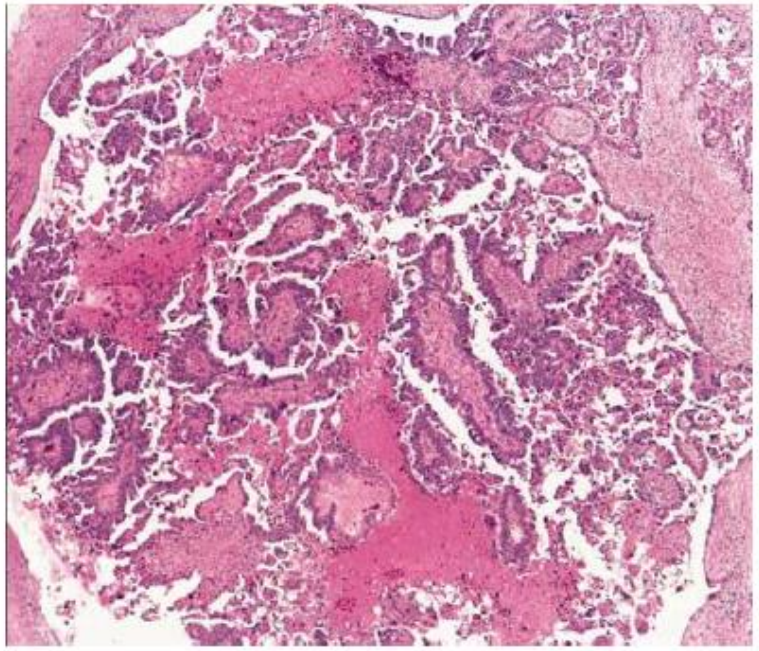
Ruolo della chirurgia nel carcinoma ovarico nell'era dei nuovi farmaci (post ASCO)

Conflit of Interest
French INCa
MSD

Is it *Surgical Effort* or *Tumor Biology* that determines cytoreduction status and overall outcome?



Can we reliably predict which patient will benefit from which approach to better inform our clinical decision making?

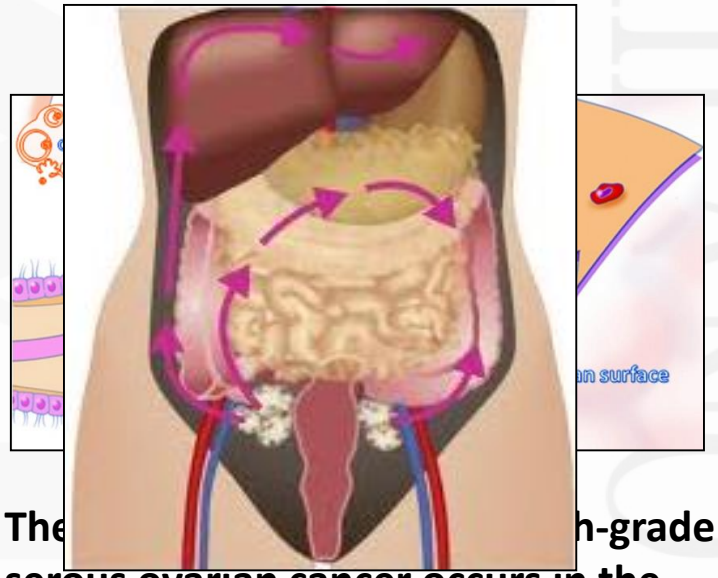
- **Biological considerations**
- **Diagnostic approach**
- **Therapeutic approach**

Ovarian cancer not "organ disease" but "loco-regional illness"

Transcelomatic dissemination

Anatomical basis

- The low tickness of tubal epithelium
- Abominal fluids circulation



The h-grade serous ovarian cancer occurs in the very thin tubal wall thus allowing the rapid detachment of cells in the abdominal cavity

- **The flow starts after the diaphragmatic movements**
- **The peristaltic pump directs clockwise the flow**

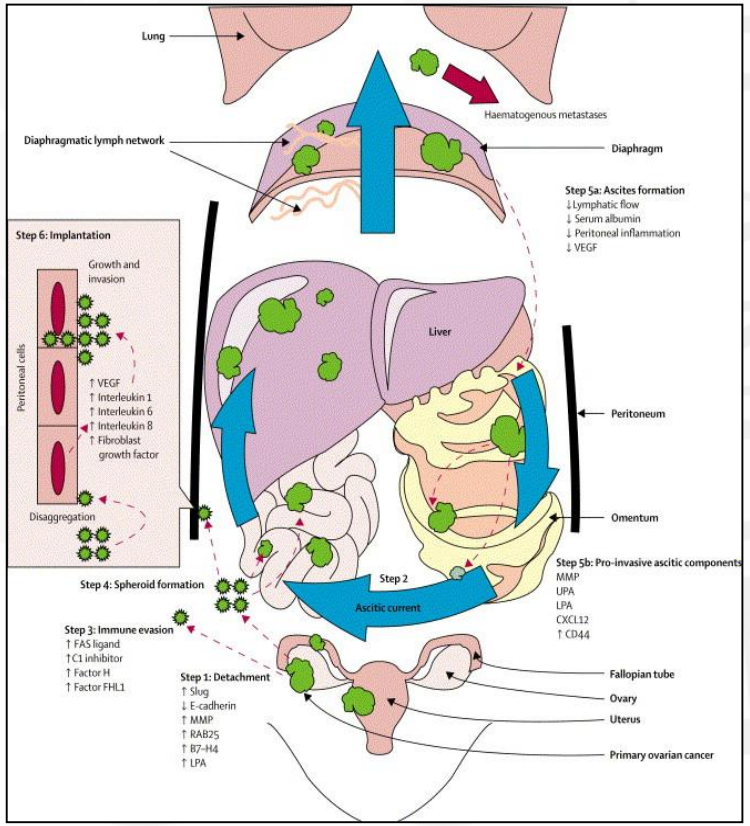
Ovarian cancer not "organ disease" but "loco-regional illness"

Transcelomatic dissemination

Biological basis

➢**A multi-step process from detachment to implantation**

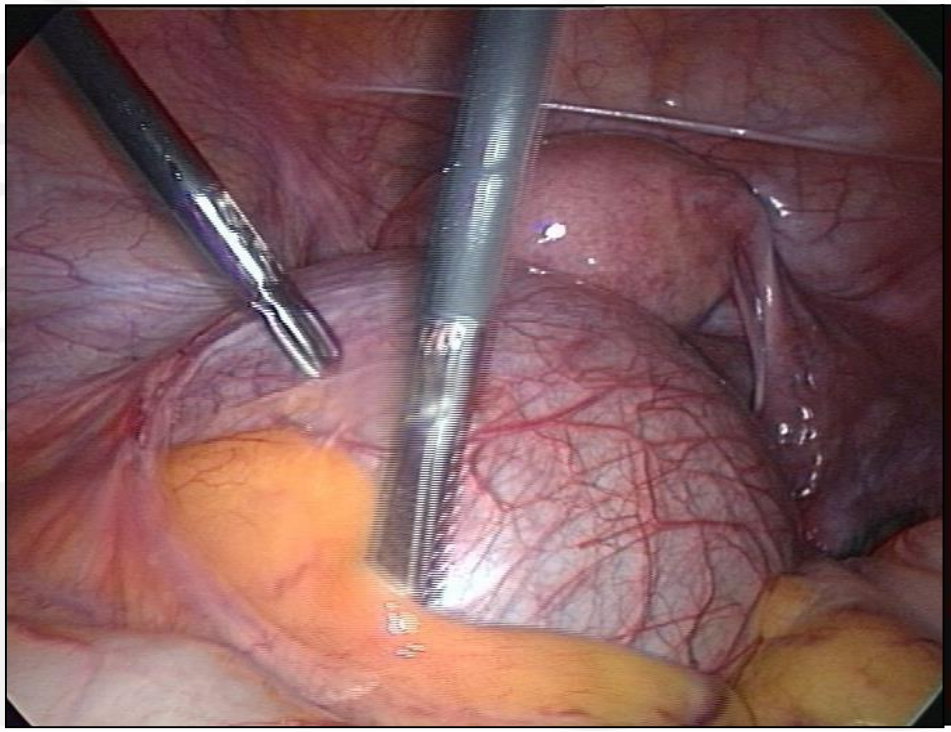
(Detachment: E-cadherin, Immune evasion: Fas-ligand, Spheroid formation Ascites formation: lymphatic flow, VEGF, peritoneal inflammation, serum albumin; Production of proinvasive ascitic components: MMP, CXCL2, CD44)

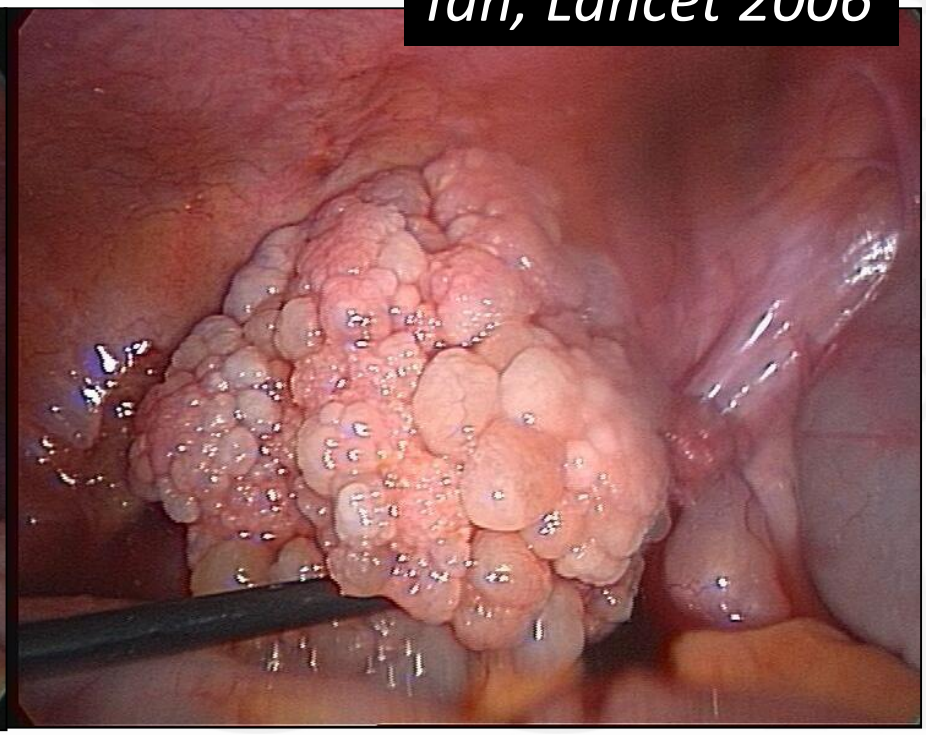


Ovarian cancer has not a celomatic origin, but a trans-celomatic spread (1)

The early removal of the disease before exposure of the peritoneum to malignant cells significantly reduces the risk of relapse, as observed in stage IA (29%) vs. stage IC (59%) disease.

Tan, Lancet 2006

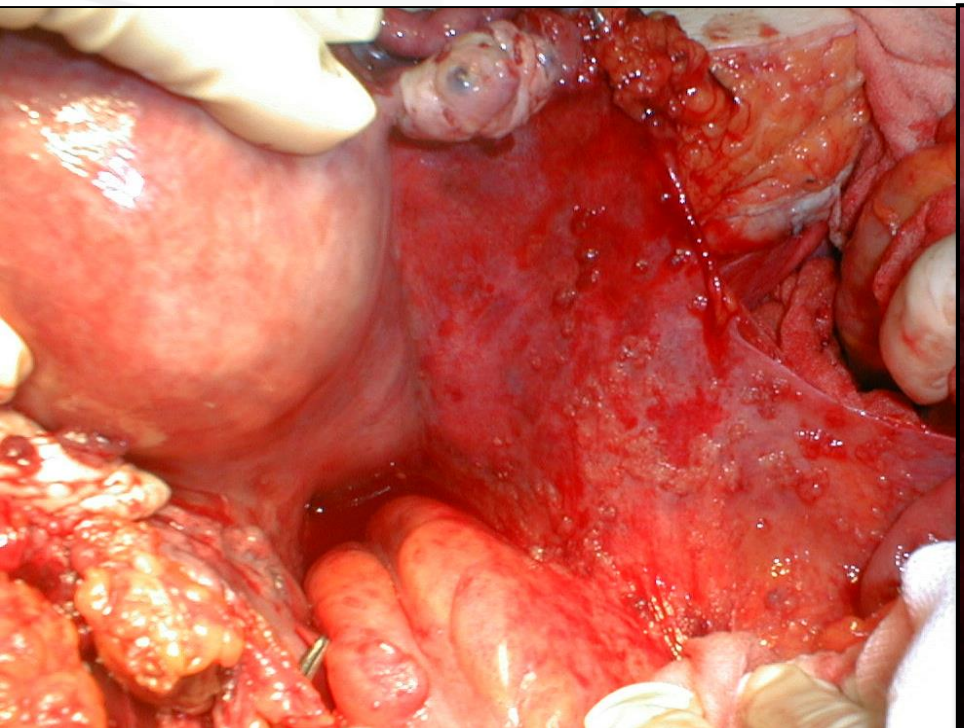


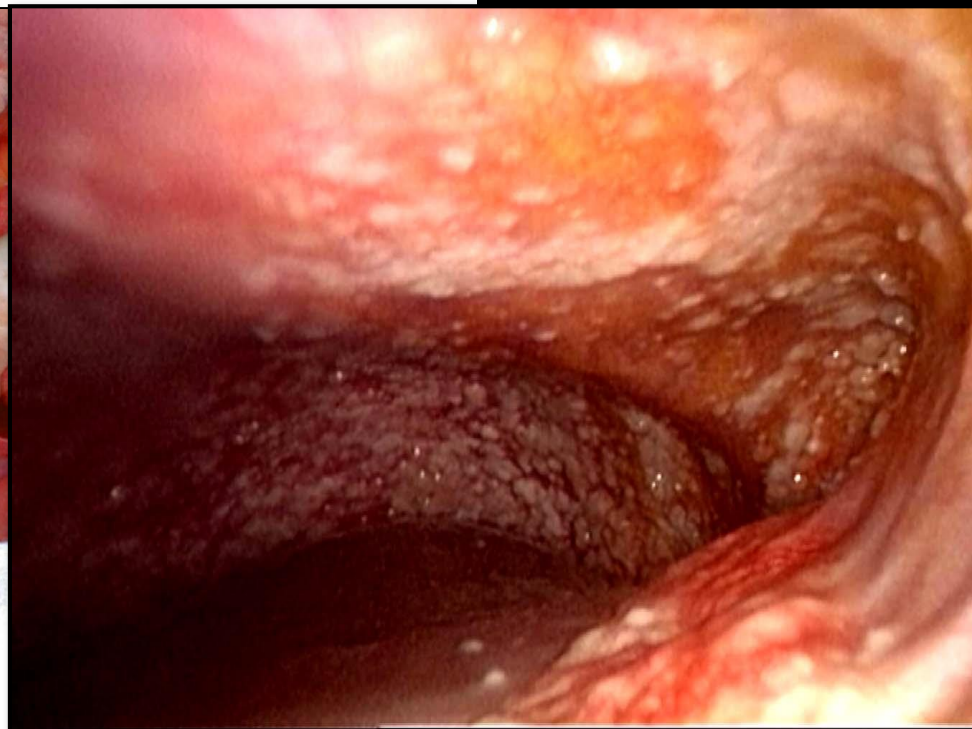


Ovarian cancer has not a celomatic origin, but a trans-celomatic spread (2)

If AOC were a celomatic disease, lesions would be distributed randomly throughout the peritoneum. On the other hand, the peritoneal involvement is more common at the greater omentum, right subphrenic region, and pouch of Douglas.

Tan, Lancet 2006

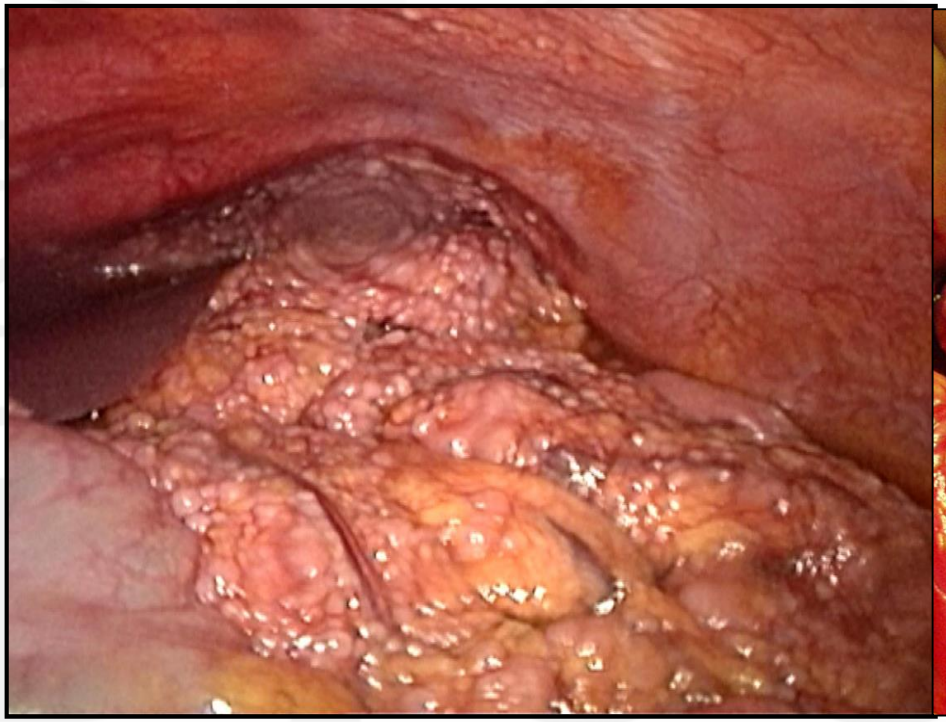


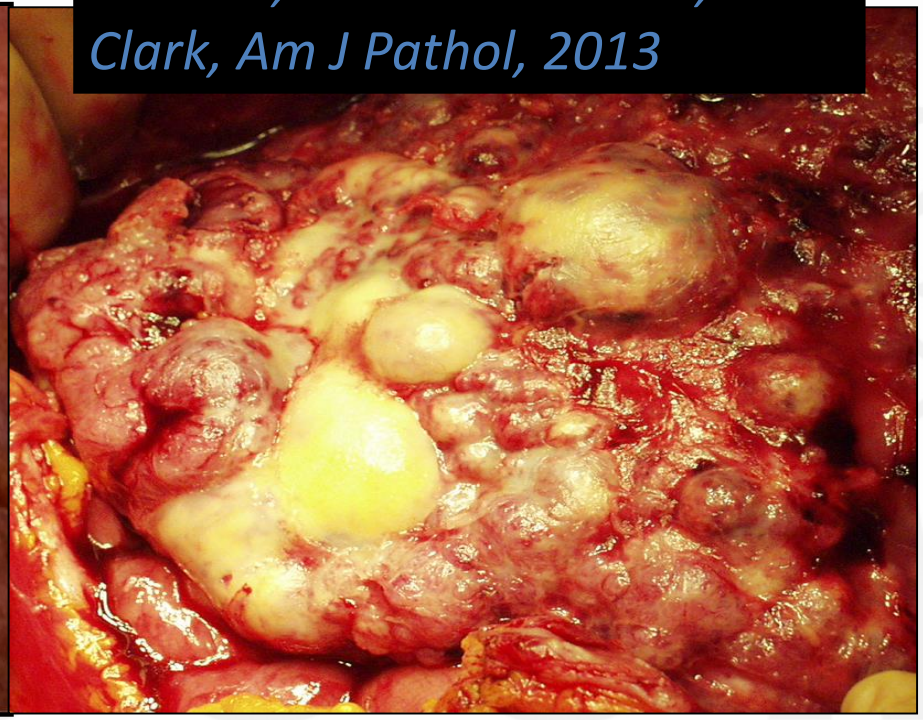


Ovarian cancer has not a celomatic origin, but a trans-celomatic spread (3)

Omental and spleno-portal fat, rich of milky spots, is able to produce an higher increase of OC cells migration compared with adipose tissue from other human anatomic sites.

Nieman, Nature Medicine, 2011
Clark, Am J Pathol, 2013





Tumor biology markers

1. **somatic and germinal BRCA mutation High grade Serous or Endometrioid ovarian cancer**

others ..??

1. Low grade serous ovarian cancer
2. Clear Cell
3. Mucinous

VOLUME 28 · NUMBER 15 · MAY 20 2010

JOURNAL OF CLINICAL ONCOLOGY

ORIGINAL REPORT

Increased Incidence of Visceral Metastases in Scottish Patients With BRCA1/2-Defective Ovarian Cancer: An Extension of the Ovarian BRCAness Phenotype

Charlie Gourley, Caroline O. Michie, Patricia Roxburgh, Timothy A. Yap, Sharon Harden, Jim Paul, Kalpana Ragupathy, Radha Todd, Russell Petty, Nick Reed, Richard L. Hayward, Paul Mitchell, Tzyvia Rye, Jan H.M. Schellens, Jan Lubinski, James Carmichael, Stan B. Kaye, Melanie Mackean, and Michelle Ferguson

From the University of Edinburgh Cancer

See accompanying article on page 2512

Table 3. Incidence of Visceral Metastases During Matched Follow-Up Period After First Progression in the Scottish Training Data Set

Location of Metastases	BRCA1/2-Deficient (n = 19)		Nonhereditary Controls (n = 38)		*P* (Mantel-Haenszel)	Estimated Odds Ratio	95% CI for Estimated Odds Ratio
	No.	%	No.	%			
Liver	8	42.1	0	0	< .001		
Lung	3	15.8	0	0	.066		
Splenic	6	31.6	1	2.6	.011	12.00	1.45 to 99.67
Other visceral	1	5.3	1	2.6	.803	2.00	0.13 to 31.98
Total visceral	11	57.9	2	5.3	< .001	21.00	2.64 to 166.80

sporadic EOC commonly remains confined to the peritoneum, BRCA1/2-deficient ovarian cancer frequently metastasizes to viscera. extend the ovarian BRCAness phenotype, imply *BRCA1/2*-deficient ovarian cancer is biologically distinct, and suggest that patients with visceral metastases

GYNECOLOGY

BRCA mutational status, initial disease presentation, and clinical outcome in high-grade serous advanced ovarian cancer: a multicenter study

Marco Petrillo, PhD; Claudia Marchetti, PhD; Rossella De Leo, MD; Angela Musella, PhD; Ettore Capoluongo, PhD; Ida Paris, PhD; Pierluigi Benedetti Panici, PhD; Giovanni Scambia, PhD; Anna Fagotti, PhD

- BRCA1/2 mutations we observed a higher incidence of peritoneal spread without ovarian mass (25.2% vs 13.9%; P value ¼ .018) and of bulky lymph nodes (30.8% vs 17.5%; P value = .010) compared with women showing BRCA1/2 wild type genotype.
- in BRCA mutated **no differences** in term of median progression-free survival were observed among women treated with primary debulking surgery and neoadjuvant chemotherapy in the group of patients with BRCA1/2 mutations (P value = .268).
- in women showing BRCA wild type genotype, median progression-free survival after primary debulking surgery was **8 months longer** compared with patients treated with neoadjuvant chemotherapy approach (26 vs 18 months; P value = .003).
- Furthermore, women with BRCA1/2 mutations showed **high peritoneal tumor load** (laparoscopic predictive index value 8; 42.1% vs 27.1%; P value = .016)

TABLE 1
Distribution of patients' clinicopathological characteristics at diagnosis according to BRCA mutational status

Characteristics	All patients	BRCAwt	BRCAmut	*P*value[a]
All	273	166 (60.8)	107 (39.2)	
Age, median (range), y[b]	54 (25–86)	58 (25–86)	50 (25–81)	.001[d]
FIGO stage				
IIIC	249 (91.2)	148 (89.2)	101 (94.4)	
IV	24 (8.8)	18 (10.8)	6 (5.6)	.136
CA125, median (range), UI/mL[b]	326 (0–10,730)	300 (0–10,730)	348 (4–8750)	.767
LPS-PIV				
<4	101 (37.0)	69 (41.6)	32 (29.9)	
4–6	82 (30.0)	52 (31.3)	30 (28.0)	
≥8	90 (33.0)	45 (27.1)	45 (42.1)	.016[d]
Ascites				
No	166 (60.8)	95 (57.2)	71 (66.4)	
Yes	107 (39.2)	71 (42.8)	36 (33.6)	.132
Ovarian mass				
No	50 (18.3)	23 (13.9)	27 (25.2)	
Yes	223 (81.7)	143 (86.1)	80 (74.8)	.018[d]
Bulky lymph nodes				
No	211 (77.3)	137 (82.5)	74 (69.2)	
Yes	62 (22.7)	29 (17.5)	33 (30.8)	.010[d]
Primary treatment strategy				
PDS	200 (73.3)	123 (74.1)	77 (72.0)	
NACT	73 (26.7)	43 (25.9)	30 (28.0)	.697
Response to NACT (RECIST criteria)				
Complete/partial response	56 (76.7)	30 (69.7)	26 (86.7)	
Stable disease/progressive disease	17 (23.3)	13 (30.3)	4 (13.3)	.158
Residual tumor at PDS[c]				
RT = 0	188 (91.7)	118 (93.7)	70 (88.6)	
RT > 0	17 (8.3)	8 (6.3)	9 (11.4)	.203
Surgical complexity[c,15]				
1–2	132 (66.0)	91 (74.1)	41 (53.2)	
3	68 (34.0)	32 (25.9)	36 (46.8)	.003[d]

Values are n (%) unless otherwise specified.

BRCAmut, BRCA1/2 mutations; *BRCAwt*, wild-type BRCA genotype; *FIGO*, International Federation of Gynecology and Obstetrics; *LPS-PIV*, laparoscopic predictive index value; *NACT*, neoadjuvant chemotherapy; *PDS*, primary debulking surgery; *RECIST*, response evaluation criteria in solid tumors; *RT*, residual tumor.

[a] Calculated by χ^2 test; [b] Calculated by Kruskal-Wallis nonparametric test; [c] Calculated only in women treated with PDS; [d] Statistically significant results.

Petrillo et al. BRCA mutational status, disease presentation, and clinical outcome in high-grade serous ovarian cancer. Am J Obstet Gynecol 2017.

TABLE 2
Distribution laparoscopic predictive index value parameters according to BRCA mutational status

LPS-PIV parameters	BRCAwt n (%)	BRCAmut n (%)	*P* value[a]
Omental cake			
Negative	68 (41.0)	38 (35.5)	
Positive	98 (59.0)	69 (64.4)	.367
Peritoneal carcinomatosis			
Negative	76 (45.8)	40 (37.4)	
Positive	90 (54.2)	67 (62.6)	.170
Diaphragmatic carcinomatosis			
Negative	87 (52.4)	50 (46.7)	
Positive	79 (47.6)	57 (53.3)	.359
Bowel infiltration			
Negative	128 (77.1)	70 (65.4)	
Positive	38 (22.9)	37 (34.6)	**.035**
Stomach infiltration			
Negative	150 (90.4)	95 (88.8)	
Positive	16 (9.6)	12 (11.2)	.675
Liver infiltration[b]			
Negative	144 (86.7)	94 (87.9)	
Positive	22 (13.3)	13 (12.1)	.790
Mesenteric retraction			
Negative	151 (91.0)	100 (93.5)	
Positive	15 (9.0)	7 (6.5)	.460

Bold values indicate statistically significant results.

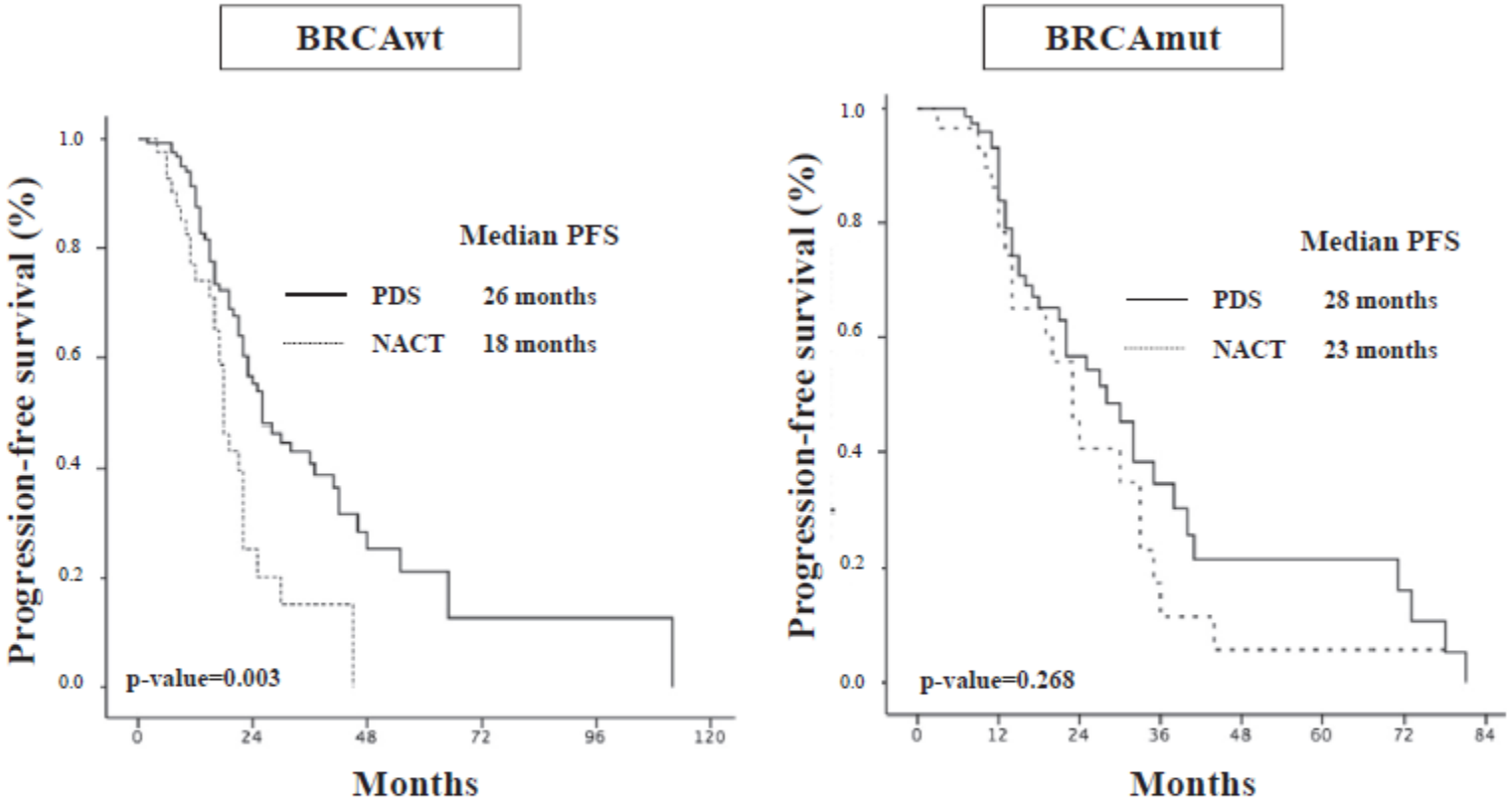
BRCAmut, BRCA1/2 mutations; *BRCAwt*, wild-type BRCA genotype; *LPS*, laparoscopic; *PIV*, predictive index value.

[a] Calculated by χ^2 test; [b] As for LPS scoring system, defined as presence of superficial lesion >2 cm, and not as parenchymal lesion.

Petrillo et al. BRCA mutational status, disease presentation, and clinical outcome in high-grade serous ovarian cancer. Am J Obstet Gynecol 2017.

FIGURE 2

Survival results and BRCA status



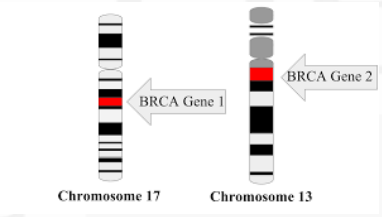
Progression-free survival (PFS) in patients treated with primary debulking surgery (PDS) and neo-adjuvant chemotherapy (NACT), according to BRCA mutational status.

BRCAmut, BRCA1/2 mutations; *BRCAwt*, wild-type BRCA genotype.

Petrillo et al. BRCA mutational status, disease presentation, and clinical outcome in high-grade serous ovarian cancer. Am J Obstet Gynecol 2017.

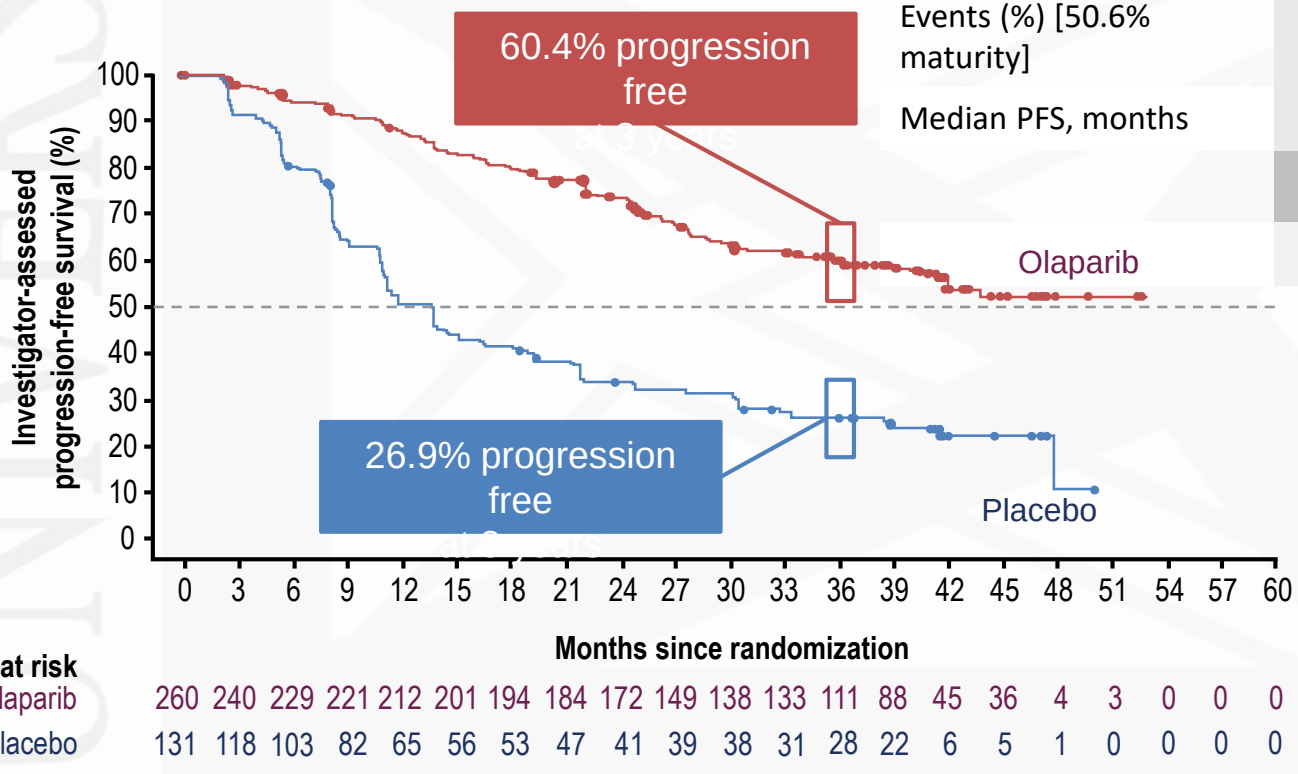
Study limitations

- biases in term of indications for BRCA testing
- the sample size is limited
- since 51 patients were excluded from a total of 324 initially found eligible, potential for selection bias may exist.
- Results might be updated with BRCA somatic testing, due to the potential shift of some cases from one group to another.



SOLO 1 TRIAL: PFS by investigator assessment

	Olaparib (N=260)	Placebo (N=131)
Events (%) [50.6% maturity]	102 (39.2)	96 (73.3)
Median PFS, months	NR	13.8
HR 0.30		
95% CI 0.23, 0.41; *P*<0.0001		



No. at risk

Olaparib	260	240	229	221	212	201	194	184	172	149	138	133	111	88	45	36	4	3	0	0	0
Placebo	131	118	103	82	65	56	53	47	41	39	38	31	28	22	6	5	1	0	0	0	0

CI, confidence interval; NR, not reached

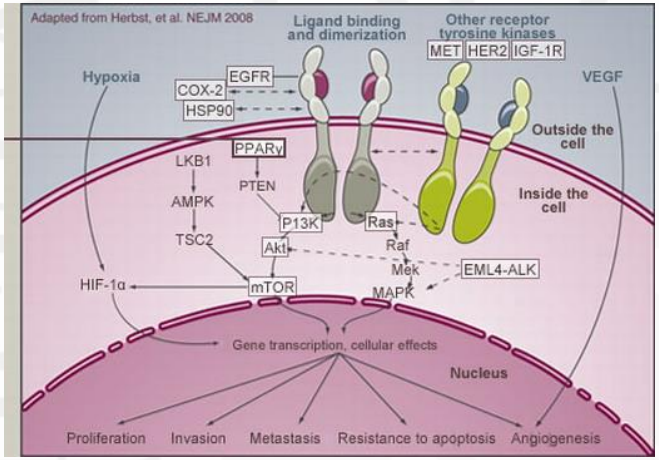
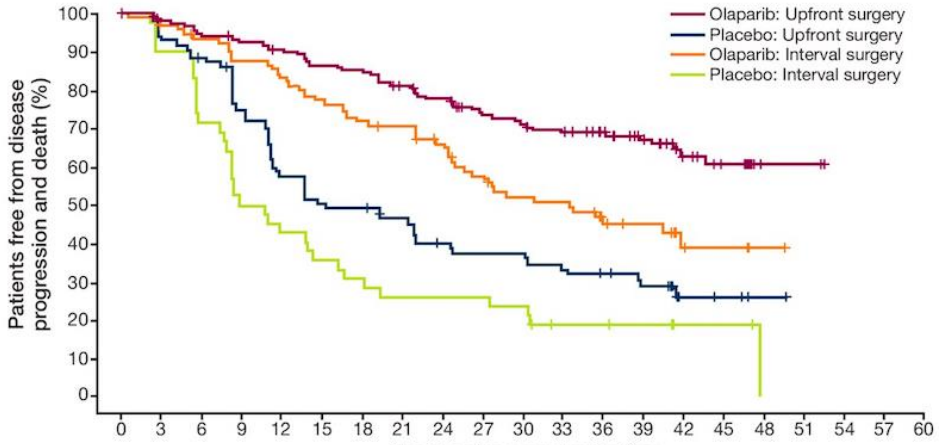


Figure 1. Kaplan-Meier estimate of investigator-assessed PFS based on timing of surgery

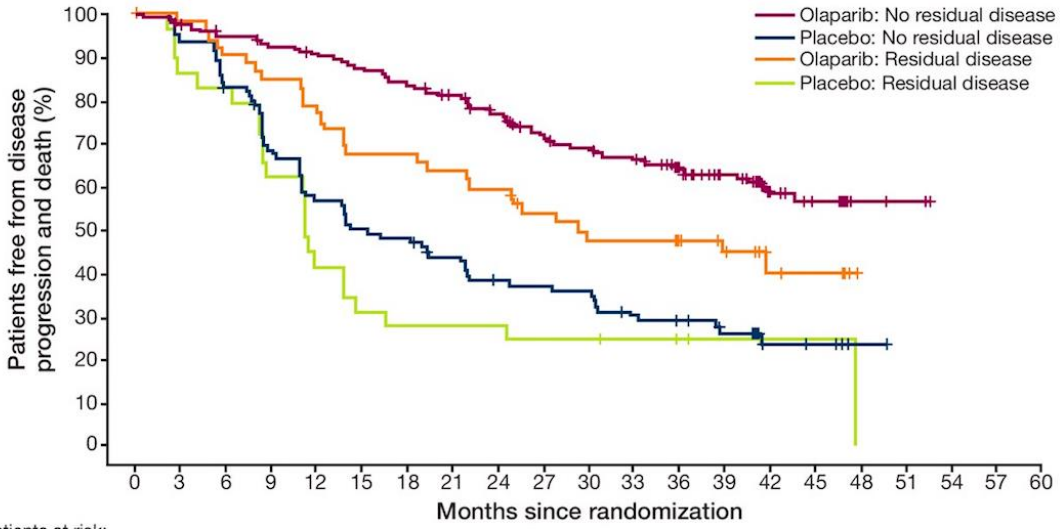


Num. patients at risk:

Olaparib: Upfront surgery	161	148	142	139	135	129	127	119	113	100	96	92	79	66	34	26	3	3	0	0	0
Placebo: Upfront surgery	85	78	73	61	47	41	40	36	30	28	28	25	22	17	4	3	1	0	0	0	0
Olaparib: Interval surgery	94	87	82	77	73	68	63	61	55	45	40	39	30	21	10	0	1	0	0	0	0
Placebo: Interval surgery	43	38	30	21	18	15	13	11	11	11	10	6	6	5	2	2	0	0	0	0	0

- PFS HRs were 0.33 (95% CI 0.23–0.46) for no residual disease following surgery (median NR for olaparib vs 15.3 months for placebo) and 0.44 (0.25–0.77) for residual disease following surgery

Figure 2. Kaplan-Meier estimate of investigator-assessed PFS based on residual disease status following surgery

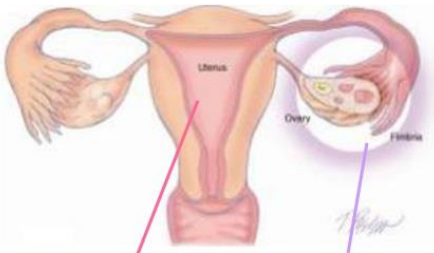


Tumor biology markers

1. somatic and germinal BRCA mutation High grade Serous or Endometrioid ovarian cancer

others ..??

1. **Low grade serous ovarian cancer**
2. **Clear Cell**
3. Mucinous



?Retrograde Menstruation

Origin

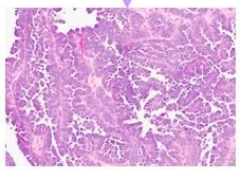
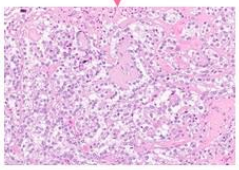
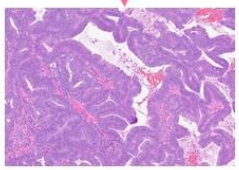
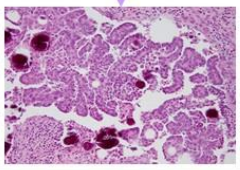
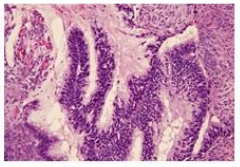
Fallopian Tube Epithelium

Endometriosis

Endometriosis

Fallopian Tube Epithelium

?Unknown

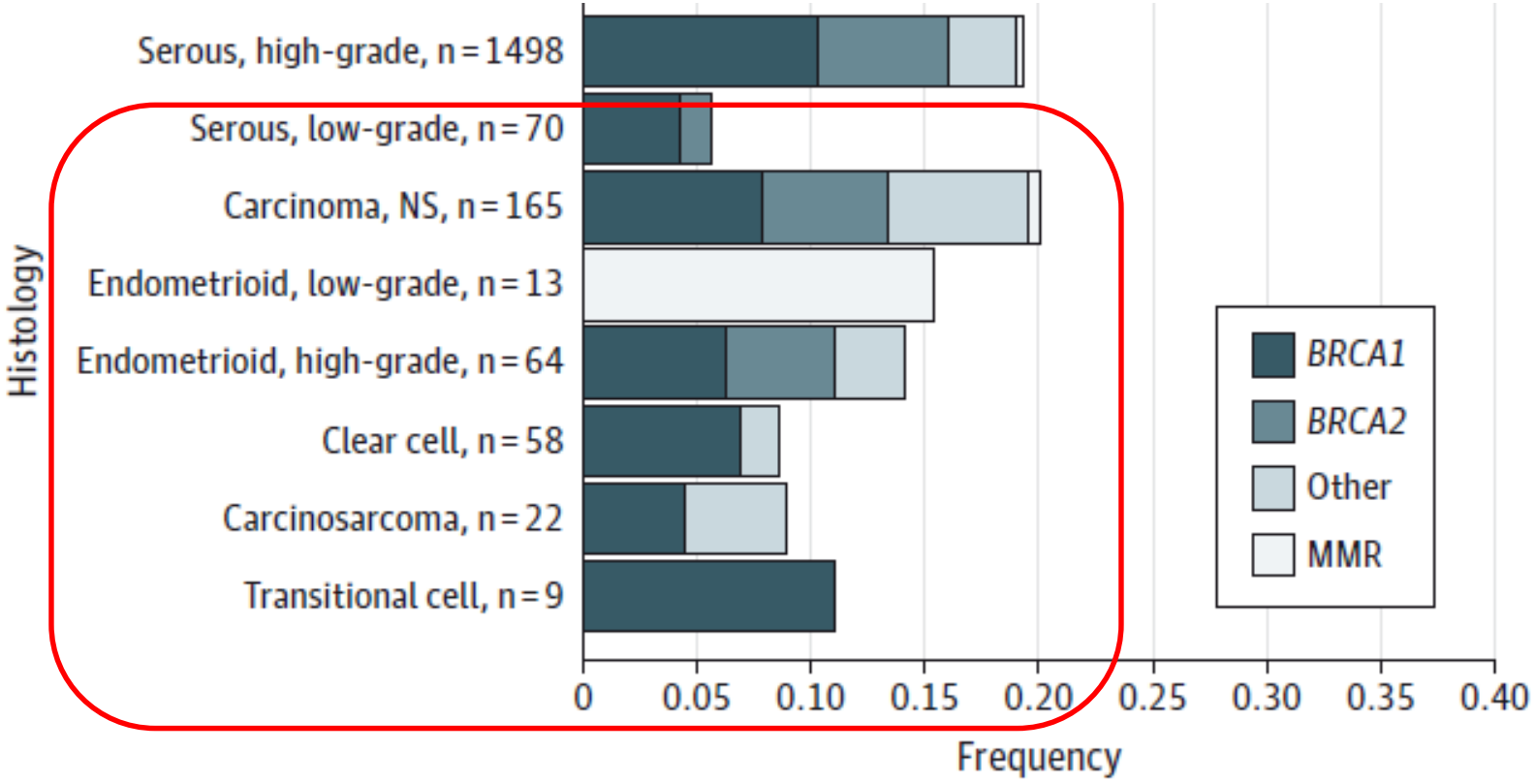






	High-Grade Serous Carcinoma	**Clear Cell Carcinoma**	**Endometrioid Carcinoma**	**Low-Grade Serous Carcinoma**	**Mucinous Carcinoma**
% of all Ovarian Carcinomas	~70%	~10%	~10%	<5%	<5%
Precursor Lesions	Serous tubal intraepithelial carcinoma (STIC)	Clear Cell Borderline Tumor	Endometrioid Borderline Tumor	Serous Borderline Tumor	Mucinous Borderline Tumor
Inherited Syndromes	BRCA1/2, Hereditary Breast and Ovarian Cancer (HBOC)	Lynch Syndrome	Lynch Syndrome	?	?
Common Mutations and Molecular Aberrations	TP53 BRCA1/2 and HRD Chromosomal instability Aneuploidy (100%)	ARID1A PIK3CA CTNNB1 PPP2R1A MSI	PTEN CTNNB1 ARID1A PPPR2R1A MSI	KRAS BRAF	KRAS HER2 amplification
Potential Molecular Targeted Therapies	PARP inhibitors, immune checkpoint inhibitors	Tyrosine kinase inhibitors	mTOR inhibitors	MEK1/2 inhibitors	Trastuzumab

Original Investigation

Inherited Mutations in Women With Ovarian Carcinoma

Barbara M. Norquist, MD; Maria I. Harrell, PhD; Mark F. Brady, PhD; Tom Walsh, PhD; Ming K. Lee, PhD; Suleyman Gulsuner, MD, PhD; Sarah S. Bernards, BS; Silvia Casadei, PhD; Qian Yi, PhD; Robert A. Burger, MD; John K. Chan, MD; Susan A. Davidson, MD; Robert S. Mannel, MD; Paul A. DiSilvestro, MD; Heather A. Lankes, PhD; Nilsa C. Ramirez, MD; Mary Claire King, PhD; Elizabeth M. Swisher, MD; Michael J. Birrer, MD, PhD



Low Grade serous OC

Upfront setting:

- Neoadjuvant chemotherapy:
  4% of response to platinum-based chemotherapy (Schmeler, Gyn Onc 2008)

- Cytoreductive surgery

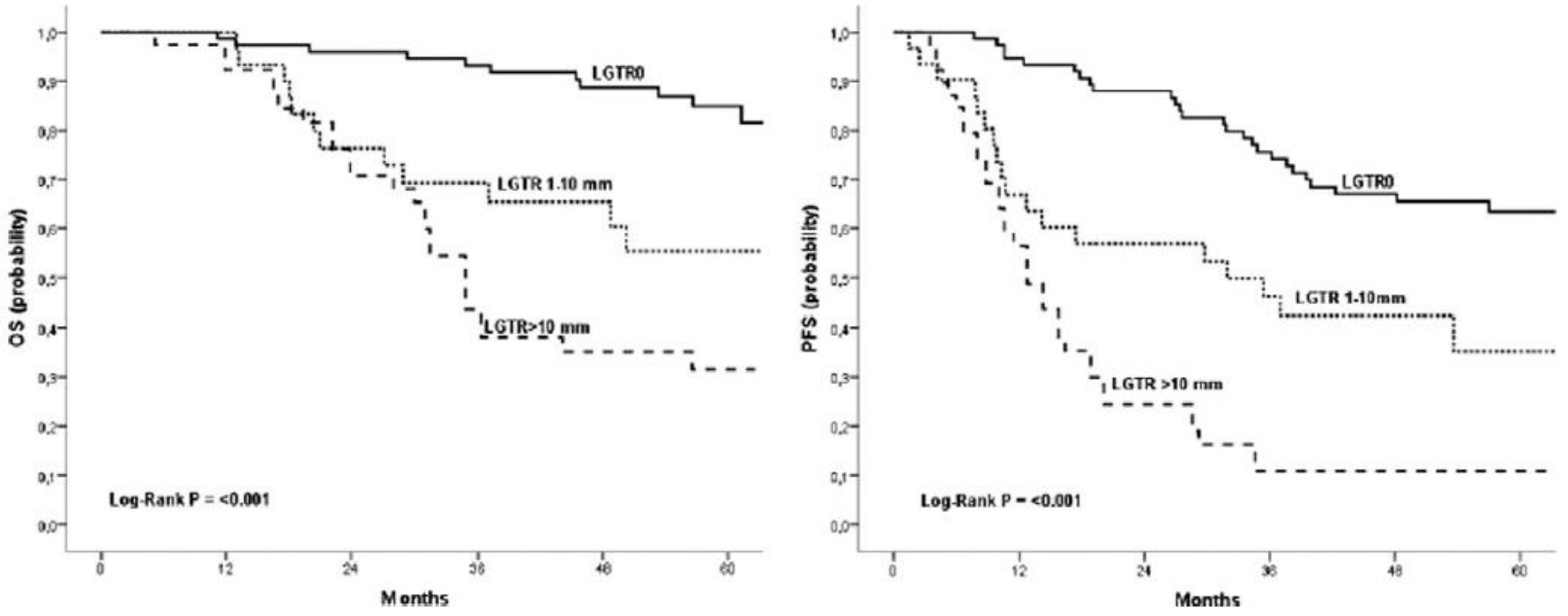


Fig. 1. Overall survival (OS) and progression free survival (PFS) in patients with LGSOC according to residual disease after primary cytoreduction; R - residual disease.

Grabowski, Gyn Onc 2016

Low Grade Serous OC (LGSOC)

First-line adiuvant treatment:

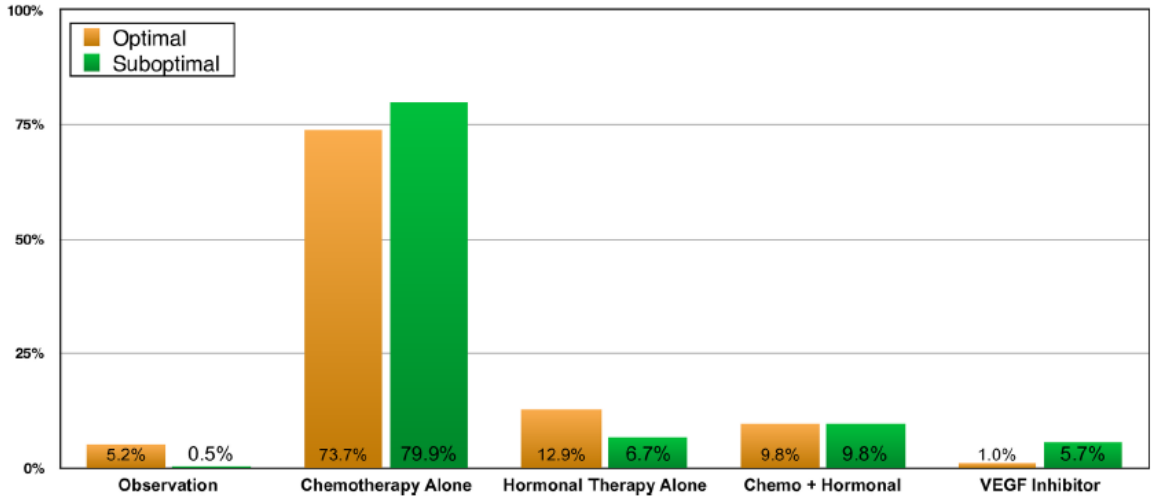


Figure 1 Management preferences in primary stage IIIC low grade serous ovarian carcinoma based on debulking status. Respondents were able to select more than one option. VEGF, vascular endothelial growth factor.

LGSOC:
identifying variations
in practice patterns
(Siemen, IJGC 2019)

Adding hormonal treatment (maintenance)

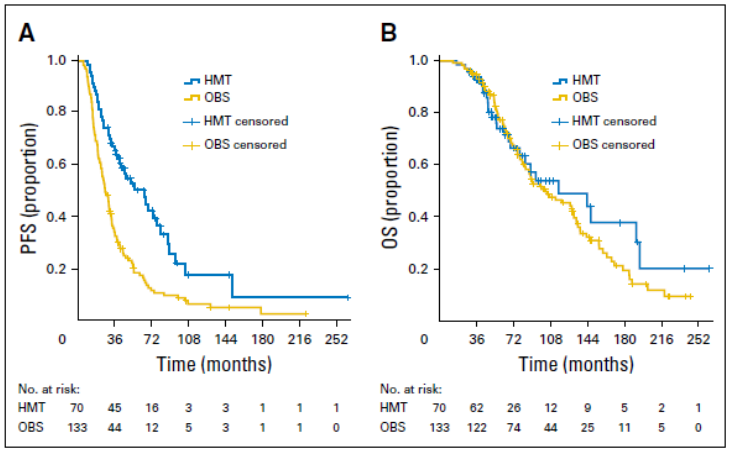
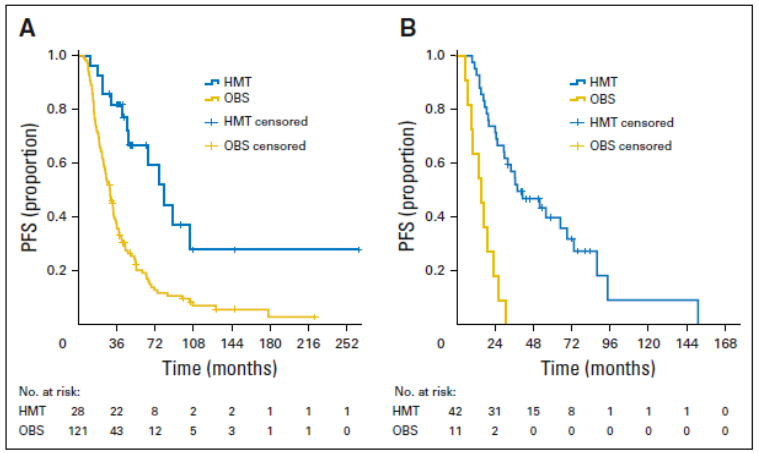


Fig 1. (A) Progression-free survival (PFS; $P < .001$) and (B) overall survival (OS; $P = .42$) for the overall study population. HMT, hormonal maintenance therapy; OBS, observation.



(Gershenson,
JCO 2017)

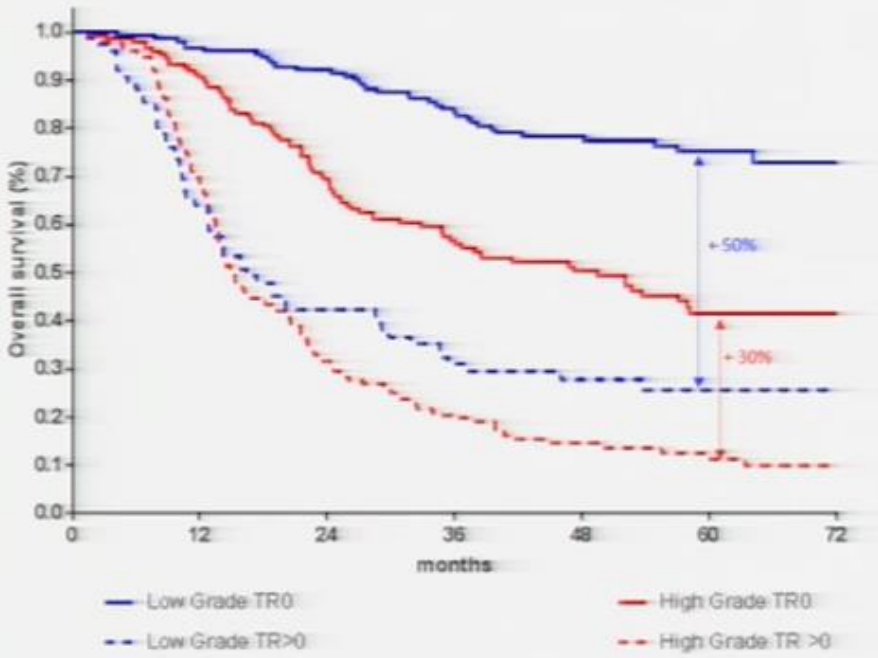
Fig 2. Progression-free survival (PFS) for patients who had (A) no evidence of disease and (B) persistent disease at completion of primary chemotherapy; stratified log-rank test by disease status, $P < .001$. HMT, hormonal maintenance therapy; OBS, observation.

High-grade vs. Low Grade serous always residual tumor

Operability and chemotherapy responsiveness in advanced low-grade serous ovarian cancer. An analysis of the AGO Study Group metadatabase

Jacek P. Grabowski [a,b,*], Philipp Harter [a], *, Florian Heitz [a], Eric Pujade-Lauraine [b], Alexander Reuss [c], Gunnar Kristensen [d], Isabelle Ray-Coquard [e], Julia Heitz [f], Alexander Traut [a], Jacobus Pfisterer [g], Andreas du Bois [a]

Gynecologic Oncology 140 (2016) 457–462



mod. from ref.

Clear cell OC

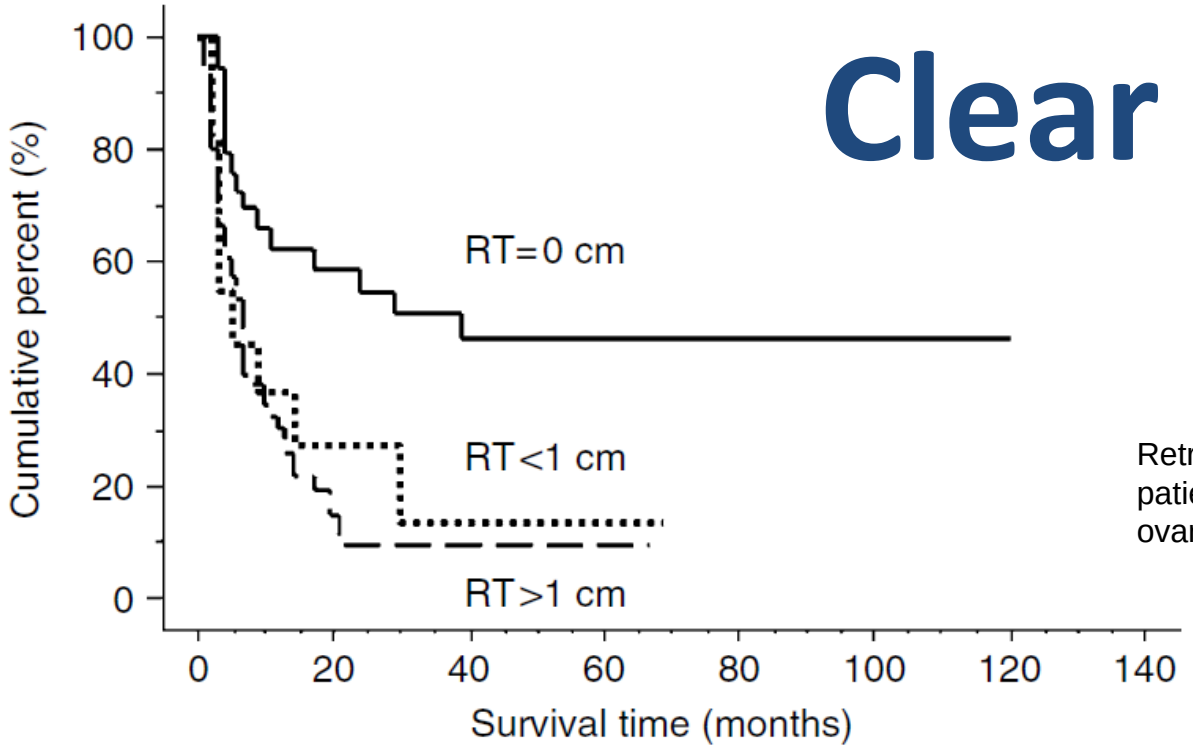


Figure 3 Progression-free survival of stage III, IV patients according to the residual tumour (RT) diameter. There is no significant prognostic difference between the patients with the tumour diameter less than 1 cm and those with the tumour diameter more than 1 cm ($P = 0.40$). The patients with no residual tumour had significantly better progression-free survival than those with the tumour less than 1 cm ($P = 0.04$) or those with tumour diameter more than 1 cm ($P < 0.01$), respectively. Median progression-free survival duration was 39 months in the patients with no residual tumour, 7 months in those with the tumour diameter less than 1 cm, and 5 months in those with residual tumour diameter more than 1 cm, respectively.

Retrospective multicenter study in 254 patients with clear cell carcinoma of the ovary

Takano, BJC 2006

Tumor biology markers

1. somatic and germinal BRCA mutation High grade Serous or Endometrioid ovarian cancer

others ..??

1. Low grade serous ovarian cancer
2. Clear Cell
3. **Mucinous**

Serous vs. Mucinous, always residual tumor

Does surgery improve prognosis or does tumorbiology overrule tumor resection?

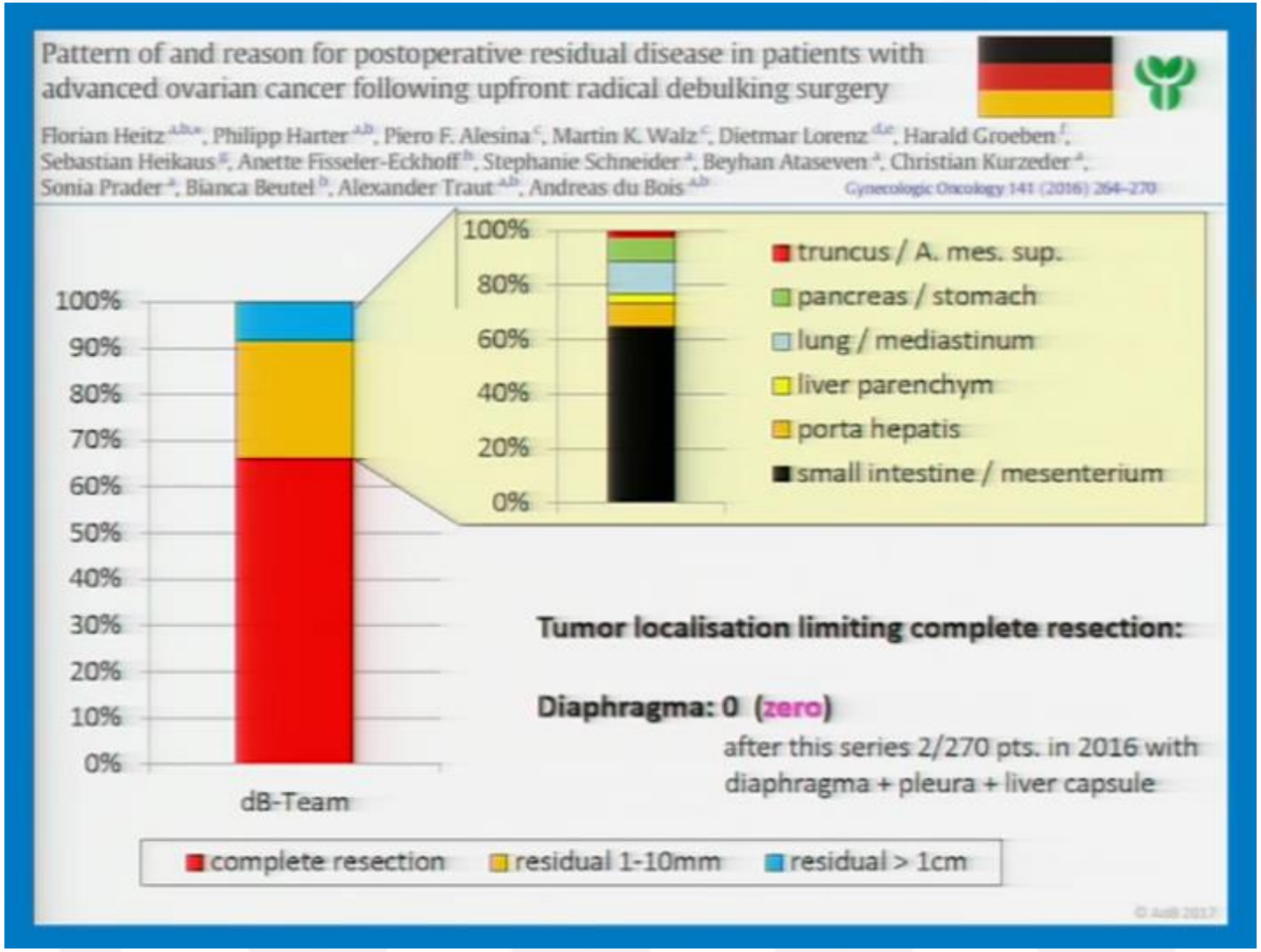
A= OS	Serous histology			Mucinous histology		
Parameter	HR	95%-CI	p-value	HR	95%-CI	p-value
Age [10yrs]	**1.15**	(1.09, 1.22)	**<.0001**	1.18	(0.98, 1.43)	0.0773
ECOG 2 vs. 0-1	**1.22**	(1.05, 1.43)	**0.0117**	**1.98**	(1.01, 3.87)	**0.0456**
residuals 1-10 mm vs. 0 mm	**2.16**	(1.84, 2.54)	**<.0001**	**2.40**	(1.35, 4.29)	**0.0031**
residual tumor > 10 mm vs. 1-10 mm	**1.16**	(1.03, 1.31)	**0.0141**	1.01	(0.62, 1.65)	0.9559
Ascites yes vs. no	**1.36**	(1.20, 1.55)	**<.0001**	1.43	(0.85, 2.40)	0.1801

Tumor biology or surgeon biology?

- **mucinous histo-type overrules most other prognostic factors**
- **complete resection is almost the only remaining prognostic factor in mucinous OC**
- **tumor reduction to 1-10mm was benefitial in serous OC only**

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

These are the landmarks of a good surgeon's biology!



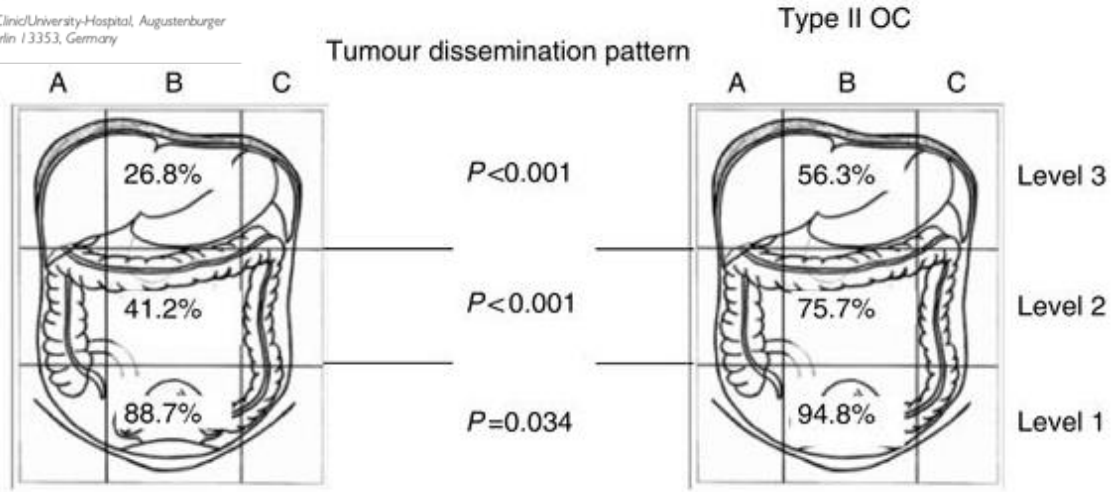
British Journal of Cancer (2011) 105, 1818 – 1824

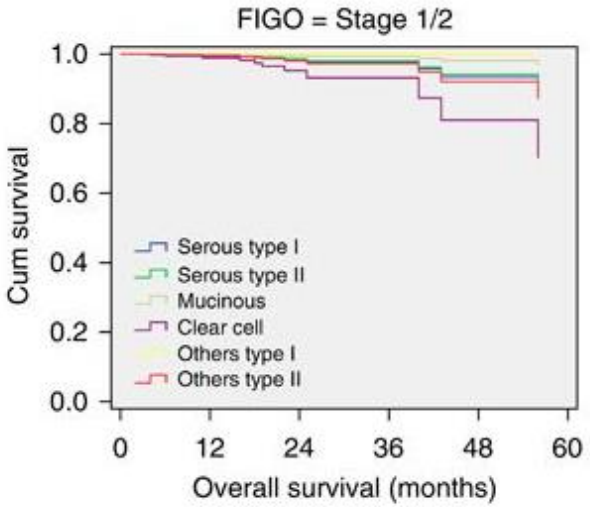
www.bjcancer.com

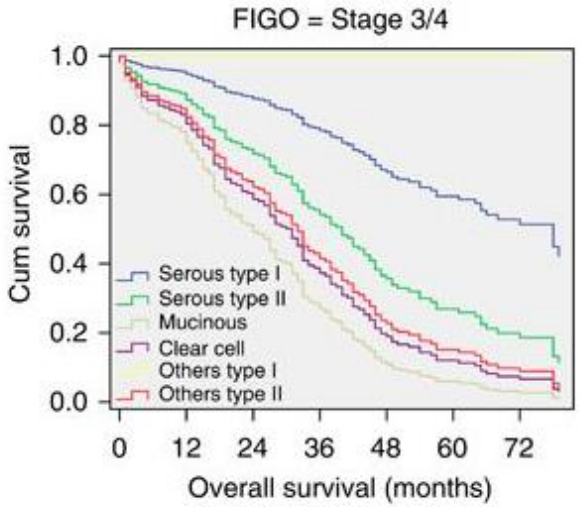
Role of histological type on surgical outcome and survival following radical primary tumour debulking of epithelial ovarian, fallopian tube and peritoneal cancers

E-I Braicu[1], J Sehouli[1], R Richter[1], K Pietzner[1], C Denkert[2] and C Fotopoulou[*,1]

[1]European Competence Center for Ovarian Cancer Department of Gynecology, Charité, Campus-Virchow-Clinic/University-Hospital, Augustenburger Platz 1, Berlin 13353, Germany; [2]Institute of Pathology, Charité Hospital, University Medicine of Berlin, Berlin 13353, Germany







- **Biological considerations**
- **Diagnostic approach**
- **Therapeutic approach**

RESEARCH www.AJOG.org

ONCOLOGY

Comparison of peritoneal carcinomatosis scoring methods in predicting resectability and prognosis in advanced ovarian cancer

Elisabeth Chéreau, MD; Marcos Ballester, MD; Frédéric Selle, MD; Annie Cortez, MD; Emile Daraï, MD, PhD; Roman Rouzier, MD, PhD

2010

To quantify more precisely the intra-abdominal extent of AOC, a number of numerical ranking systems have been proposed, such as: the Peritoneal Cancer Index (PCI) by Sugarbaker; the Eisenkop's score and the Fagotti's score (PIV). The major difference among them is represented by the laparoscopic approach in the last one, thus keeping pace with the times

Correlation matrix between scores (correlation coefficient r)

Variable	Aletti	Eisenkop	PCI	Fagotti	FIGO	Fagotti-modified
Aletti	1	0.8[a]	0.76[a]	0.59[a]	0.44[b]	0.41[c]
Eisenkop	—	1	0.94[a]	0.81[a]	0.64[a]	0.78[a]
PCI	—	—	1	0.84[a]	0.59[a]	0.8[a]
Fagotti	—	—	—	1	0.61[a]	0.8[a]
FIGO	—	—	—	—	1	0.6[a]
Fagotti-modified	—	—	—	—	—	1

FIGO, International Federation of Obstetrics and Gynecology; *PCI*, peritoneal cancer index.

[a] $P < .0001$; [b] $P < .01$; [c] $P < .001$.

- **Biological considerations**
- **Diagnostic approach**
- **Therapeutic approach**

Radical Surgery in Advanced Ovarian Cancer

“ old” but “still”

the gold standard

“Old”… in comparison to New Innovations

J. Obstet. Gynaec. Brit. Cwlth.
Nov. 1968. Vol. 75. pp. 1155–1160.

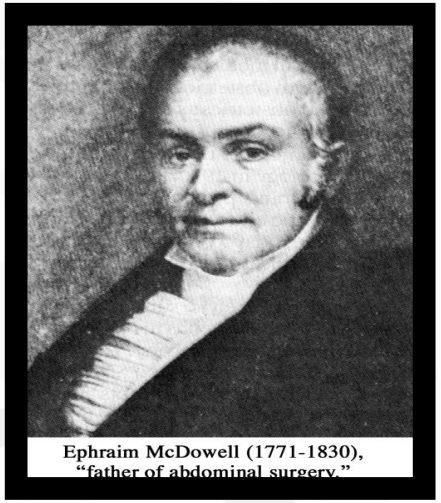
A RADICAL OPERATION FOR FIXED OVARIAN TUMOURS

BY

C. N. HUDSON,* M.Chir., F.R.C.S., M.R.C.O.G., *Senior Lecturer*
Departments of Obstetrics and Gynaecology, University of Ibadan, Nigeria, and St. Bartholomew's Hospital, London

McDowell. Eclectic Repertory Anal Rev

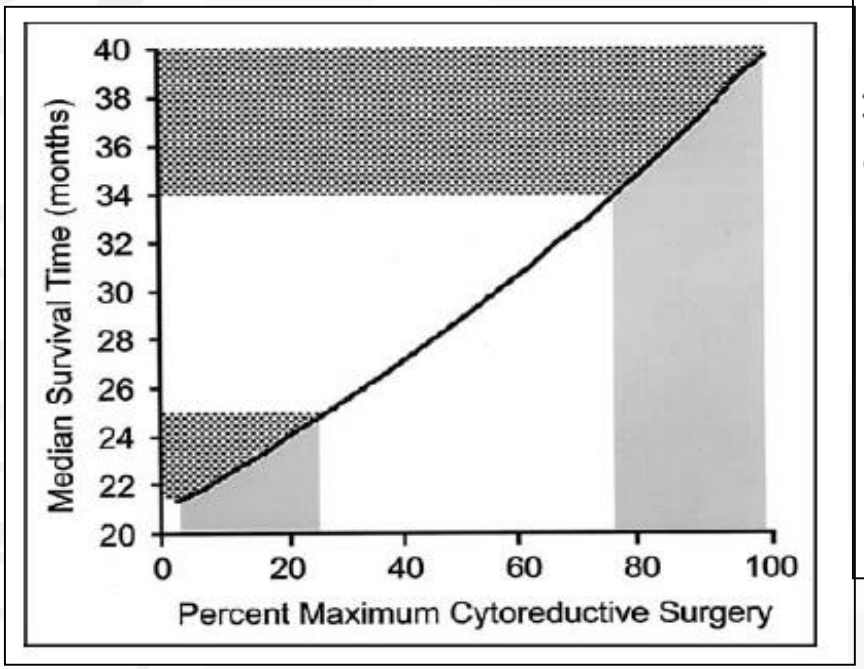
1817: 7: 242 (1809)



Ephraim McDowell (1771-1830), “father of abdominal surgery.”

But… “still“ gold standard

Survival effect of maximal cytoreductive surgery for advanced OC during the platinum era



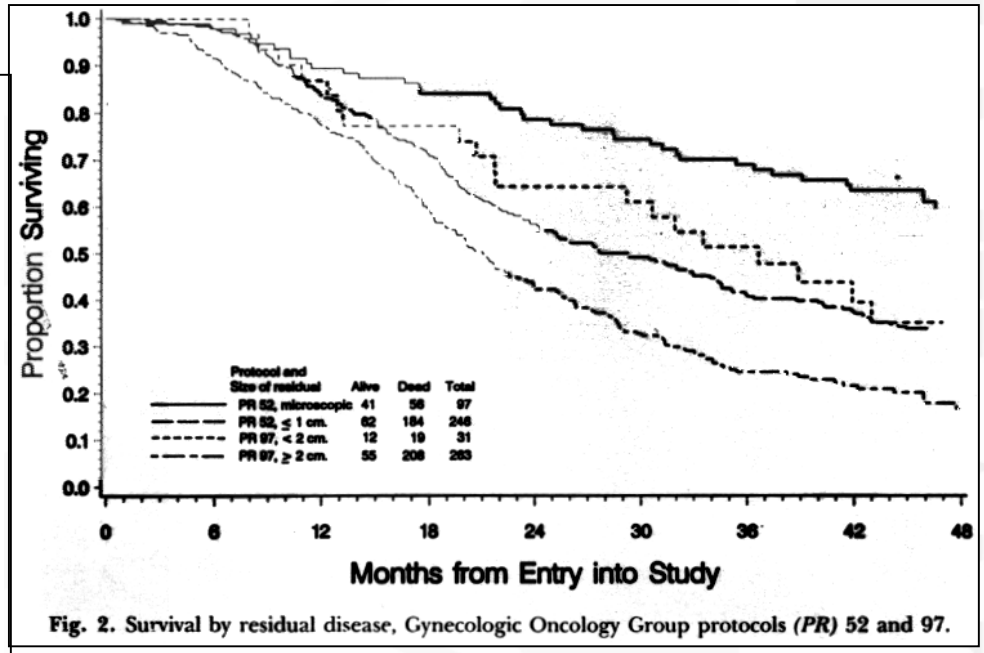


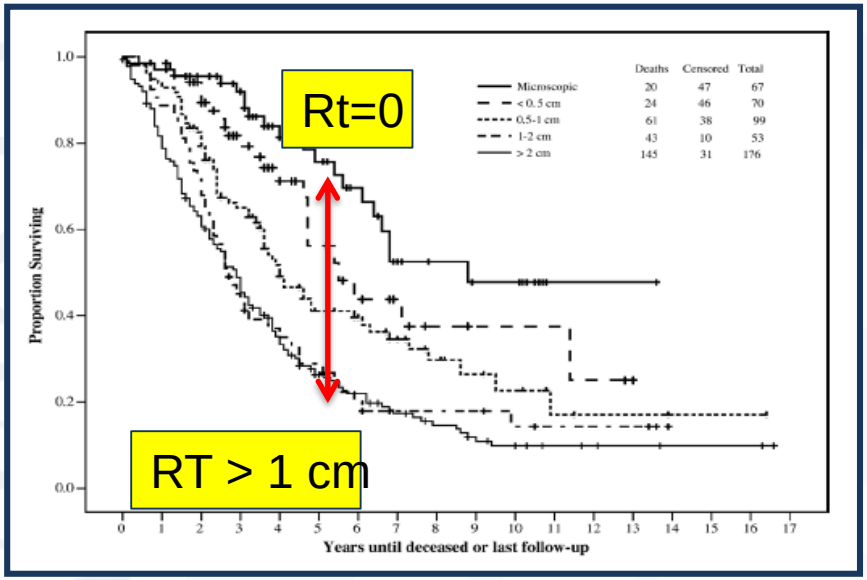
Fig. 2. Survival by residual disease, Gynecologic Oncology Group protocols *(PR)* 52 and 97.

Hoskins , 1994

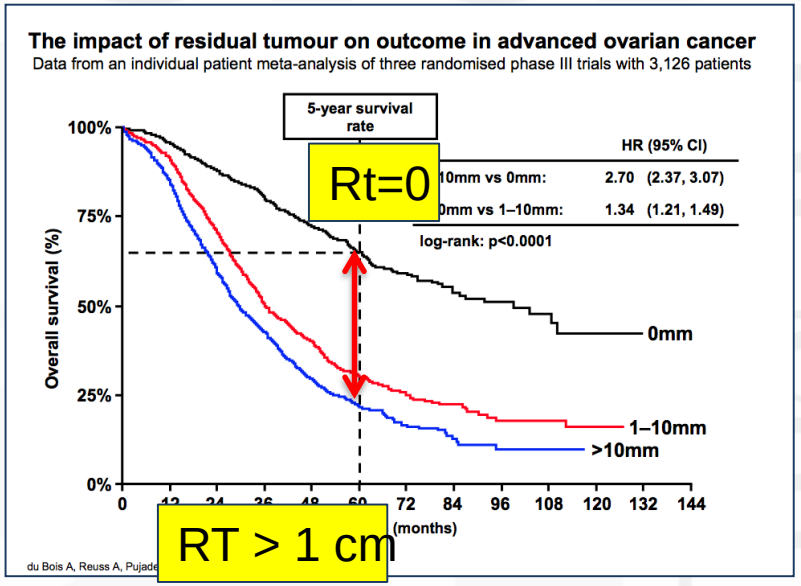
Each 10% increase of optimal cytoreduction rate produces a 5.5% increase in median survival

Bristow , 2002

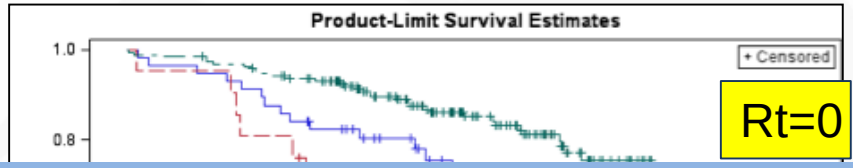
But… “still“ gold standard



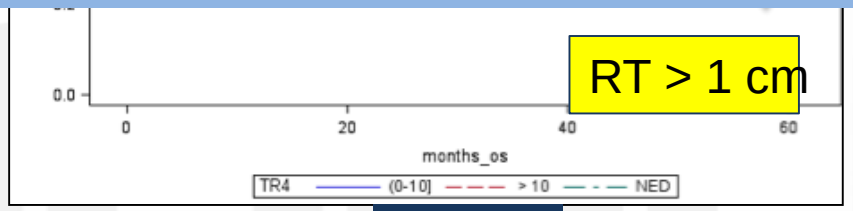
D.Chi



Du Bois



“… all patients with no residual tumor had the best prognosis and in view of these results we believe that the gold standard of primary surgery should be considered as leaving no macroscopic tumor”



Peiretti

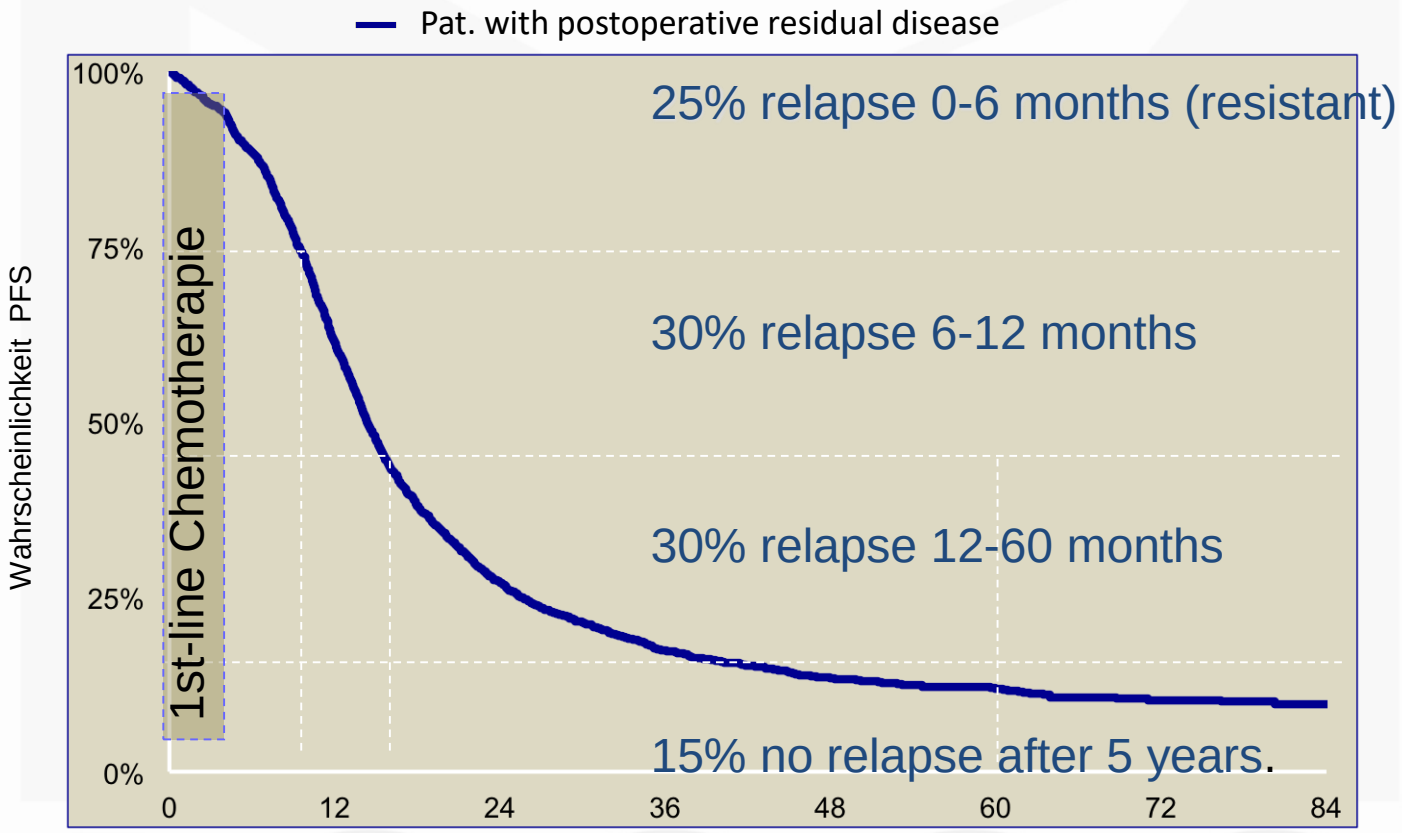
But… "still" gold standard

The benefit of tumour resection in relation to initial tumour burden

Initial FIGO stage	No macroscopic residual tumour		Any residual tumour		HR (95% CI)	Absolute gain in median OS:
	Patients (n)	Median survival (months)				
FIGO IIB–IIIB	497	108.6	317	48.3	0.37 (0.30, 0.47)	+60.3 months
FIGO IIIC	486	81.1	1,293	34.2	0.36 (0.31, 0.42)	+46.9 months
FIGO IV	63	54.6	467	24.6	0.49 (0.34, 0.70)	+30.0 months

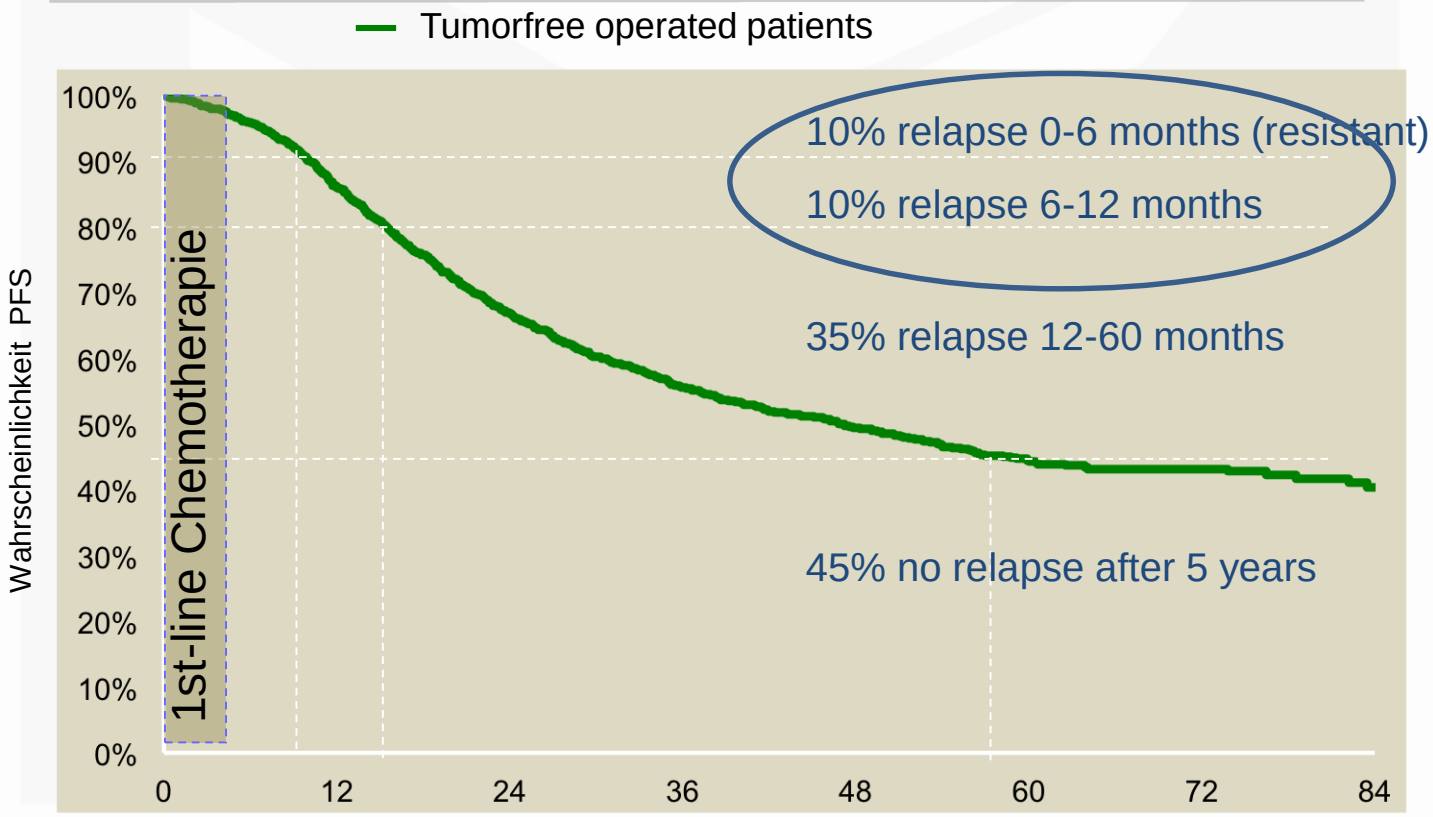
du Bois A, Reuss A, Pujade-Lauraine E, et al. Cancer 2009;15:1234–44

Quality of primary surgery defines type and pattern of relapse – patients with residual disease-



AGO metadatenbank OVAR 3,5 and 7:
N=1,921, E=1,672, median PFS (95%CI): 14.3 mos. (13.9- 14.9)

Quality of primary surgery defines type and pattern of relapse – tumofree patients-



AGO Metadatenbank OVAR 3,5 und 7:
N=1,003, E=540, Median PFS (95%CI): 47.2 mos. (40.2 - 53.9)

“New” limits

- Resection of extraabdominal metastases: cardiophrenic LN, pleurectomies, mediastinoscopy
- Resections in the lesser sac, coeliac trunc, diaphragmatic crura
- Bowel resections with modern stapler techniques without stoma formation
- Liver/ pancreatic surgery

We are ready to select patients

for a different surgery according to **molecular features** ?

Challenge of the future

Is it „only“ about residual disease?

Molecular profiling

Prognostic markers

Molecular predictive of drug Sensitivity/resistence

VARIABLES TO BE CONSIDERED

Comorbidity

Age/ps

patients

Geriatric T

Distribution

STAGE

Histotype

Abnormality

Mutations

Tumor biology

DNA dam/rep

drugs

Chemo therapy

schedules

Motivaton

Surgery

Team

Surgical skill

"Nurse, get on the internet, go to SURGERY.COM, scroll down and click on the 'Are you totally lost?' icon."

Size of RT