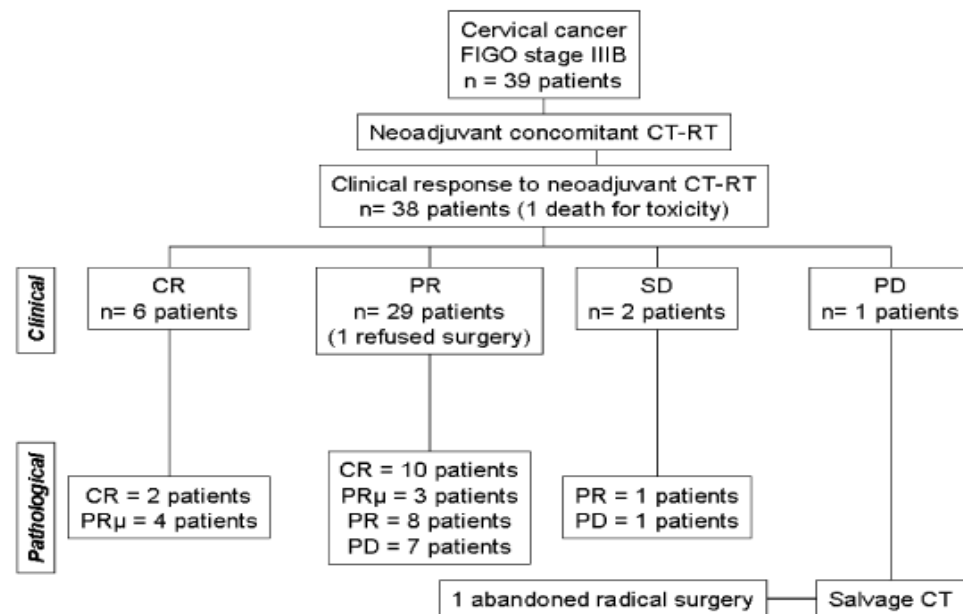
Feasibility, Complications, and Clinical Outcome

Francesco Fanfani, MD,* Anna Fagotti,* Gabriella Ferrandina,† Francesco Raspagliesi,‡ Antonino Ditto,‡ Anna Maria Cerrotta,§ Alessio Morganti,|| Daniela Smaniotto,¶ and Giovanni Scambia*

International Journal of Gynecological Cancer 2009

TABLE 1. Preoperative clinicopathological characteristics of the study population (N = 39)

Clinicopathological Characteristic	
Age, median (range), yr	53 (35–80)
Histotype	
Squamous	37 (94.9%)
Adenocarcinoma	2 (5.1%)
Tumor volume	
≥4 cm	32 (80.0%)
MRI lymph node status	
Positive pelvic nodes	20 (56.4%)
Positive aortic nodes	7 (17.9%)
Grade of differentiation	
G1	6 (15.4%)
G2	10 (25.7%)
G3	23 (58.9%)



Complicanze

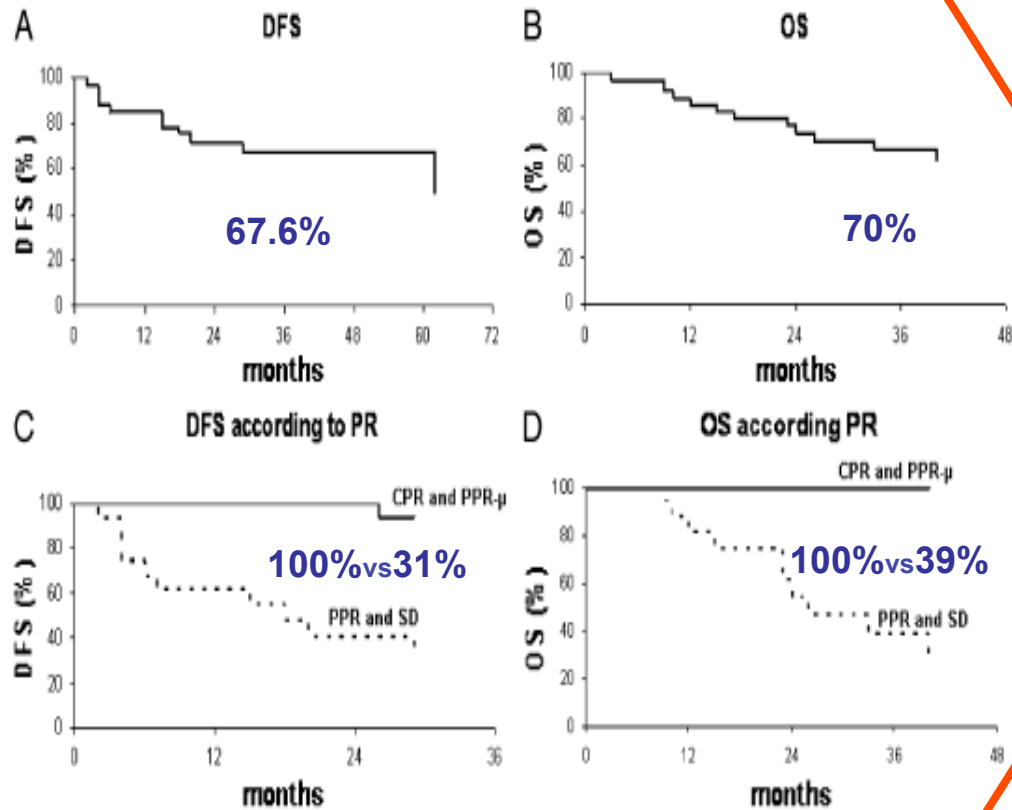
Overall rate surgical compl **31.4%**
20.0% grade 3 toxicity

TABLE 2. Intraoperative and postoperative complications classified according to glossary by Chassagne et al¹¹

	n (%)	Chassagne Glossary Classification
Intraoperative Complications		
Transfusion (patients)	18 (51.4)	—
EBL >1000	3 (8.6)	—
Vascular IO injury	4 (11.4)	G1
Vesical lesion	2 (5.7)	G1
Rectal lesion	1 (2.8)	G1
Ureteral lesion	1 (2.8)	G1
Early postoperative complications		
Urinary retention needing self-catheterization	15 (42.8)	G2
Rectoureterovaginal fistula	1 (2.8)	G3
Pneumothorax	1 (2.8)	—
Rectovaginal fistula	1 (2.8)	G3
Wound infection	1 (2.8)	G2
Pelvic abscess	1 (2.8)	G1
Late postoperative complications		
Ureteronephrosis	9 (25.7)	G1
Long-term neurological vesical dysfunction	5 (14.3)	G3
Lymphocyst	4 (11.4)	G1
Persistent leg edema	3 (8.6)	G1
Bowel occlusion	2 (5.7)	G1
Vesicovaginal fistula	2 (5.7)	G2
DVT	1 (2.8)	G1
Chronic renal failure	1 (2.8)	G3

Deep venous thrombosis (DVT), estimated blood loss (EBL).

OUTCOME



CONCLUSIONI

Radical surgery
following chemoradiotherapy
can be performed
with an acceptable rate of
complications
even in stage IIIb patients

Fanfani F. *International Journal of Gynecological Cancer*

Punti in Discussione

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5. Prospettive future

RTCT neoadiuvante in stadi avanzati del cervicocarcinoma

	RS	RT/CT neoadiuvante
	Trimbos 2004	
Median OT	240	
Median EBL	---	
Transfusion (%)	32%	
Mortality	<1%	
Fistula	2%	
Ureteral stenosis/renal failure	3%	
Bowel (sub)occlusion	1%	
DVT	3%	
Wound dehiscence	4%	
Fever	---	
Symptomatic Lymphocysts	5%	

Sicurezza

RTCT neoadiuvante in stadi avanzati del cervicocarcinoma

	RS	RT/CT neoadiuvante	
	Trimbos 2004	Jurado 1999	
Median OT	240	---	
Median EBL	---	---	
Transfusion (%)	32%	---	
Mortality	<1%	---	
Fistula	2%	10%	
Ureteral stenosis/renal failure	3%	12.5 + 5.0%	
Bowel (sub)occlusion	1%	7.5%	
DVT	3%	2.5%	
Wound dehiscence	4%	2.5%	
Fever	---	20%	
Symptomatic Lymphocysts	5%	5%	

Sicurezza

RTCT neoadiuvante in stadi avanzati del cervicocarcinoma

	RS	RT/CT neoadiuvante	
	Trimbos 2004	Jurado 1999	UCSC 2007
Median OT	240	---	215
Median EBL	---	---	500
Transfusion (%)	32%	---	32%
Mortality	<1%	---	1%
Fistula	2%	10%	1.3%
Ureteral stenosis/renal failure	3%	12.5 + 5.0%	7.3%
Bowel (sub)occlusion	1%	7.5%	4.2%
DVT	3%	2.5%	1%
Wound dehiscence	4%	2.5%	2.0%
Fever	---	20%	18%
Symptomatic Lymphocysts	5%	5%	3.3%

Sicurezza

RTCT neoadiuvante in stadi avanzati del cervicocarcinoma

	RS	RT/CT neoadiuvante		
	Trimbos 2004	Jurado 1999	UCSC 2007	UCSC 2013
Median OT	240	---	215	210
Median EBL	---	---	500	250
Transfusion (%)	32%	---	32%	n.r
Mortality	<1%	---	1%	<1%
Fistula	2%	10%	1.3%	1.6%
Ureteral stenosis/renal failure	3%	12.5 + 5.0%	7.3%	5.4%
Bowel (sub)occlusion	1%	7.5%	4.2%	2.4%
DVT	3%	2.5%	1%	0%
Wound dehiscence	4%	2.5%	2.0%	2.1%
Fever	---	20%	18%	18.8%
Symptomatic Lymphocysts	5%	5%	3.3%	1.3%

Sicurezza

CHIRURGIA
Massa Critica

Uterine cancer in Maryland: Impact of surgeon case volume and other prognostic factors on short-term mortality

Teresa P. Díaz-Montes ^{a,*}, Marianna L. Zahurak ^b, Robert L. Giuntoli II ^a,
Ginger J. Gardner ^a, Robert E. Bristow ^a

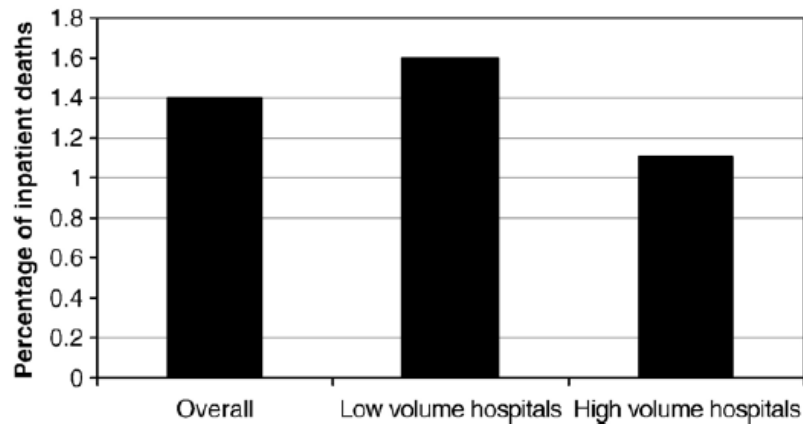
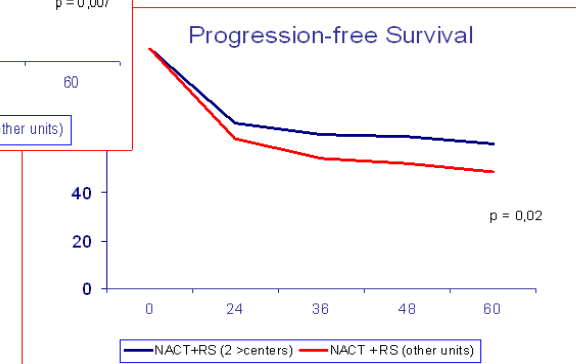
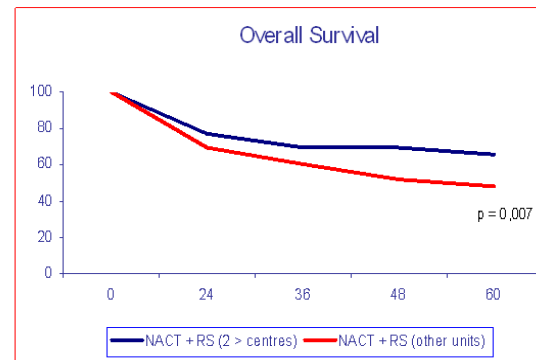


Fig. 2. In-hospital death rate among women that underwent surgical treatment for uterine cancer in Maryland, 1994–2005 according to hospital volume.



Sicurezza

PATTERNS OF RADIOTHERAPY PRACTICE FOR PATIENTS WITH
CARCINOMA OF THE UTERINE CERVIX: A PATTERNS OF CARE STUDY

PATRICIA J. EIFEL, M.D.,* JENNIFER MOUGHAN, M.S.,[†] BETH ERICKSON, M.D.,[‡]
TOM IAROCCI, M.D., M.S.,[†] DEBORA GRANT, R.N., M.S.N.,[†] AND JEAN OWEN, PH.D.[†]

- i parametri di una RT ottimale (uso della brachiterapia, dose totale e tempo totale del trattamento) son meglio rispettati nei centri di riferimento, che trattano più di 500 pz/anno
- Un quarto dei centri valutati trattavano meno di 3 pazienti/anno, con ricaduta negativa sulla qualità della terapia

Punti in Discussione

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2. Fattibilità negli stadi avanzati
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4. **Complicanze tardive e QoL** dopo trattamento RT/CT + chirurgia radicale
5. Prospettive future

Table 2. Grade 3 sequelae correlated with stage

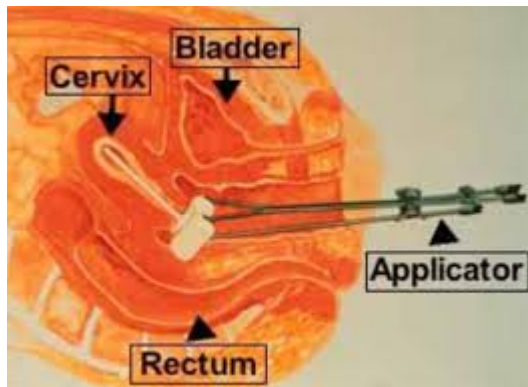
	Stage, number (%)				
	IB	IIA	IIB	III	IVA
Total number of patients treated	493	151	433	350	29
Number of patients with sequelae	24 (5)	15 (10)	45 (10)	33 (9)	3 (10)
Number of complications	28 (6)	25 (17)	61 (14)	41 (12)	4 (14)
Rectum-rectosigmoid					
Rectovaginal fistula	4 (0.8)	2 (1)	11 (2)	11 (3)	1 (3)
Rectouterine fistula	1 (0.2)				
Colonvaginal fistula			1 (0.2)		
Rectal stricture	3 (0.6)	4 (3)	4 (0.9)	2 (0.6)	
Proctitis					
Rectal ulcer					
Sigmoid perforation					
Small bowel					
Small bowel obstruction					
Small bowel perforation					
Enterocolic fistula					
Enterocutaneous fistula		1 (0.7)	–	1 (0.3)	
Enterovaginal fistula			3 (0.7)		
Enteritis/cachexia				1 (0.3)	
Urinary					
Vesicovaginal fistula	3 (0.6)	2 (1)	6 (1)	8 (2)	2 (7)
Ureterovaginal fistula				1 (0.3)	
Cystitis	2 (0.4)				
Bladder ulcer				1 (0.3)	
Ureteral stricture	5 (1)	5 (3)	7 (2)	4 (1)	1 (3)
Other					
Postoperative abscess			1 (0.2)		
Pulmonary embolus				1 (0.3)	
Hemorrhage		1 (0.7)	1 (0.2)		
Pelvic infection	1 (0.2)	1 (0.7)	1 (0.2)		
Neuropathy			1 (0.2)		
Thrombosis of pelvic blood vessels		1 (0.7)			
Radiation myelitis	1 (0.2)				

IB**IIA****IIB****III****IVA****6%****17%****14%****12%****14%**

Brachiterapia: effetti tardivi comuni

Complicanze rettali 22.1%

- Gradi I/II 19.4%,
- Gradi III/IV 1.8%,
- Grado V (fatali) 0.9%



Complicanze tenuali 4.4%

- Gradi I/II 3.5%
- Gradi III/IV 0.9%

Complicanze tratto urinario 14.2%

- Gradi I/II 11.5%
- Gradi III/IV 2.7%

**COMPLETION SURGERY AFTER CONCOMITANT CHEMORADIATION IN
LOCALLY ADVANCED CERVICAL CANCER: A COMPREHENSIVE ANALYSIS OF
PATTERN OF POSTOPERATIVE COMPLICATIONS**

Gabriella Ferrandina¹, Alfredo Ercoli², Anna Fagotti³, Francesco Fanfani⁴, Valerio Gallotta¹,
Alessandro P. Margariti¹, Maria Giovanna Salerno⁵, Vito Chiantera⁶, Francesco Legge⁶, Gabriella
Macchia⁷, Alessio G. Morganti⁷, Vincenzo Valentini⁸, Giovanni Scambia¹

362 pazienti consecutive

**IB2-IVA FIGO LACC trattate con RT/CT neoadiuvante +
CH**

singola Istituzione

Complicanze tardive

Table 3. Type of late postoperative complications according to organ system and grade

ORGAN SYSTEM	N	TYPE
ALL	31	
Urinary	20	
G2	14	Ureteral stenosis requiring surgery with subsequent normal renal function (N=5) Hematuria requiring hospitalization and/or vesical therapy (N=4) Urinary retention requiring self-catheterization (N=2) Urinary incontinence (N=3)
G3	5	Ureteral stenosis with subsequent inadequate renal function (n=3) Urinary retention with long term catheterization (N=1) Total incontinence (N=1)
G4	1	Septicaemia ^a
Gastro-intestinal	7	
G1	1	Post-operative obstruction settling on conservative treatment (N=1)
G2	5	Persistent symptoms or sign of rectal origin requiring medical and/or dietary treatment (N=3) Chronic obstruction not requiring surgery (N=2)
G3	1	Any signs or symptoms requiring surgery not resulting in normal activity
Vascular	2	
G1	2	Lymphocele (N=1) Thrombophlebitis (N=1)
Other	2	
G1	1	Wound dehiscence not requiring surgery
G3	1	Severe dyspareunia

^a Early G3 urinary complication

93 pazienti



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Quality of life and psychological distress in locally advanced cervical cancer patients administered pre-operative chemoradiotherapy

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Distribution of all subscales SF-36 scores in early and locally advanced cervical cancer patients

SF-36 subscale	EEC	LACC	<i>p</i> value *
	Mean ± SD	Mean ± SD	
Physical Functioning (PF) ←	85.4 ± 16.2	69.0 ± 13.1	0.0007
Role Physical (RP)	65.0 ± 21.4	60.7 ± 32.9	0.8
Bodily Pain (P)	70.8 ± 25.0	69.0 ± 28.7	0.6
General Health (GH)	63.0 ± 21.8	60.2 ± 22.7	0.3
Vitality (VT)	60.7 ± 20.3	58.6 ± 19.4	0.4
Social Functioning (SF)	66.6 ± 23.0	68.3 ± 24.7	0.5
Role Emotional (RE)	65.5 ± 21.8	61.9 ± 33.2	0.5
Mental Health (MH)	65.4 ± 20.7	62.8 ± 20.4	0.3
Physical Component Scale (PCS)	48.3 ± 10.8	44.2 ± 10.4	0.075
Mental component Scale (MCS)	43.2 ± 10.1	43.0 ± 10.8	0.9

QoL scores **paragonabili**

QoL

Punti in Discussione

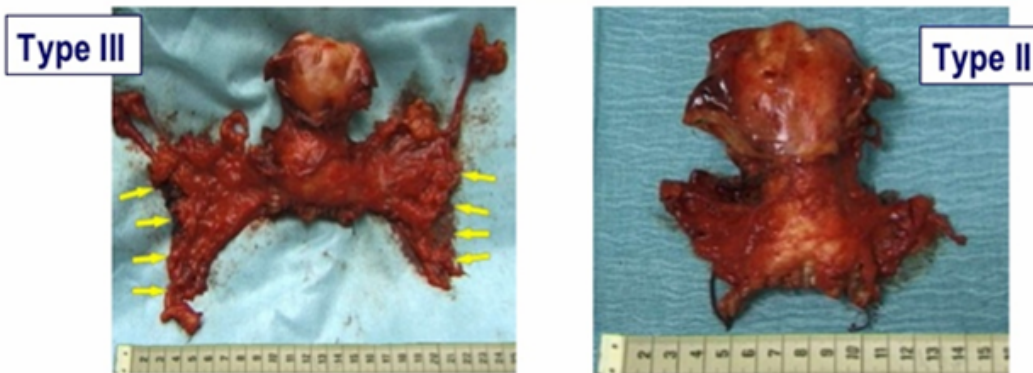
1. Outcomes rispetto a trattamento standard
2. Fattibilità negli stadi avanzati
3. Sicurezza della chirurgia radicale dopo RT/CT preoperatoria
4. Complicanze tardive e QoL dopo trattamento RT/CT + chirurgia radicale
5. **Prospettive future**

Is There a Place for a Less Extensive Radical Surgery in Locally Advanced Cervical Cancer Patients?

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Types of hysterectomy- Piver



Complication	Type II	Type III
Urinary fistulas	0.3%	4.8%
Digestive fistulas	0.3%	1%
Deaths	0.5%	0.3%
Thromboembolism	1.1%	7%
Urinary dysfunction	0.8%	40%

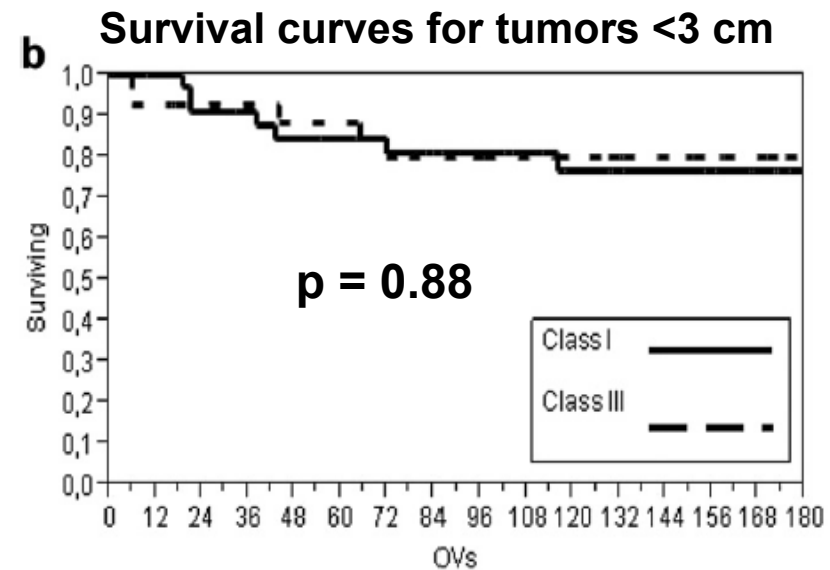
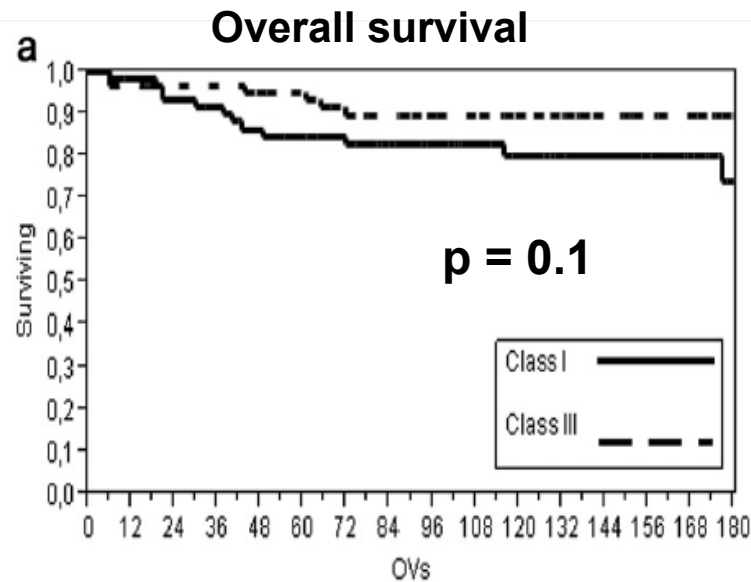
Magrina, 1995

Modulazione CH



Class I versus class III radical hysterectomy in stage IB1-IIA cervical cancer.
A prospective randomized study

F. Landoni ^a, A. Manco ^b, I. Zapardiel ^{a,*}, V. Zanagnolo ^a, C. Mangioni ^b





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Multimodality approach in extra cervical locally advanced cervical cancer:
Chemoradiation, surgery and **intra-operative radiation therapy**. A phase II trial

G. Giorda ^{a,*}, G. Boz ^b, A. Gadducci ^c, E. Lucia ^a, G. De Piero ^a, A. De Paoli ^b, R. Innocente ^b,
M. Trovò ^b, R. Sorio ^d, E. Campagnutta ^a

- IORT migliora controllo locale [IFR =4 of 35 (11%)] ma non influenza OS
- OS rimane scadente se persiste residuo di malattia extracervicale sebbene venga rimosso chirurgicamente

IORT



Identificazione di nuovi fattori di prognosi

- COX-2 status/SCC/Anemia
- CT-RT response: RM-US- PET/TC

Incremento del controllo locale

- Nuovi farmaci (molecole, dosaggi, schedule)
- Modificatori biologici della risposta
- Incremento della dose totale di radioterapia
- Chemioterapia adiuvante
- Immunoterapia

grazie



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UPDATE ON CHEMORADIATION AND CERVICAL CANCER

NOVEL PROMISING STRATEGIES and DRUGS in CRT

- ✓ **CONCURRENT RADIOTHERAPY WITH PACLITAXEL/CARBOPLATIN CHEMOTHERAPY AS DEFINITIVE TREATMENT FOR LACC**
Lee G, Gynecol Oncol 2007
33pts enrolled; 100% RR (70% CR, 30% PR); 3yrs DFS 50-90%, 3yrs OS 50-91%
- ✓ **CAPECITABINE AND RADIOTHERAPY FOR LACC: PHASE II RESULTS**
Domingo E, ASCO 2008
- ✓ **CONCURRENT MITOMYCIN C, 5-FLUOROURACIL AND RADIOTHERAPY IN LACC: A RANDOMIZED TRIAL**
Lorvidahya, Int J Radiat Oncol Biol Phys 2003
- ✓ **EFFICACY OF WEEKLY CARBOPLATIN (AUC2) FOLLOWED BY CHEMORADIATION (70 Gy total dose) IN LACC**
Higgins RV, Gynecol Oncol 2003
High response rate (90%) with low grade GI and hematological toxicities
- ✓ **DOSE DENSE CARBOPLATIN (AUC2) AND PACLITAXEL (80 MQ/MSQ) WEEKLY FOR 6 CYCLES FOLLOWED BY CHEMORADIATION**
Mccormak M, ESGO 2009
Preliminary data suggests a very high RR (80%) with acceptable toxicity profile

FUTURE PERSPECTIVES

- ✓ **Developing target based therapy**
- ✓ **Identification of gene expression signatures as predictors of outcome after CRT** (*JB Weidhass, Clinical Cancer Research 2009*)