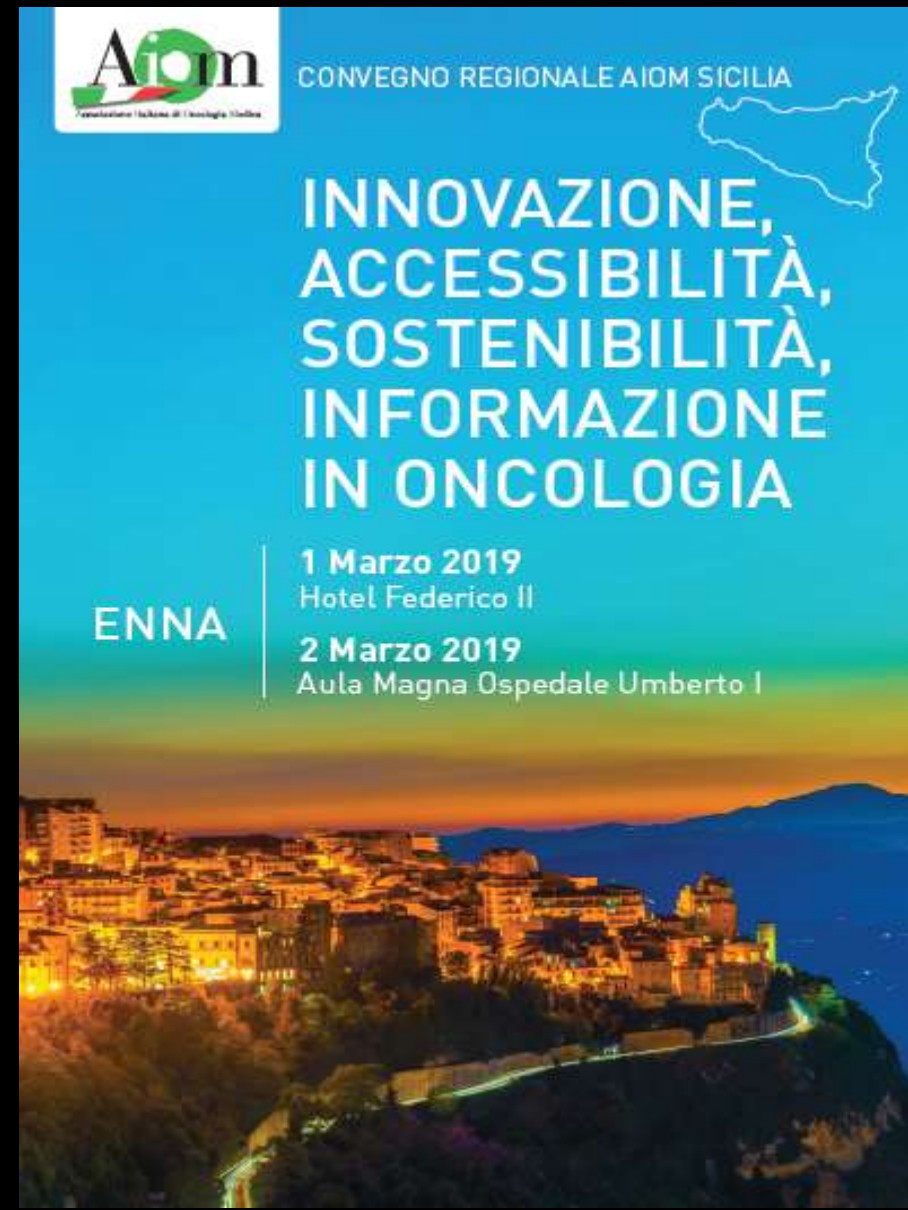




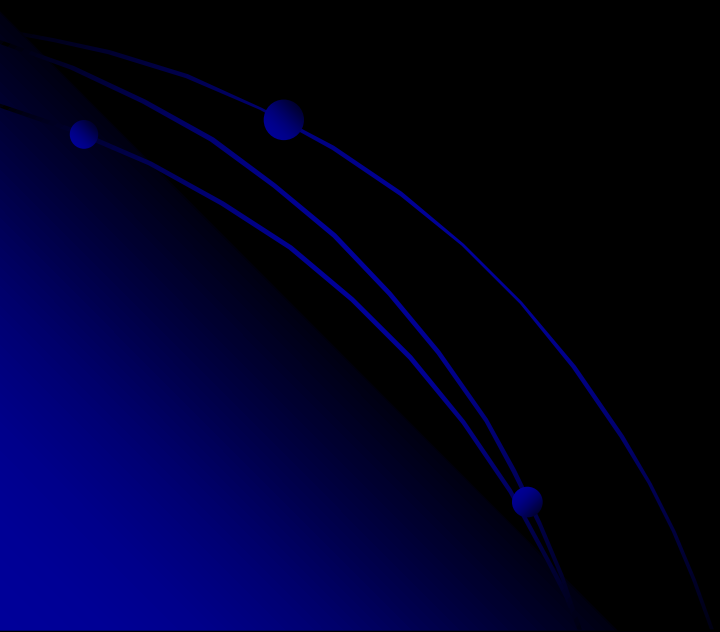
Azienda Ospedaliera "Cannizzaro"  
Catania  
Dipartimento Materno-Infantile  
U.O. di Ostetricia e Ginecologia

La chirurgia del  
tumore ovarico:  
uf-front vs chirurgia  
dopo chemioterapia  
neoadiuvante.



# Surgery

## WHO ?



# Outcomes of advanced stage OC according to specialty of surgeon performing initial surgery

## ARTICLES

### Associations Between Hospital and Surgeon Procedure Volumes and Patient Outcomes After Ovarian Cancer Resection

*Deborah Schrag, Craig Earle, Feng Xu, Katherine S. Panageas, K. Robin Yabroff, Robert E. Bristow, Edward L. Trimble, Joan L. Warren*



Available online at [www.sciencedirect.com](http://www.sciencedirect.com)

ScienceDirect

Gynecologic Oncology 105 (2007) 801–812

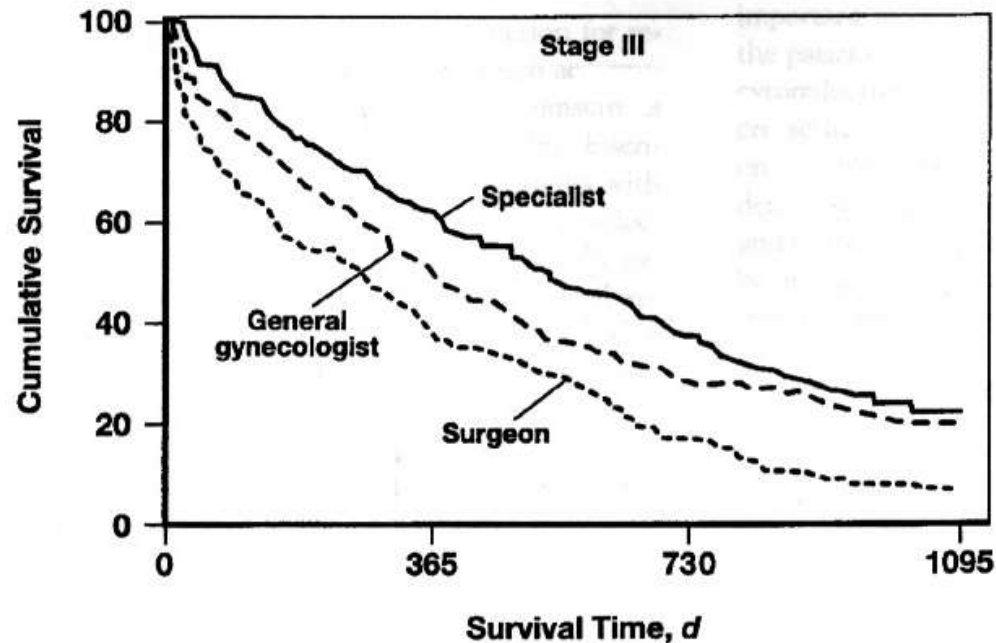
Gynecologic  
Oncology

[www.elsevier.com/locate/ynmg](http://www.elsevier.com/locate/ynmg)

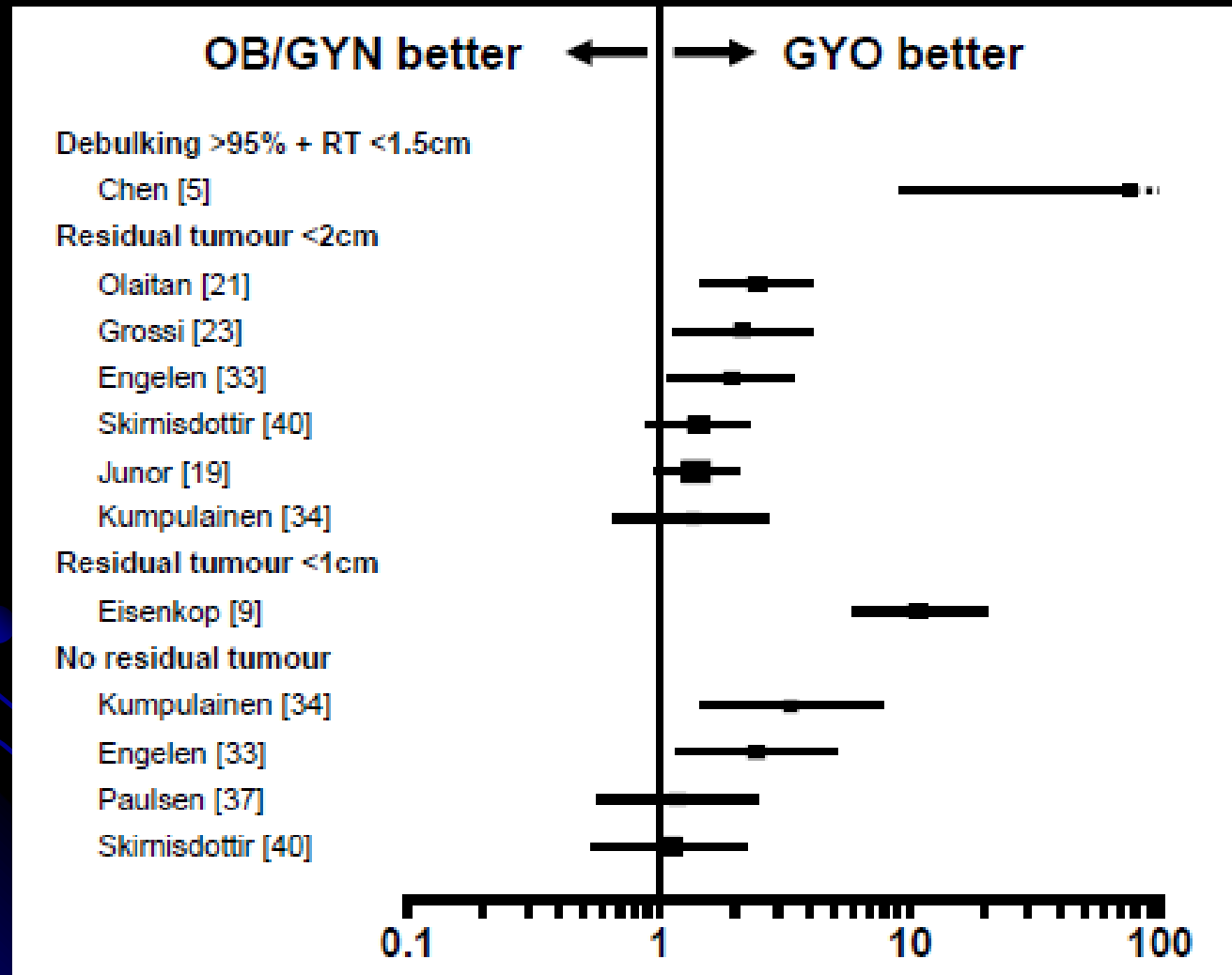
Review

The outcomes of ovarian cancer treatment are better when provided by gynecologic oncologists and in specialized hospitals: A systematic review

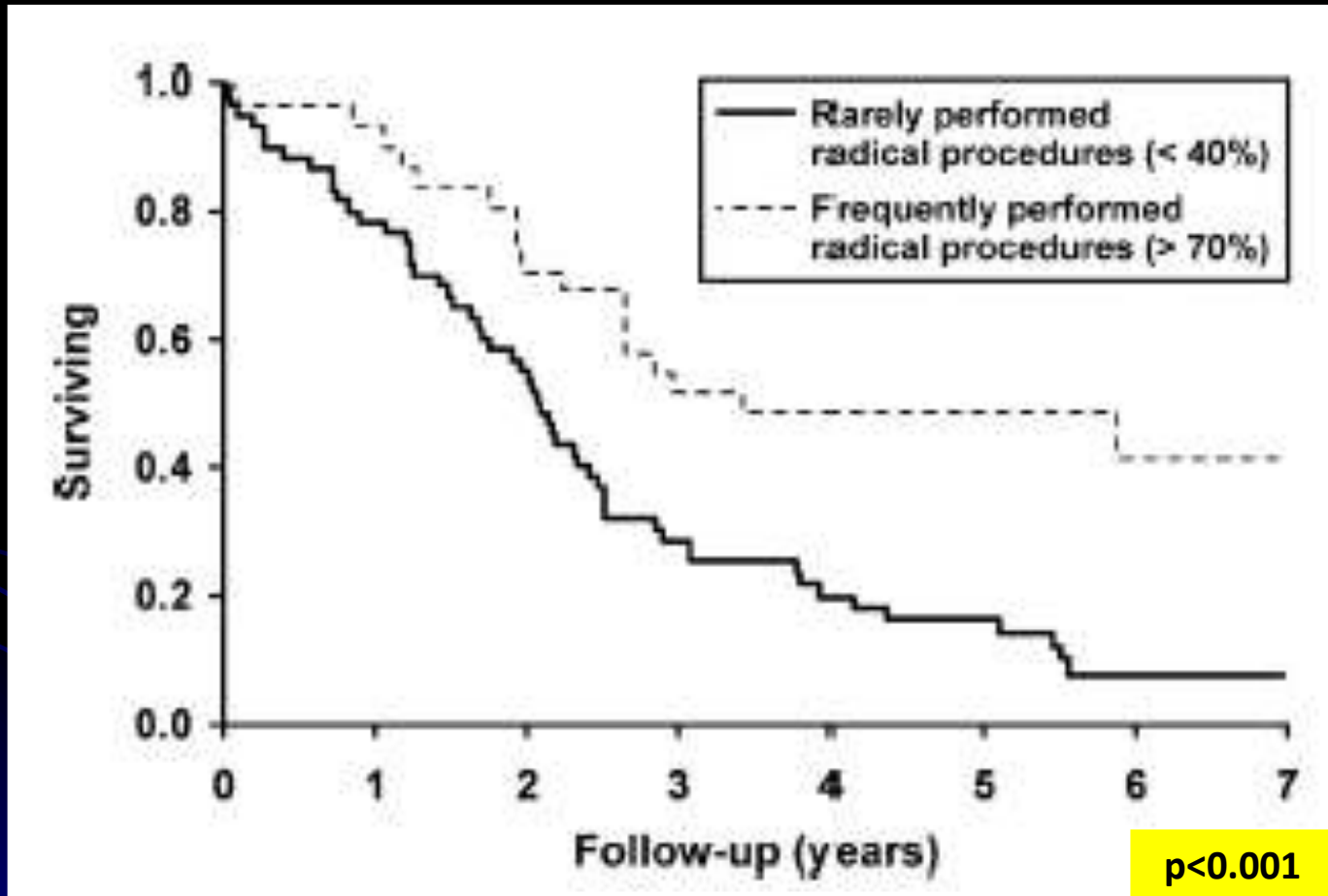
Flora Vernooij <sup>a,\*</sup>, Peter Heintz <sup>a</sup>, Els Witteveen <sup>b</sup>, Yolanda van der Graaf <sup>c</sup>



# Outcomes of advanced stage OC according to specialty of surgeon performing initial surgery



# Effect of surgeon tendency to perform aggressive surgery on overall survival in stage IIIC





# European Society of Gynaecologic Oncology Quality Indicators for Advanced Ovarian Cancer Surgery

*Denis Querleu, MD,\* François Planchamp, MSc,\* Luis Chiva, MD,† Christina Fotopoulou, MD,‡ Desmond Barton, MD,§ David Cibula, MD,|| Giovanni Aletti, MD,¶ Silvestro Carinelli, MD,¶ Carien Creutzberg, MD,# Ben Davidson, MD, PhD,\*\* Philip Harter, MD,†† Lene Lundvall, MD,‡‡ Christian Marth, MD,§§ Philippe Morice, MD, PhD,|||| Arash Rafii, MD, PhD,¶¶ Isabelle Ray-Coquard, MD, PhD,### Andrea Rockall, MD,‡ Cristiana Sessa, MD,\*\*\* Ate van der Zee, MD,††† Ignace Vergote, MD,‡‡‡ and Andreas du Bois, MD††*

**Objectives:** The surgical management of advanced ovarian cancer involves complex surgery. Implementation of a quality management program has a major impact on survival. The goal of this work was to develop a list of quality indicators (QIs) for advanced ovarian cancer surgery that can be used to audit and improve the clinical practice. This task has been carried out under the auspices of the European Society of Gynaecologic Oncology (ESGO).

# Quality Indicators

## OUTCOME

- Rate of complete surgical resection
- Existence of a structural prospective reporting of post-operative complications

## STRUCTURAL

- Pre-intra and post-operative management
- Center participating in clinical trials

## PROCESS

- Required preoperative work-up
- Minimum required elements in operative reports
- Minimum required elements in pathology reports
- Treatment planned and reviewed at a multidisciplinary team
- Surgery performed by a gynecologic oncologist or a trained surgeon specifically dedicated to Gyn cancer
- Number of cytoreductive surgeries performed for center

**TABLE 2. Presentation of QIs**

**QI 1—Rate of Complete Surgical Resection**

Type  Outcome indicator

**Description** Complete abdominal surgical resection is defined by the absence of remaining macroscopic lesions after careful exploration of the abdomen. Whenever feasible, localized thoracic disease is resected. Surgery can be decided upfront, or planned after neoadjuvant chemotherapy. However, the quality assurance program must take into account that patients who can be operated upfront with a reasonable complication rate benefit most from primary debulking surgery.

**Specifications**

- (i) Complete resection rate (all patients):
  - Numerator: no. patients with advanced ovarian cancer undergoing complete surgical resection
  - Denominator: all incoming patients with advanced ovarian cancer
- (ii) Proportion of stage III–IV patients who are operated upfront:
  - Numerator: stage III–IV patients undergoing primary cytoreductive surgery
  - Denominator: all incoming patients with untreated advanced ovarian cancer

**Target(s)**



- (i) Complete resection rate (all patients):
  - Optimal target: >65%
  - Minimum required target: >50%
- (ii) Proportion of primary debulking surgeries (stage III–IV patients):  $\geq 50\%$

**Scoring rule**

- (i) 5 if the optimal target is met, 3 if the minimum required target is met
- (ii) 3 if the target is met



## QI 2—No. Cytoreductive Surgeries Performed Per Center and Per Surgeon Per Year

Type	 Structural indicator (no. upfront or interval cytoreductive surgeries performed per center)  Process indicator (no. surgeries per surgeon per year)
Description	Only surgeries with an initial objective of complete cytoreduction are recorded. Exploratory endoscopies, exploratory laparotomies, or surgeries limited to tissue biopsy that do not include at least a bilateral salpingo-oophorectomy (if applicable), hysterectomy (if applicable), and a comprehensive peritoneal staging including omentectomy are not included.
Specifications	Numerator: (i) no. cytoreductive surgeries as defined previously performed per center per year; (ii) no. cytoreductive surgeries as defined previously performed per surgeon per year. Secondary and tertiary procedures are accepted. Denominator: not applicable
Target(s)	(i) No. surgeries performed per center per year: <ul style="list-style-type: none"><li>• Optimal target: <math>n \geq 100</math></li><li>• Intermediate target: <math>n \geq 50</math></li><li>• Minimum required target: <math>n \geq 20</math></li></ul> (ii) $\geq 95\%$ of surgeries are performed or supervised by surgeons operating at least 10 patients a year
Scoring rule	(i) 5 if the optimal target is met, 3 if the intermediate target is met, 1 if the minimum required target is met (ii) 3 if the target is met

### Q13—Surgery Performed by a Gynecologic Oncologist or a Trained Surgeon Specifically Dedicated to Gynecological Cancers Management

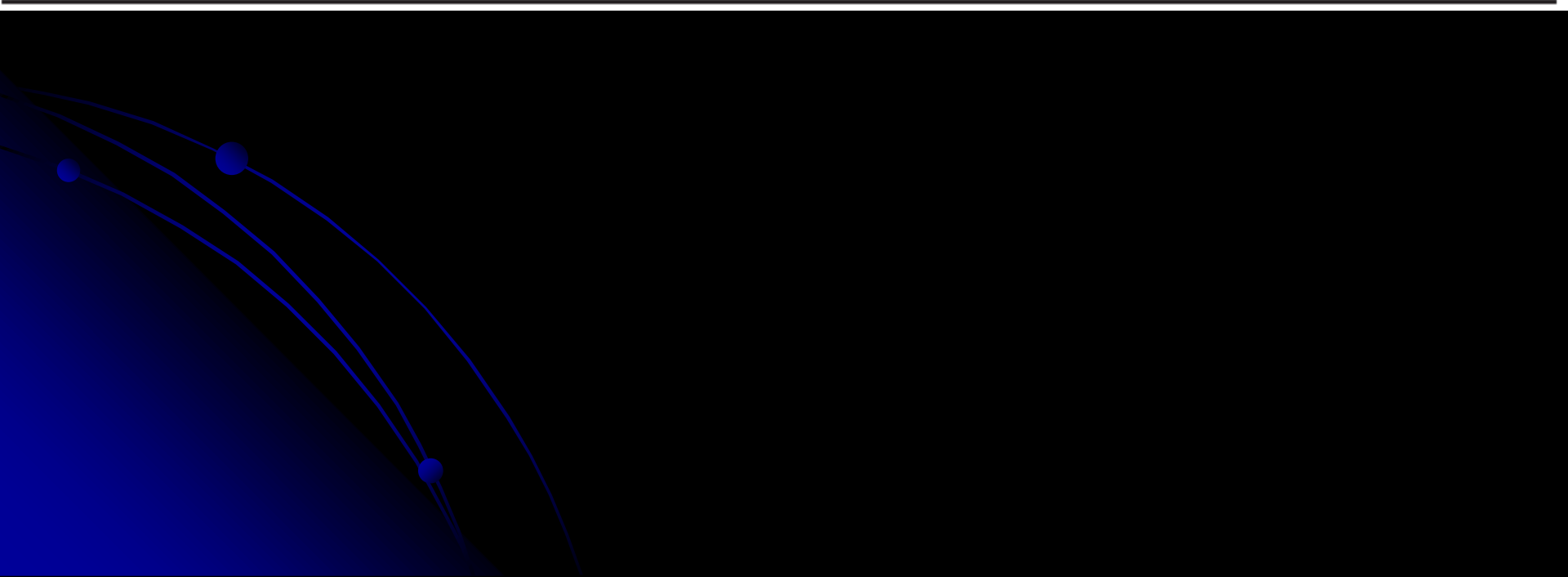
Type  Process indicator

Description Surgery is performed by a certified gynecologic oncologist or, in countries where certification is not organized, by a trained surgeon dedicated to the management of gynecologic cancer (accounting for more than 50% of his practice) or having completed an ESGO-accredited fellowship. Skills to successfully complete abdominal and pelvic surgery procedures necessary to achieve complete cytoreduction must be available.

Specifications Numerator: no. patients with advanced ovarian cancer operated by a specialist (as defined previously)  
Denominator: all patients undergoing surgery for advanced ovarian cancer

Target(s)  $\geq 90\%$

Scoring rule 3 if the target is met



#### QI 4—Center Participating in Clinical Trials in Gynecologic Oncology

Type  Structural indicator

Description The center actively accrues patients in clinical trials in gynecologic oncology

Specifications Numerator: not applicable  
Denominator: not applicable

Target(s) Not applicable

Scoring rule 3 if the center actively accrues patients in clinical trials in gynecologic oncology

#### QI 5—Treatment Planned and Reviewed at a Multidisciplinary Team Meeting

Type  Process indicator

Description The decision for any major therapeutic intervention has been taken by a multidisciplinary team (MDT) including at least a surgical specialist as defined previously (QI 2 and QI 3), a radiologist, a pathologist (if a biopsy is available), and a physician certified to deliver chemotherapy (a gynecologic oncologist in countries where the subspecialty is structured and/or a medical oncologist with special interest in gynecologic oncology).

Specifications Numerator: no. patients with advanced ovarian cancer for whom the decision for therapeutic intervention(s) has been taken by an MDT  
Denominator: all patients with advanced ovarian cancer undergoing therapeutic intervention(s)

Target(s)  $\geq 95\%$

Scoring rule 3 if the target is met



## QI 6—Required Preoperative Workup

Type  Process indicator

Description Unresectable parenchymal metastases have been ruled out by imaging. Ovarian and peritoneal malignancy secondary to gastrointestinal cancer has been ruled out by suitable methods, for example, plasma CA 125 and CEA levels, and/or by biopsy under radiologic or laparoscopic guidance.

Specifications Numerator: no. patients with advanced ovarian cancer who had undergone cytoreductive surgery and who were offered minimum preoperative workup as defined previously

Denominator: all patients with suspected advanced ovarian cancer who underwent cytoreductive surgery

Target(s)  $\geq 95\%$

Scoring rule 3 if the target is met

## QI 7—Preoperative, Intraoperative, and Postoperative Management

Type  Structural indicator

Description The minimal requirements are (1) intermediate care facility, and access to an intensive care unit in the center are available; and (2) an active perioperative management program is established\*

Specifications Numerator: not applicable


Denominator: not applicable

Target(s) Not applicable

Scoring rule 3 if the minimal requirements are met.



## QI 8—Minimum Required Elements in Operative Reports

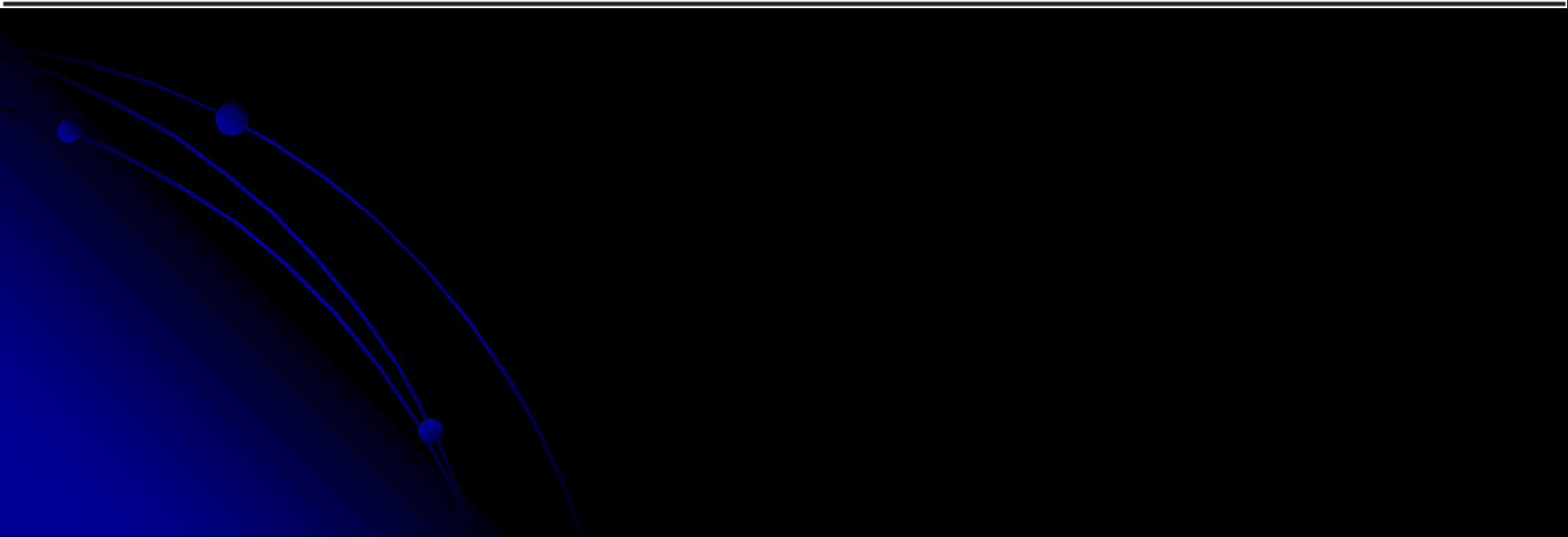
Type  Process indicator

**Description** Operative report is structured. Size and location of disease at the beginning of the operation must be described. All the areas of the abdominal cavity† must be described. If applicable, the size and location of residual disease at the end of the operation, and the reasons for not achieving complete cytoreduction must be reported.

**Specifications** Numerator: no. patients with advanced ovarian cancer undergoing cytoreductive surgery who have a complete operative report that contains all required elements as defined previously  
Denominator: all patients with advanced ovarian cancer undergoing cytoreductive surgery

**Target(s)** 90%

**Scoring rule** 3 if the target is met



## QI 9—Minimum Required Elements in Pathology Reports

Type  Process indicator

Description Pathology report contains all the required elements listed in the International Collaboration on Cancer Reporting (ICCR) histopathology reporting guide.†§


Specifications Numerator: no. patients with advanced ovarian cancer undergoing cytoreductive surgery who have a complete pathology report that contains all required elements as defined in ICCR histopathology reporting guide

Denominator: all patients with advanced ovarian cancer undergoing cytoreductive surgery

Target(s)  $\geq 90\%$ . The tolerance within this target reflects situations where it is not possible to report all components of the data set due to poor quality of specimen.

Scoring rule 3 if the target is met

## QI 10—Existence of a Structured Prospective Reporting of Postoperative Complications

Type  Outcome indicator

Description Data to be recorded are reoperations, interventional radiology, readmissions, secondary transfers to intermediate or intensive care units, and deaths.

Specifications Numerator: no. recorded serious postoperative complications or deaths occurred among patients with advanced ovarian cancer who have undergone cytoreduction

Denominator: all complications occurred among patients with advanced ovarian cancer who have undergone cytoreduction

Target(s) Optimal target: 100% of complications are prospectively recorded  
Minimum required target: selected cases are discussed at morbidity and mortality conferences

Scoring rule 3 if the optimal target is met, 1 if the minimum required target is met



It is hoped that  
governments and health care administrations  
will understand that  
implementing  
a global quality assurance program  
is currently a  
• necessary and cost-effective way  
to improve the outcome of patients with  
ovarian cancer



The ESGO  
QIs  
and  
certification program  
may be  
a major tool  
to facilitate this achievement.



# CHIRURGIA NEL CANCRO DELL'OVAIO

## PAZIENTI A BASSO RISCHIO (a buona prognosi)

- Epiteliali: Stadio IA o IB, grado 1-2
- Borderline
- Tumori non epiteliali

(Sopravvivenza a 5 anni > 90 %)

## PAZIENTI AD ALTO RISCHIO (a cattiva prognosi)

Epiteliali: Stadio IA o IB di grado 3 o stadio IC o II o istotipo indifferenziato

(sopravvivenza a 5 anni → 50-60 %)

Epiteliali: Stadio III e IV

(sopravvivenza a 5 anni → 20%)

# CHIRURGIA NEL CANCRO DELL'OVAIO

**PAZIENTI AD ALTO RISCHIO**  
**(a cattiva prognosi)**

Stadio IA o IB di grado 3 o stadio IC o II o  
istotipo indifferenziato  
**(sopravvivenza a 5 anni → 50-60%)**



**Chirurgia demolitiva/stadiativa**

# CHIRURGIA NEL CANCRO DELL'OVAIO

PAZIENTI AD ALTO RISCHIO  
(a cattiva prognosi)

Stadio III e IV  
(sopravvivenza a 5 anni → 20%)



Chirurgia demolitiva prima o dopo NACT?

**PDS:** Primary cytoreductive surgery

**IDS:** Interval Debulking surgery





# PDS

Primary  
citoreductive  
surgery



## A5: What role does surgery play today?

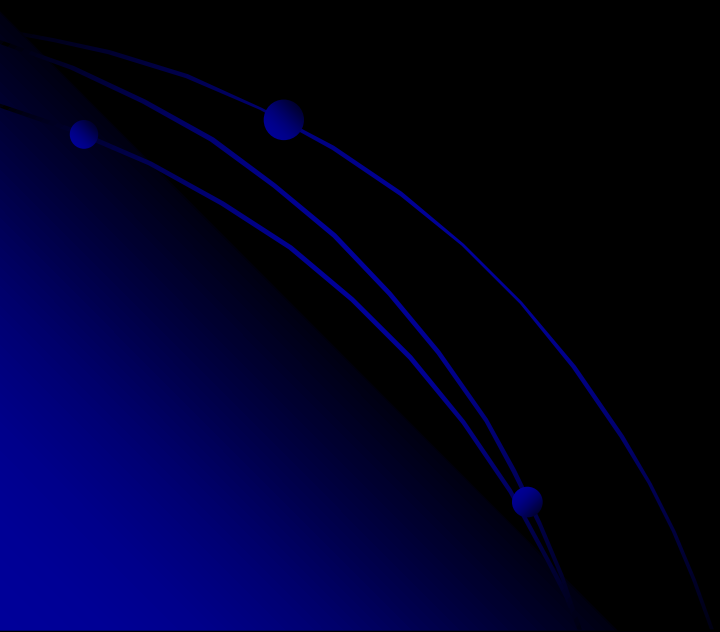
- Surgical staging should be mandatory and should be performed by a gynecologic oncologist.
- **The ultimate goal is cytoreduction to microscopic disease.**

There is evidence that reduction to < 1 cm macroscopic disease is associated with some benefit.

The term "optimal" cytoreduction should be reserved for those with no macroscopic residual disease.

- Documentation must be provided as to the level of cytoreduction (at least microscopic vs. macroscopic).
- **Delayed primary surgery following neoadjuvant chemotherapy is an option for selected patients with stage IIIC and IV ovarian cancer as included in EORTC 55971.**

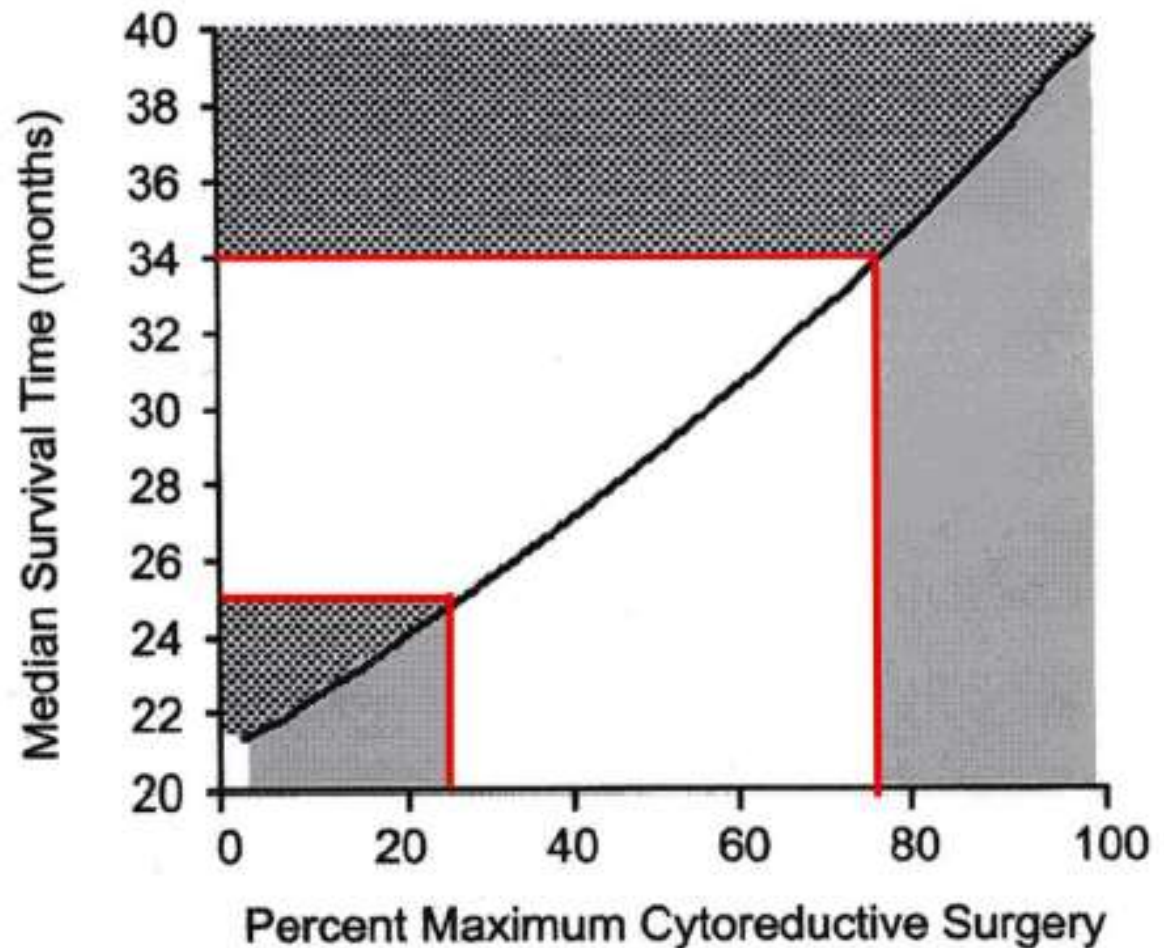
WHY ?



# Greater Success at Cyto reduction is Associated with Greater Median Survival

**75% Max. CytoRS  
corresponds to a 34  
mo. median survival**

**25% Max. CytoRS  
corresponds to a 25  
mo. median survival**





# SURGERY IN OVARIAN CANCER

- Ovarian cancer is potentially curable by surgery: the cure rate is, however, poor because in **most patients the disease is diagnosed at an advanced stage when overall five-year survival is only about 30%**

(Jemal et al, 2005, Ca Cancer J Clin)

- Meta-analysis has confirmed that maximal surgical cytoreduction is one of the most powerful determinants of cohort survival in **FIGO III-IV ovarian cancer** (Bristow et al, 2002, JCO)

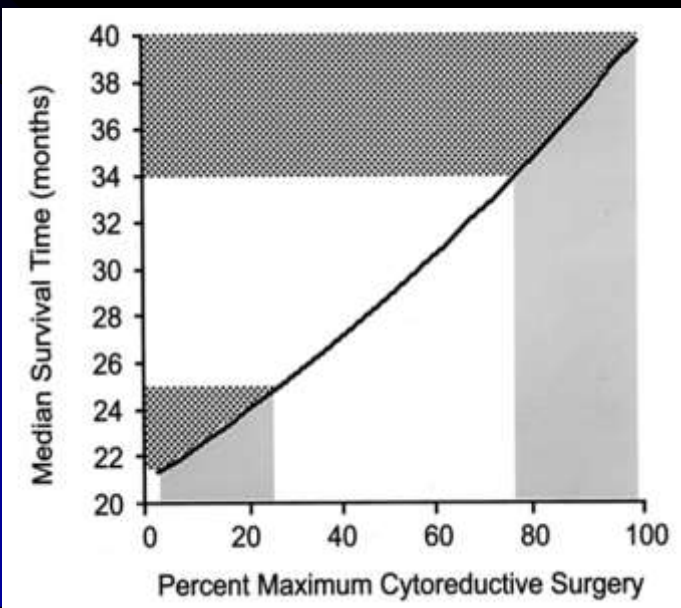
## Survival Effect of Maximal Cytoreductive Surgery for Advanced Ovarian Carcinoma During the Platinum Era: A Meta-Analysis

By Robert E. Bristow, Rafael S. Tomacruz, Deborah K. Armstrong, Edward L. Trimble, and F.J. Montz

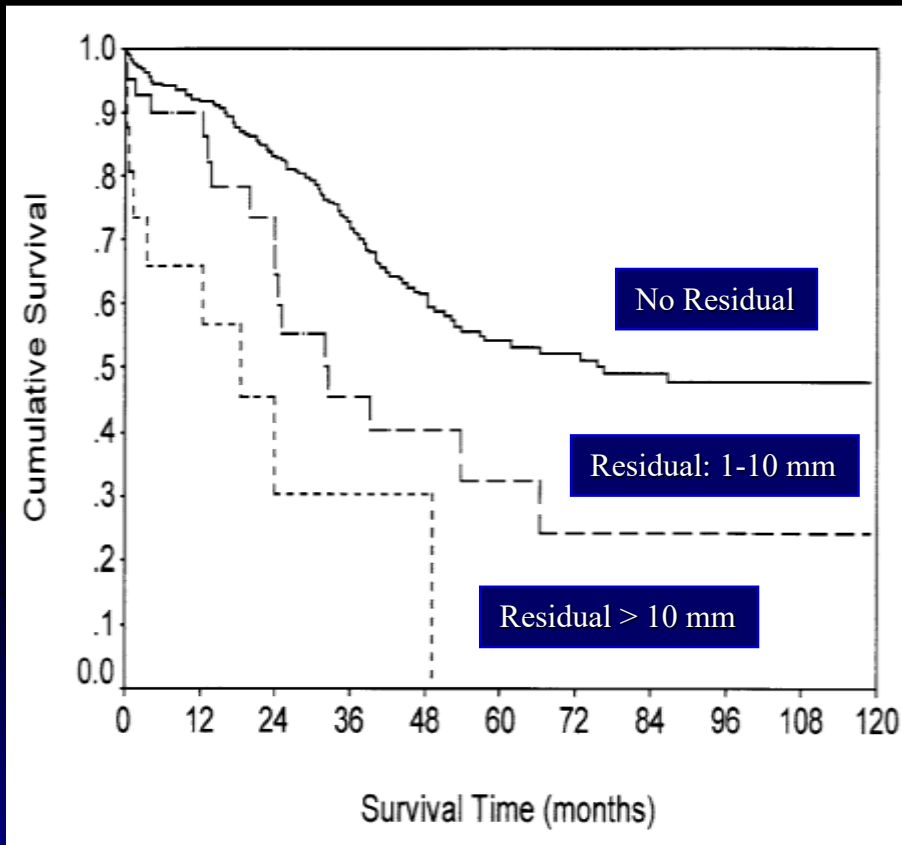
**10% increase in maximal  
cytoreductive surgery**



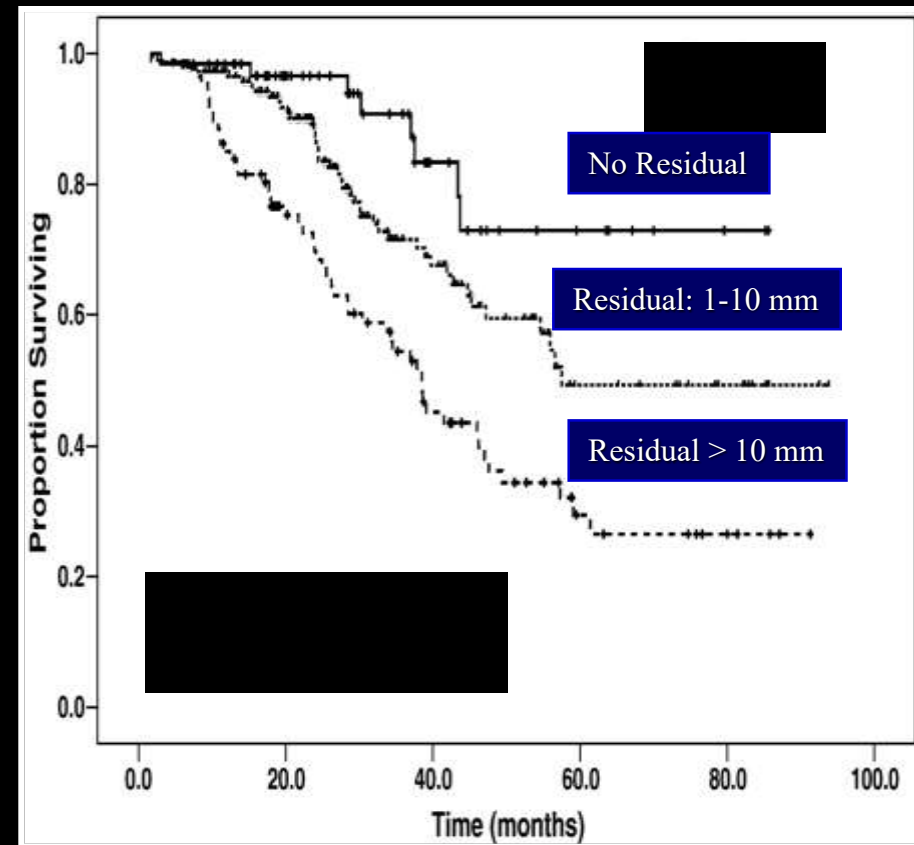
**5.5 % increase in median survival time**



# Primary Cytoreductive - Literature data

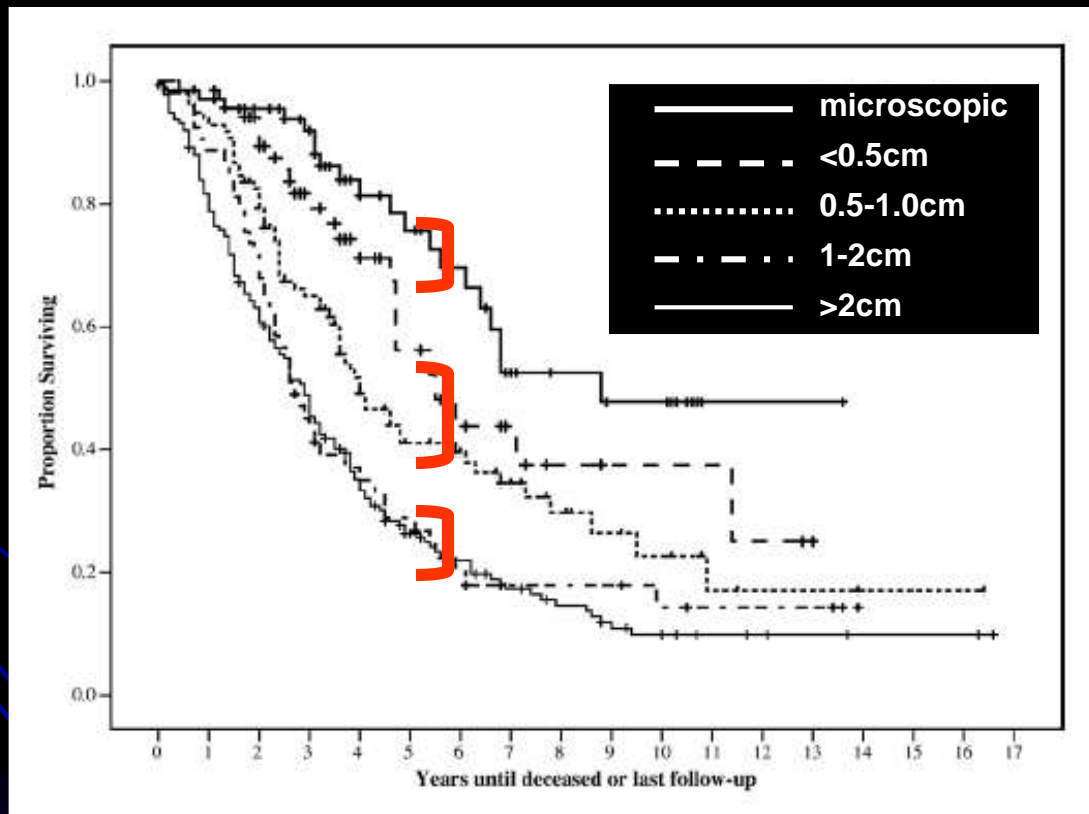


Eisenkop et al. *Gynecol Oncol* 90:390, 2003



Eisenhauer et al. *Gynecol Oncol* 108, 2008

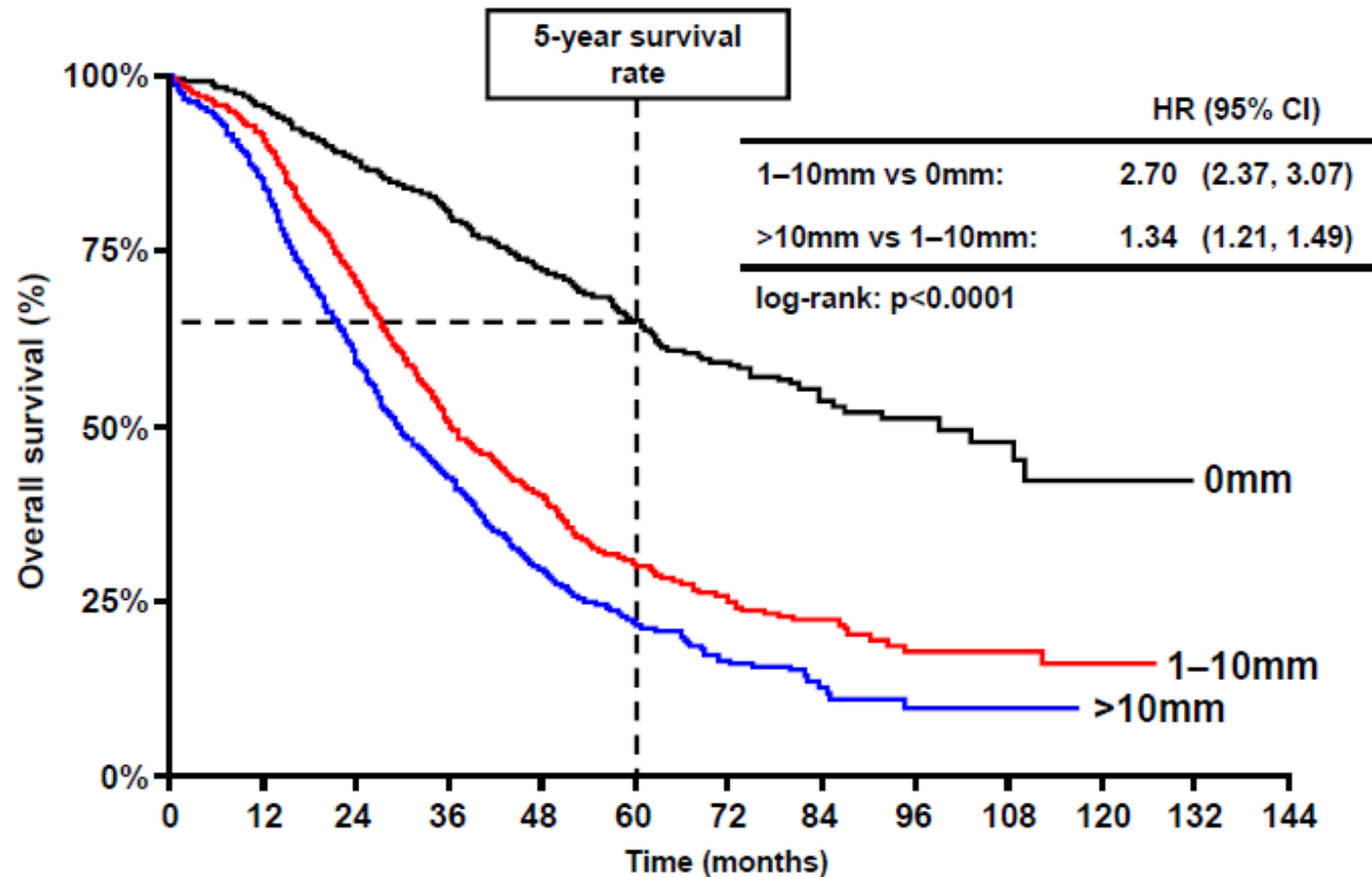
# What is the Optimal Goal of Primary Cytoreductive Surgery for Bulky Stage IIIC Epithelial Ovarian Cancer?



# RESIDUAL DISEASE (RD)

## The impact of residual tumour on outcome in advanced ovarian cancer

Data from an individual patient meta-analysis of three randomised phase III trials with 3,126 patients



du Bois A, Reuss A, Pujade-Lauraine E, et al. Cancer 2009;15:1234–44

# Mayo Clinic Experience

## Stage IIIC Ovarian Cancer

Residual Disease	% 5-Year Survival
None	76
<1 cm	31
1-2 cm	13
>2 cm	5

# Association between debulking status and chemotherapy outcome

## 1. Suboptimal debulked patients have less chance for a complete response

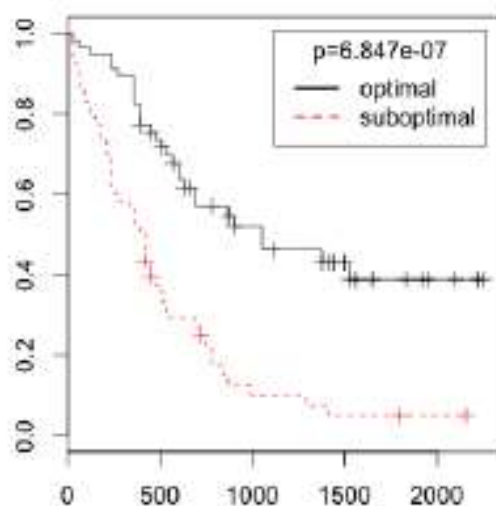
TCGA dataset (n=412):

	complete	incomplete
optimal	229	72
suboptimal	54	57

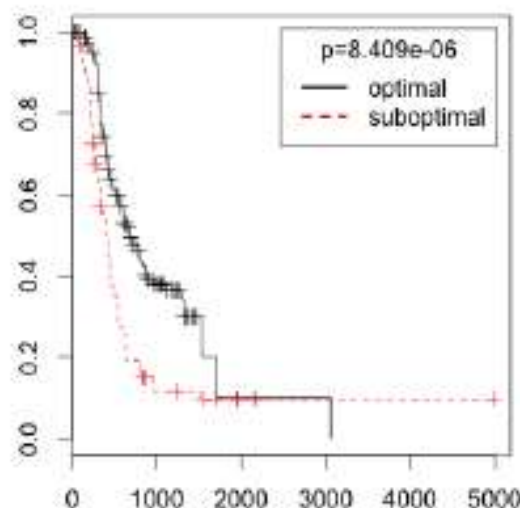
Pearson's Chi-square:  
 $p = 1.9 \times 10^{-7}$

## 2. Patients with suboptimally debulked tumor has significant shorter PFS (even after complete chemo-response)

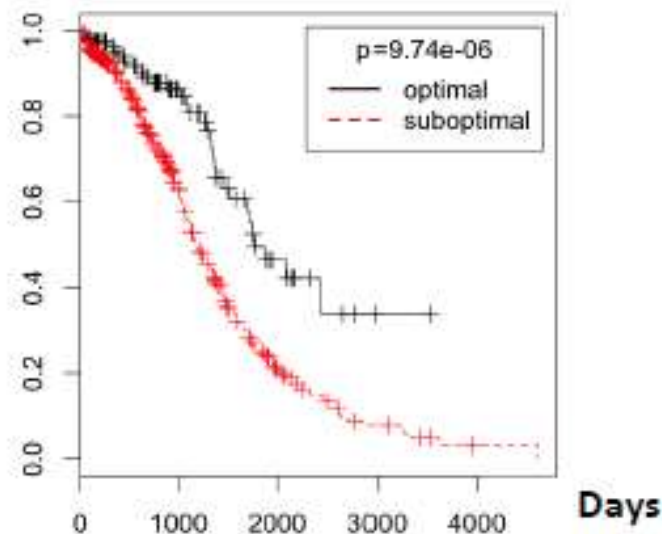
Yoshihara-110



Tothill-260



TCGA n=503





# Unresolved questions

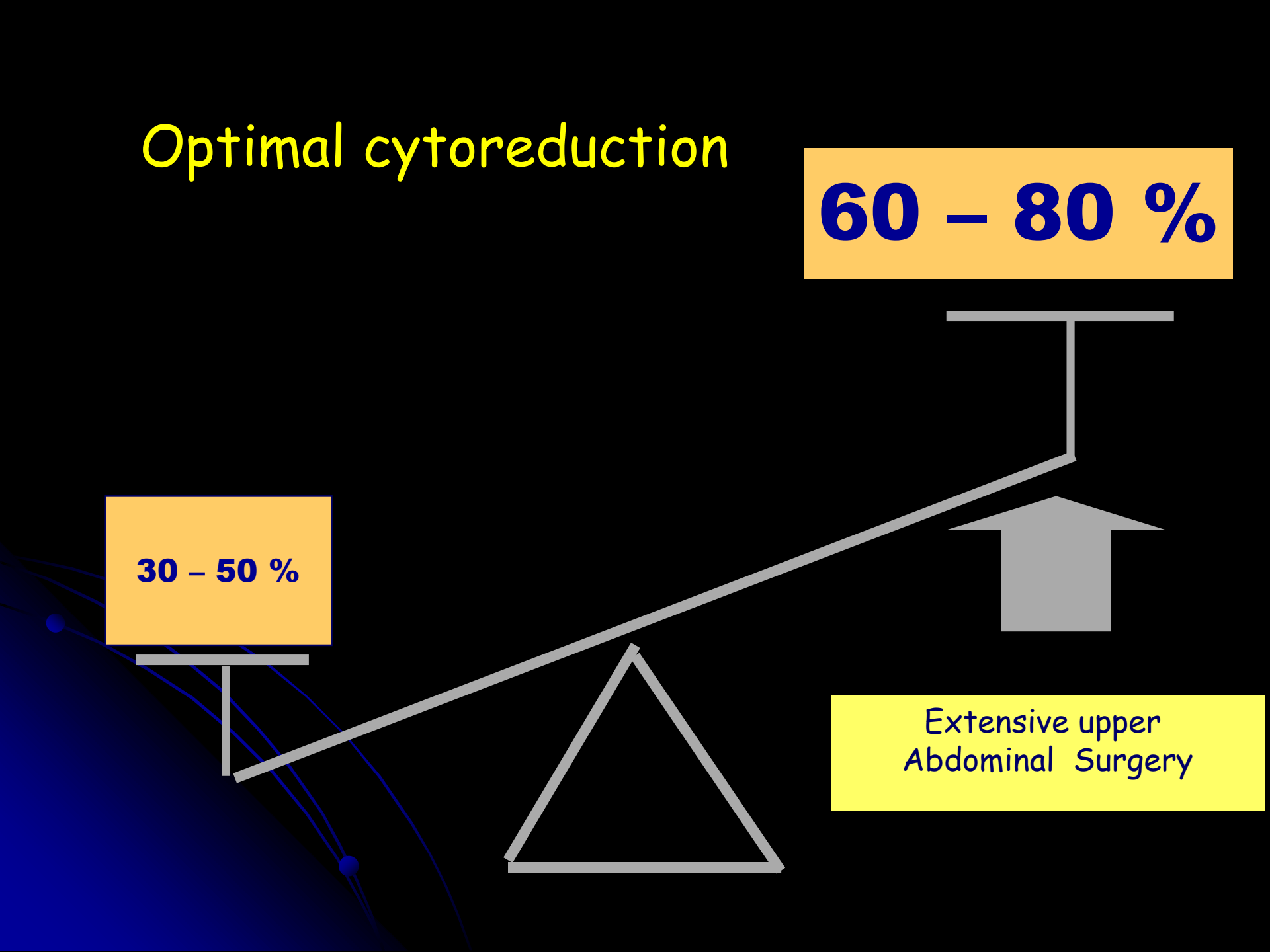
- What is successful cytoreduction surgery due to:
  - Exclusively the surgical factors
  - the intrinsic biology of the tumor
- The benefit of optimal debulking to chemo-therapy is due to
  - Reduced tumor burden
  - the intrinsic biology of the tumor
- Possibility of targeting the biological signature underlying the suboptimal debulked ovarian tumors

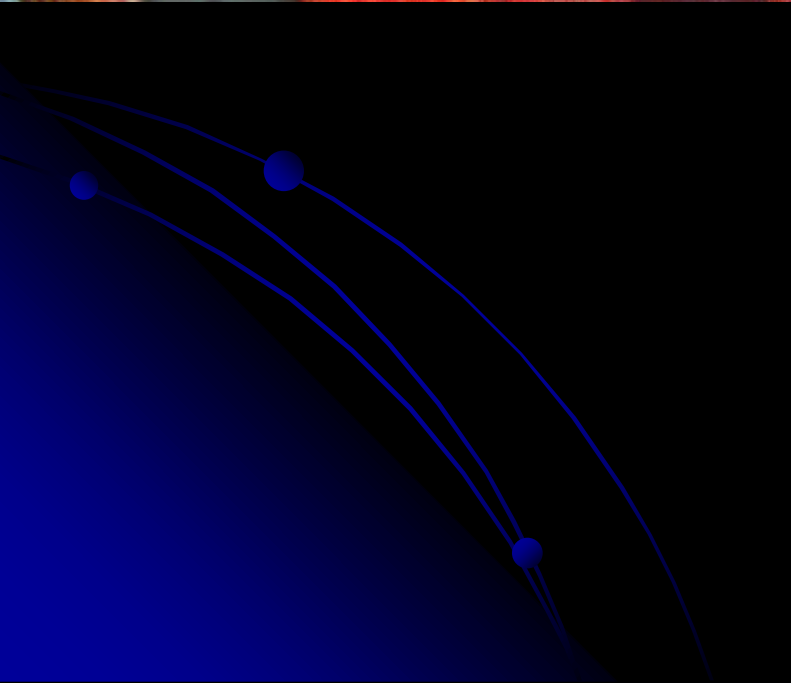
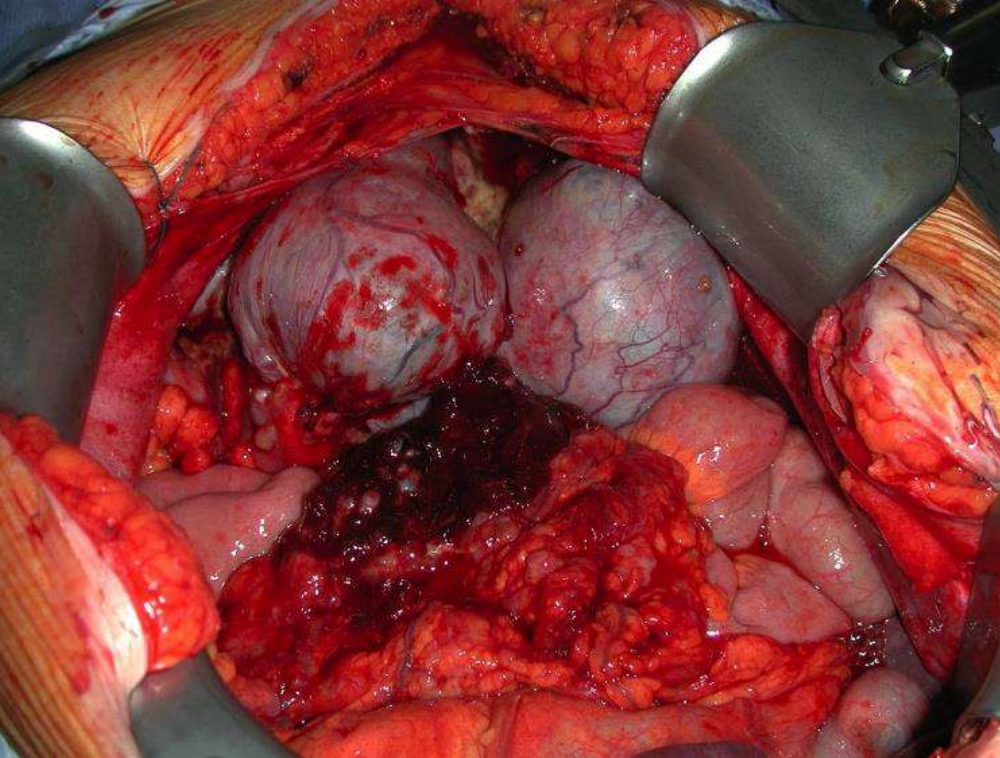
# Optimal cytoreduction

**60 – 80 %**

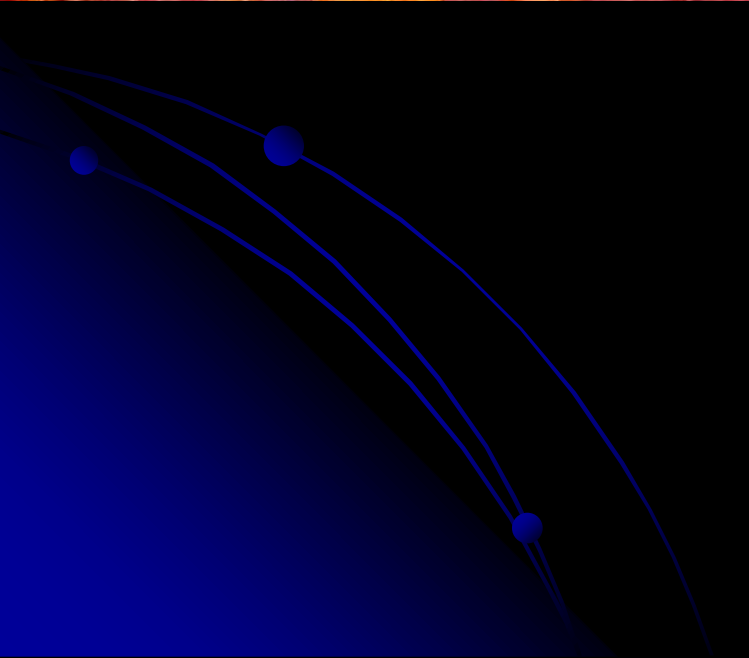
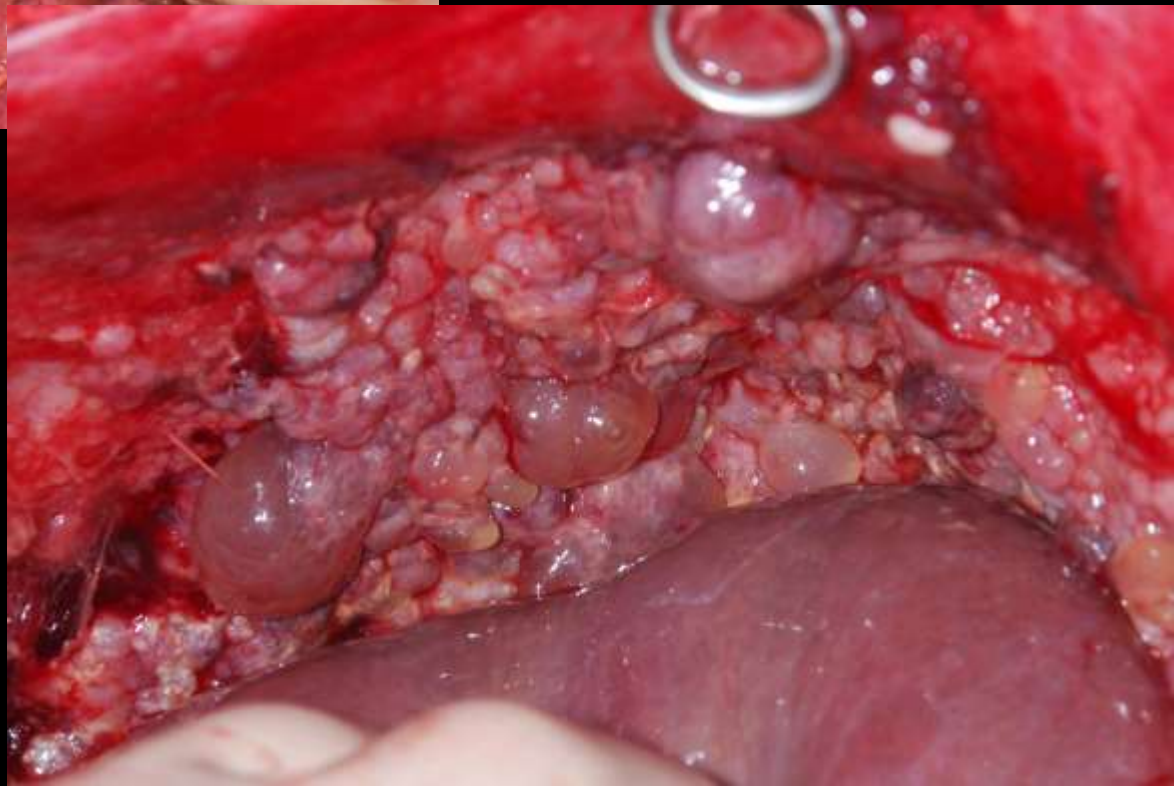
**30 – 50 %**

Extensive upper  
Abdominal Surgery

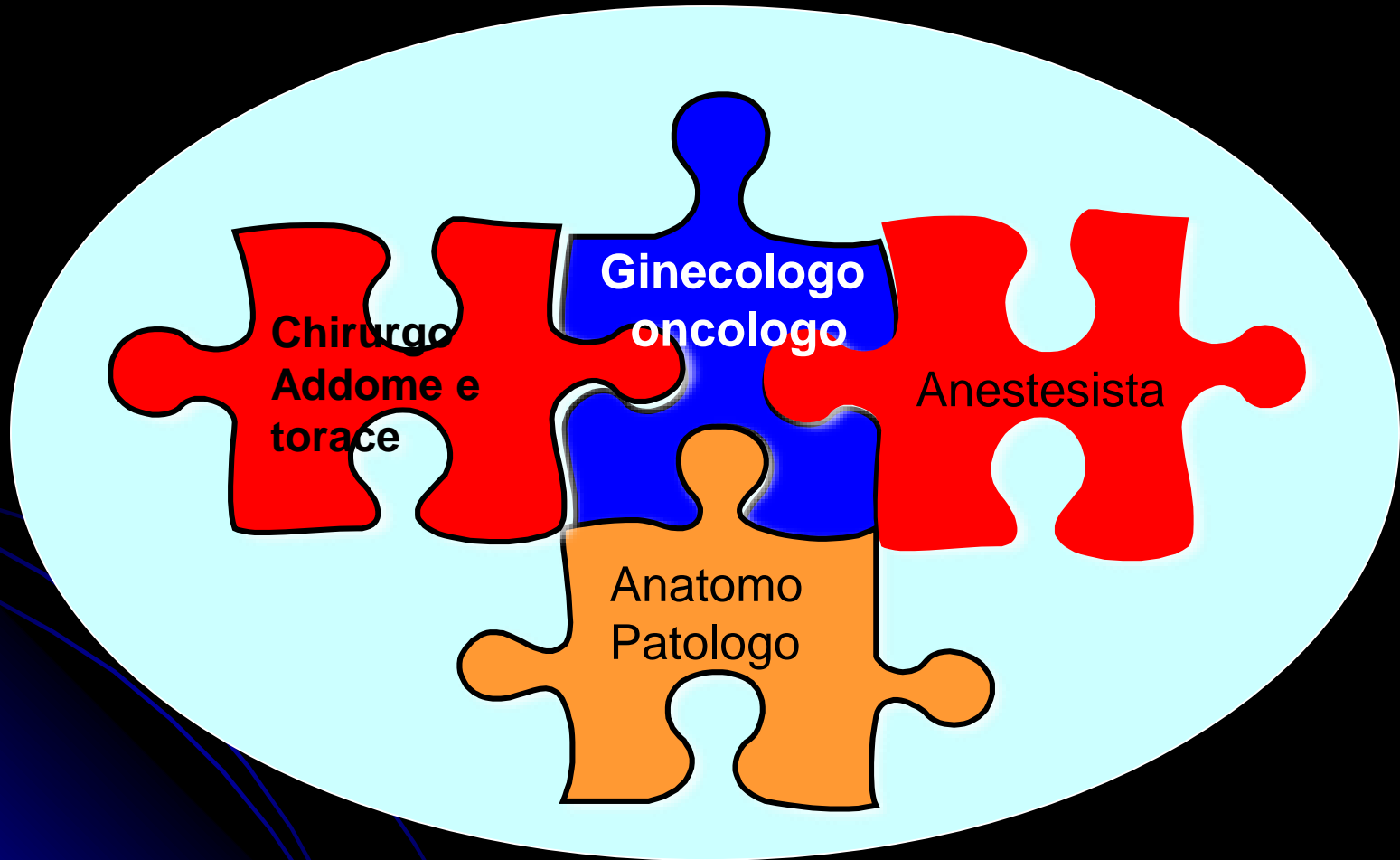








# Multidisciplinarietà





# Complessità



- Chirurgica

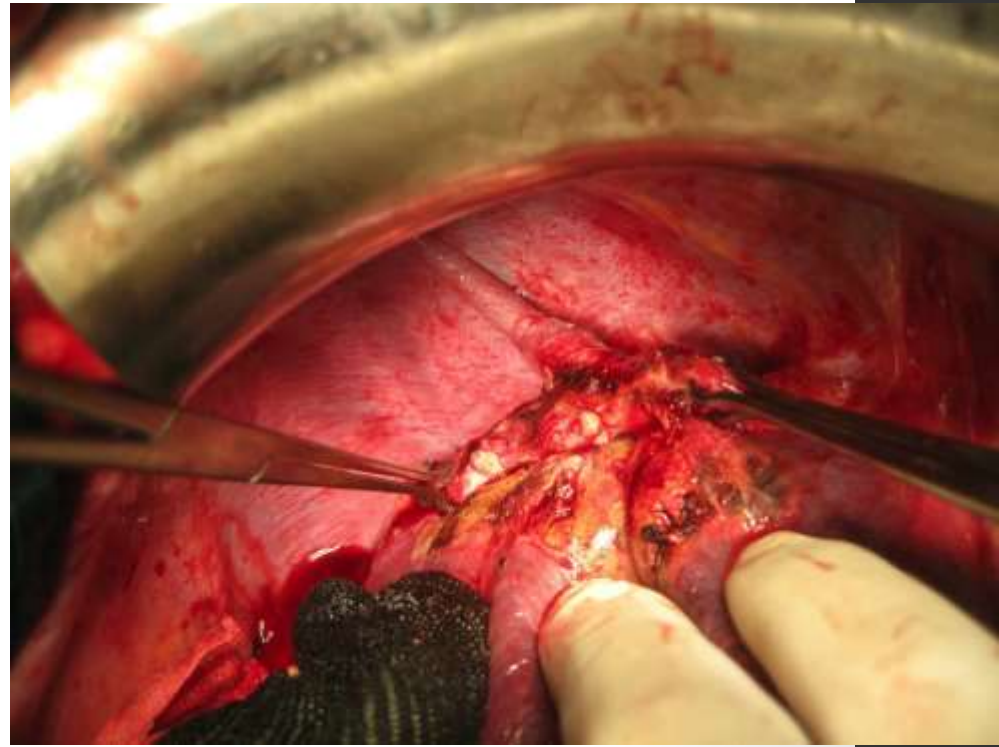


- Clinica



# CYTOREDUCTIVE SURGERY: **goal**

- **GOAL: NO MACROSCOPIC RESIDUAL DISEASE !!!**
- **SOME BENEFITS MAY BE FOUND IN PATIENTS DEBULKED TO MINIMAL RD**
  - ✓ Potential benefit for resistant clones, poorly vascularized areas, reduction VEGF, EGF, PDGF
- **SYMPTOMS PALLIATION**
  - ✓ Bowel obstruction
  - ✓ Reduce ascites formation



# CYTOREDUCTIVE SURGERY: team work

## PREOPERATIVE

- Nurses, secretary
- Radiologist/US
- Anesthesiologist

## INTRAOPERATIVE

- Hepatobiliary/Thoracic/Vascular/General Surgery
- Pathology
- Anesthesiology/OR nurses

## POSTOPERATIVE

- ICU team
- Psychologists
- Gyne/Medical Oncologists



# CYTOREDUCTIVE SURGERY: **strategies**

## Criteria for Primary Chemotherapy and Interval Debulking Surgery in FIGO Stage IIIC and IV

- Involvement of the superior mesenteric artery
- Diffuse deep infiltration of the radix mesenterii of the small bowel
- Diffuse and confluent carcinomatosis of the small bowel
- Multiple parenchymal liver or lung metastases
- Tumor infiltrating the vessels of the hepatoduodenal lig or celiac trunk
- Brain metastases

**UNRESECTABLE**

- Impaired performance status and comorbidity not allowing a “maximal surgical effort” to achieve a complete resection
- Patients nonacceptance of potential supportive measures as blood transfusion or temporary stomas

**INOPERABLE**

# CYTOREDUCTIVE SURGERY

## Intraoperative evaluation

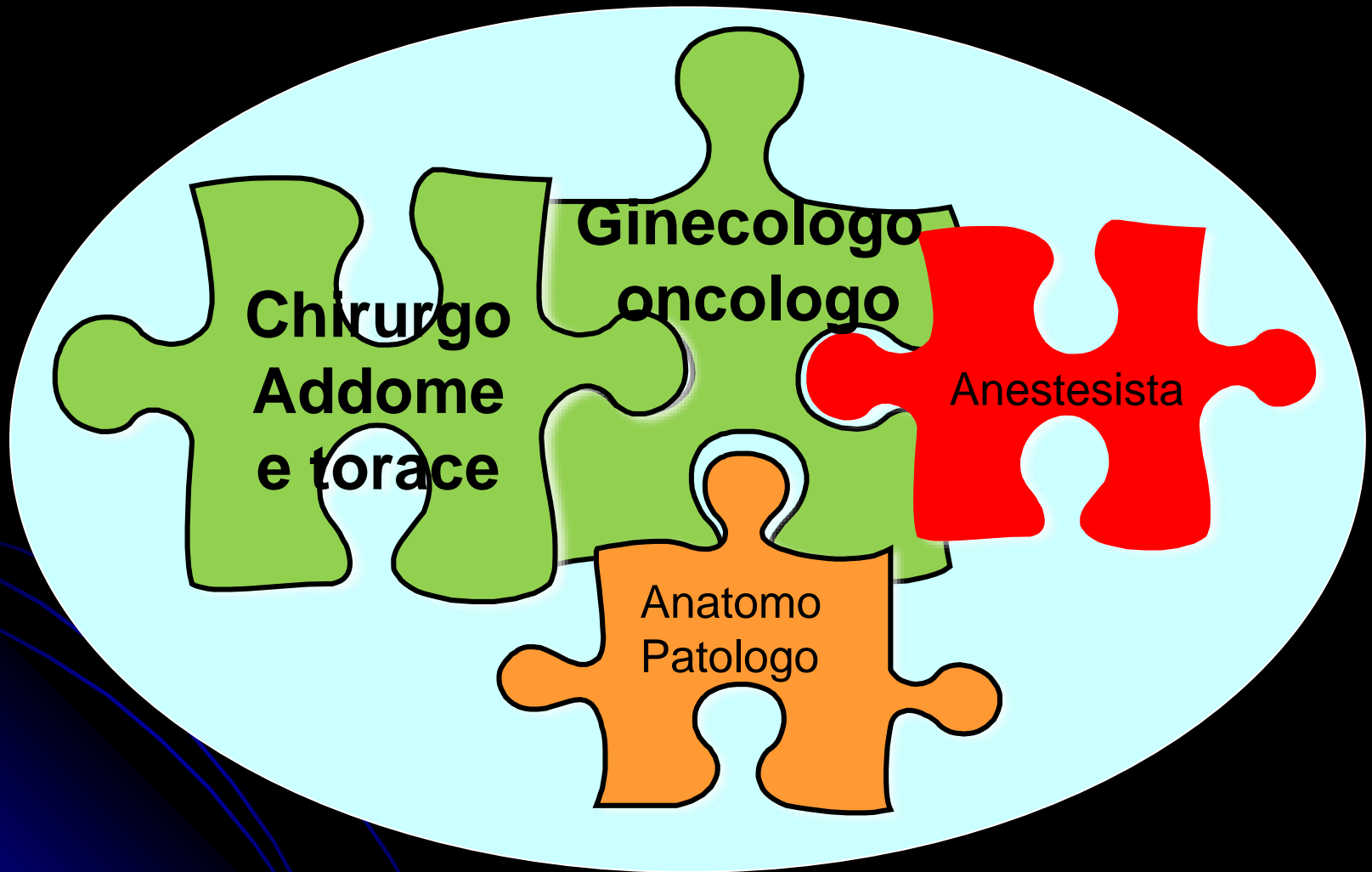
### STEP 1: SMALL LAPAROTOMY OR LAPAROSCOPY



Systematic evaluation without create morbidity and not passing the  
“point of no return”



# Multidisciplinarietà



# CYTOREDUCTIVE SURGERY

## Intraoperative evaluation

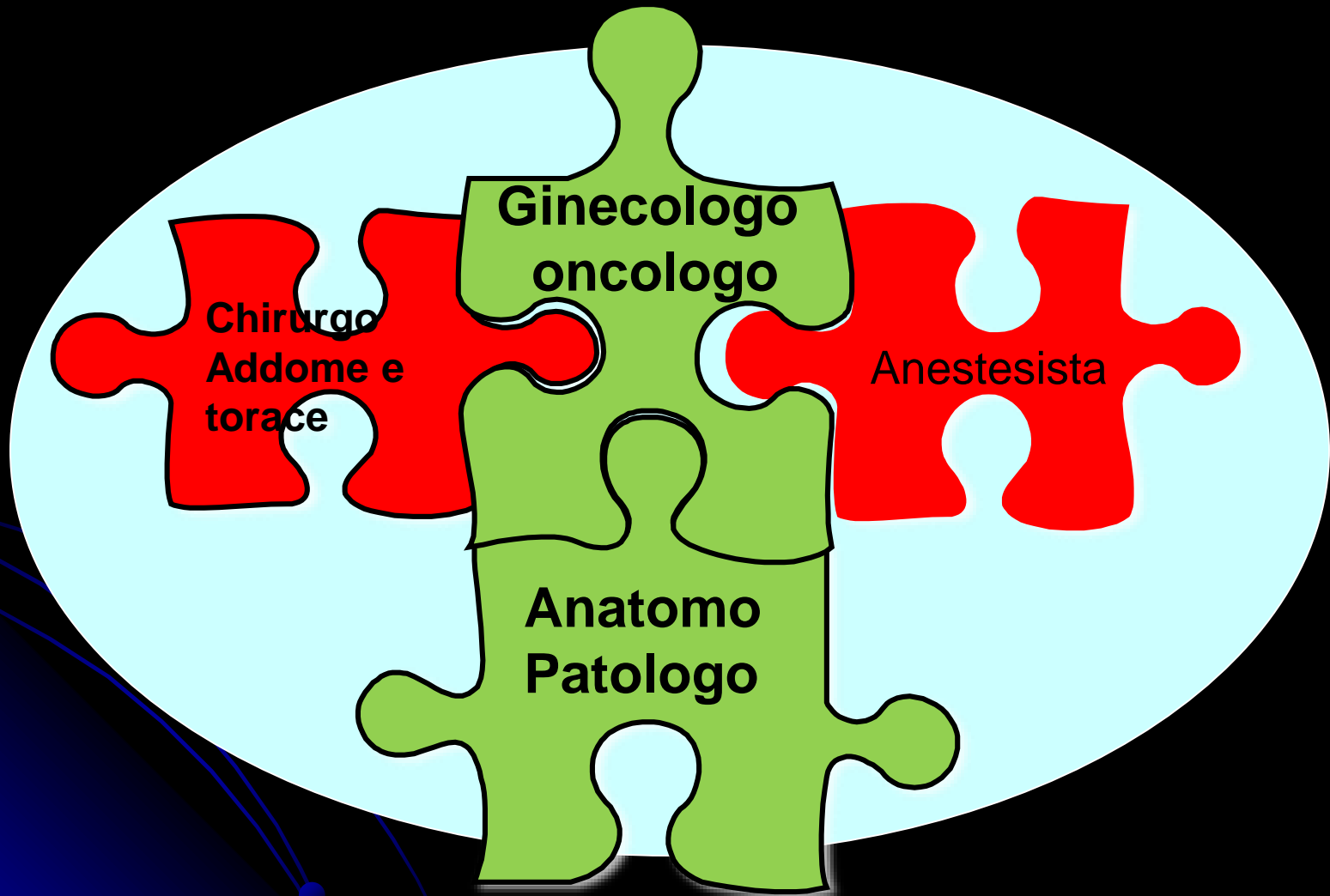
### STEP 2: BIOPSY

#### Specimen of tumor for Frozen Section:

- ? Primary or metastatic
- ? Low or High grade
- ? Borderline
- ? Non epithelial ovarian tumor



# Multidisciplinarietà



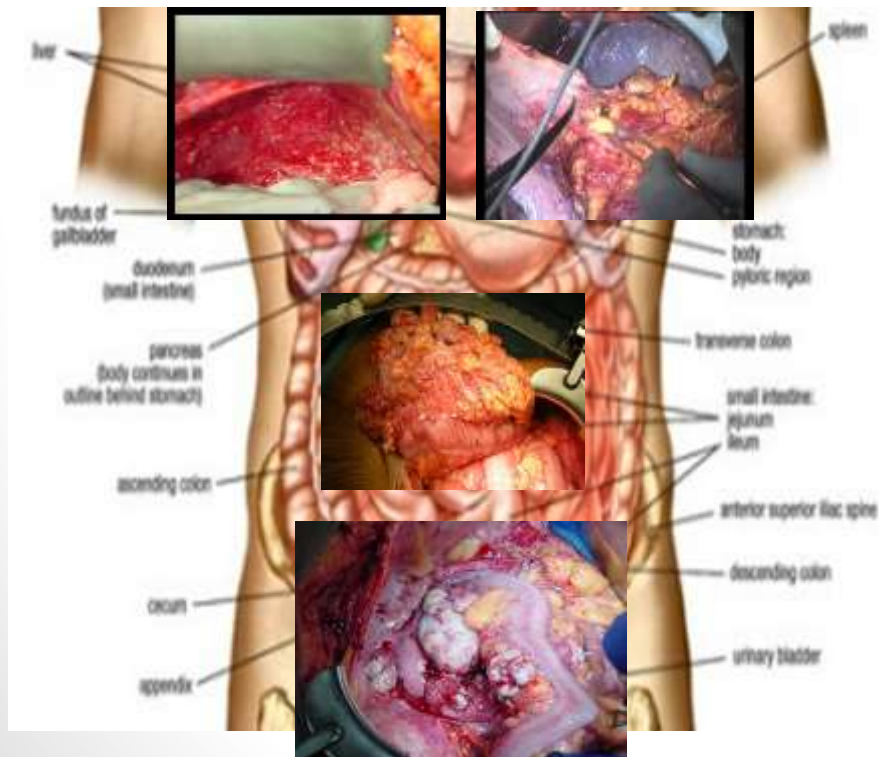
# CYTOREDUCTIVE SURGERY

## Intraoperative evaluation

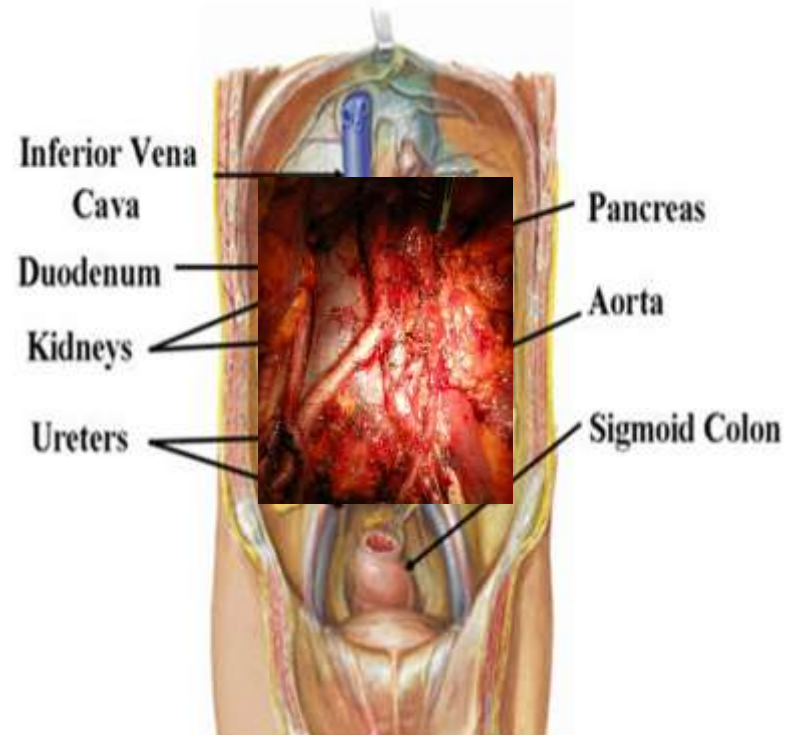
### STEP 3: SURGICAL EVALUATION

#### SURGICAL ZONES

##### PERITONEUM



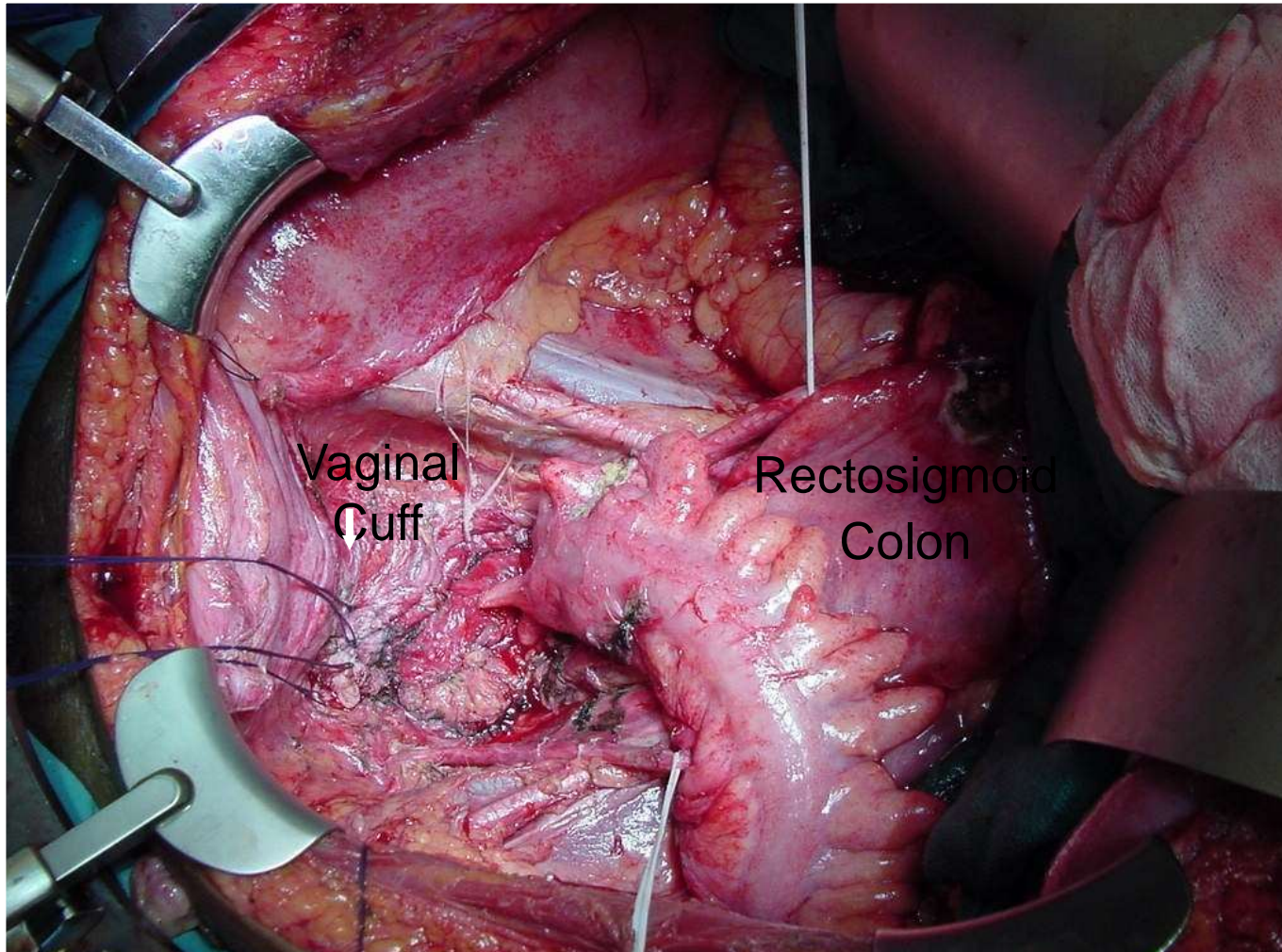
##### RETROPERITONEUM





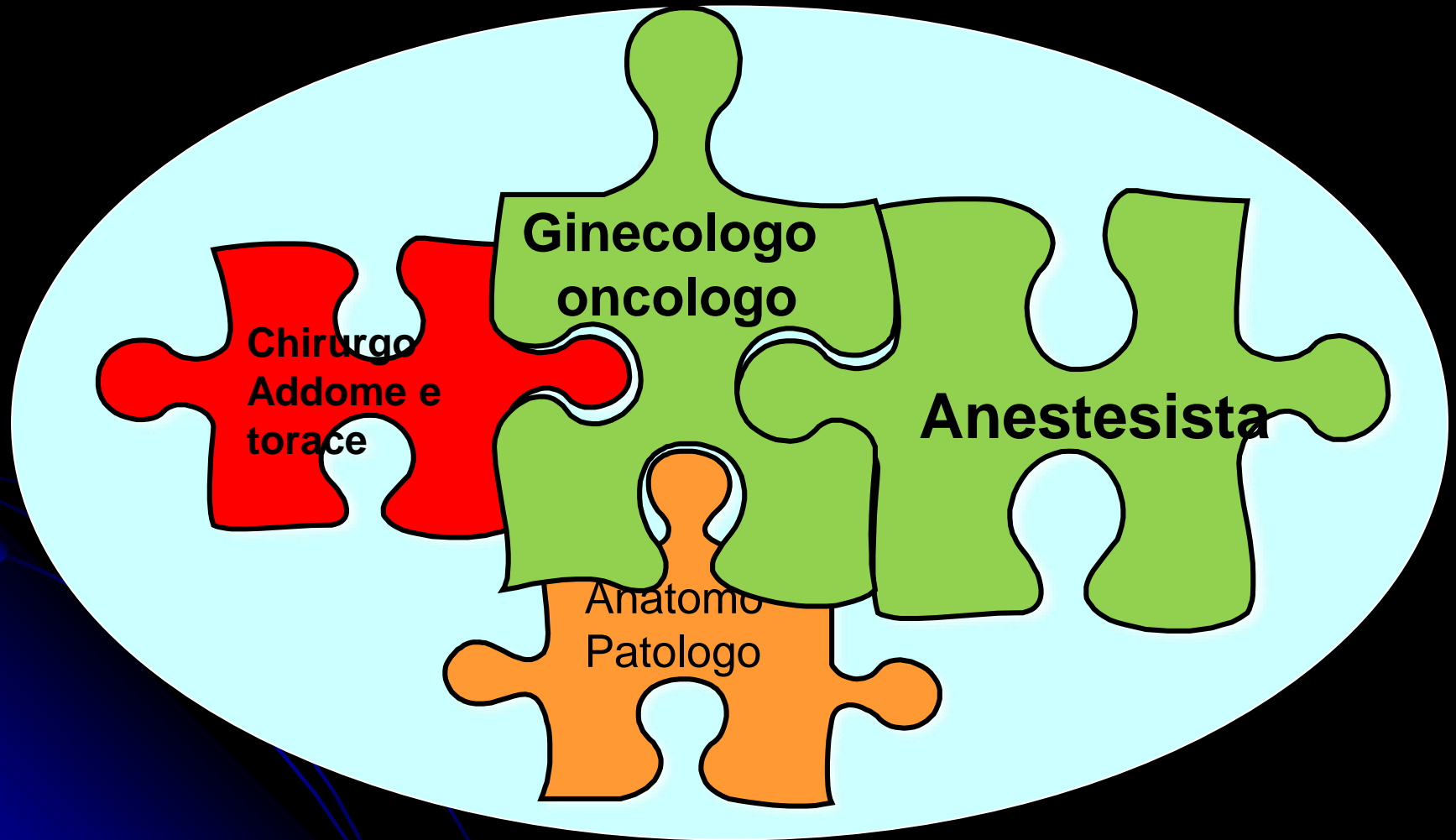
# ZONE 1: PELVIS

## RADICAL OOPHORECTOMY





# Multidisciplinarietà



# Primary citoreductive Surgery

When ?

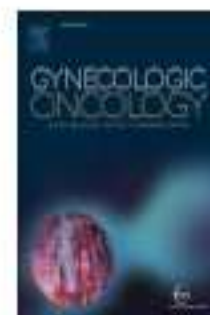




Contents lists available at ScienceDirect

## Gynecologic Oncology

journal homepage: [www.elsevier.com/locate/ygyno](http://www.elsevier.com/locate/ygyno)



# Risk-prediction model of severe postoperative complications after primary debulking surgery for advanced ovarian cancer



Amanika Kumar<sup>a</sup>, Jo Marie Janco<sup>a</sup>, Andrea Mariani<sup>a</sup>, Jamie N. Bakkum-Gamez<sup>a</sup>, Carrie L. Langstraat<sup>a</sup>, Amy L. Weaver<sup>b</sup>, Michaela E. McGree<sup>b</sup>, William A. Cliby<sup>a,\*</sup>

<sup>a</sup> Department of Obstetrics and Gynecology, Division of Gynecologic Surgery, Mayo Clinic, Rochester, MN, United States

<sup>b</sup> Division of Biomedical Statistics and Informatics, Mayo Clinic, Rochester, MN, United States

## HIGHLIGHTS

- Postoperative complications after primary debulking surgery for advanced epithelial ovarian cancer are common and predictable based on risk factors.
- Age, albumin <3.5 g/dL, surgical complexity, stage, ASA, and BMI influence morbidity and mortality after debulking surgery.
- Risk stratification may help in pre-operative counseling for patients with advanced ovarian cancer.

## 30 day morbidity

### Odds Ratio Estimates and Wald Confidence Intervals

Variable	Estimate	95% CI	
Age	1.207	0.995	1.464
ASA 3,4	<b>1.507</b>	0.992	2.287
Albumin <3.5 g/dL vs ≥3.5 g/dL	<b>1.678</b>	0.967	2.910
Surgical complexity: Intermediate vs low	0.827	0.453	1.513
Surgical complexity: High vs low	<b>1.917</b>	1.036	3.548
stage 4 vs 3	<b>1.617</b>	1.032	2.534
BMI <25.0 vs BMI 25.0-39.9	1.353	0.890	2.058
BMI 40.0+ vs BMI 25.0-39.9	<b>2.814</b>	1.327	5.966

### Independent Predictors

**AGE**

**Performance Status**

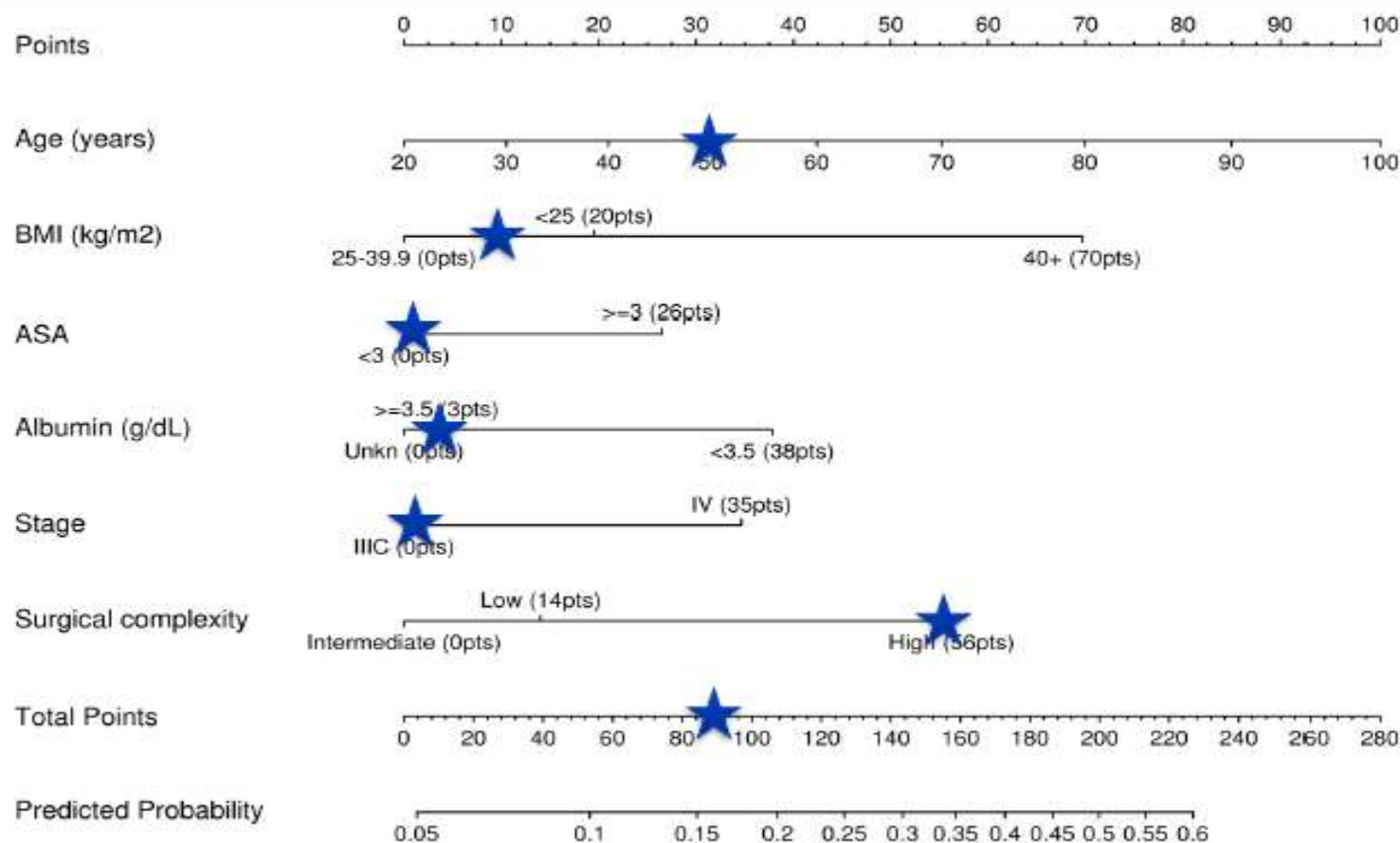
**Albumin**

**Stage**

**BMI**

**Surgical Complexity**

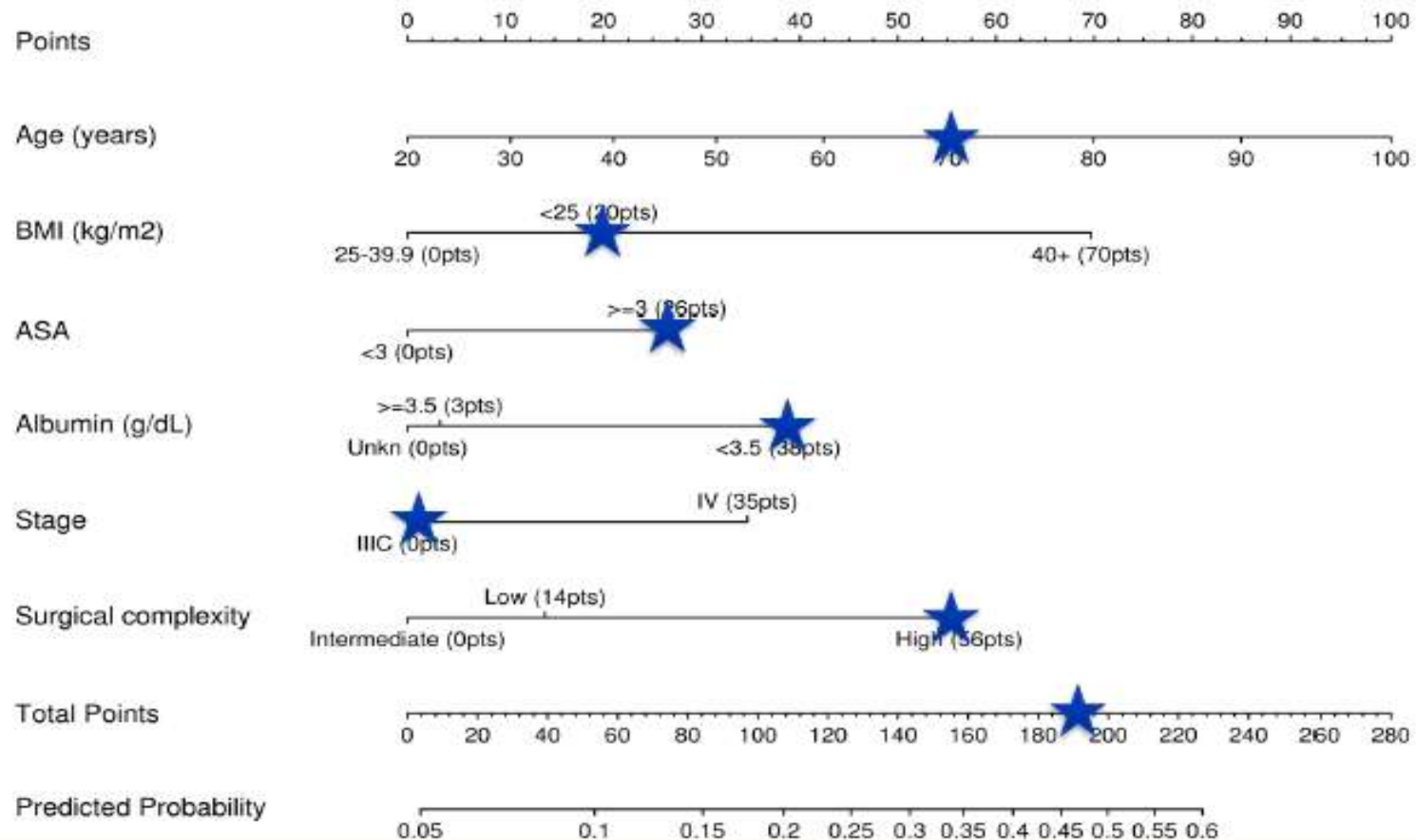
## 30 day morbidity



90 points = 16% risk of Grade 3 Complication



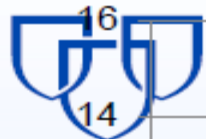
# 30 day morbidity



195 points = 48% risk of Grade 3 Complication

## Reducing M/M

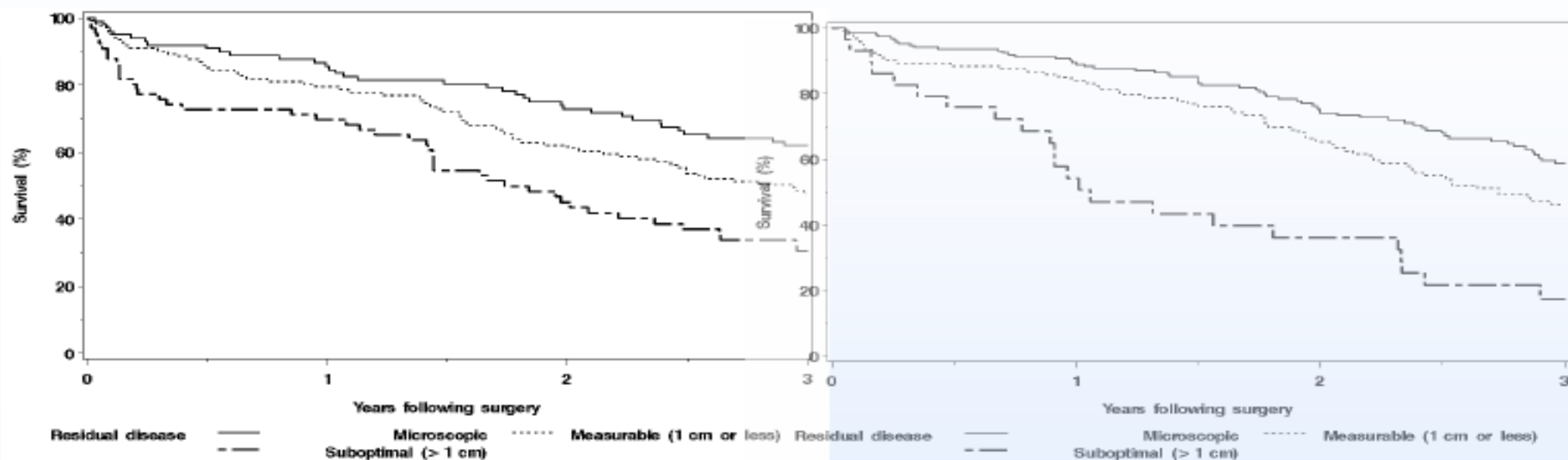
- Improved technique
  - SSI
  - Anastomotic leak
  - Enhanced recovery
- Triage of highest risk patients
- Horizon: more accurate triage systems
  - Nomograms
  - Age and PS are crude measures of reserve
  - Frailty Index



## Stage IIIC/IV PDS: Trends in 90d mortality



# Extending Surgical Efforts in OVCA Mayo Clinic



**2003-2006**

**RD0: 99 (34%)**  
**RD<1: 122 (43%)**  
**RD>1: 66 (23%)**



**2007-2011**

**185 (55%)**  
**120 (36%)**  
**29 (9%)**

## Effective Debulking

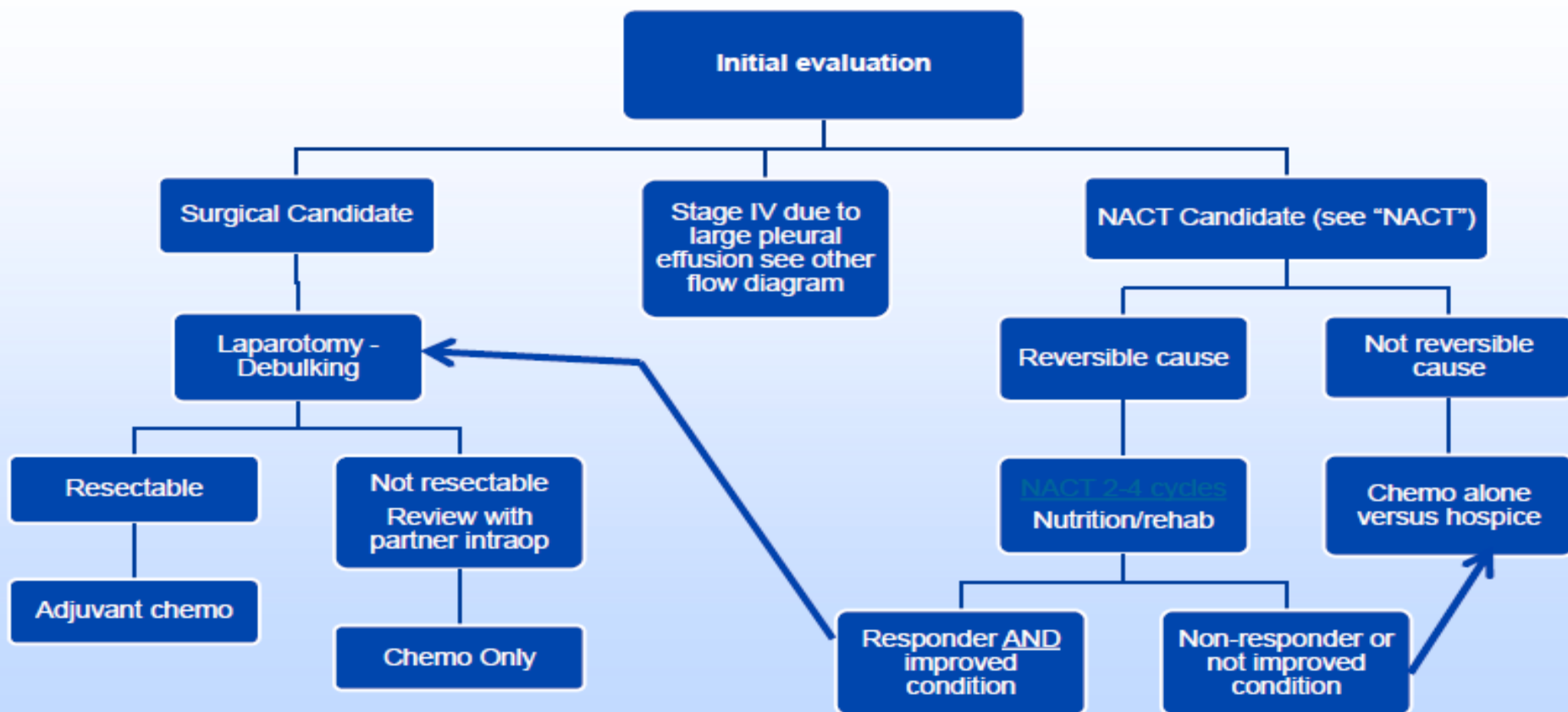
Not **for** everyone: Not **by** everyone

---

- Wide range of ability to reach RD0 and RD<1cm
- Survival Benefit
- Majority of patients can tolerate a maximal effort
- Must get patients who can tolerate complex surgery to expert centers



# Advanced Stage Epithelial OVCA - Overview



# IDS

Interval Debulking  
surgery



# Ovarian Cancer: First-Line Treatment Algorithm

Neoadjuvant  
chemotherapy?

Primary cytoreductive surgery

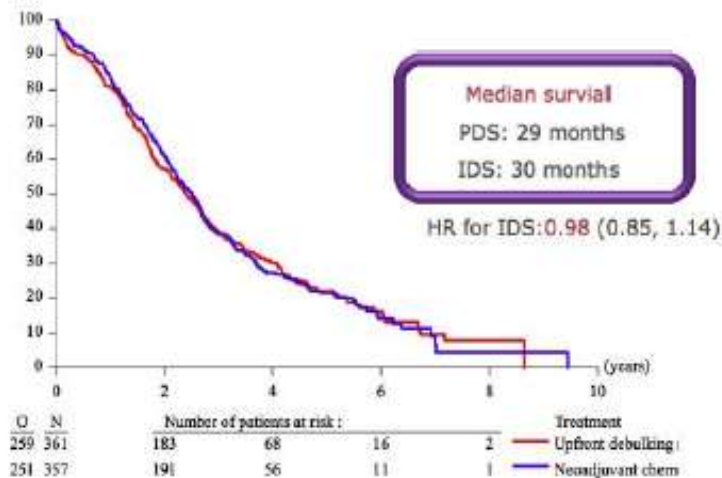
Carboplatin + paclitaxel three-weekly

# Neoadjuvant Chemotherapy or Primary Surgery in Stage IIIC or IV Ovarian Cancer



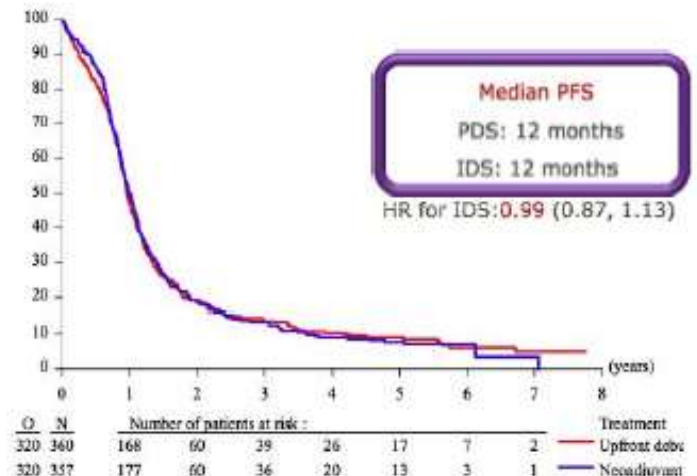
## NACT + IDS vs PDS: ITT

### Overall survival



## NACT + IDS vs PDS: ITT

### Progression-free survival



# Trial EORTC-GCG/NCIC-CTG

## NACT + IDS *versus* PCS

### Critica

Bassa  
% di R0

No residual per country	Primary OP (n=310)	NACT-----IDS (n=322)
Belgium	63%	87%
The Netherlands	4%	28%
Italy	6%	39%
Norway	8%	50%
Spain	10%	42%
UK	10%	43%
Canada	11%	41%
No residual after surgery	19.4%	51.2%



# Trial EORTC-GCG/NCIC-CTG

## NACT + IDS versus PCS

### Critica

Arruolamento lento...

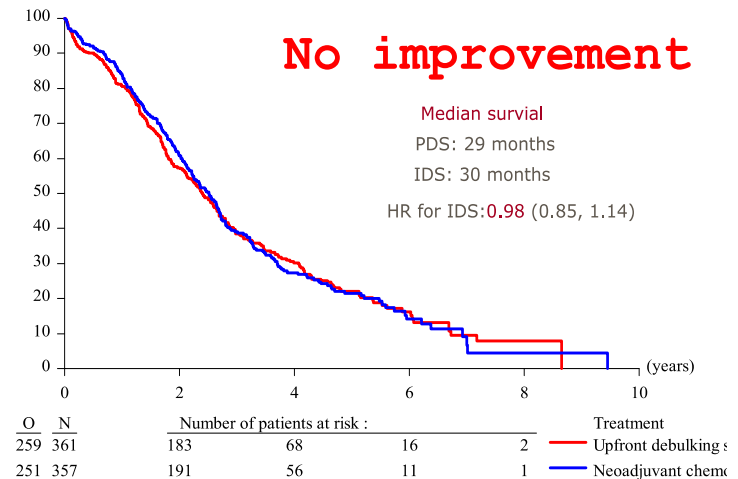
Country	Randomized Pts	Pts per year	Centers	Pts x year x center
Belgium	131	16	3	5.5
The Netherlands	100	12.5	4	3.1
Italy	30	3.8	5	0.8
Norway	77	9.6	2	4.8
Spain	59	7.4	3	2.5
UK	96	12	11	1.1
Canada	75	9.4	11	0.9
<b>Total</b>	<b>568</b>	<b>71</b>	<b>39</b>	<b>1.8</b>

# Quali sono i rischi dell'impiego della chemioterapia neoadiuvante?

NO residual per country (PP1)	PDS (n = 329)	NACT -> IDS (n = 306/339)
Belgium (n=133)	63%	87%
The Netherlands (n=104)	40%	77%
Sweden (n=23)	4%	28%
Norway (n=82)	8%	50%
Italy (n=38)	6%	39%
Spain (n=62)	10%	42%
UK (n=101)	10%	43%
Canada (n=84)	11%	41%
Total no residual	19.4%	51.2%
Total < 1 cm	41.6%	80.7%

EORTC/NCIC Study: NACT + Interval-OP vs. Primary OP

Overall survival



Wrongly interpreted as NACT is equivalent to primary surgery in FIGO IIIc/IV OC

**+ 31.8%**

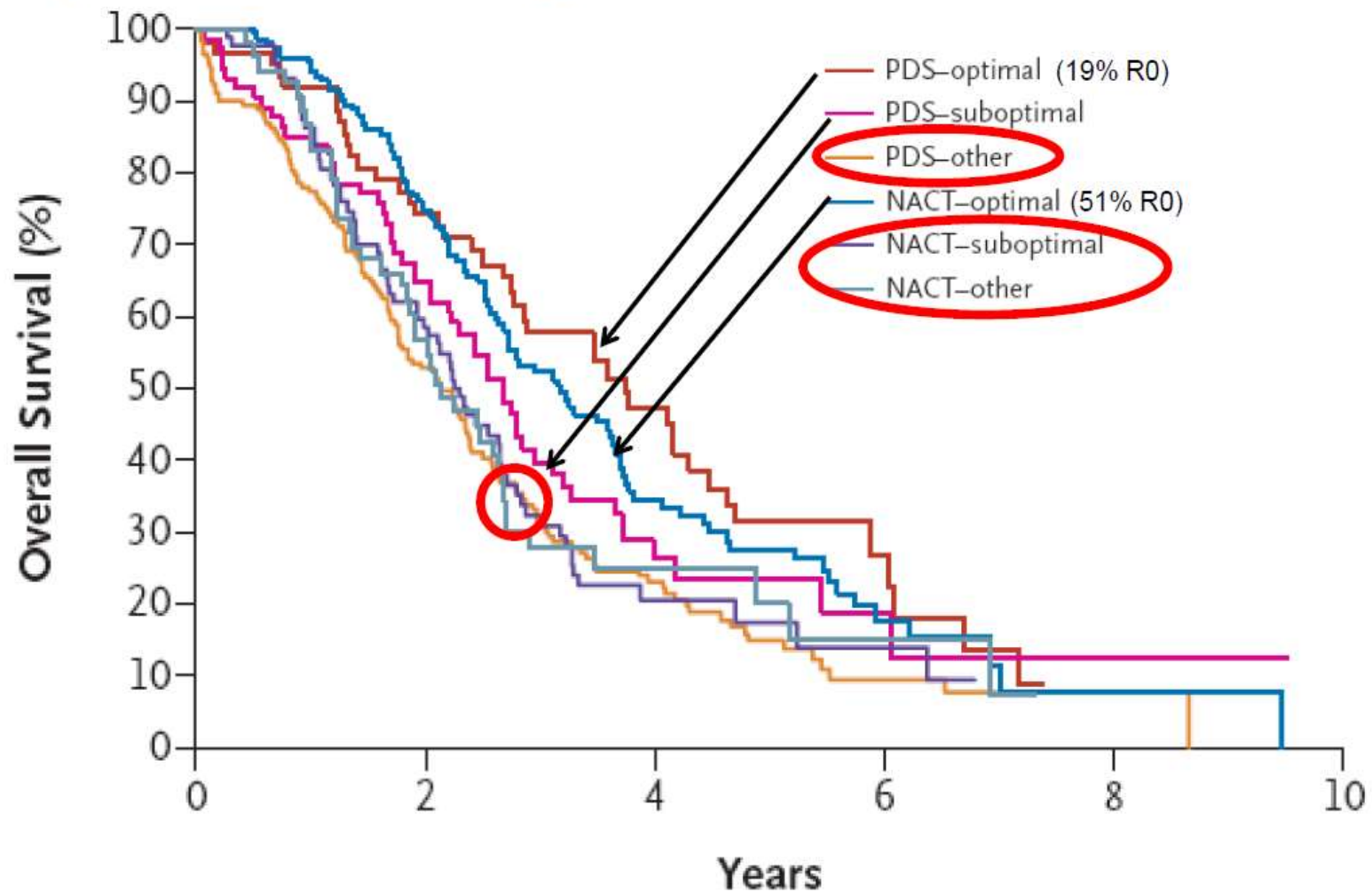
**+ 39.1%**

**La chemioterapia neoadiuvante rende le procedure chirurgiche più semplici ma non più efficaci**

# Quali pazienti traggono beneficio dalla NACT?

Pazienti con residuo tumorale maggiore di 1 cm.

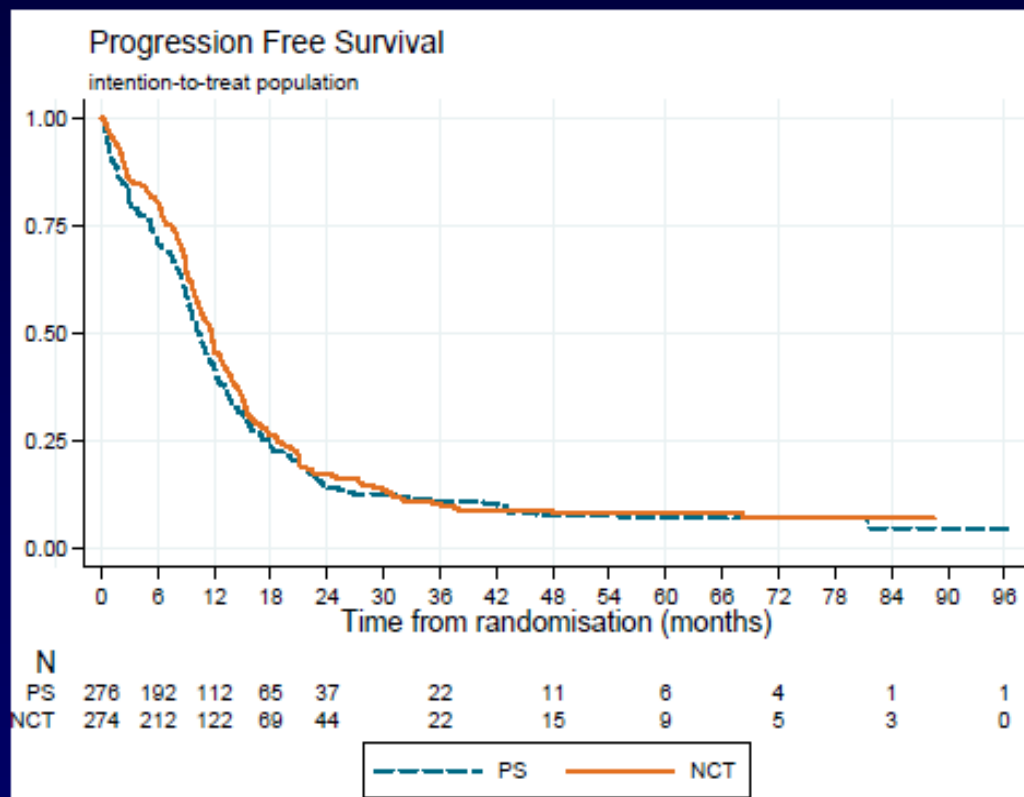
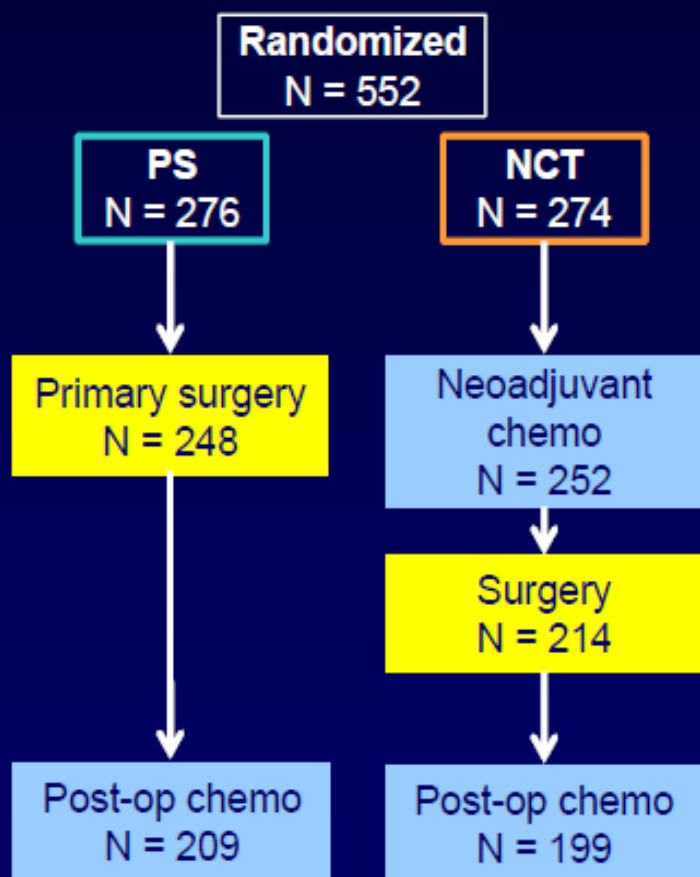
## Optimal Debulking and treatment arm: PP1



Optimal = no residual tumor

# Chemotherapy or Upfront Surgery for Newly Diagnosed Advanced Ovarian Cancer

Results from the MRC CHORUS trial



# ASCO 2013

## CHORUS trial: Surgery details

		<b>PS (N=250)*</b>	<b>NACT (N=216)*</b>
<b>Optimal debulking</b>	<b>0cm</b>	<b>37 (16%)</b>	<b>77 (40%)</b>
	<b>≤1cm</b>	<b>57 (25%)</b>	<b>67 (35%)</b>
	<b>&gt;1cm</b>	<b>135 (61%)</b>	<b>49 (25%)</b>
	<i>Missing</i>	<i>21</i>	<i>23</i>
<b>Length of operation (minutes)</b>	<b>Median</b>	<b>120</b>	<b>120</b>
	<b>(Range)</b>	<b>(30 – 450)</b>	<b>(30 – 330)</b>

\* Includes: PS - 2 pts who had NACT + surgery; NACT – 2 pts who had PS



# Both Trials Highly Criticized for the Low Resection Rate, Short Duration of Surgery, and Poor Survival

VOLUME 29 • NUMBER 31 • NOVEMBER 1 2011

JOURNAL OF CLINICAL ONCOLOGY

COMMENTS AND CONTROVERSIES

## Is the Easier Way Ever the Better Way?

Dennis S. Chi, *Memorial Sloan-Kettering Cancer Center, New York, NY*  
Robert E. Bristow, *University of California, Irvine Medical Center, Irvine, CA*  
Deborah K. Armstrong, *Johns Hopkins Kimmel Cancer Center, Baltimore, MD*  
Beth Y. Karlan, *Cedars-Sinai Medical Center, Los Angeles, CA*

Moreover, 5 hours to 6 hours in the operating room resulting in an optimal cytoreduction may provide the patient with a median survival of 50 months to 100 months (as reported in the literature with successful surgery),

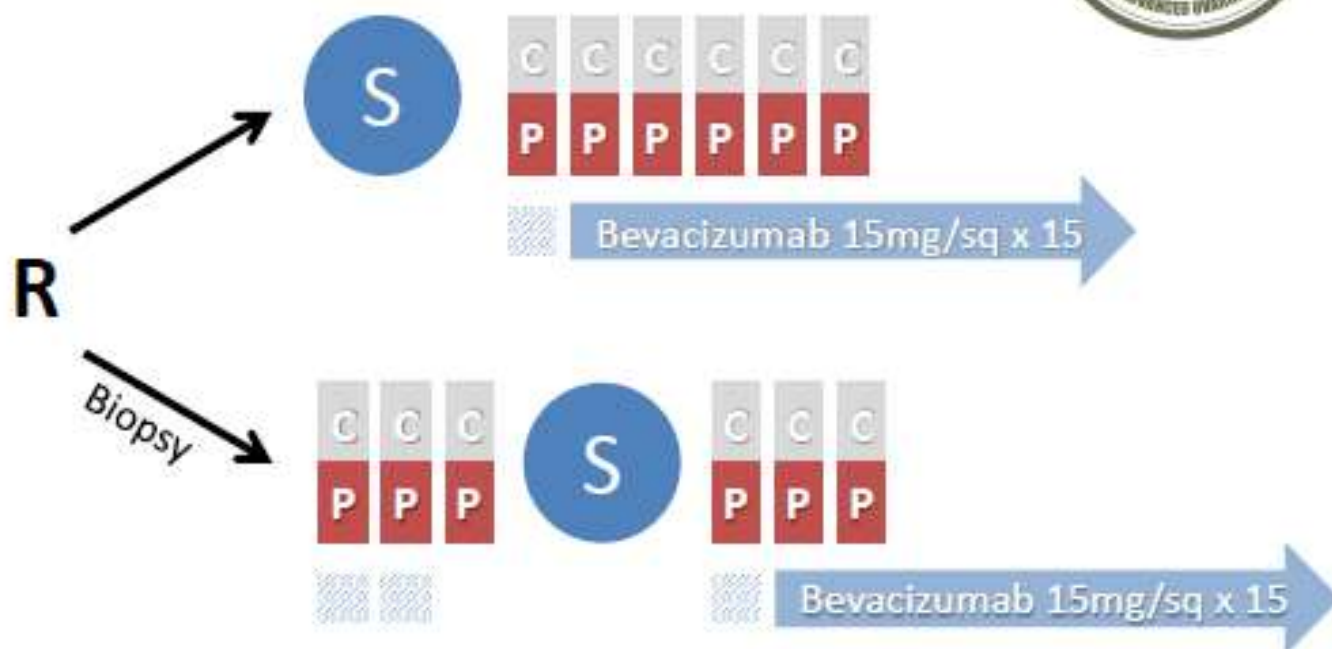
whereas interval cytoreductive surgery lasting 2 hours to 3 hours after NACT is consistently associated with a median survival of only 30 months to 36 months, even after complete gross resection is attained in this setting

# TRUST

## Trial on Radical Upfront Surgical Therapy

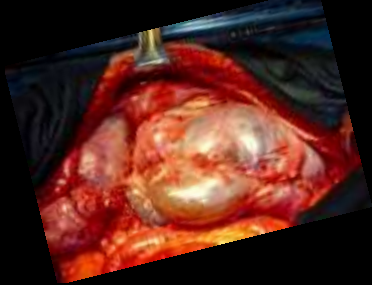


Pts. with ovarian-,  
fallopian-tube or  
peritoneal-cancer  
FIGO stage IIIB, IIIC  
and resectable stage IV



- *Primary Endpoint OS ITT population.*
- *Secondary Endpoints PFS, resection rates, M'nM after 6 months, QoL, „fragility Index“*
- *Strata: FIGO stage (III / IV), group/country, ECOG 0 vs 1/2*
- *Qualification process for participating centers to ensure high surgical quality*

**S** surgery   **C** Carboplatin AUC5   **P** Paclitaxel 175 mg/sq   ➡ Bev. 15mg 15 mon  
suggested therapy, also weekly paclitaxel possible / or omission of Bev



# Conclusioni

- La chirurgia ha un ruolo **DETERMINANTE** nel trattamento del tumore dell'ovaio in stadio avanzato.
- Il team chirurgico deve essere in grado di approcciare oltre alla pelvi anche l'alto addome.
- Le complicanze chirurgiche sono accettabili in mani esperte.
- Necessaria la centralizzazione dei casi per un più corretto approccio.
- Il RT dopo chirurgia rimane il fattore prognostico più importante.....



# Conclusioni 1

- La chemioterapia neoadiuvante **non è uno standard** e non migliora gli outcome attuali
- L'abuso nell'impiego della chemioterapia neoadiuvante **può essere dannosa** perchè posticipa o non permette alle pazienti di accedere a trattamenti potenzialmente curativi.
- La chirurgia primaria nelle pazienti con malattia localmente avanzata con RT < 1 cm è lo **standard**  
**Modifica la sopravvivenza della paziente**

# Conclusioni 2

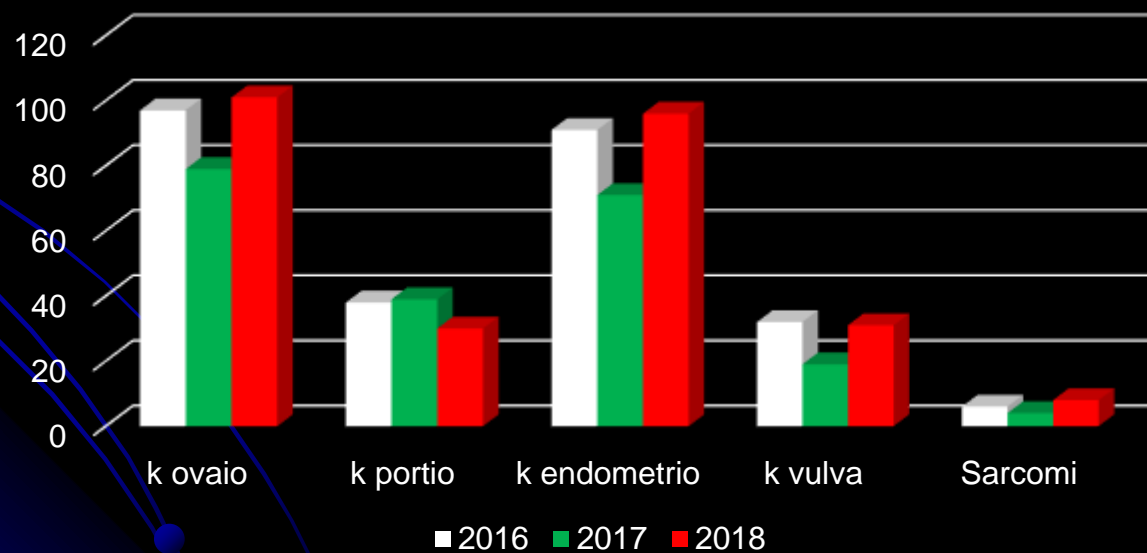
- La **terapia neoadiuvante** dovrebbe essere limitata a **pazienti selezionate** che non hanno possibilità di ricevere un intervento chirurgico ottimale in upfront a causa di comorbidità o delle sedi di malattia.
- La **scarsa competenza chirurgica** non deve essere mai la causa dell'impiego della chemioterapia neoadiuvante.



2018

K endometrio	96
Sarcoma uterino	8
<b>K ovaio</b>	<b>101</b>
K portio	30
K vulva	31
K vagina	5

Titolo del grafico





*Grazie!*

# Theoretical Benefits of Optimal Cytoreductive Surgery for Advanced Ovarian Carcinoma

- Removal of large bulky tumors with poor blood supply
- Improved sensitivity of residual masses to postoperative chemotherapy
- Greater likelihood of tumor eradication before chemoresistance develops

# Complessità



- Chirurgica



- Clinica





Patient Safety !!  
The shortest cancer survival is  
an operative death

C.P Morrow



## 90 day mortality

Points

0 10 20 30 40 50 60 70 80 90 100

Same examples:

50yo, BMI 28, ASA 2, Hemoglobin 4.2, IIIC, High complexity

**3 points = 0.1%**

70yo, BMI 23, ASA 2, Hemoglobin 3.3, IIIC, High Complexity

**104 points = 30%**

Predicted Probability

0.01 0.02 0.05 0.1 0.15 0.2 0.3 0.4 0.5 0.6



# Chemotherapy Candidates

## Definite

- Low Albumin
- Age 75-79, **AND** 1 of the following:
  - ECOG >1 (ASA 3-4)
  - Stage IV disease (moderate to large pleural effusion or parenchymal liver mets)
  - Complex surgery likely (more than hyst/BSO/omentectomy): consider Laparoscopy if unclear
- Age over 80

## Probable NACT

- Recent VTE
- Recent Laparotomy elsewhere
- MI or new stent in the past 6 months
  - Cards consult risk/benefit

Re-Assess after chemotherapy for response, condition and surgery vs. chemo only

# TRUST-Quality Manual



STUDY OF  
PRIMARY RADICAL CYTOREDUCTIVE SURGERY FOR  
ADVANCED EPITHELIAL OVARIAN CANCER

**TRUST**

Protocol ID:  
**AGO-OVAR OP.7**

A prospectively randomised open multi-centre study  
A project of the AGO study group

**TRUST Quality Control Manual**

Version: V01MASTER international  
Date: 02.03.2016



Authors: S. Mahner, A. du Bois