Optimal Multi-modality Therapy For Gynaecological Cancers

Endometrial Cancer

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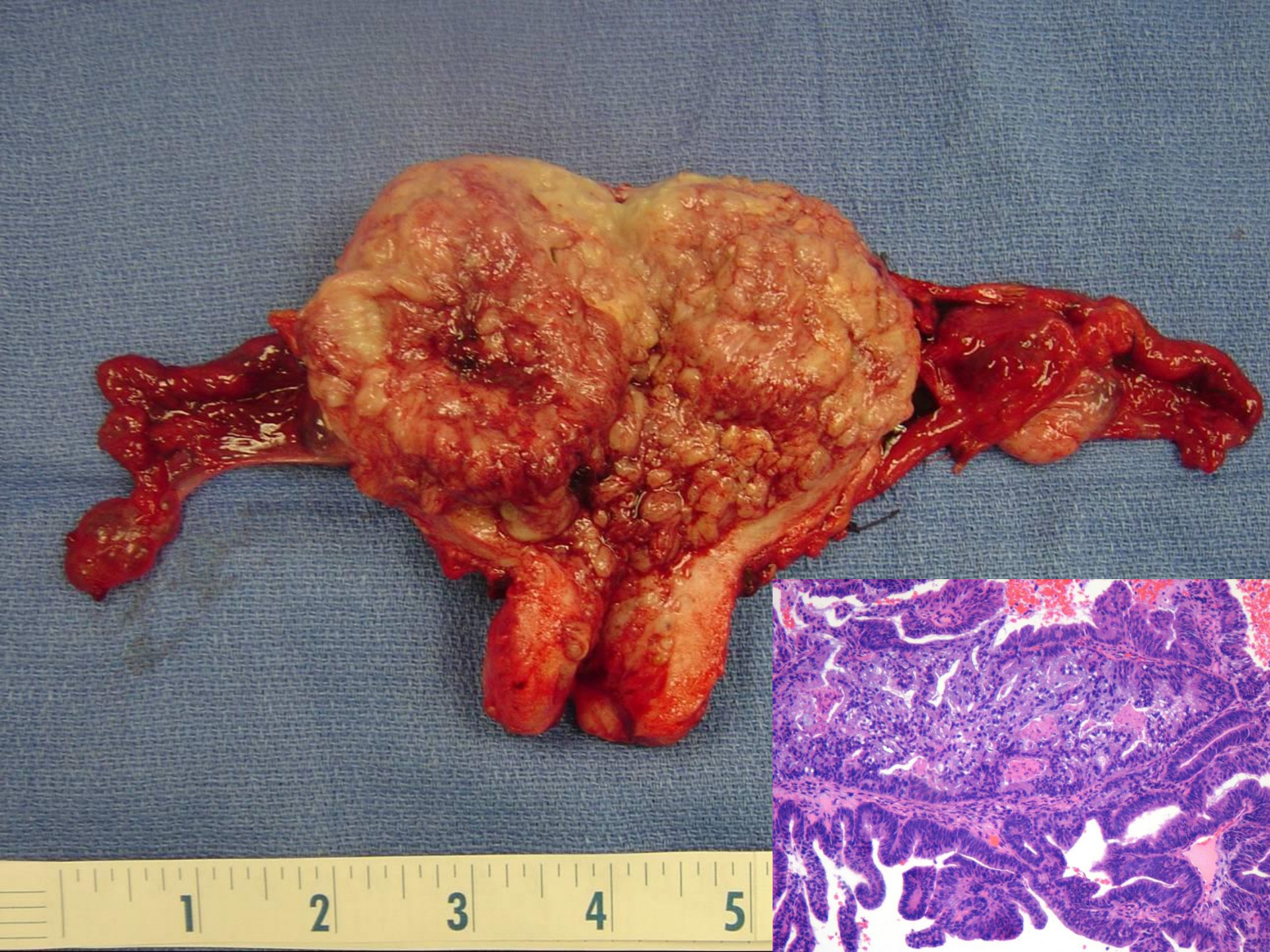
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Endometrial Cancer: Annual Incidence and Mortality

ACS Estimates

Year	Cases	Deaths
1987	35,000	2,900
2015	54,870	10,170

American Cancer Society 2015

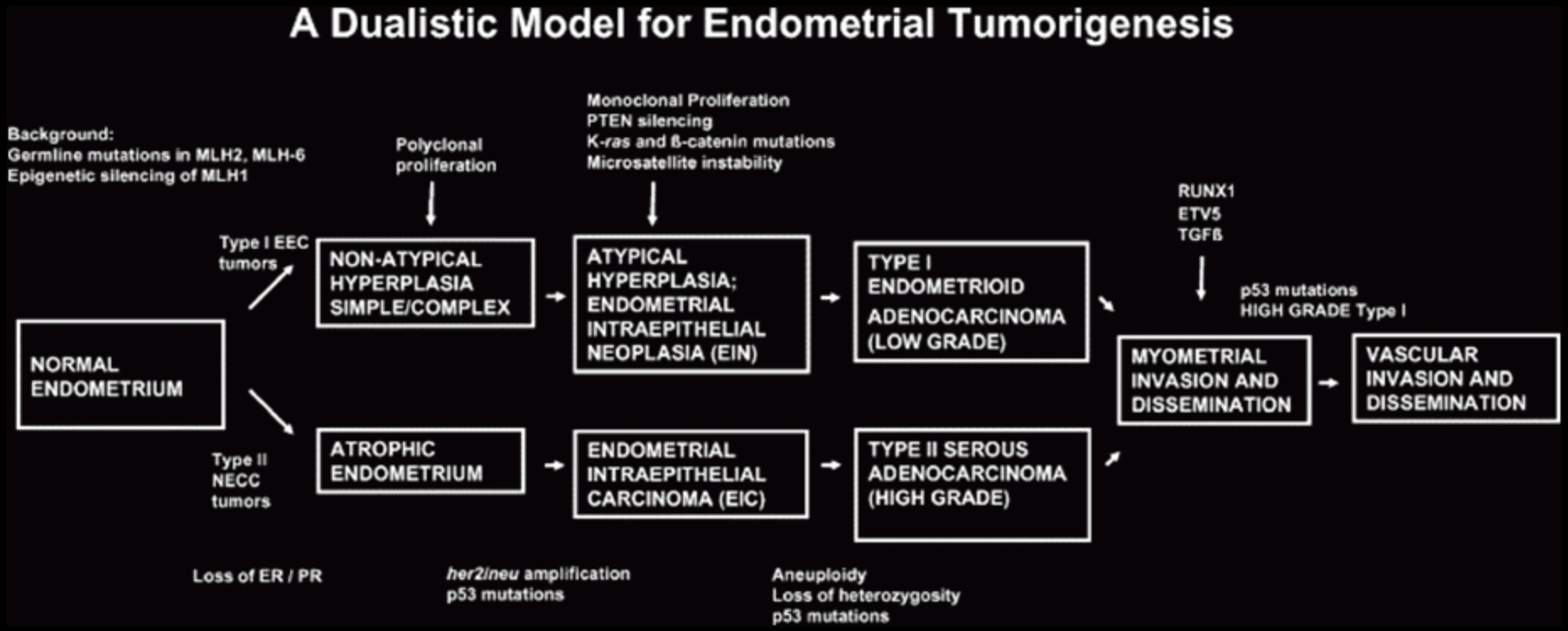
Endometrial Cancer: Types

Table 33-3. Type I and II Endometrial Carcinoma: Distinguishing Features

Feature	Type I	Type II
Unopposed estrogen	Present	Absent
Menopausal status	Pre- and perimenopausal	Postmenopausal
Hyperplasia	Present	Absent
Race	White	Black
Grade	Low	High
Myometrial invasion	Minimal	Deep
Specific subtypes	Endometrioid	Serous, clear cell
Behavior	Stable	Aggressive

From Kurman, 1994, with permission.

Bokhman. Gyn Onc 15:10 ‘83



Doll. J Steroid Biochem Mol Biol 108:221 '08

Table. — Genetic Alterations in Endometrial Cancer: Percentage Frequency of Genetic Mutations Identified in Type 1 and 2 Endometrial Cancers

Genetic Alteration	Type 1 Carcinoma (%)	Type 2 Carcinoma (%)
PTEN inactivation	50–80	10
K-ras mutation	15–30	0–5
β-catenin mutation	20–40	0–3
Microsatellite instability	20–40	0–5
p53 mutation	10–20	80–90
HER-2/neu	10–30	40–80
p16 inactivation	10	40
E-cadherin	10–20	60–90

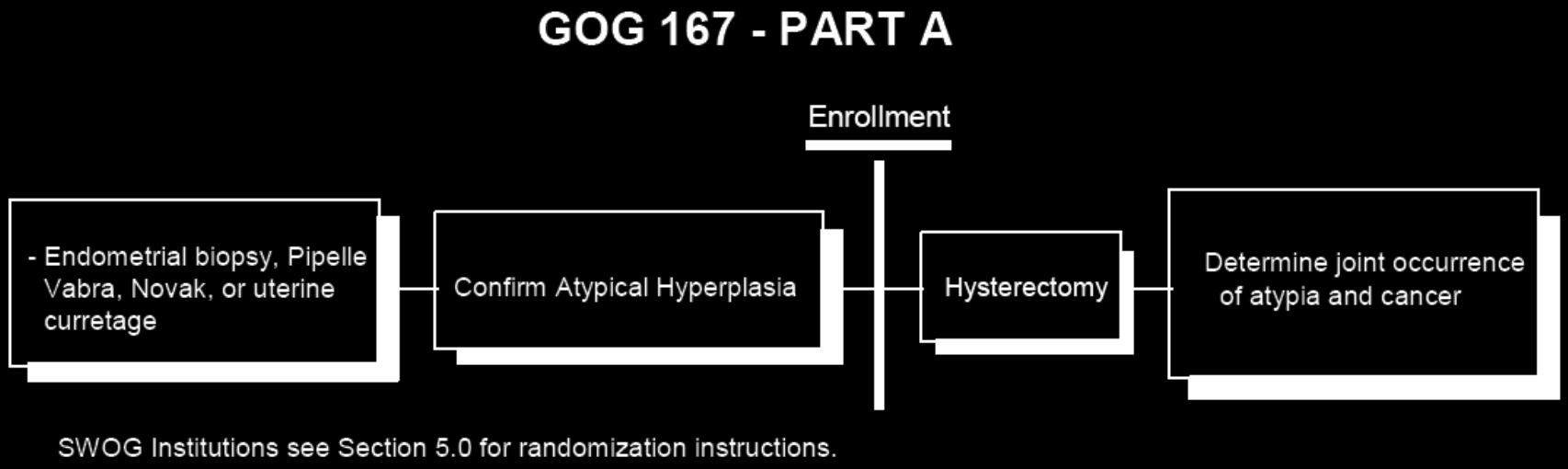
Bansal et al. Ca Control 16:13 ‘09

Atypical Endometrial Hyperplasia

TABLE 5
Atypical Endometrial Hyperplasia and Concurrent Endometrioid Carcinoma of the Uterus

Study	Type of study	No. of patients	Percentage of patients with concurrent carcinoma	Percentage of patients with myoinvasion
Gusberg and Kaplan, 1963[12]	Retrospective, single-institution case series	18	20.0	Not recorded
Tavassoli and Kraus, 1978[15]	Retrospective, single-institution case series	48	25.0	2.1
Kurman and Norris, 1982[16]	Retrospective, referral case series	89	17.0	7.9
Janicek and Rosenshein, 1994[22]	Retrospective, single-institution case series	44	43.0	39.0
Dunton et al., 1996[23]	Retrospective, single-institution case series	23	52.0	26.0
Current study	Prospective, multiinstitutional cohort	289	43.0	13.2

Atypical Endometrial Hyperplasia



- AEH dx not confirmed in 61%
- Ca found in 40% (31% > IA GI)
  - 37% in confirmed AEH
  - 67% with no agreement
    - Zaino et al. Cancer 106:804 ‘06
    - Trimble et al. Cancer 106:812 ‘06

LNG-IUS for Endometrial Hyperplasia

Table 2. Fraction of regression of hyperplasia and the confidence intervals (95% CI) in each category of endometrial hyperplasia in the three therapy groups

Intervention	SH Fraction of regress. (95% CI)	CH Fraction of regress. (95% CI)	ACH Fraction of regress. (95% CI)
LNG-IUS	6/6 = 1.0 (0.54–1.0)	41/41 = 1.0 (0.91–1.0)	6/6 = 1.0 (0.54–1.0)
Oral continuous	6/6 = 1.0 (0.54–1.0)	33/34 = 0.97 (0.84–1.0)	7/8 = 0.88 (0.47–1.0)
Oral cyclic	7/11 = 0.64 (0.31–0.89)	26/36 = 0.72 (0.55–0.86)	3/5 = 0.6 (0.14–0.95)
Total	19/30 = 0.64 (0.44–0.80)	100/111 = 0.90 (0.83–0.95)	16/19 = 0.84 (0.60–0.97)

SH, simple hyperplasia; CH, complex hyperplasia; ACH, atypical complex hyperplasia.[1,28]

- Multicentre randomised trial, N=170
- Responses were obtained for all the women in the LNG-IUS group (53/53, 95% CI 0.93–1.0) and for 96% of the women in the continuous oral group (46/48, 95% CI0.86–0.99).
- Only 69% of the women in the cyclic oral group were responders (36/52, 95% CI 0.55–0.81).
  - Orbo et al. BJOG 121:477 ‘14

Endometrial Cancer Histopathologic correlation

- 22% (144/621) of patients had metastatic disease
- 11% (70/621) had LN metastases (pelvic &/or PAN)
- Fewer than 10% of metastatic nodes were palpably enlarged
- Depth of myometrial invasion increased with tumor grade (dedifferentiation)
- Risk of lymph node metastasis increased with
  - Depth of myometrial invasion
  - tumor grade (i.e. tumor dedifferentiation)

    - Creasman, Ca 60(8S)2035 ‘87

Risk of Pelvic Node Metastasis

Invasion	Grade 1	Grade 2	Grade 3
Endometrium only	0%	3%	0%
Inner 1/3	3%	5%	9%
Middle 1/3	0%	9%	5%
Outer 1/3	11%	19%	34%

Creasman WT, et al. Cancer 1987;60:2035-2041

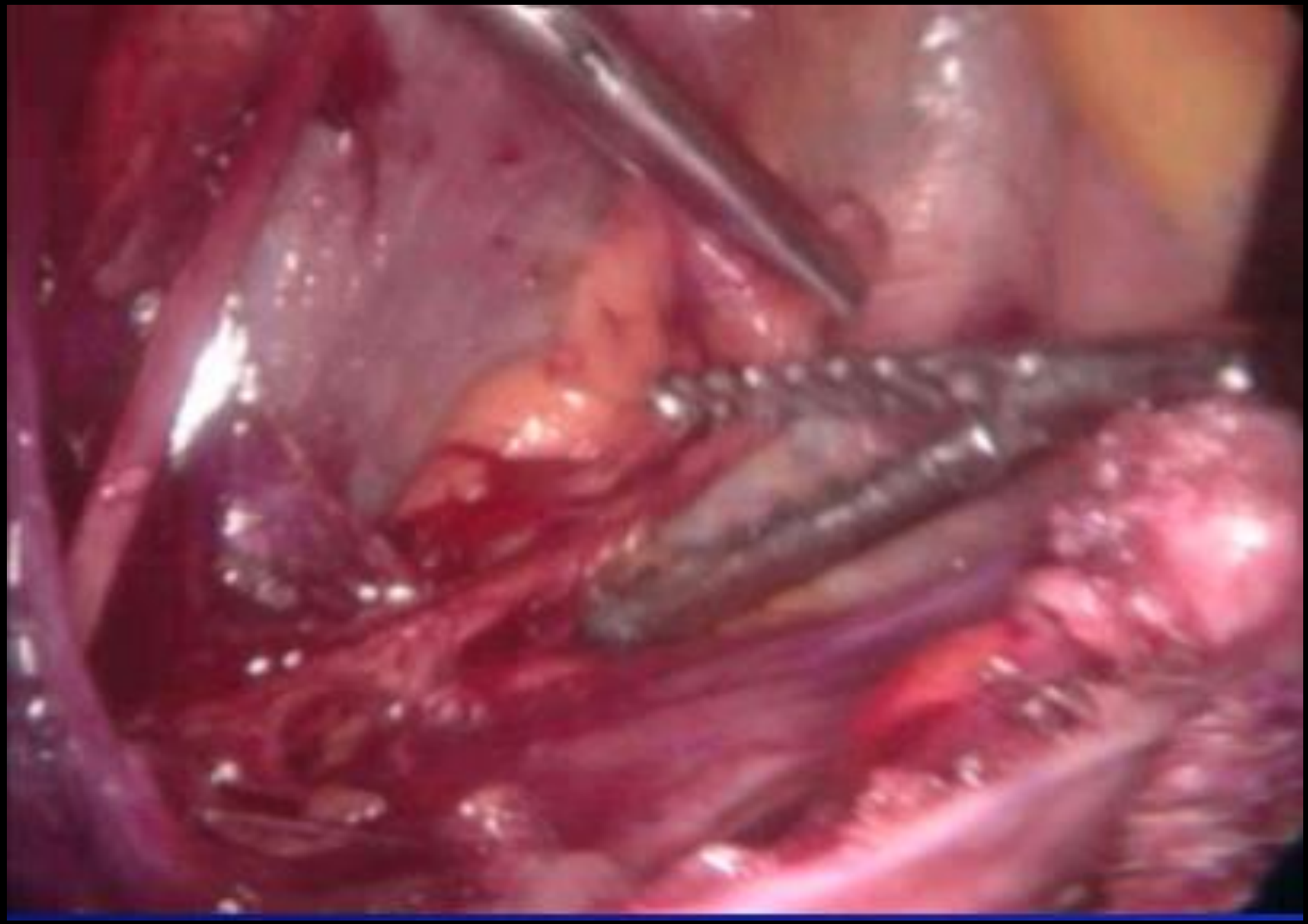
Endometrial Cancer: Nodal Involvement

Situation	% Positive Nodes
G1, no myometrial invasion, no extrauterine disease.	<1%
G2 or G3, inner 1/3 invasion, no extrauterine disease	5-9% Pelvic 4% Aortic
G3, outer muscle, and/or extrauterine disease	20-60% Pelvic 10-30% Aortic

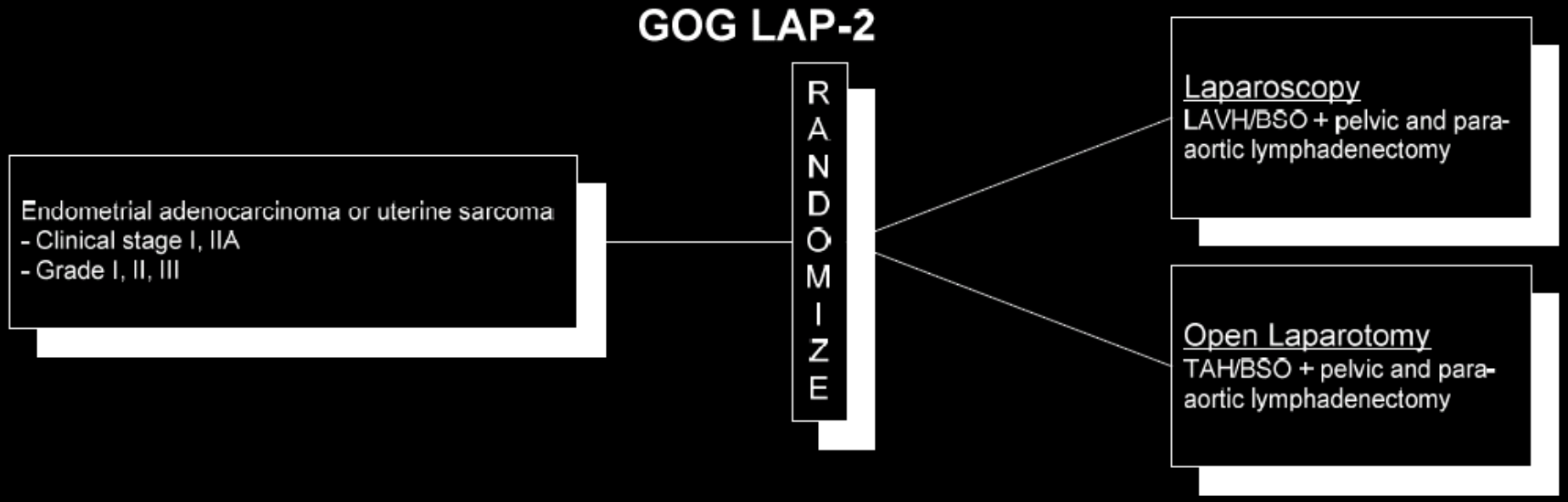
Endometrial Cancer

FIGO 2009

FIGO Stage	Criteria
IA	No invasion or <=1/2 myometrial invasion
IB	>1/2 myometrial invasion
II	Extension to cervical stroma
IIIA	Extension to uterine serosa and/or adnexae
IIIB	Extension to vagina and/or parametrium and/or pelvic peritoneum
IIIC1	Metastasis to pelvic nodes
IIIC2	Metastasis to para-aortic nodes with/without pelvic node metastasis
IVA	Extension to bladder and/or rectal mucosa
IVB	Distant mets including intraabdominal and/or inguinal nodes



Phase III Randomized Clinical Trial of Laparoscopic Pelvic and Para Aortic Node Sampling with Vaginal Hysterectomy and BSO Versus Open Laparotomy with Pelvic and Para Aortic Node Sampling and Abdominal Hysterectomy and BSO in Endometrial Adenocarcinoma and Uterine Sarcoma, Clinical Stage I, IIA, Grade I, II, III



Staging

GOG LAP-2

- Laparoscopic (n=1696) vs laparotomy (n=920)
- Laparoscopy: 74% completed
- Lymphadenectomy 92% vs 96%, p<0.0001
- Operative minutes 204 vs 130, p<0.001
- Post op complications >G2: 14% vs 21%, p<0.0001
- Hospital days 3 vs 4, p<0.001
- “Laparoscopic surgical staging is feasible and safe”
  - Walker et al. J Clin Oncol 27:2531 “09

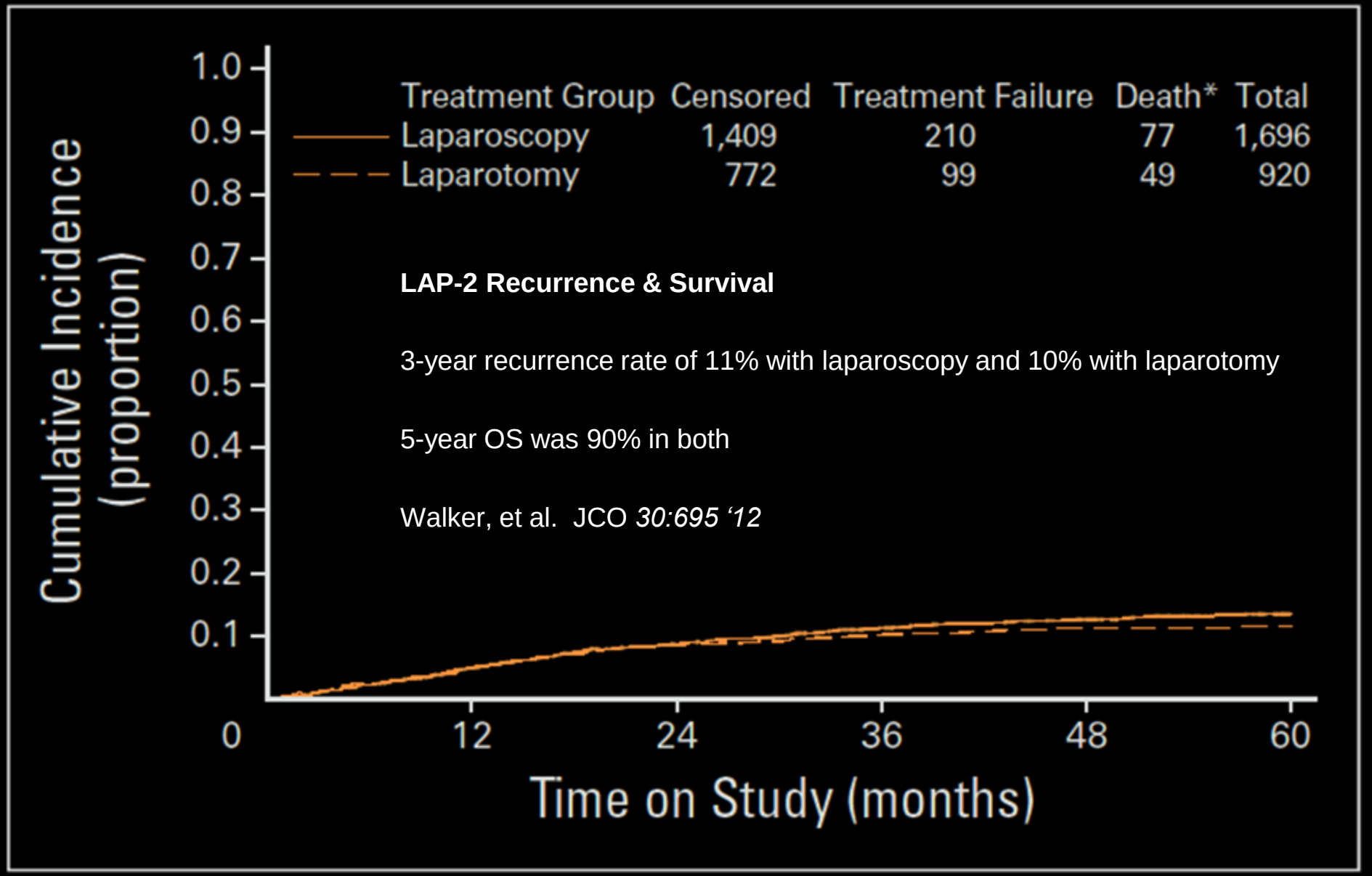


Fig 2. Cumulative incidence of recurrence by randomly assigned treatment group. (*) Deaths prior to recurrence.

THE LANCET

Articles

Efficacy of systematic pelvic lymphadenectomy in endometrial cancer (MRC ASTEC trial): a randomised study

*The writing committee on behalf of the ASTEC study group**

Summary

Background Hysterectomy and bilateral salpingo-oophorectomy (BSO) is the standard surgery for stage I endometrial cancer. Systematic pelvic lymphadenectomy has been used to establish whether there is extra-uterine disease and as a therapeutic procedure; however, randomised trials need to be done to assess therapeutic efficacy. The ASTEC surgical trial investigated whether pelvic lymphadenectomy could improve survival of women with endometrial cancer.

Methods From 85 centres in four countries, 1408 women with histologically proven endometrial carcinoma thought preoperatively to be confined to the corpus were randomly allocated by a minimisation method to standard surgery (hysterectomy and BSO, peritoneal washings, and palpation of para-aortic nodes; n=704) or standard surgery plus lymphadenectomy (n=704). The primary outcome measure was overall survival. To control for postsurgical treatment, women with early-stage disease at intermediate or high risk of recurrence were randomised (independent of lymph-node status) into the ASTEC radiotherapy trial. Analysis was by intention to treat. This study is registered, number ISRCTN 16571884.

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See Online/Comment
DOI:10.1016/S0140-6736(08)61768-7

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JNCI JOURNAL OF THE NATIONAL CANCER INSTITUTE

Systematic Pelvic Lymphadenectomy vs No Lymphadenectomy in Early-Stage Endometrial Carcinoma: Randomized Clinical Trial

Pierluigi Benedetti Panici, Stefano Basile, Francesco Maneschi, Andrea Alberto Lissoni, Mauro Signorelli, Giovanni Scambia, Roberto Angioli, Saverio Tateo, Giorgia Mangili, Dionyssios Katsaros, Gaetano Garozzo, Elio Campagnutta, Nicoletta Donadello, Stefano Greggi, Mauro Melpignano, Francesco Raspagliesi, Nicola Ragni, Gennaro Cormio, Roberto Grassi, Massimo Franchi, Diana Giannarelli, Roldano Fossati, Valter Torri, Mariangela Amoroso, Clara Crocè, Costantino Mangioni

Background Pelvic lymph nodes are the most common site of extrauterine tumor spread in early-stage endometrial cancer, but the clinical impact of lymphadenectomy has not been addressed in randomized studies. We conducted a randomized clinical trial to determine whether the addition of pelvic systematic lymphadenectomy to standard hysterectomy with bilateral salpingo-oophorectomy improves overall and disease-free survival.

Methods From October 1, 1996, through March 31, 2006, 514 eligible patients with preoperative International Federation of Gynecology and Obstetrics stage I endometrial carcinoma were randomly assigned to undergo pelvic systematic lymphadenectomy (n = 264) or no lymphadenectomy (n = 250). Patients' clinical data, pathological tumor characteristics, and operative and early postoperative data were recorded at discharge from hospital. Late postoperative complications, adjuvant therapy, and follow-up data were collected 6 months after surgery. Survival was analyzed by use of the log-rank test and a Cox multivariable regression analysis. All statistical tests were two-sided.

Results The median number of lymph nodes removed was 30 (interquartile range = 22–42) in the pelvic systematic lymphadenectomy arm and 0 (interquartile range = 0–0) in the no-lymphadenectomy arm ($P < .001$). Both early and late postoperative complications occurred statistically significantly more frequently in patients who had received pelvic systematic lymphadenectomy (81 patients in the lymphadenectomy arm and 34 patients in the no-lymphadenectomy arm, $P = .001$). Pelvic systematic lymphadenectomy improved surgical staging as statistically significantly more patients with lymph node metastases were found in the lymphadenectomy arm than in the no-lymphadenectomy arm (13.3% vs 3.2%, difference = 10.1%, 95% confidence interval [CI] = 5.3% to 14.9%, $P < .001$). At a median follow-up of 49 months, 78 events (ie, recurrence or death) had been observed and 53 patients had died. The unadjusted risks for first event and death were similar between the two arms (hazard ratio [HR] for first event = 1.10, 95% CI = 0.70 to 1.71, $P = .68$, and HR for death = 1.20, 95% CI = 0.70 to 2.07, $P = .50$). The 5-year disease-free and overall survival rates in an intention-to-treat analysis were similar between arms (81.0% and 85.9% in the lymphadenectomy arm and 81.7% and 90.0% in the no-lymphadenectomy arm, respectively).

Conclusion Although systematic pelvic lymphadenectomy statistically significantly improved surgical staging, it did not improve disease-free or overall survival.

J Natl Cancer Inst 2008;100:1707–1716

Nodal Metastasis Risk in Endometrioid Endometrial Cancer

Michael R. Milam, MD, MPH, James Java, MA, Joan L. Walker, MD, Daniel S. Metzinger, MD, Lynn P. Parker, MD, and Robert L. Coleman, MD, for the Gynecologic Oncology Group

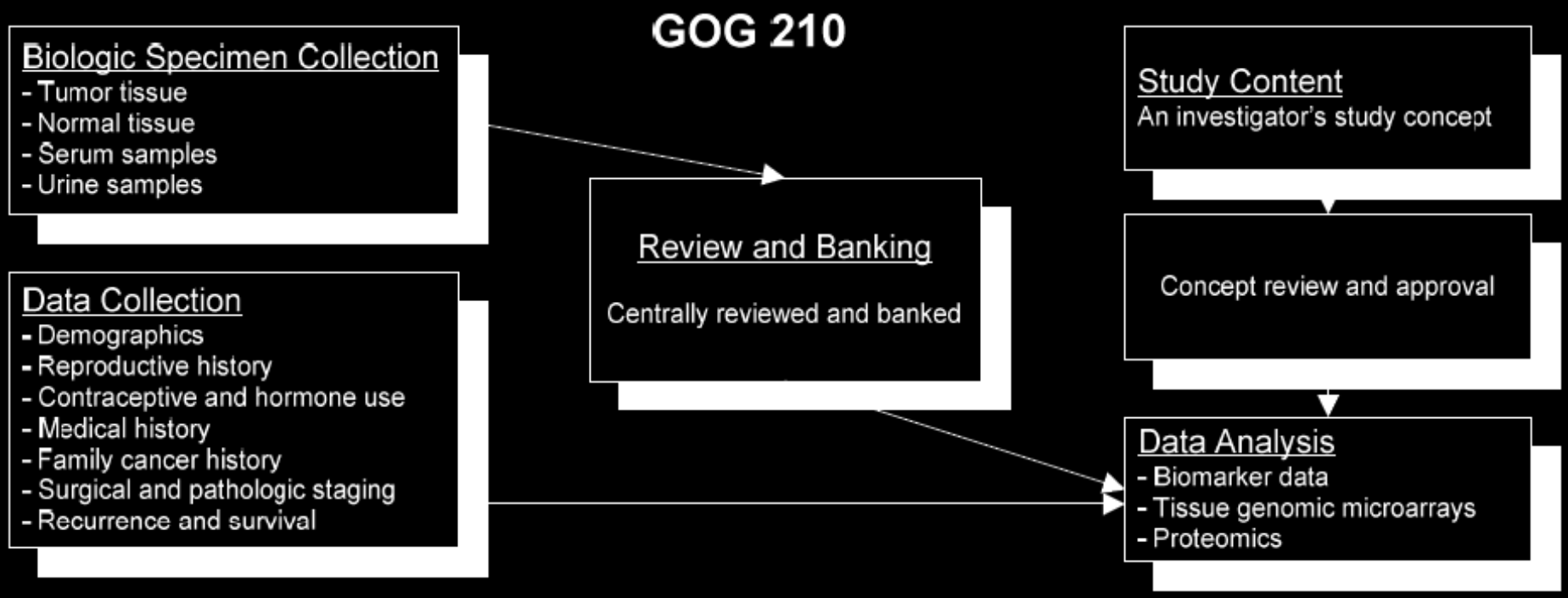
- N = 971 endometrioid from LAP-2
- Tumor < 2cm, < 50% invasion, G1-2 identified 40% at low risk (0.8%) of node mets
- High risk 6.3 X risk of node mets
  - (95% CI 1.67–23.8, P=.007)
- "Low-risk …criteria may be used to help guide treatment planning"
    - Ob Gyn 119:286 '12

Robotics for surgical staging of endometrial cancer

- Da Vinci surgical Robotic system was FDA approved in gynecology in April 2005
- Studies have compared robotics to traditional laparotomy and laparoscopy for endometrial cancer staging
  - Improved visualization (3-D imaging), wrist-like instrument rotation, tremor ablation and motion scaling
  - Lower EBL, lower conversion rates, can accommodate higher BMI pts, shorter operative time, significantly shorter learning curve, lower complication rates

(Boggess 2008; Bell 2008; Lowe 2009; Hoekstra 2009; Seamon, 2009; Holloway 2009; Cardenas-Goicoechea; 2010)

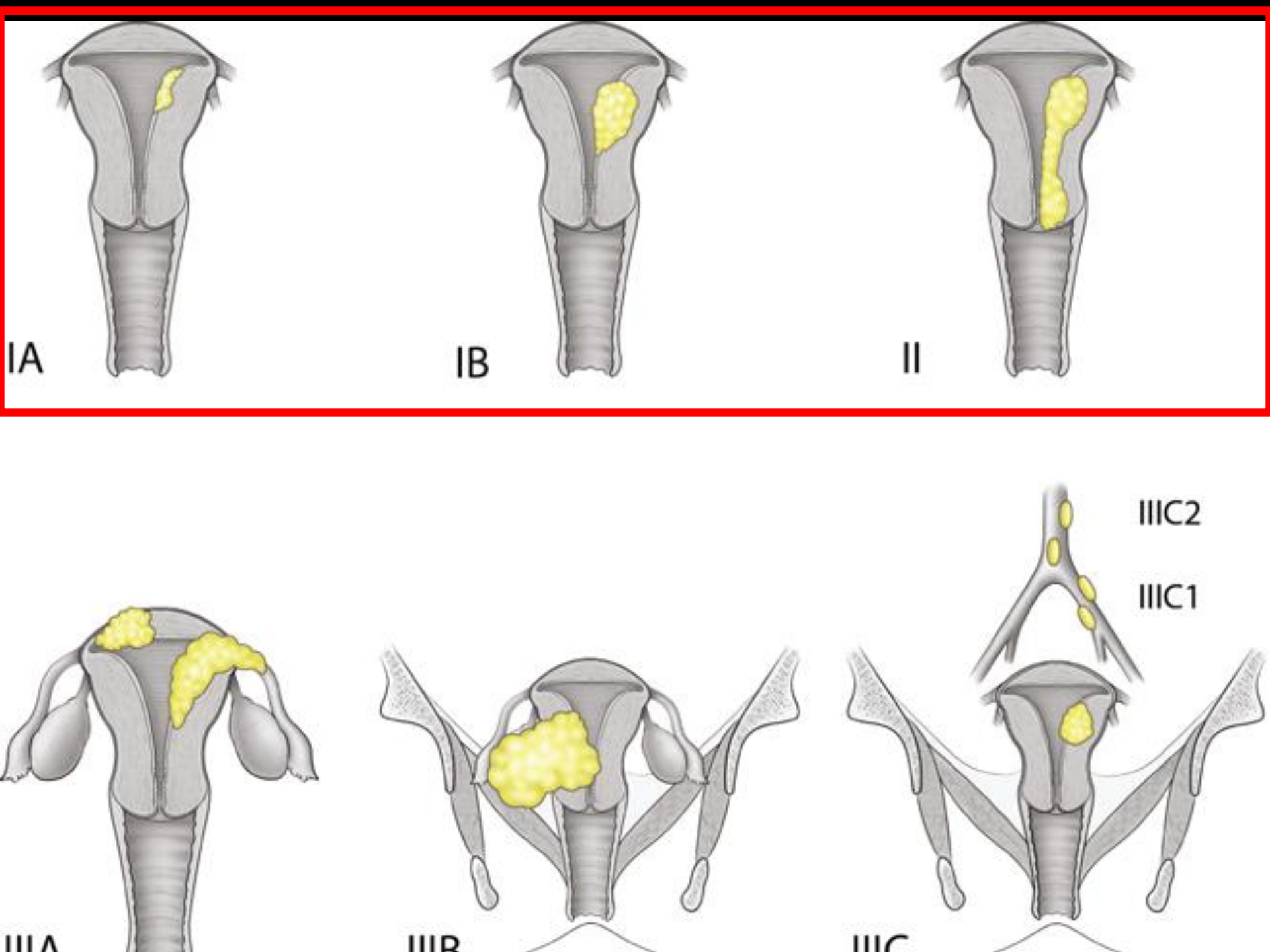
Molecular Staging



- 9/22/2003
- 6096/3500
- Closed 12/2011

GOG-210 Associated Studies

ID	PI	Type	Grant	Status
2006-1	Cohn	Copy number alterations and metastasis	DOD grants P30 CA016056	Genes Chrom Ca 2010;49:791-802
8014	Boren	microRNAs associated with metastasis	CTSA UL1 RR024982	Testing
8015	Gunter	Hormone and IGF-axis and recurrence	R01 CA133010	Specimen Dist / Testing
8016	Maxwell	Genomic/proteomic profile and recurrence	DOD grants	Testing
8017	Zighelboim	ATR mutations and recurrence/progression	R21 pending	Specimen Dist / Testing
8020	Goodfellow	Endometrial SPORE: FGFR2 mutations, methylation profiling, DNA repair defects, ERK signaling, SNPs	P50 CA134254 R21 CA133295 GOG YI Award	Specimen Dist / Testing / Analysis / Manuscript Development
8022	Rocconi	Racial admixture and recurrence/progression	GOG YI Award	Specimen Distr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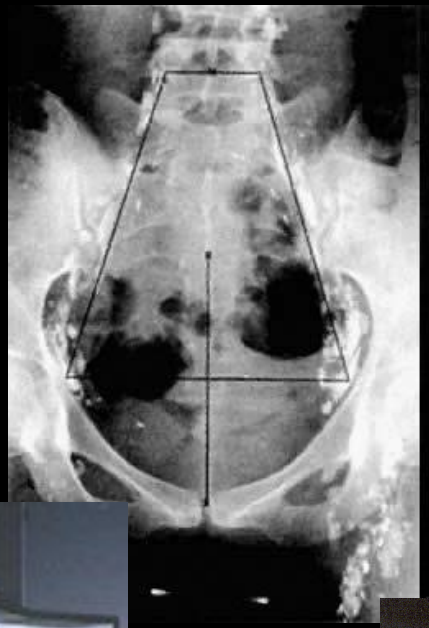
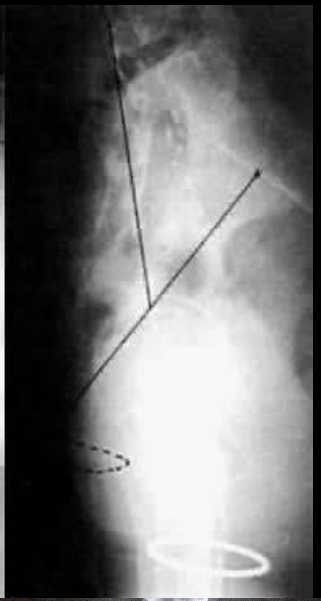
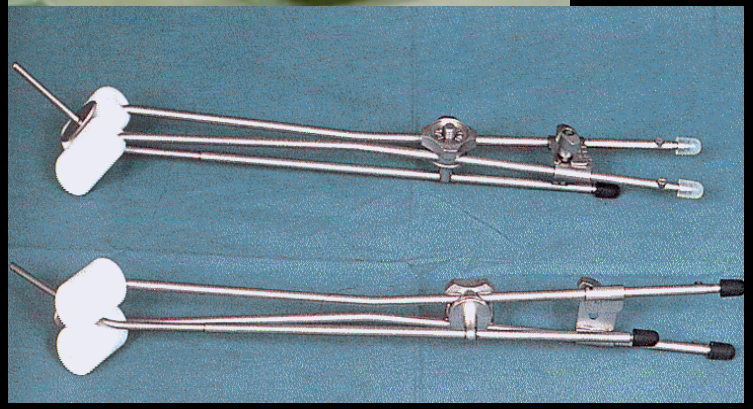
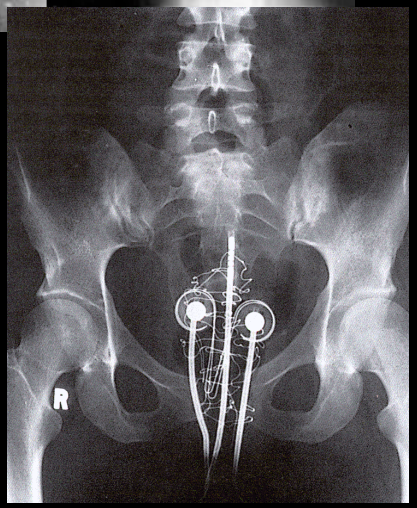
Radiation Therapy

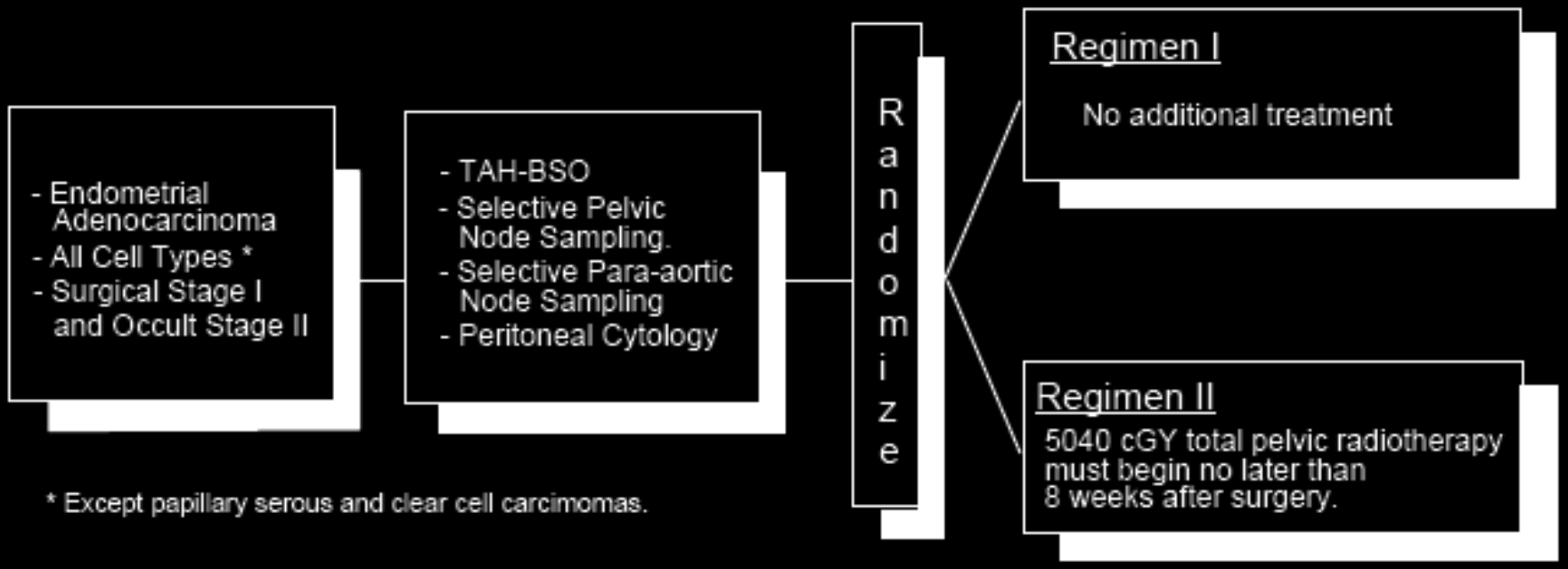








GOG #99: Surgery +/- Adjunctive Radiation Therapy in Intermediate Risk Endometrial Adenocarcinoma

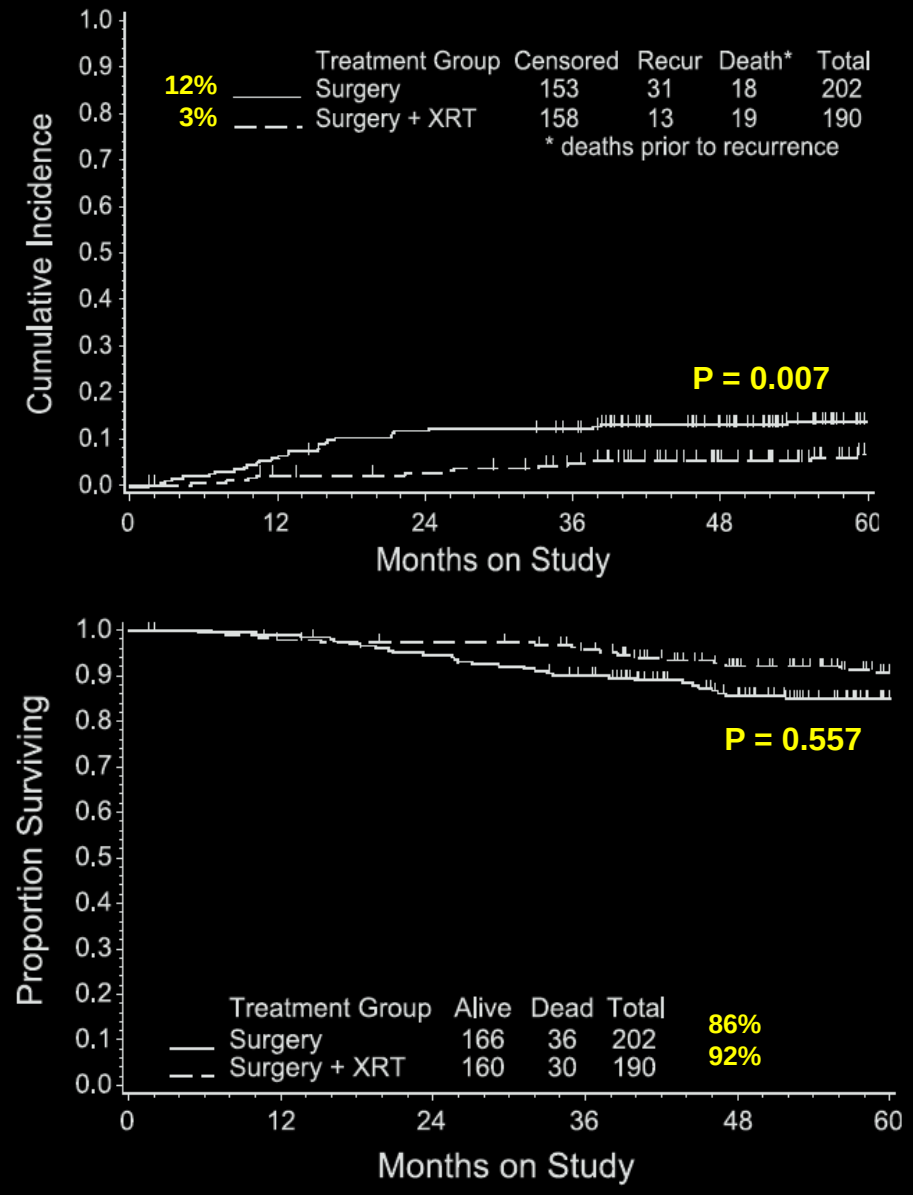


* Except papillary serous and clear cell carcinomas.

GOG #99

- 6/87 – 7/95
- 392 eligible
- Most lb, G1/2, adeno
- 6% vs 14% G3/4 tox
- More heme, GI, GU, skin tox p<.0001
- 44 recurrences
- >50% deaths not CA

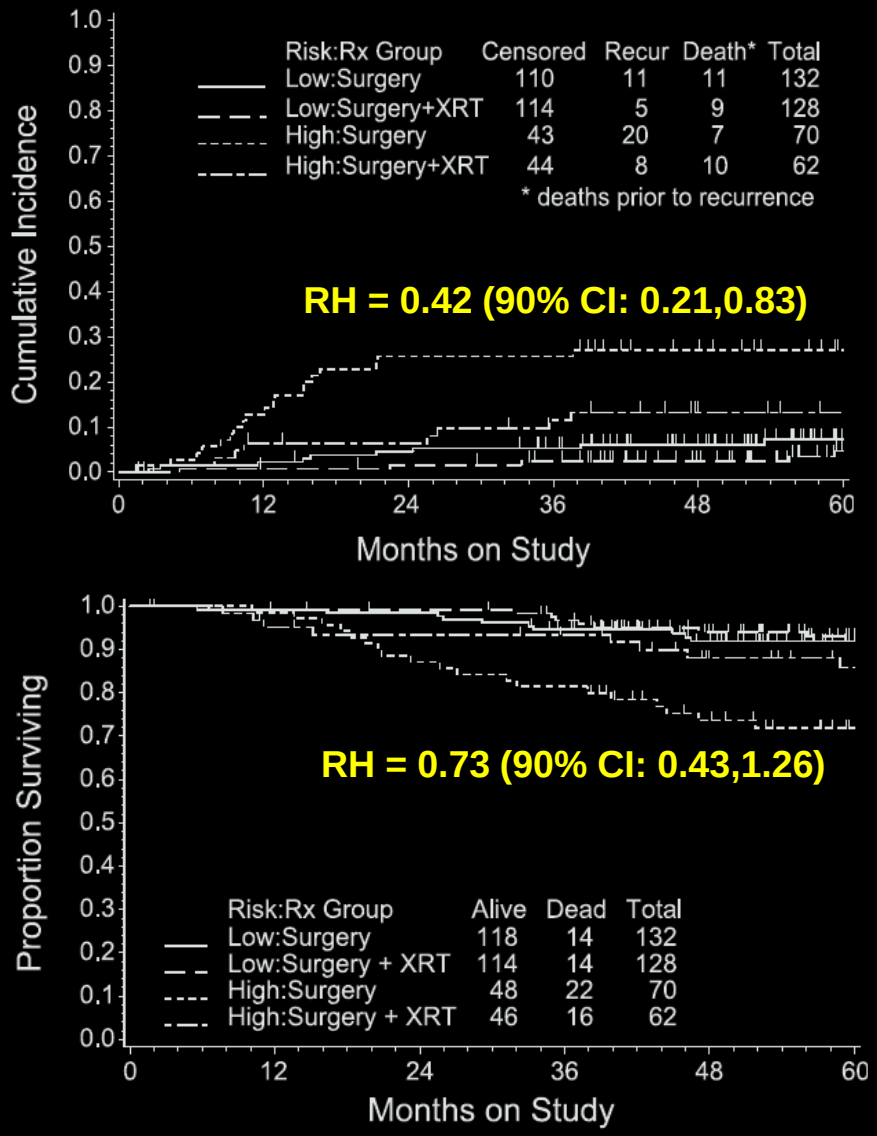
  – Keys et al. Gyn Onc 92:744 ‘04



GOG #99

- High intermediate risk:
  - G2/3, LVSI, >2/3 invasion
  - >50 yrs + 2
  - >70 yrs + 1

    - Keys et al. Gyn Onc 92:744 '04



GOG #99

- Conclusion: "strong evidence for … RT in … high intermediate risk. … not recommended for … lower risk"
- Take home:
  - RT will cut recurrence from 27% to 13%, death from 26% to 12% in HIR
  - But, increase toxicity 6% to 14%
  - Thus, 100 patients will be treated to benefit 14

    - Keys et al. Gyn Onc 92:744 '04

Adjuvant Radiotherapy for Stage I Endometrial Cancer: Cochrane Database of Systematic Reviews

- Gynaecological Cancer Group
- “in patients without any of the high risk factors … greater risk of endometrial carcinoma-related deaths”
  - Kong, et al. DOI: 10.1002/14651858.CD003916.pub2 ‘07

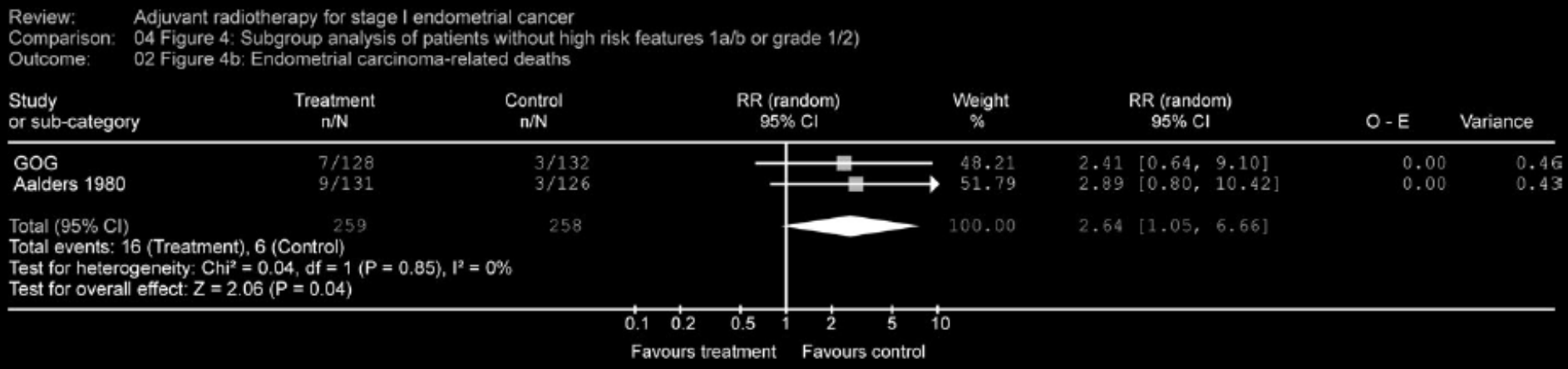
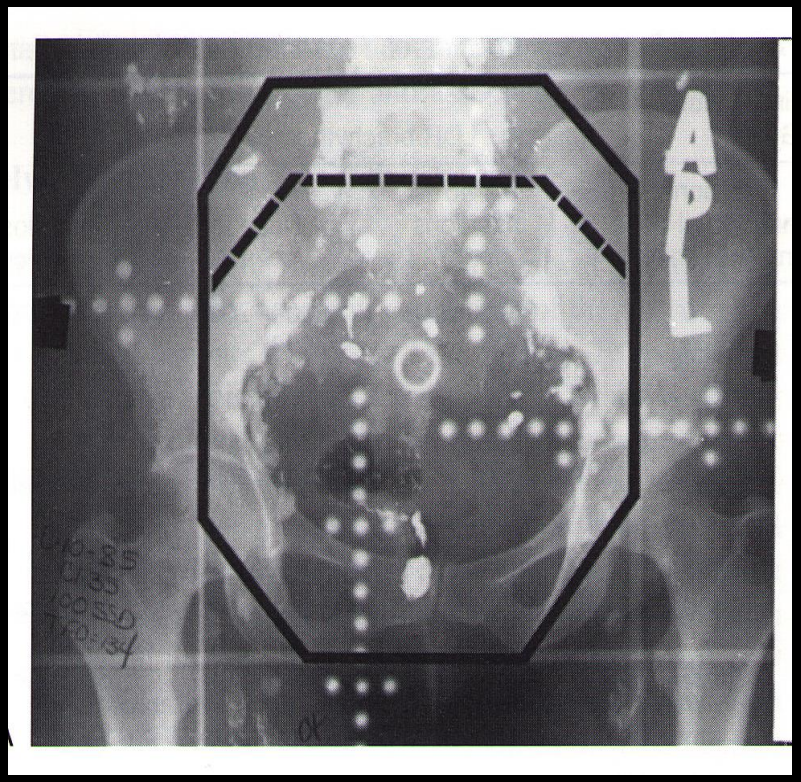
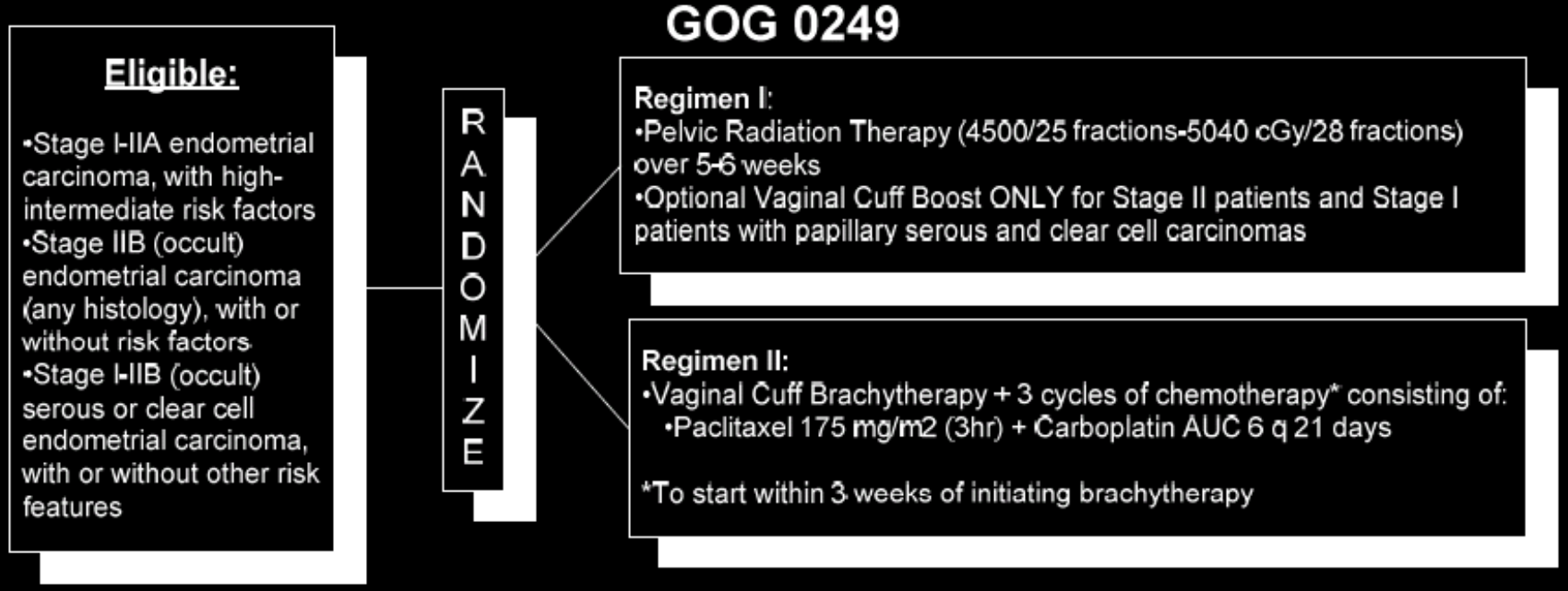


Figure 4. Subgroup analysis of patients without high-risk features, i.e. patients with either stage Ia/b or grade 1/2. (A) Death from all causes. (B) Endometrial carcinoma-related death.

Radiation +/- Chemo

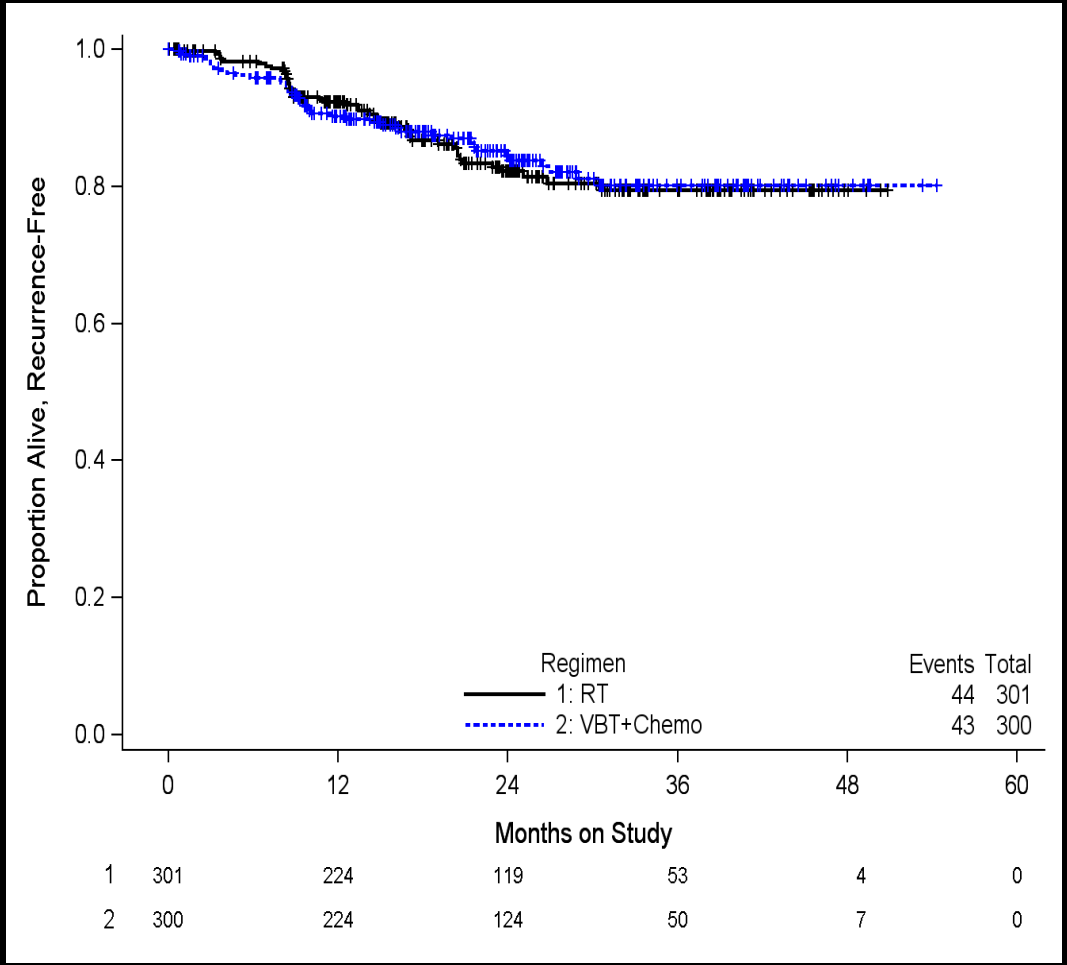


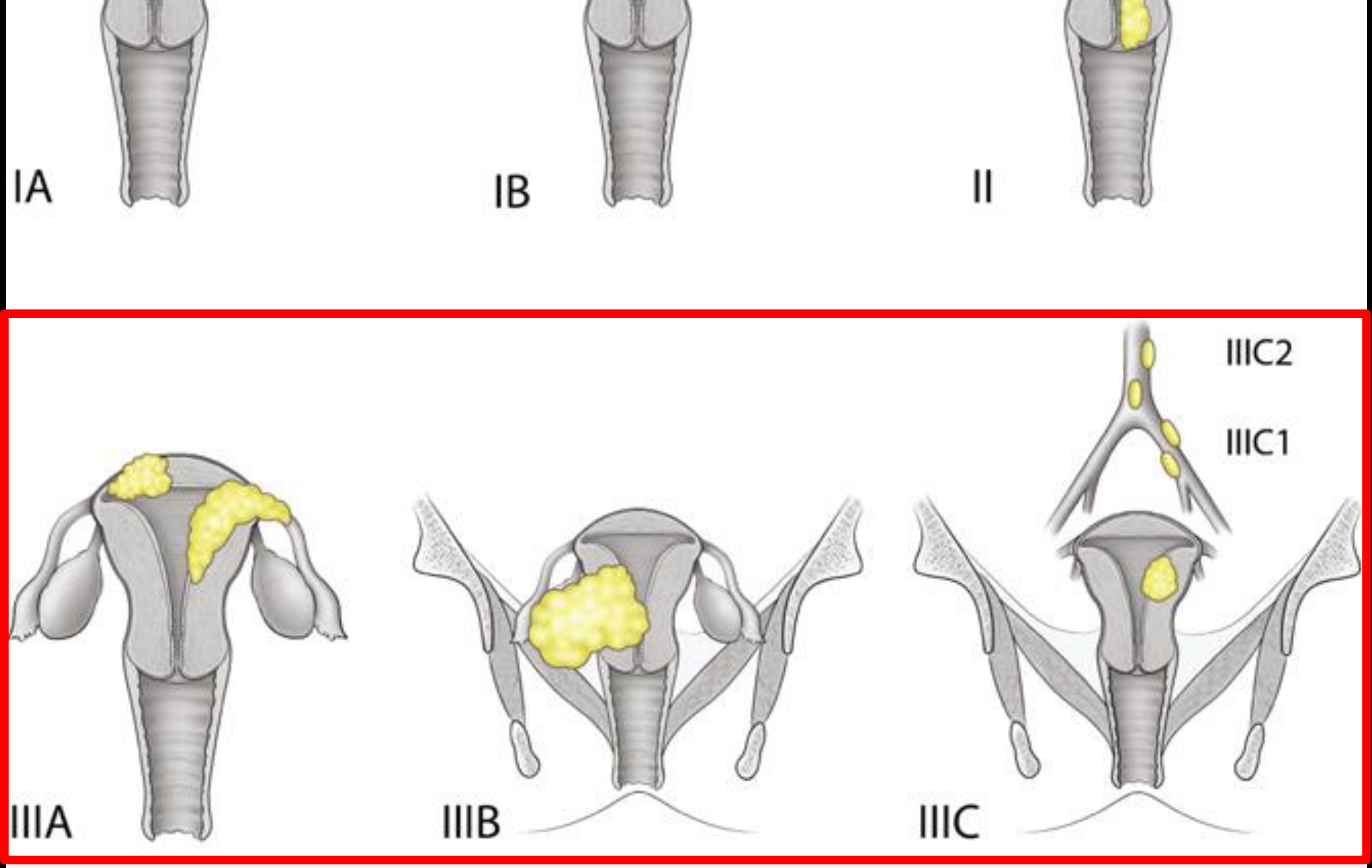
Phase III Trial of Pelvic Radiation Therapy Versus Vaginal Cuff Brachytherapy Followed by Paclitaxel/Carboplatin Chemotherapy in Patients with High Risk, Early Stage Endometrial Carcinoma



GOG 249: Recurrence-Free Survival

- Over 600 pts enrolled
- Median F/U 24 mo
- 87 events
- Pelvic Failures
  - 2 in RT arm (0.6%)
  - 19 in VCB/Chemo arm (6.3%)
- Death from disease
  - 12 in RT arm
  - 18 in VCB/C arm
    - McMeekin et al. Gyn Onc 134:438 “14

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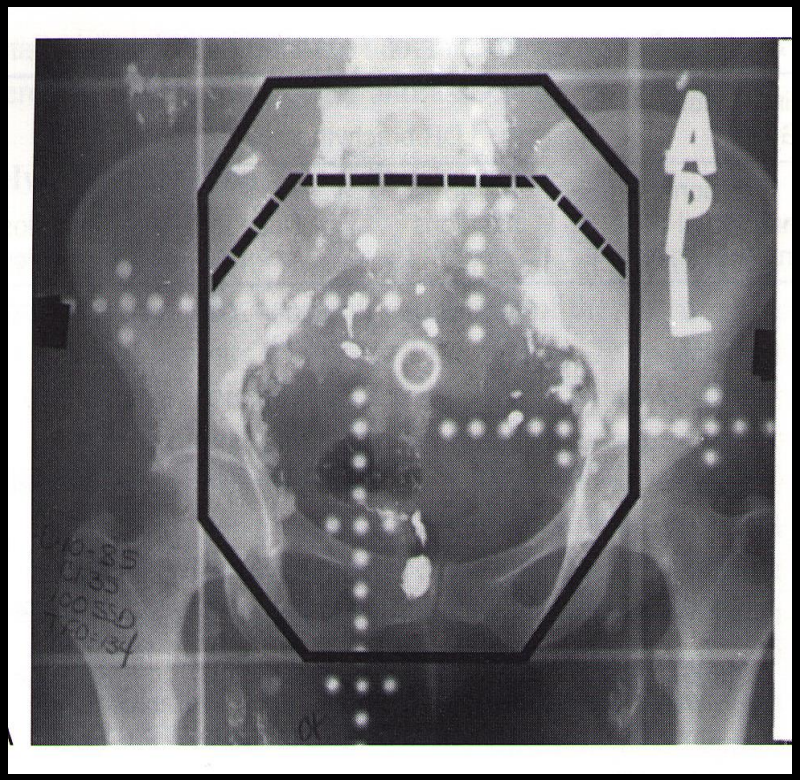
Chemo vs. Radiation

Vs.



GOG 122

- Endometrial carcinoma
- Surgical stage III/IV
  with
  (distant metastasis excluded)
- Hysterectomy and BSO

With either:

- Para-aortic nodes negative.
  or
- Unknown para-aortic node status.
  or
- Positive para-aortic nodes with
  Biopsy negative scalene nodes,
  and negative chest CT scan.

Randomize

Regimen I

Whole Abdomen
Radiation Therapy

Regimen II

Doxorubicin
60* mg/m2.
Cisplatin
50 mg/m2.

* Maximum total dose is 420 mg/m2.

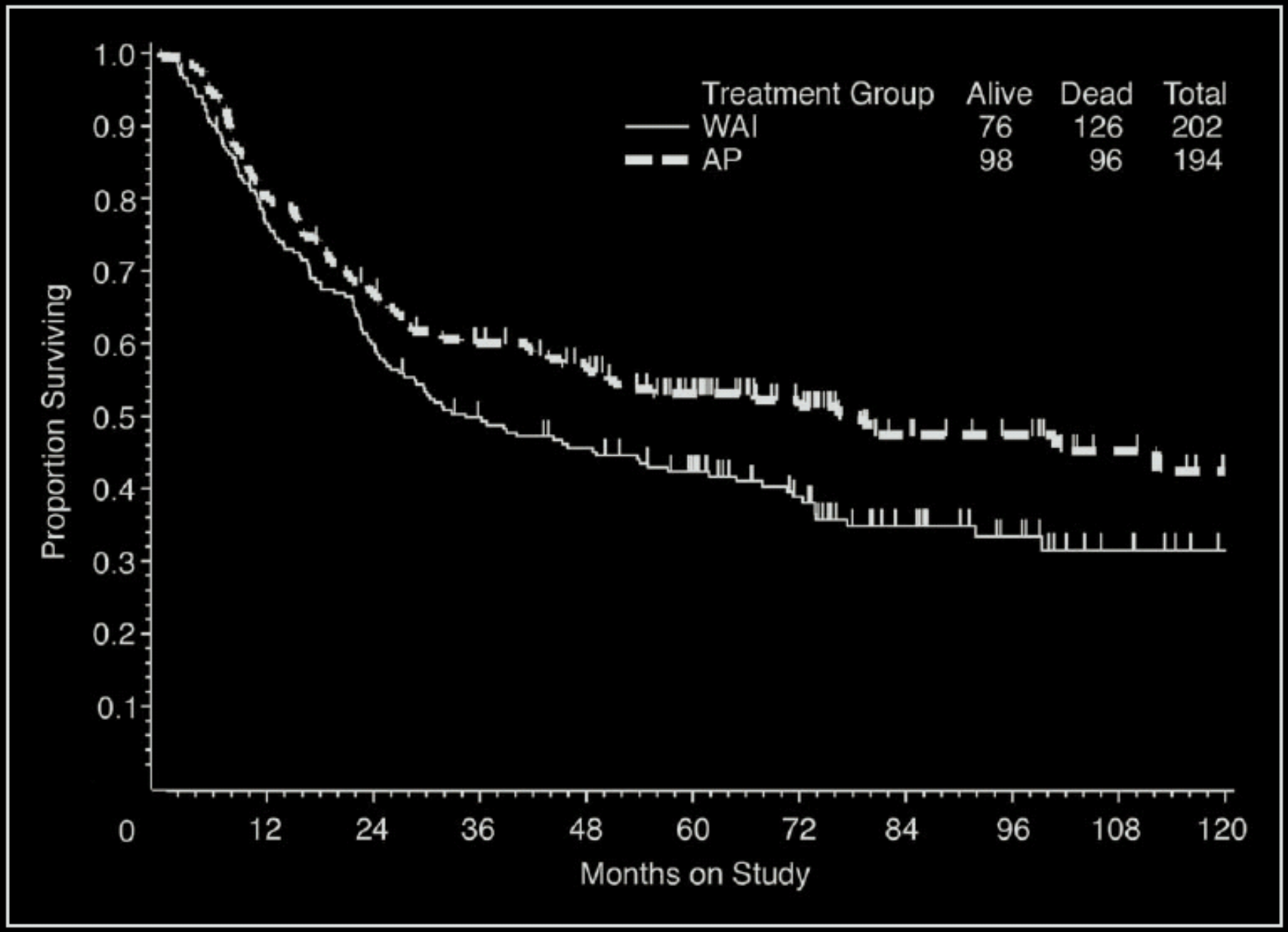


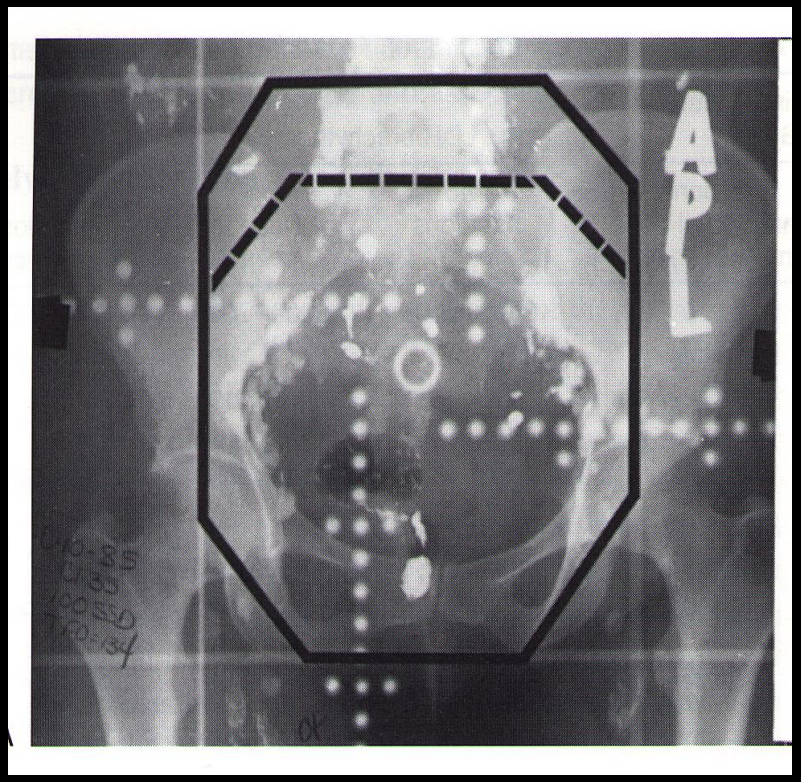
Fig 2. Survival by randomized treatment group. AP, doxorubicin and cisplatin; WAI, whole-abdominal irradiation.

GOG #122: Phase III Whole-Abdominal Irradiation vs. Doxorubicin + Cisplatin in Optimal Advanced Endometrial Carcinoma

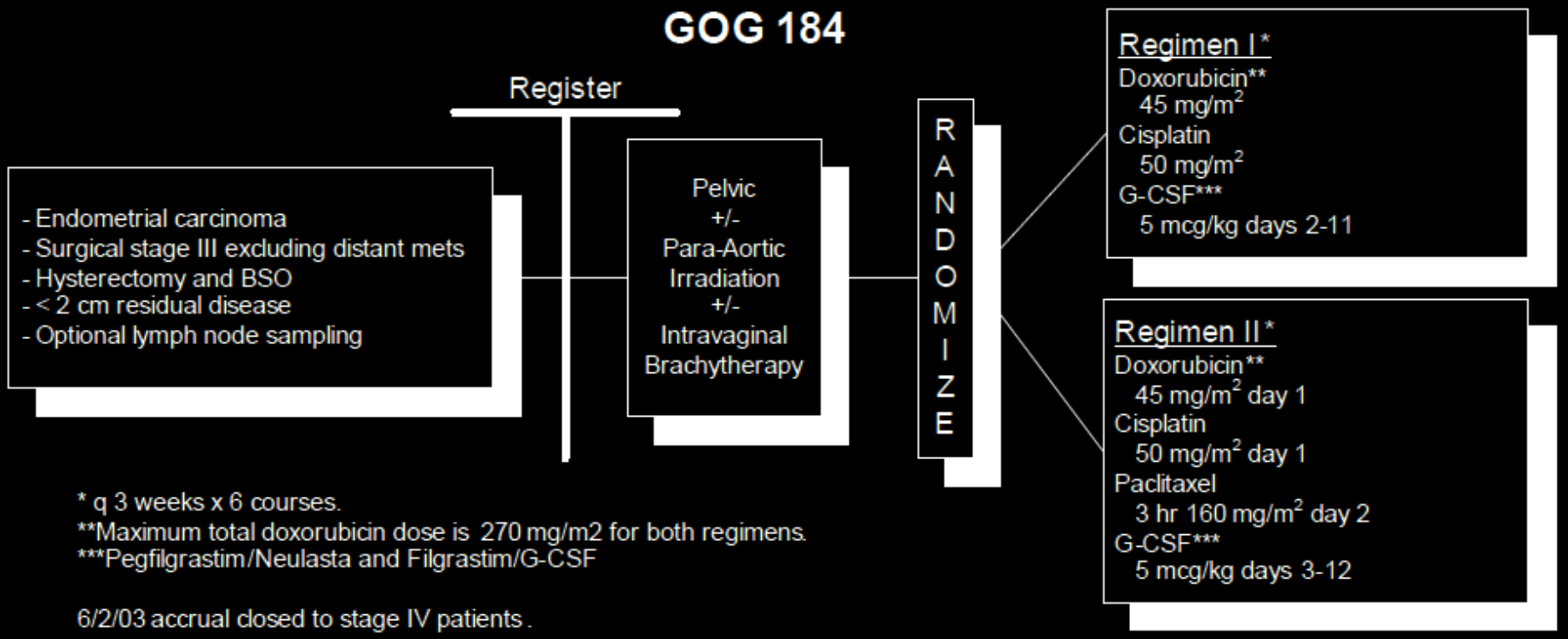
- WAI 3000 cGy (150 cGy X 20) vs. DOX 60 → CDDP 50 mg/m2 iv q 3 wks X 8
- 5/92 - 2/00, n=422
- Adverse effects were much more common with AP
- 24 months ($p<0.01$):
  - disease-free (WAI: 46%, AP: 59%)
  - Alive (WAI: 59%, AP: 70%)
- "AP … improves PFS and S"

  - Randall et al. J Clin Oncol 24;36-44, 2006

Radiation + Chemo



GOG #184: Tumor Volume-Directed Pelvic +/- Para-Aortic Irradiation Followed by Cisplatin and Doxorubicin +/- Paclitaxel for Advanced Endometrial Carcinoma



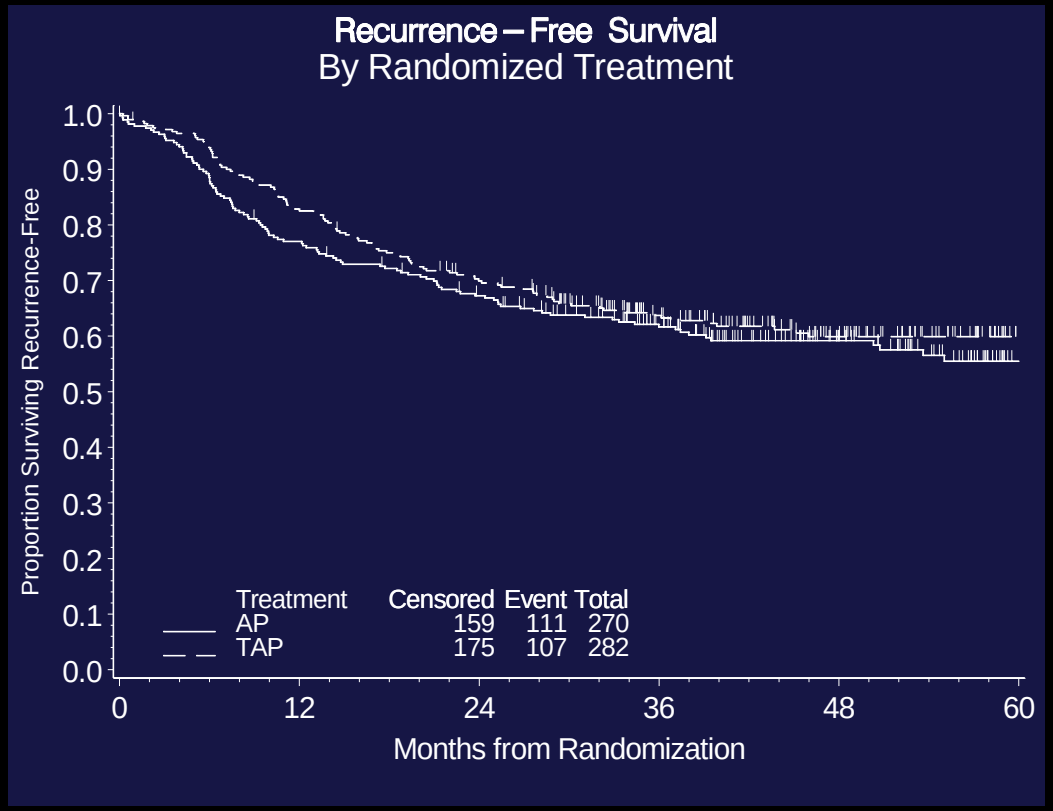
* q 3 weeks x 6 courses.
**Maximum total doxorubicin dose is 270 mg/m2 for both regimens.
***Pegfilgrastim/Neulasta and Filgrastim/G-CSF

6/2/03 accrual closed to stage IV patients.

Endometrial Carcinoma

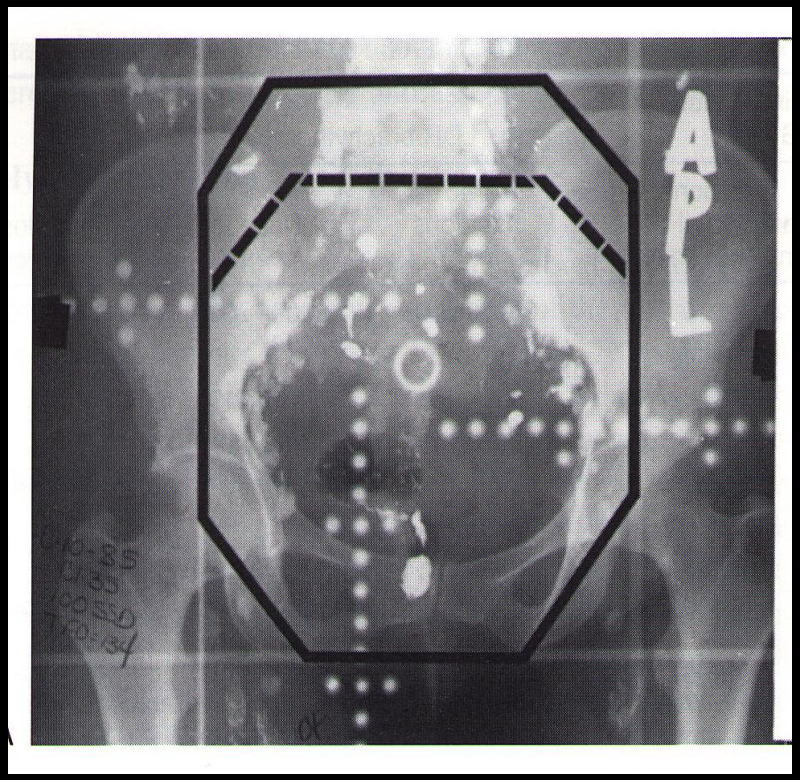
Advanced Minimal Residual

- GOG 184
  - 80% completed 6 cycles
  - More heme, neuro, myalgia in TAP, p<.01
  - 36 mo. RFS: 62% vs 64%
    - 50% reduction in death in gross residual disease for TAP
  - “addition of paclitaxel ... not associated with a significant improvement in RFS”

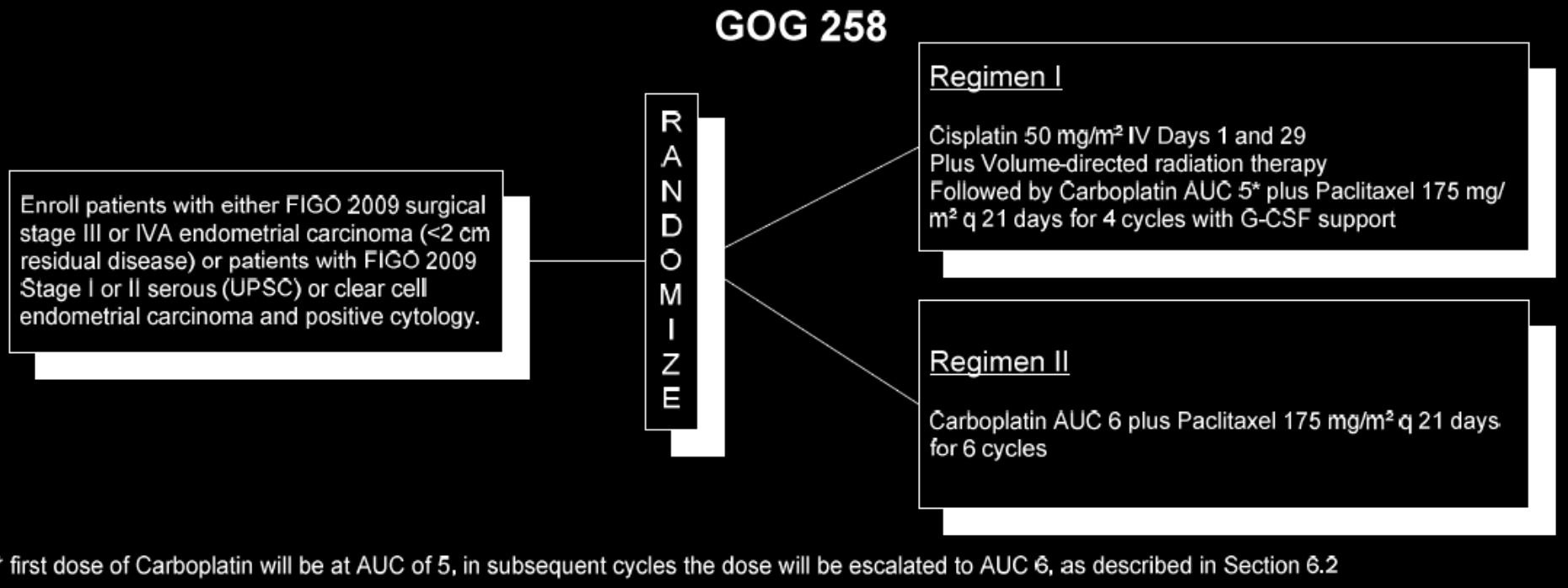


Gynecol Oncol 112:543, 2009

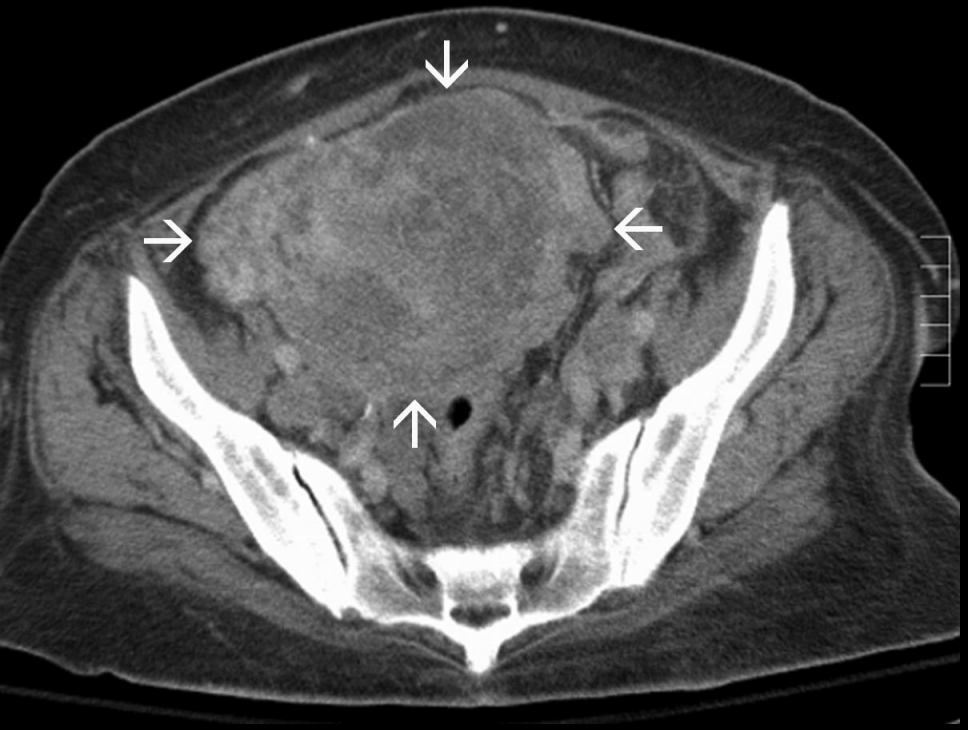
Chemo +/- Radiation

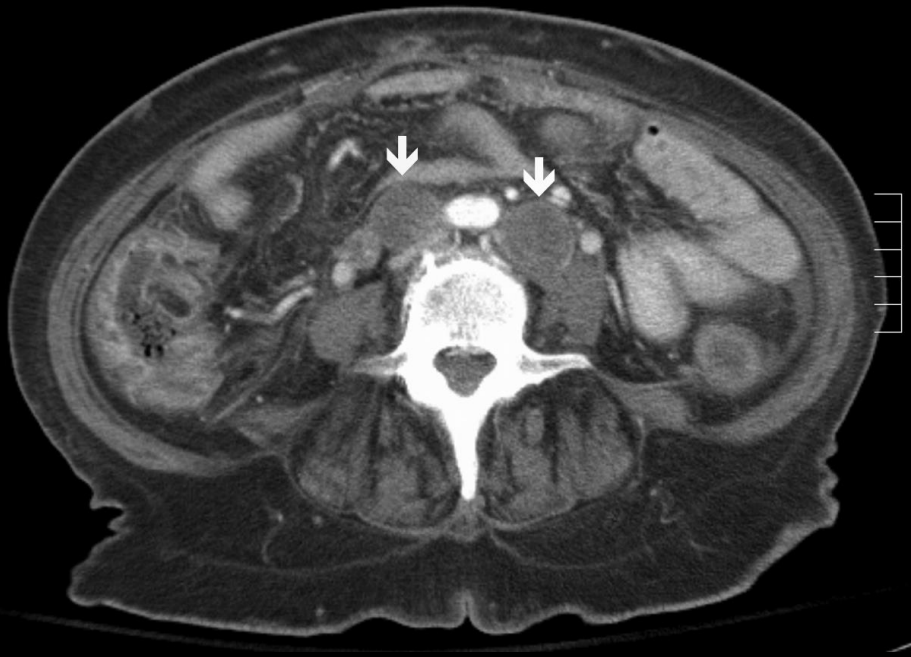


Endometrial: Stage III/IV



- 6/29/2009 – 7/28/2014: Completed
- Endorsed by RTOG
- 813/804 accrued

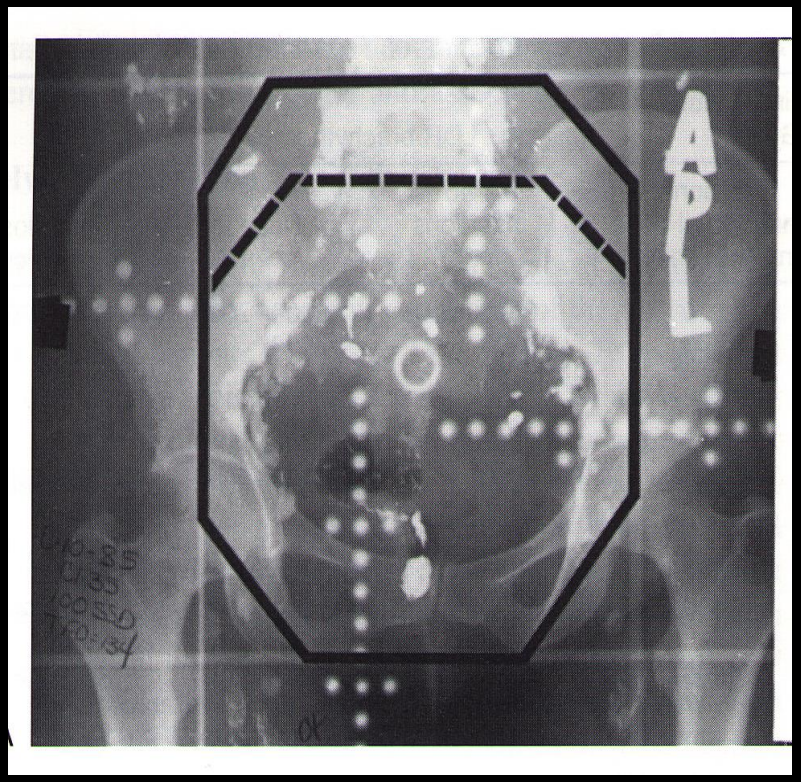




Endometrial Cancer: Recurrence

- 80% of recurrences happen first 3 years
- Most will be symptomatic
- 50% vaginal recurrences cured
- Rare to cure distant recurrences

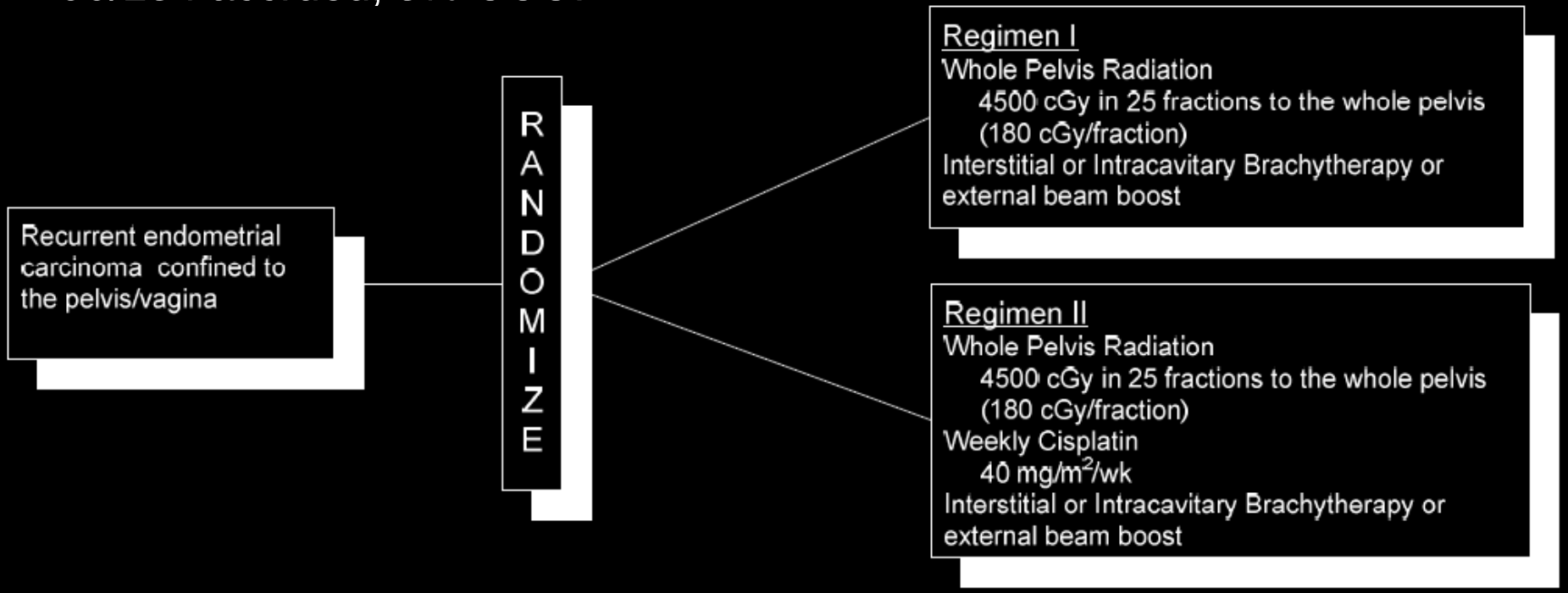
Radiation +/- Chemo



Pelvic Recurrence

- 2/25/2008
- Endorsed by RTOG
- 90/154 accrued, 5% CCOP

GOG 238



Institution IMRT Credentialing is required when IMRT is to be used before registering any patient on this trial. A Knowledge Assessment for this study must be completed by the treating radiation oncologist before registering patients on this trial.

For patients with tumors involving the distal vagina and clinically negative groins, the bilateral inguino-femoral lymph node regions should be treated to 4500 cGy.

3-D conformal or IMRT boost is allowed for patients who are not candidates for brachytherapy.

Chemo vs. Chemo

Randomized Study of Doxorubicin Plus Cisplatin Versus Doxorubicin Plus Cisplatin Plus 3-Hour Paclitaxel With G-CSF Support in Patients With Primary Stage III & IV or Recurrent Endometrial Carcinoma

GOG 177

- Stage III, IV or Recurrent Endometrial Carcinoma
- Measurable Disease
- No Prior Cytotoxic Chemotherapy

Tumor blocks or slides submitted

Randomize

Regimen I

Doxorubicin*
60 mg/m2 IV day 1 q 21 days x 7

Cisplatin
50 mg/m2 IV day 1 q 21 days x 7

G-CSF
As specified in protocol section 6.0

Regimen II

Doxorubicin
45 mg\m2 IV day 1 q 21 days x 7

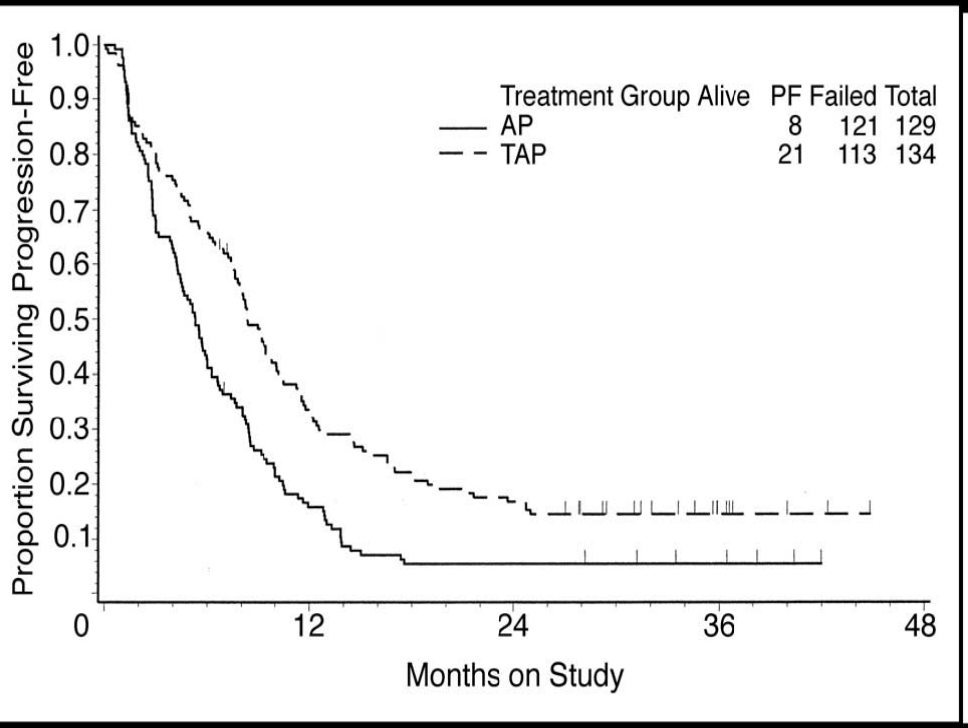
Cisplatin
50 mg/m2 day 1 q 21 days x 7

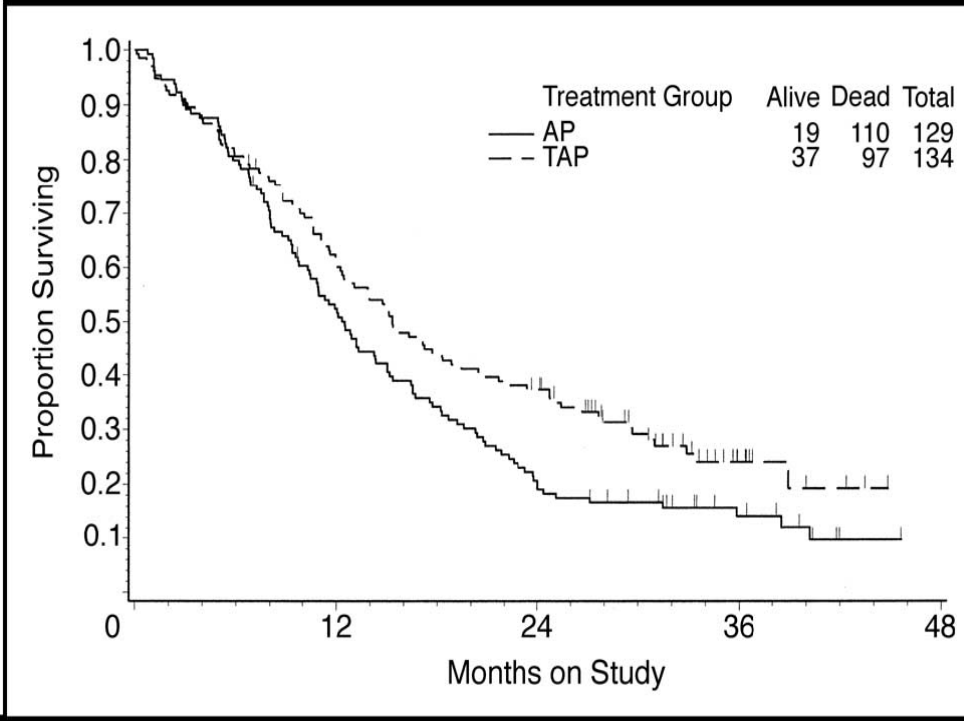
Paclitaxel
160 mg/m2 day 2 over 3 hrs q 21 days x 7

G-CSF
5 mcg\kg days 3-12, q 21 days x 7

* Patients with prior radiotherapy or who are over the age of 65 will have initial Doxorubicin dose reduced to 45 mg/m2.

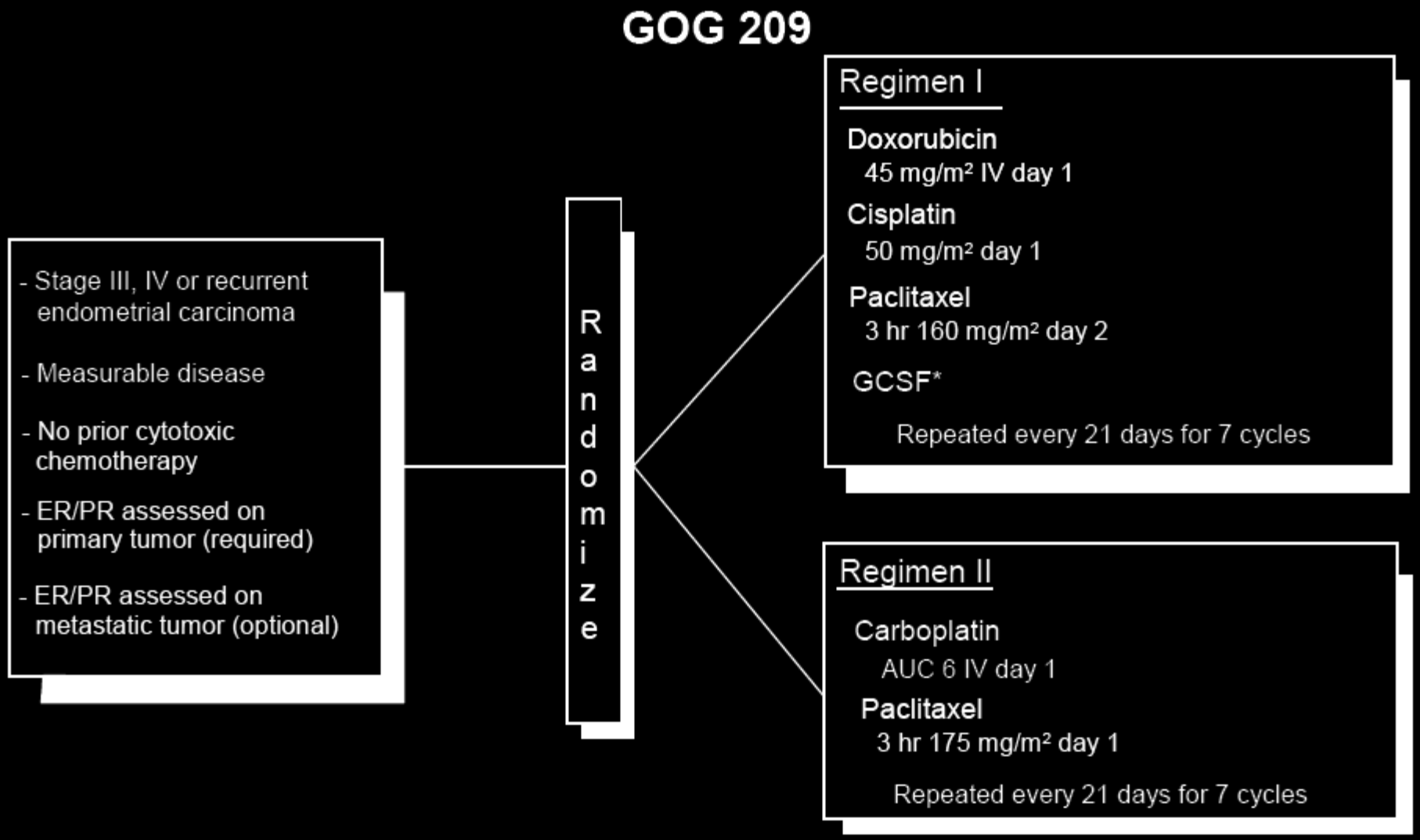
Phase III Trial of Doxorubicin Plus Cisplatin With or Without Paclitaxel Plus Filgrastim in Advanced Endometrial Carcinoma: GOG Protocol 177





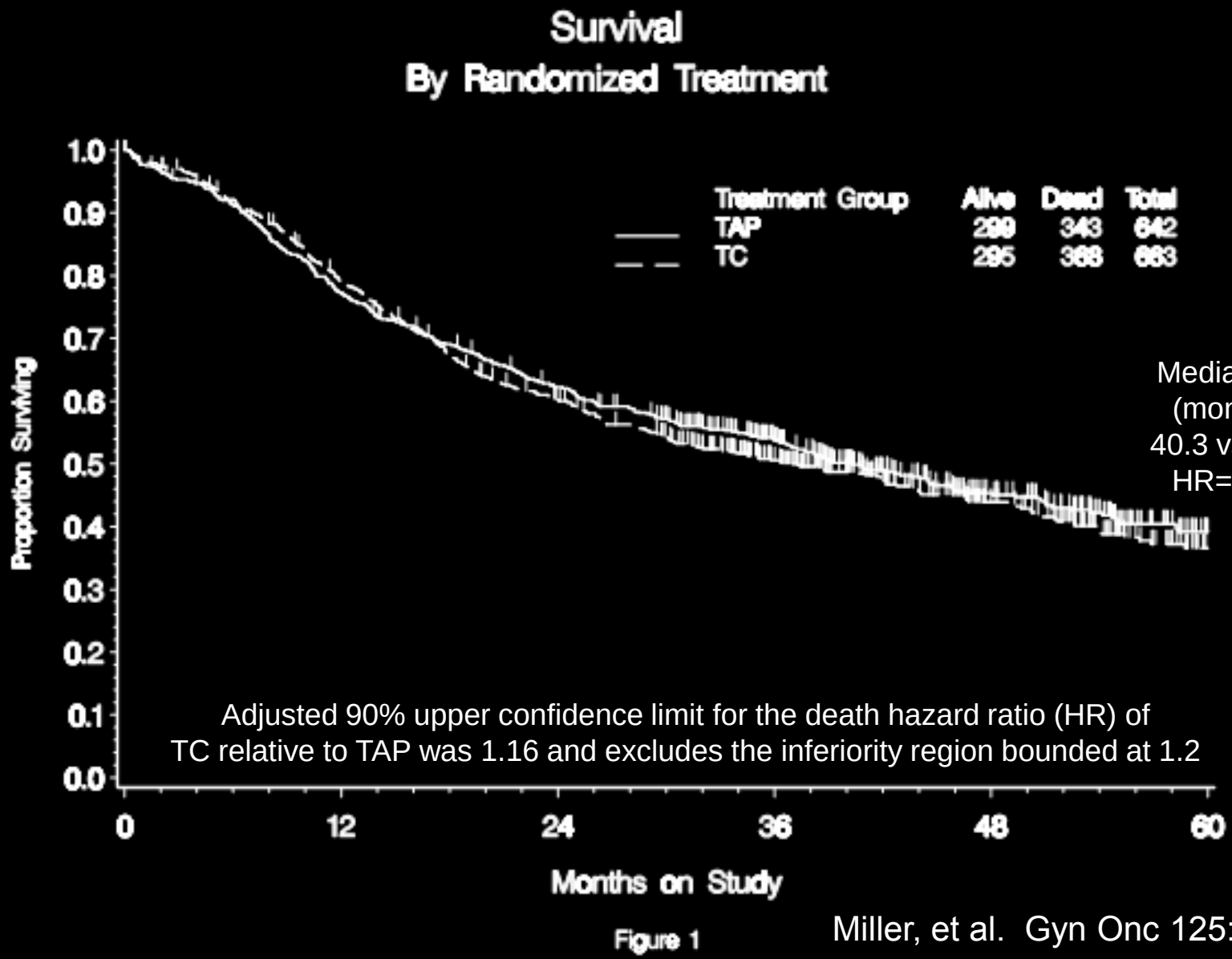
Fleming GF et al *J Clin Oncol* 2004;22:2159-66

Randomized Phase III Trial of Doxorubicin/Cisplatin/Paclitaxel and G-CSF Versus Carboplatin/Paclitaxel in Patients with Stage III and IV or Recurrent Endometrial Cancer



Filgrastim (G-CSF, Neupogen) 5 mcg/kg days 3-12 or Pegfilgrastin (G-CSF) 6 mg day 3.

GOG209: Survival



Miller, et al. Gyn Onc 125:771 ’12

Biologic therapies in endometrial cancer evaluated by the Gynecologic Oncology Group.

Agent	*N*	ORR (%)	PFS at 6 months (%)	Progression-free survival (median, months)	Overall survival (median, months)
Thalidomide[4]	34	12.5	8.3	1.7	6.3
Gefitinib[12]	26	3.8	15.4	1.8	7.1
Lapatinib[13]	30	3.3	10	1.8	7.3
Bevacizumab[5]	52	13.5	40.4	4.2	10.5
Aflibercept[6]	44	6.8	40.9[a]	2.9	14.6
Brivanib[8]	43	18.6	30.2	3.3	10.7
Nintedanib	32	9.4	21.9	3.3[b]	10.1[c]

[a] The proportion of patients EFS at 6 months in this study was 23%, which was significantly less than 40.9%. Patients who went off of study therapy for toxicity were often scanned for progression less frequently, which probably produced an artificially high frequency of patients PFS at 6 months. The longer median OS may have resulted in part from selection bias.

[b] The 90% CI for median PFS is 1.9–3.84 months.

[c] The 90% CI for median OS is 6.0–14.0 months.

Dizon et al. Gyn Onc 135:441 '14

Gynecologic Oncology 138 (2015) 507–512

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journal homepage: www.elsevier.com/locate/ygyno

A phase II evaluation of cediranib in the treatment of recurrent or persistent endometrial cancer: An NRG Oncology/Gynecologic Oncology Group study☆,☆☆

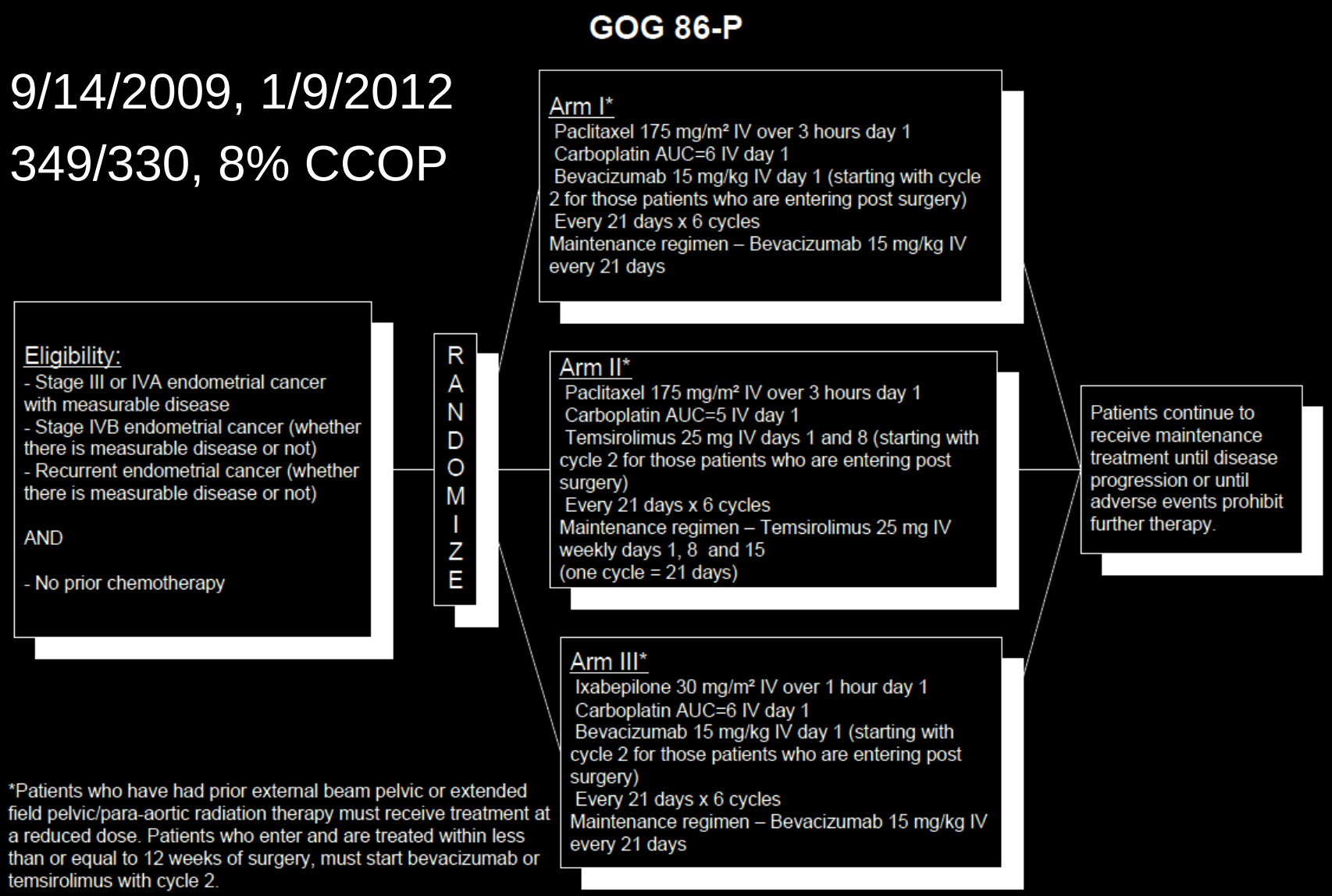
David Bender [a,*], Michael W. Sill [b], Heather A. Lankes [b], Henry D. Reyes [a], Christopher J. Darus [c], James E. Delmore [d], Jacob Rotmensch [e], Heidi J. Gray [f], Robert S. Mannel [g], Jeanne M. Schilder [h], Mark I. Hunter [i], Carolyn K. McCourt [j,1], Megan I. Samuelson [a], Kimberly K. Leslie [a]

- N = 53
- ORR 12%,
- PFS: median 3.6 mo, 29% 6 mo
- OS: 12.5 mo

- Cediranib is an active multi-tyrosine kinase inhibitor in uterine cancer.
- Cediranib for recurrent uterine cancer had a 33% six-month progression free survival.
- Cediranib is a safe and well-tolerated oral treatment for recurrent uterine cancer.

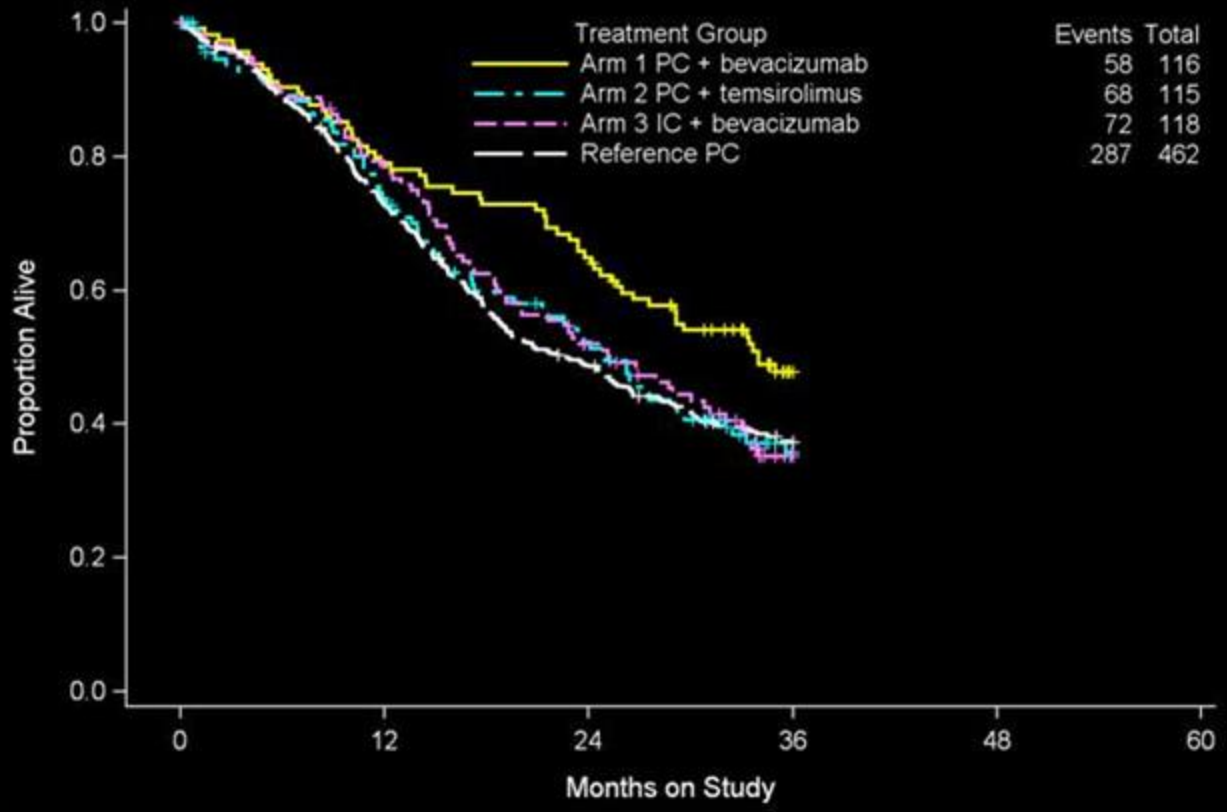
Endometrial: Stage IV or Measurable

- 9/14/2009, 1/9/2012
- 349/330, 8% CCOP



Endometrial focus

GOG86P: OS



Arm	*Median Point Estimate*
1	**34.0 (p<0.039)**
2	25.0
3	25.2
Reference	22.7

PRESENTED AT: ASCO Annual '15 Meeting

GOG0286B

GOG-286B

Report Based on Data Through: 05/01/2015

A Randomized Phase II/III Study of Paclitaxel/Carboplatin/Metformin (NSC#91485) Versus Paclitaxel/Carboplatin/Placebo as Initial Therapy for Measurable Stage III or IVA, Stage IVB, or Recurrent Endometrial Cancer

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ELIGIBILITY

Stage III or IVA endometrial cancer with measurable disease

Stage IVB endometrial cancer (whether there is measurable disease or not)

Recurrent endometrial cancer (whether there is measurable disease or not)

AND

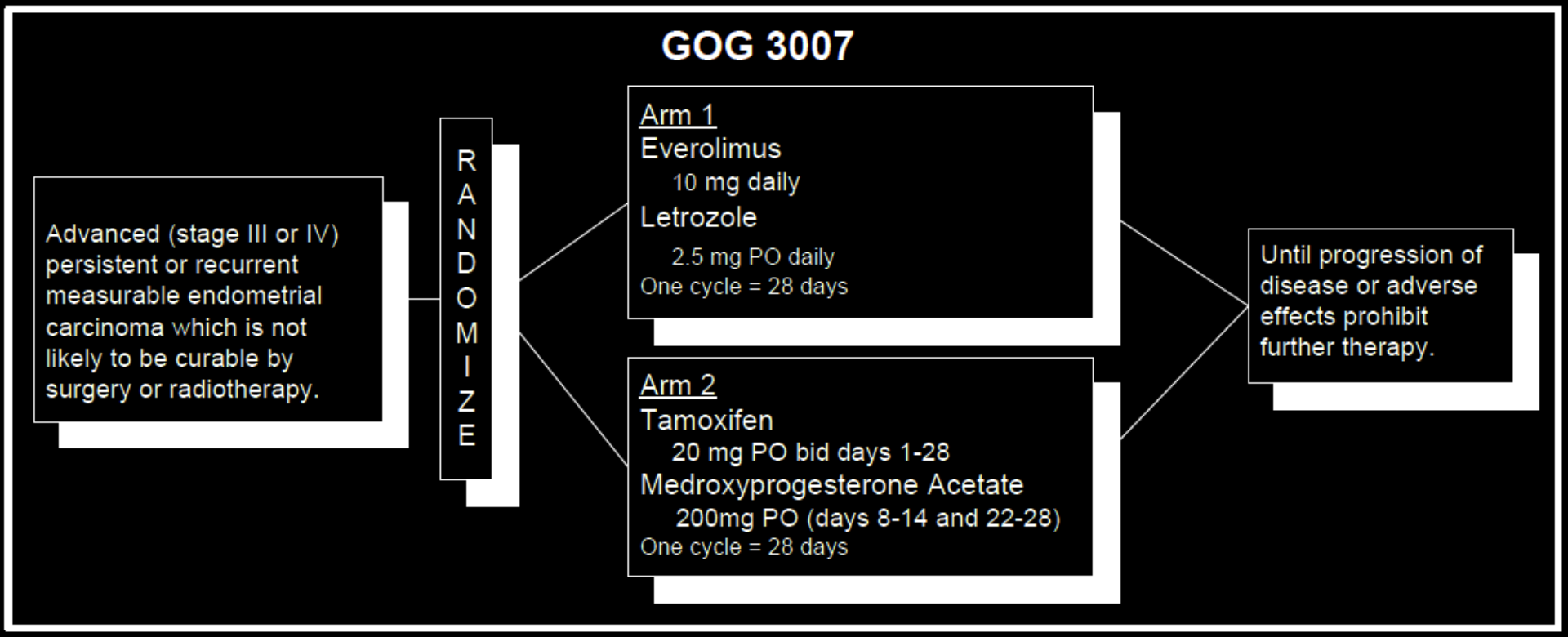
NO PRIOR CHEMOTHERAPY

Opened 3/17/2014
184/540

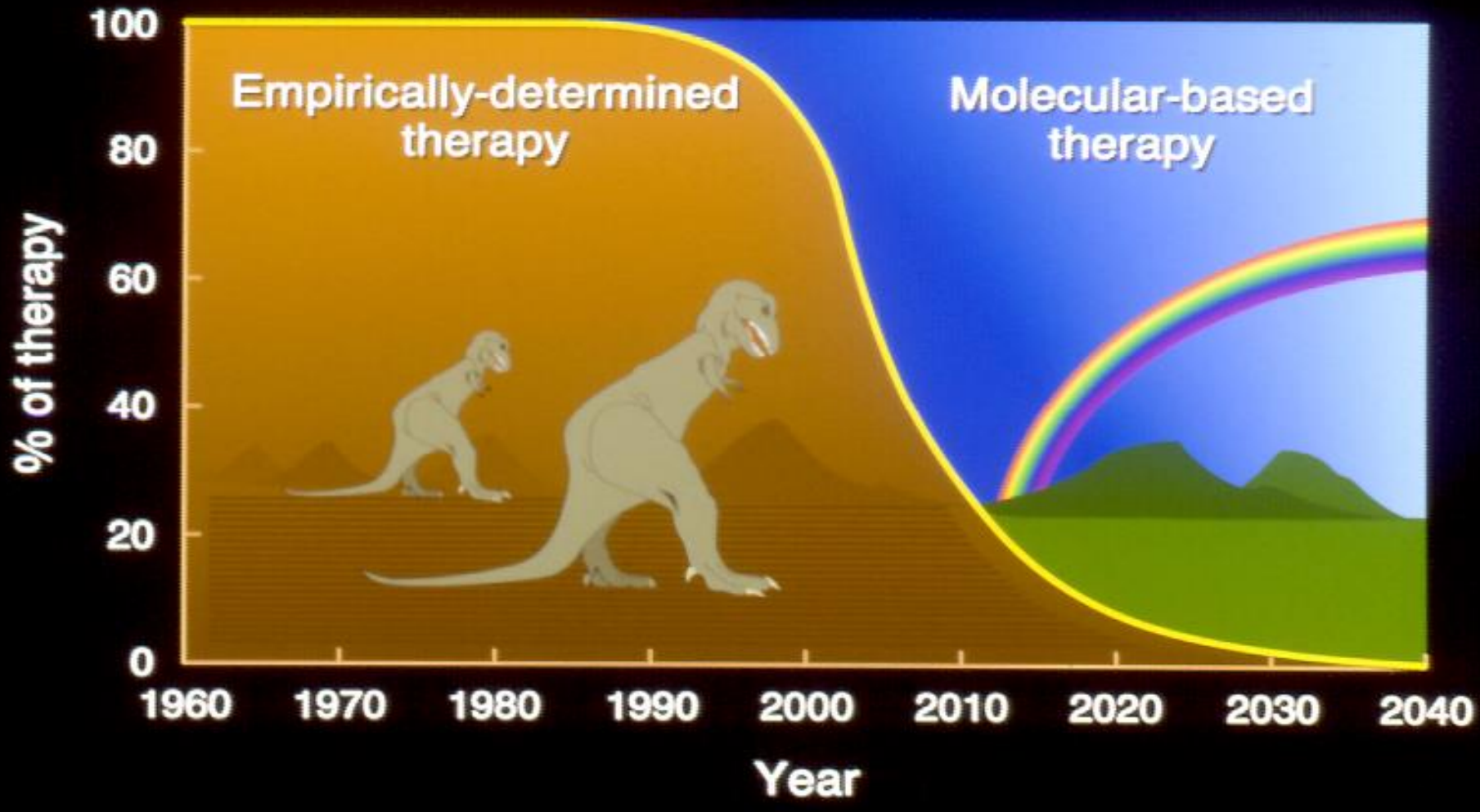
GOG #119: Phase II Alternating Tamoxifen plus Medroxyprogesterone for Advanced, Recurrent, or Metastatic Endometrial Cancer

- TMX 20 mg po bid + MPA 200 mg po qd X 1 wk qow
- 6/91-2/96, n=60
- CR 10% + PR 23% = 33% (95% CI: 21-46%)
- PFS = 3 mo., OS = 13 mo.
- “active treatment ”
  - Whitney et al. Gyn Onc 92:4 ‘04

A Randomized Phase II Trial of Everolimus and Letrozole or Hormonal Therapy (Tamoxifen/Medroxyprogesterone Acetate) in Women with Advanced, Persistent, or Recurrent Endometrial Carcinoma



Opened 2/19/2015


Empirically-determined therapy
Molecular-based therapy
% of therapy
100
80
60
40
20
0
1960
1970
1980
1990
2000
2010
2020
2030
2040
Year