

Recent Developments in the Transmission of Human Life

19-21 January 2023

Berlin, Germany

Welcome to all Participants

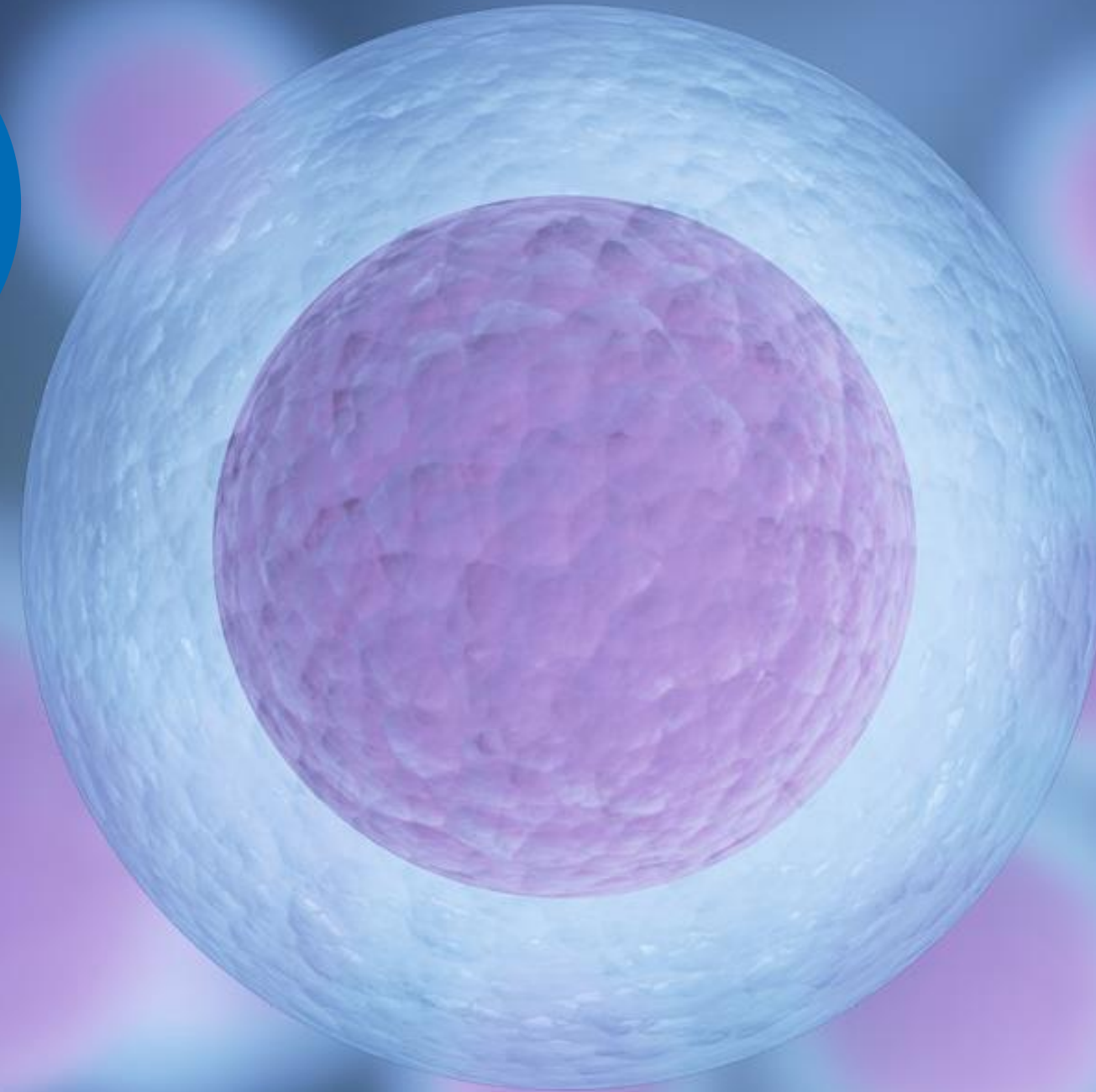


Recent Developments in the Transmission of Human Life

Laparoscopy in advanced ovarian
cancer

How far can we go ?

Prof. Christophe Pomel
Dr. Sabrina Madad



Faculty Disclosure

Roche, AstraZeneca, MSD, Clovis, Pharmamar, Storz

FERTILITY SPARING SURGERY IN OVARIAN CANCER?

~10% of all patients with epithelial ovarian carcinoma are younger than 40 years old and may have not completed their childbearing

ELIGIBLE PATIENT?

- **HISTOLOGY: LOW GRADE serous, endometrioid or mucinous expansile subtype**
- **STAGE: IA (FIGO 2014)**
- **IC1? 50% of isolated recurrence on the remaining ovary**
- **AGE? OVARIAN RESERVE? CO-MORBIDITIES?**

1. Ditto A, Bogani G, Martinelli F, et al. Fertility-sparing surgery in highrisk ovarian cancer. J Gynecol Oncol 2015;26:350–1.
2. Bentivegna E, Gouy S, Maulard A et al. Fertility-sparing surgery in epithelial ovarian cancer: a systematic review of oncological issues. AnnOncol 2016; 27(11):
3. Satoh T, Hatae M, Watanabe Y et al. Outcomes of fertility-sparing surgery for stage I epithelial ovarian cancer: a proposal for patient selection. J Clin Oncol 2010; 28(10): 1727–1732.
4. Fruscio R, Corso S, Ceppi L et al. Conservative management of early-stage epithelial ovarian cancer: results of a large retrospective series. Ann Oncol 2013; 24(1): 138–144

Melamed, Alexander MD, MPH; Rizzo, Anthony E. MD; Nitecki, Roni MD; Gockley, Allison A. MD; Bregar, Amy J. MD, MS; Schorge, John O. MD; del Carmen, Marcela G. MD, MPH; Rauh-Hain, J. Alejandro MD. All-Cause Mortality After Fertility-Sparing Surgery for Stage I Epithelial Ovarian Cancer. **Obstetrics & Gynecology 130(1):p 71-79, July 2017. |**

ONCOLOGICAL OUTCOMES

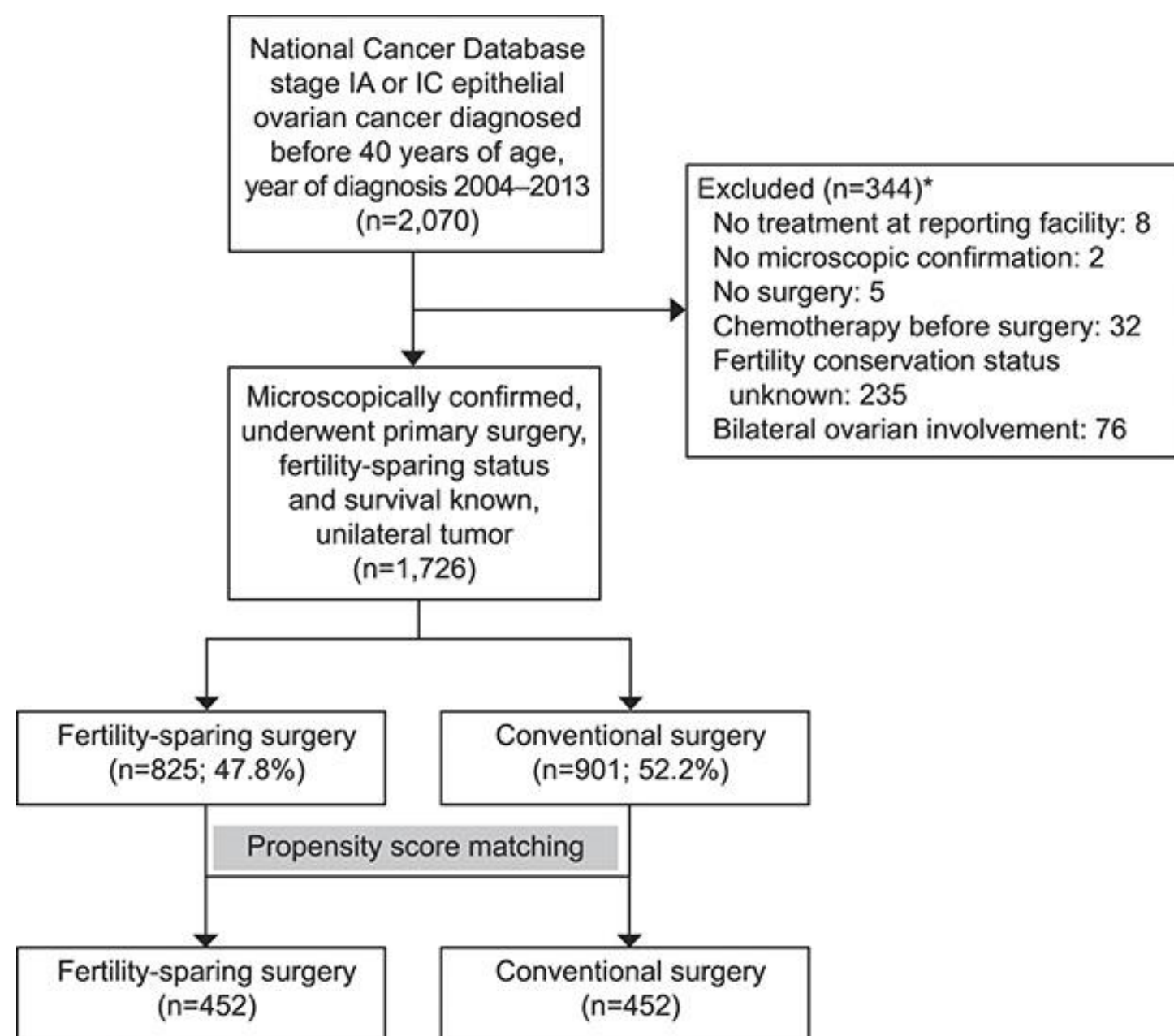
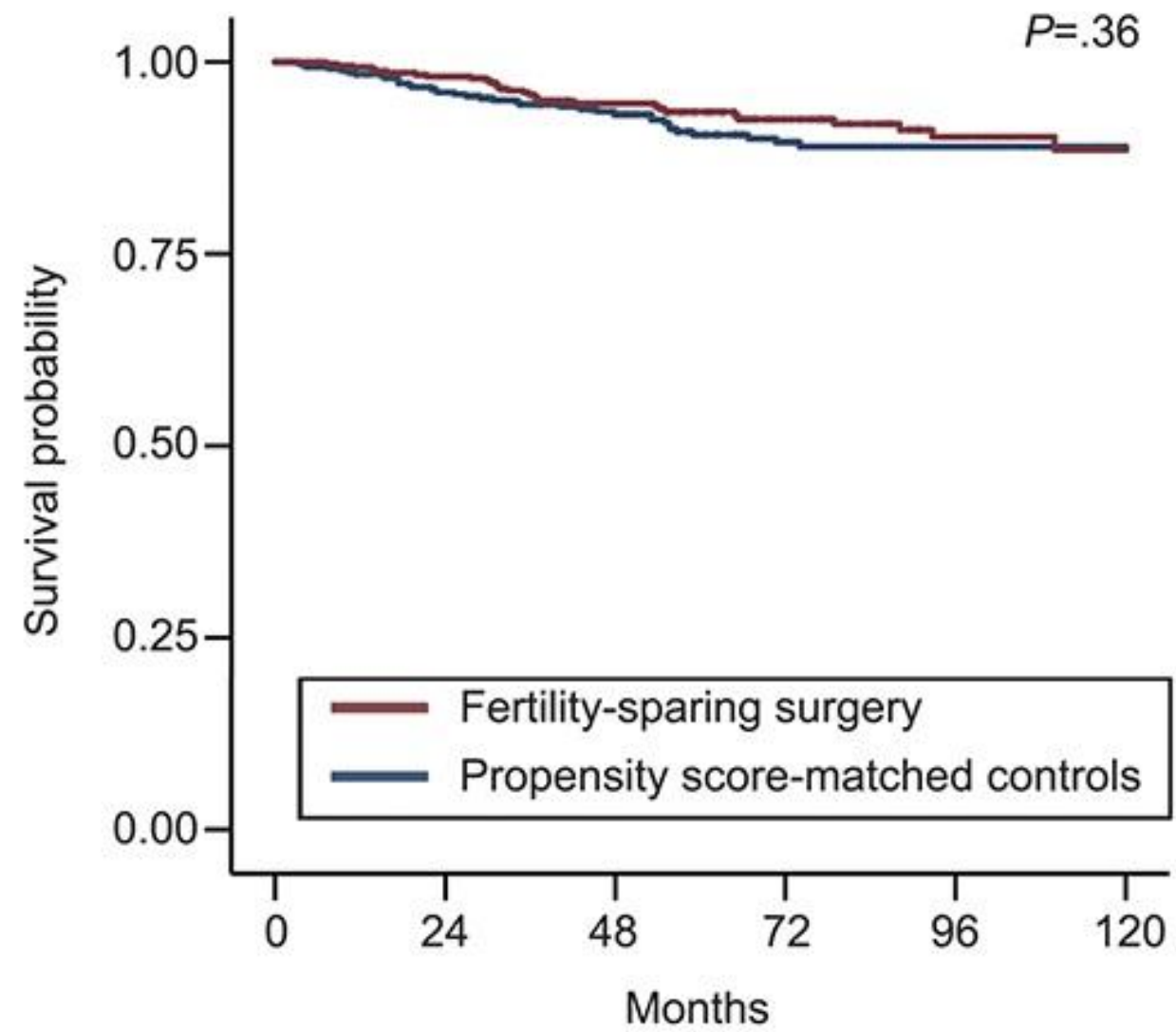


Table 1. Characteristics of Women With Stage IA and Unilateral IC Epithelial Ovarian Cancer Who Underwent Fertility-Sparing and Conventional Surgery, Before and After Propensity Score Matching (continued)

Characteristic	All Patients (N=1,726)			Propensity Score-Matched Patients* (n=904)		
	Fertility-Sparing (n=825)	Conventional (n=901)	<i>P</i> [†]	Fertility-Sparing (n=452)	Conventional (n=452)	<i>P</i> [†]
Stage			.26			.83
IA	546 (66.2)	573 (63.6)		291 (64.4)	294 (65.0)	
IC	279 (33.8)	328 (36.4)		161 (35.6)	158 (35.0)	
Histologic type			<.001			.94
Clear cell	53 (6.4)	99 (11.0)		42 (9.3)	41 (9.1)	
Endometrioid	207 (25.1)	316 (35.1)		152 (33.6)	141 (31.2)	
Mucinous	362 (43.9)	284 (31.5)		160 (35.4)	168 (37.2)	
Other adenocarcinoma	98 (11.9)	115 (12.8)		47 (10.4)	47 (10.4)	
Serous	105 (12.7)	87 (9.7)		51 (11.3)	55 (12.2)	
Grade			.002			.85
1	298 (36.1)	340 (37.7)		168 (37.2)	170 (37.6)	
2	201 (24.4)	251 (27.9)		123 (27.2)	118 (26.1)	
3	111 (13.5)	143 (15.9)		67 (14.8)	61 (13.5)	
Unknown	215 (26.1)	167 (18.5)		94 (20.8)	103 (22.8)	
Tumor size (cm)			.41			.92
Less than 1.0	40 (4.8)	33 (3.7)		18 (4.0)	19 (4.2)	
1.0–4.9	146 (17.7)	146 (16.2)		77 (17.0)	74 (16.4)	
5.0–9.9	106 (12.8)	139 (15.4)		69 (15.3)	61 (13.5)	
10–19.9	218 (26.4)	249 (27.6)		119 (26.3)	126 (27.9)	
20 or greater	129 (15.6)	127 (14.1)		68 (15.0)	62 (13.7)	
Unknown	186 (22.5)	207 (23.0)		101 (22.3)	110 (24.3)	
Lymphadenectomy			<.001			1.0
Yes	510 (61.8)	754 (83.7)		341 (75.4)	340 (75.2)	
No	312 (37.8)	143 (15.9)		108 (23.9)	109 (24.1)	
Unknown	3 (0.4)	4 (0.4)		3 (0.7)	3 (0.7)	
Chemotherapy			<.001			.76
Yes	288 (34.9)	425 (47.2)		199 (44.0)	188 (41.6)	
No	504 (61.1)	439 (48.7)		235 (52.0)	245 (54.2)	
Unknown	33 (4.0)	37 (4.1)		18 (4.0)	19 (4.2)	

Data are median (interquartile range) or n (%) unless otherwise specified.

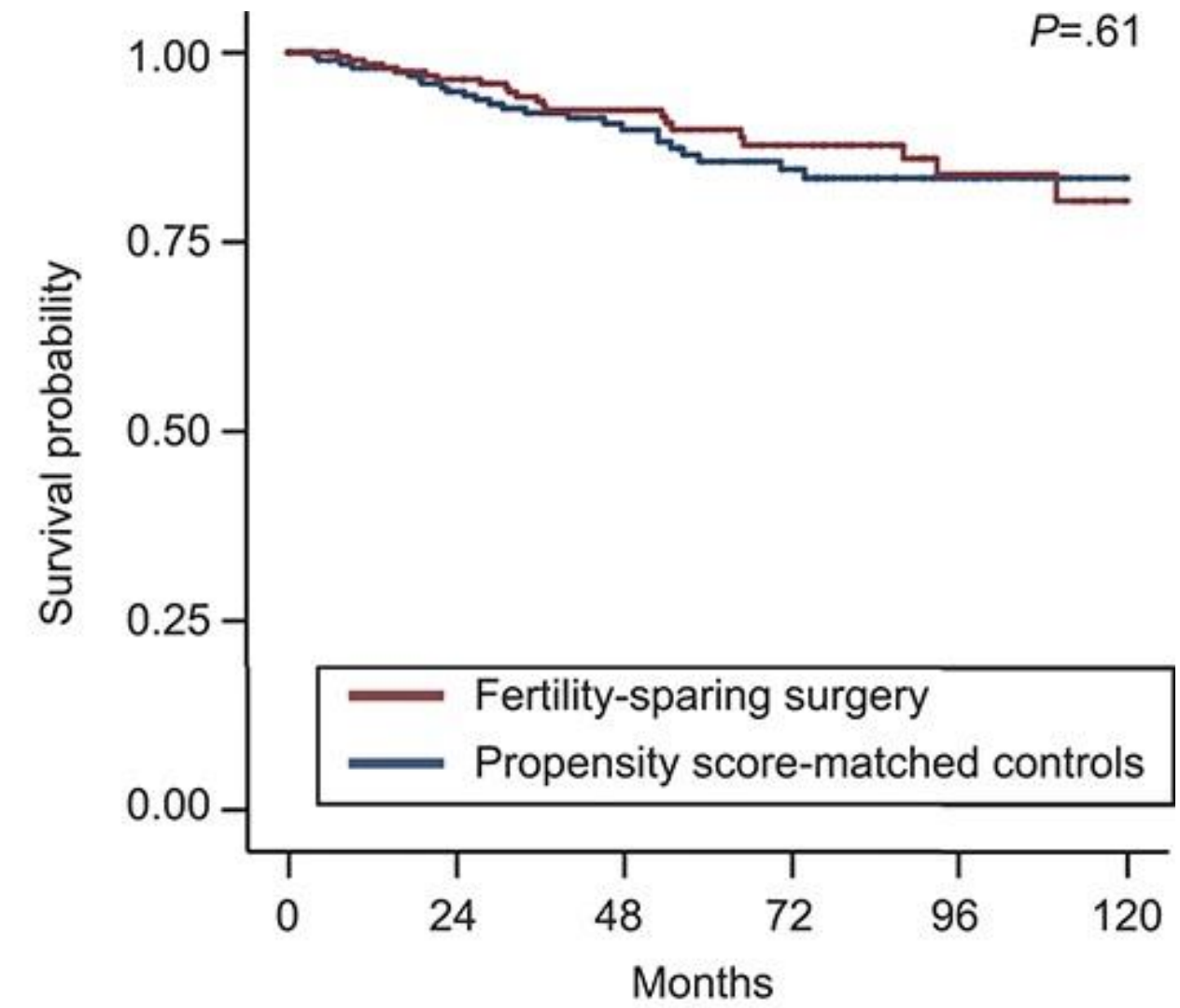
* Each patient undergoing fertility-sparing surgery was matched, using a 1:1 nearest-neighbor algorithm, to the patient who was most similar on observed covariates but underwent conventional surgery. The propensity score model was based on all tabulated characteristics.



Number at risk		0	24	48	72	96	120
Fertility-sparing	Conventional	452	396	286	175	93	30
Fertility-sparing	Conventional	452	397	278	172	87	31

A

A. All matched patients.



Number at risk		0	24	48	72	96	120
Fertility-sparing	Conventional	211	182	125	73	39	14
Fertility-sparing	Conventional	201	180	117	78	38	16

B

B. Survival curves for matched patients who had at least one high-risk feature (stage IC, clear cell histology, or high grade).

FERTILITY SPARING SURGERY

- UNILATERAL SALPINGO-OOPHORECTOMY
- COMPLETE SURGICAL STAGING

Laparoscopy in ovarian cancer

How far can we go ?

In the late nineties and the beginning of 21 th century the use of laparoscopy in the field of gynaecologic cancer has increase dramatically with lots of retrospective data suggesting the safety of the minimal invasive surgery...

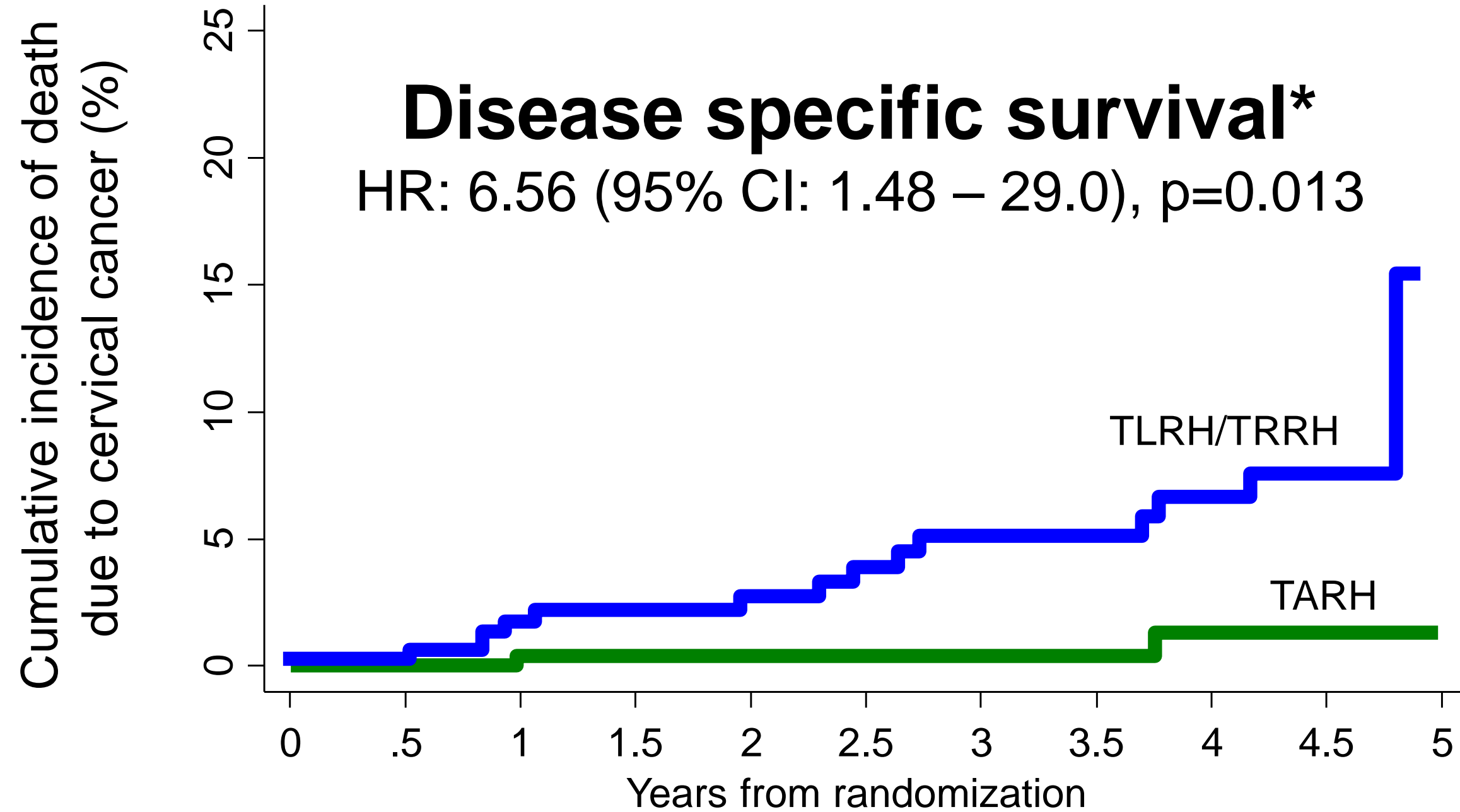
Since...

**Phase III Randomized Trial of Laparoscopic or Robotic
Radical Hysterectomy vs. Abdominal Radical Hysterectomy
in Patients with Early-Stage Cervical Cancer:
LACC Trial**

Pedro T. Ramirez, Michael Frumovitz, Rene Pareja, Aldo Lopez, Marcelo Vieira, Reitan Ribeiro, Alessandro Buda,
Xiaojian Yan, Kristy P Robledo, Val Gebiski, Robert L Coleman, Andreas Obermair

**Primary Objective
LACC Trial**

Compare disease-free survival at 4.5 years amongst patients who underwent a total **laparoscopic or robotic radical hysterectomy (TLRH/TRRH)** vs. a **total abdominal radical hysterectomy (TARH)** for early stage cervical cancer.



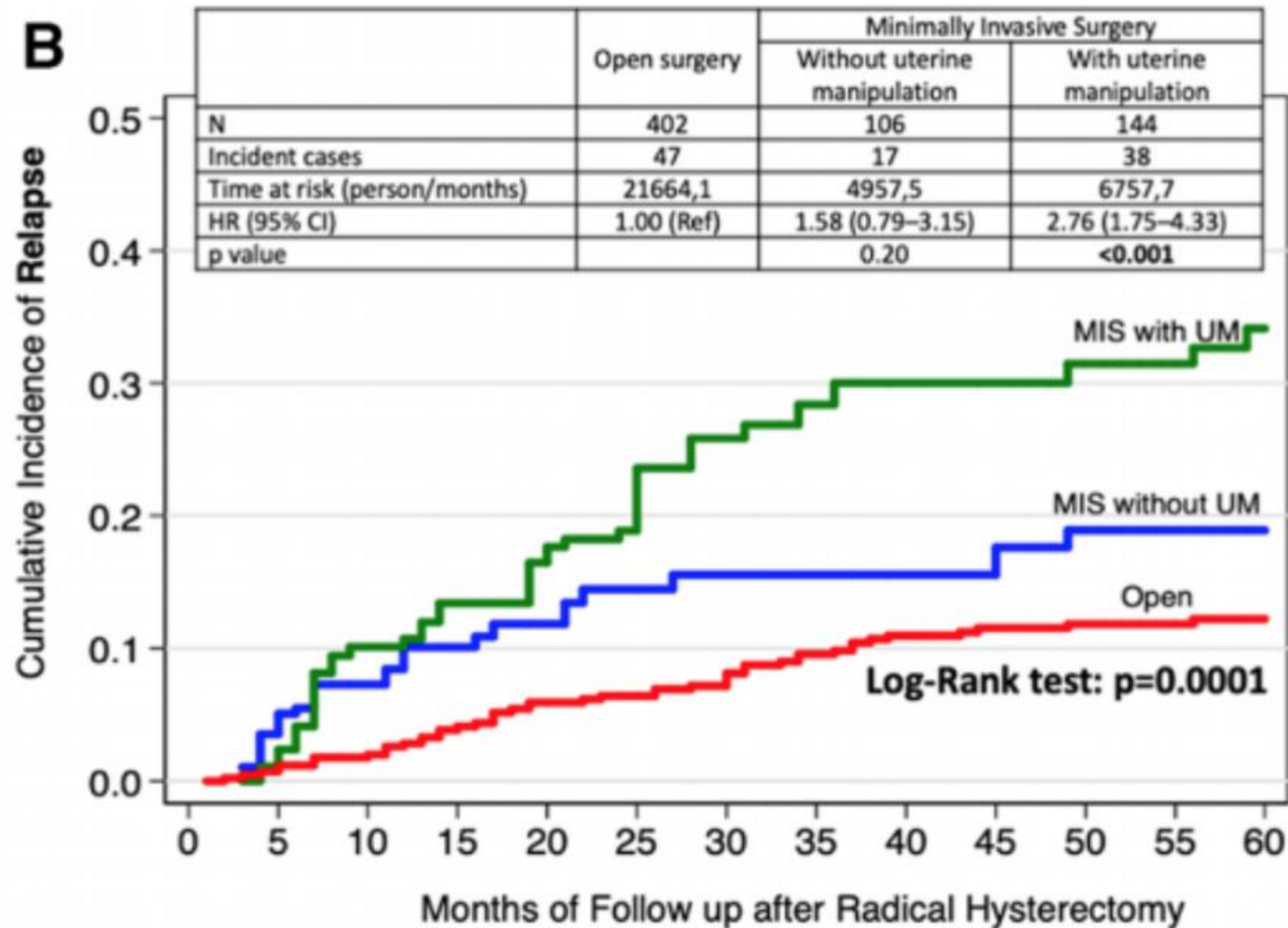
Number at risk

TARH	312	282	237	190	164	146	136	125	104	90	7
TLRH	319	297	249	198	174	163	150	133	113	87	5

SUCCOR Study

SUCCOR study: an international European cohort observational study comparing minimally invasive surgery versus open abdominal radical hysterectomy in patients with stage IB1 cervical cancer L. Shiva et al.

→ Uterine manipulation



PUBMED: 12/2022

Laparoscopy early stage ovarian cancer

327 publications...

But 0 RCT level A evidence

Randomized clinical trials about the use of laparoscopy in early stage ovarian cancer = 0

Cochrane Database Syst Rev, 2016 vol. 10(10) CD005344
Laparoscopy versus laparotomy for FIGO stage I ovarian cancer.

Falcetta, FS; Lawrie, TA; Medeiros, LR; da Rosa, MI; Edelweiss, MI; Stein, AT; Zelmanowicz, A; Moraes, AB; Zanini, RR; Rosa, DD
This review has found no good-quality evidence to help quantify the risks and benefits of laparoscopy for the management of early-stage ovarian cancer as routine clinical practice.

PUBMED 12/2022: Operative laparoscopy for interval debulking ovarian cancer

176 references...

But 0 RCT level A evidence

Randomized clinical trials about the use of laparoscopy interval debulking surgery= 0

Gynecol Obstet Fertil Senol, 2021 vol. 49(10) pp. 736-743

[Epithelial ovarian cancers and minimally invasive cytoreductive surgery after neoadjuvant chemotherapy: A systematic review].

Achen, G; Koual, M; Bentivegna, E; Fournier, L; Nguyen Xuan, HT; Delanoy, N; Bats, AS; Azaïs, H

Laparoscopic versus open pancreatoduodenectomy for pancreatic or periampullary tumours (LEOPARD-2): a multicentre, patient-blinded, randomised controlled phase 2/3 trial

Jony van Hilst, Thijs de Rooij, Koop Bosscha, David J Brinkman, Susan van Dieren, Marcel G Dijkgraaf, Michael F Gerhards, Ignace H de Hingh, Tom M Karsten, Daniel J Lips, Misha D Luyer, Olivier R Busch, Sebastiaan Festen, Marc G Besselink*, for the Dutch Pancreatic Cancer Group*

Interpretation Although not statistically significant, laparoscopic pancreatoduodenectomy was associated with more complication-related deaths than was open pancreatoduodenectomy, and there was no difference between groups in time to functional recovery. These safety concerns were unexpected and worrisome, especially in the setting of trained surgeons working in centres performing 20 or more pancreatoduodenectomies annually. Experience, learning curve, and annual volume might have influenced the outcomes; future research should focus on these issues.

Effect of Laparoscopic-Assisted Resection vs Open Resection on Pathological Outcomes in Rectal Cancer

The ALaCaRT Randomized Clinical Trial

Andrew R. L. Stevenson, MB BS, FRACS^{1,2}; Michael J. Solomon, MB BCH, MSc, FRCSI, FRACS³; John W. Lumley, MBBS, FRACS⁴; [et al](#)

» [Author Affiliations](#) | [Article Information](#)

JAMA. 2015;314(13):1356-1363. doi:10.1001/jama.2015.12009

Published in final edited form as:

JAMA. 2015 October 06; 314(13): 1346–1355. doi:10.1001/jama.2015.10529.

Effect of Laparoscopic-Assisted Resection vs Open Resection of Stage II or III Rectal Cancer on Pathologic Outcomes:

The ACOSOG Z6051 Randomized Clinical Trial

“Among patients with T1-T3 rectal tumors, noninferiority of laparoscopic surgery compared with open surgery for successful resection was not established. Although the overall quality of surgery was high, these findings do not provide sufficient evidence for the routine use of laparoscopic surgery.”

Surgery in ovarian cancer:

a unique goal: NO RESIDUAL TUMOUR

« EVALUATION OF THE RESECTABILITY »

Reason for unresectability...

1. Poor Medical
conditions
PS/ASA/Age

2.
Anatomical/functional/
reasons...
Small bowel +++
Distant liver or lung
metastases

3. Surgical
insufficiency...
Human/Material

Laparoscopy +++

The same as HIPEC for colorectal surgery...

Laterza et al. In Vivo. 2009 Jan-Feb;23(1):187-90.

Table II. Literature and present study data on effectiveness of laparoscopic evaluation in predicting the completeness of cytoreduction.

Authors (ref.)	Year	No. of patients	Disease	Sensitivity (%)	Specificity (%)	Accuracy (%)	PPV (%)	NPV (%)
Pomel <i>et al.</i> (12)	2005	11	PM, ovarian and colorectal cancer PC	100	NA	91	87.5	NA
Valle and Garofalo (13)	2006	97	PM, PMP, GI and breast PC Sarcomas	100	NA	98	98	NA
Present study	2008	33	PM	100	75	97	97	100

PM: peritoneal mesothelioma; PMP: pseudomixoma peritonei; PC: peritoneal carcinomatosis; GI: gastrointestinal; NA: not available; PPV: positive predictive value; NPV: negative predictive value.

Advantage of laparoscopy

1 Biopsies

2 simple

PCI scopy = PCI tomy

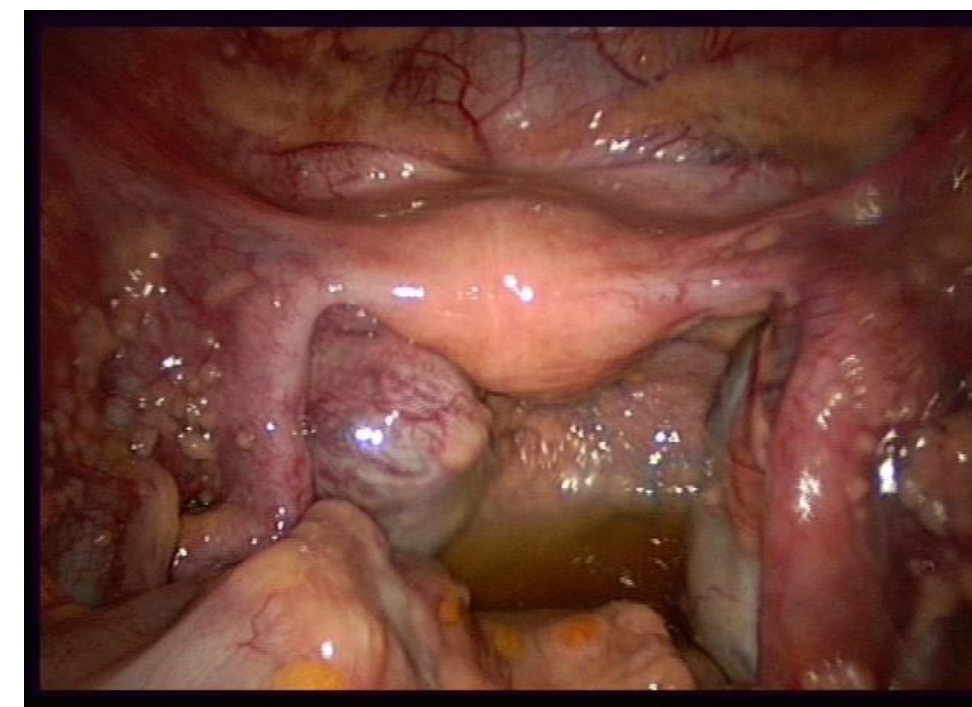
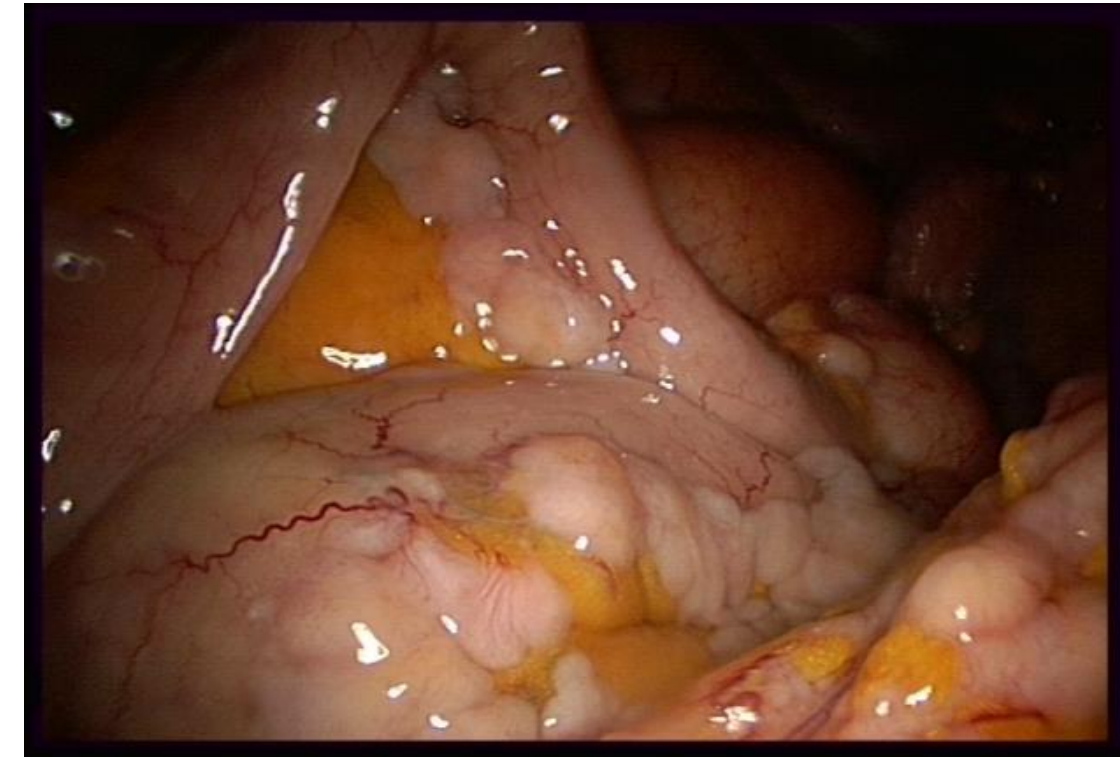
Small bowel

omentum

pelvis

Anterior part of the diaphragm

Abdominal wall, parieto-colic gutters...



Pitfalls of LAPAROSCOPY

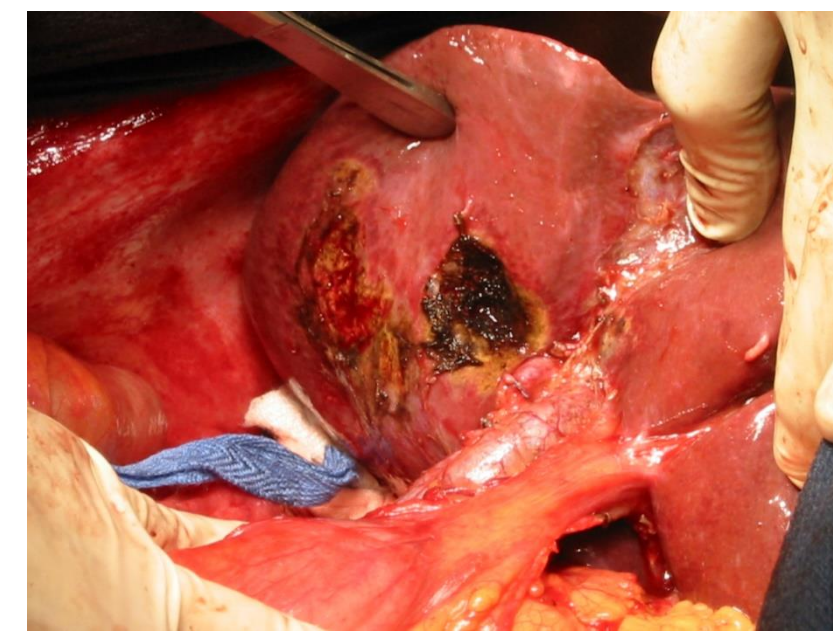
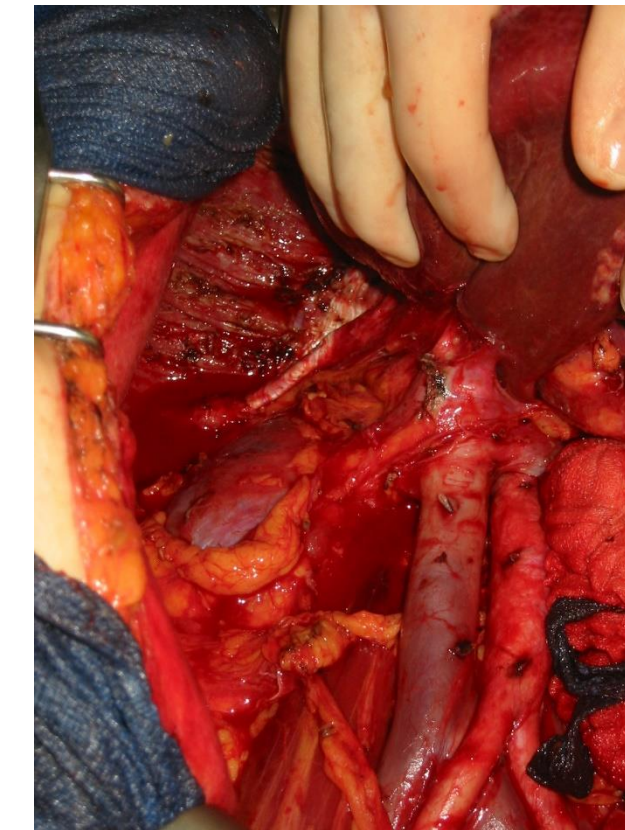
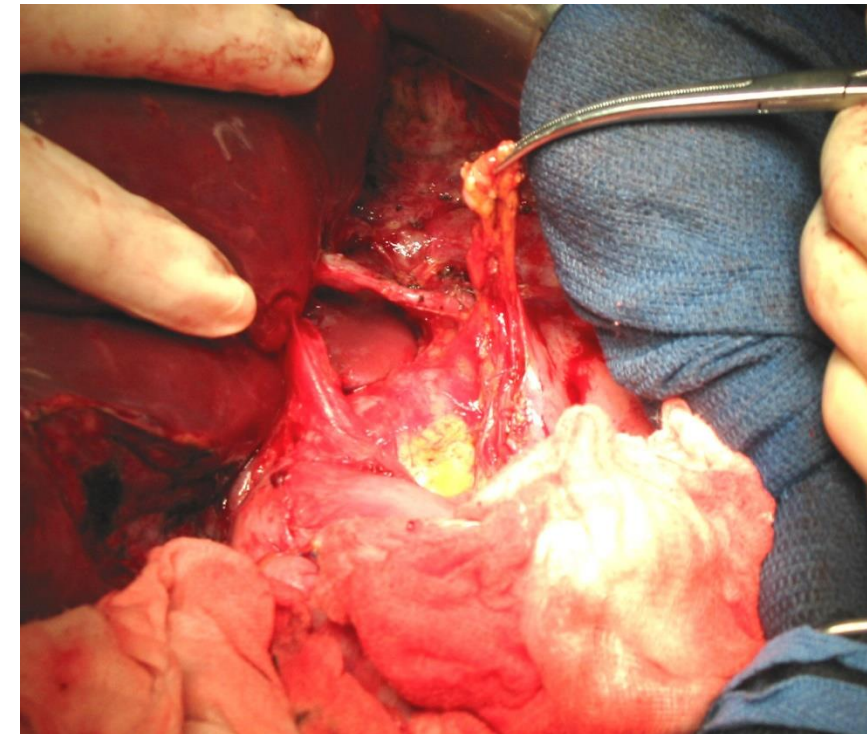
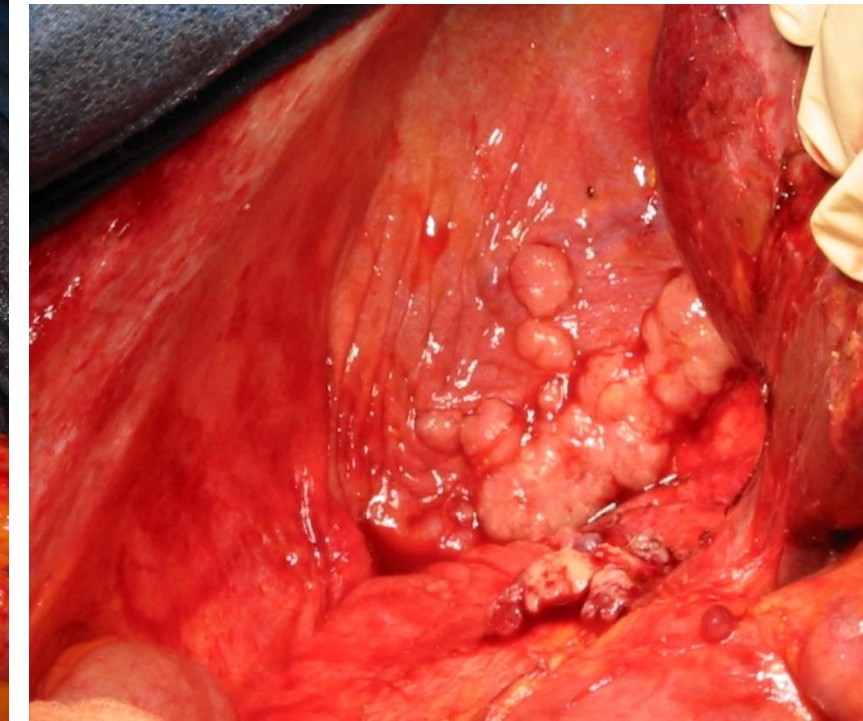
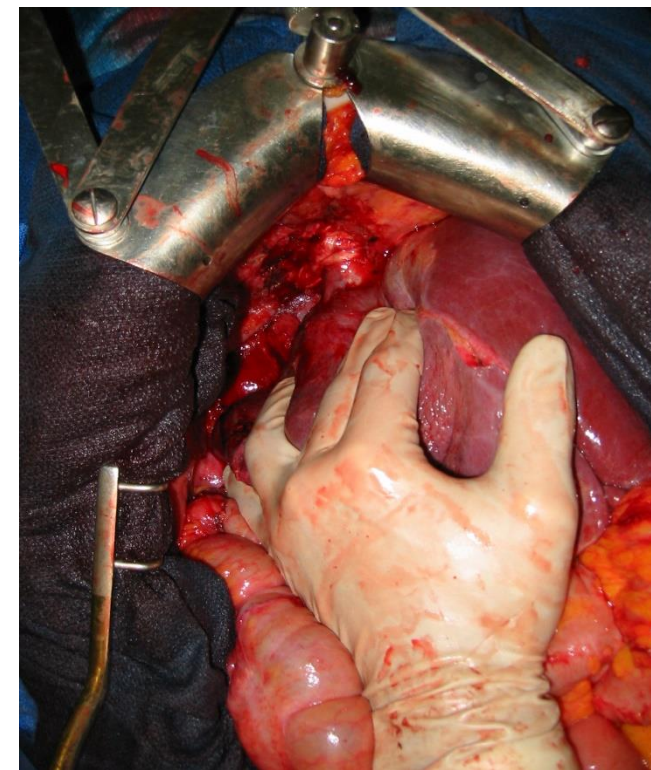
PCI scopy < PCI tomy

Fixed omental cakes that reduce visibility of the small bowel+++

Infiltration of supra-hepatic vessels and porta
(extremely rare in first line treatment)

Lesser sac with infiltration of gastric vessels

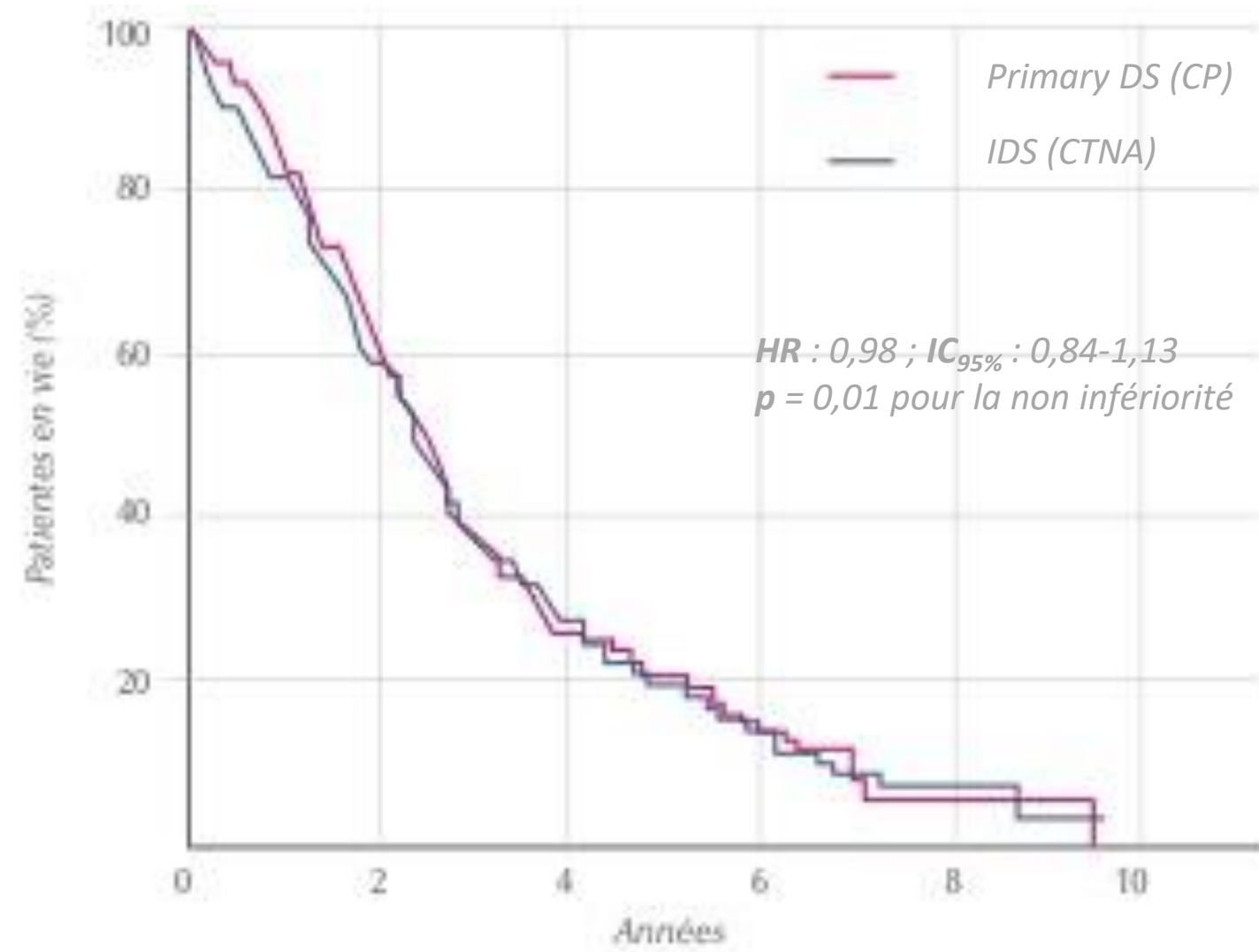
Coeliac trunk



Is there a place of operative laparoscopy in AOC ?

Rate of NEO ADJUVANT CHEMOTHERAPY (NAC)

50 à 70 % IN « EXPERT CENTRES »... ! (Luyckx et al.)



(EORTC 55971)

		At risk				
PDS	253	336	189	62	14	2
IDS	245	334	195	46	13	2

	EORTC (2010)		CHORUS (2015)		JCOG	
	PDS	NAC	PDS	NAC	PDS	NAC
Age	62 (25-86)	63 (33-81)	66 (26-87)	65 (34-88)	59 (30-75)	60 (36-75)
PS 2-3	40 (12%)	44 (13%)	54 (20%)	53 (19%)	19 (13%)	21 (14%)
Stage IV	77 (23%)	81 (24%)	70 (25%)	68 (25%)	49 (33%)	47 (31%)
CA 125	1130	1180	NA	NA	1950	1556
Clear Cell/ mucinous	14 (4%)	15 (4%)	6 (2%)	17 (8%)	14 (10%)	6 (5%)

Survival analyses from a randomized trial of primary debulking surgery versus neoadjuvant chemotherapy for advanced epithelial ovarian cancer with high tumor load (SCORPION trial) (NCT01461850)

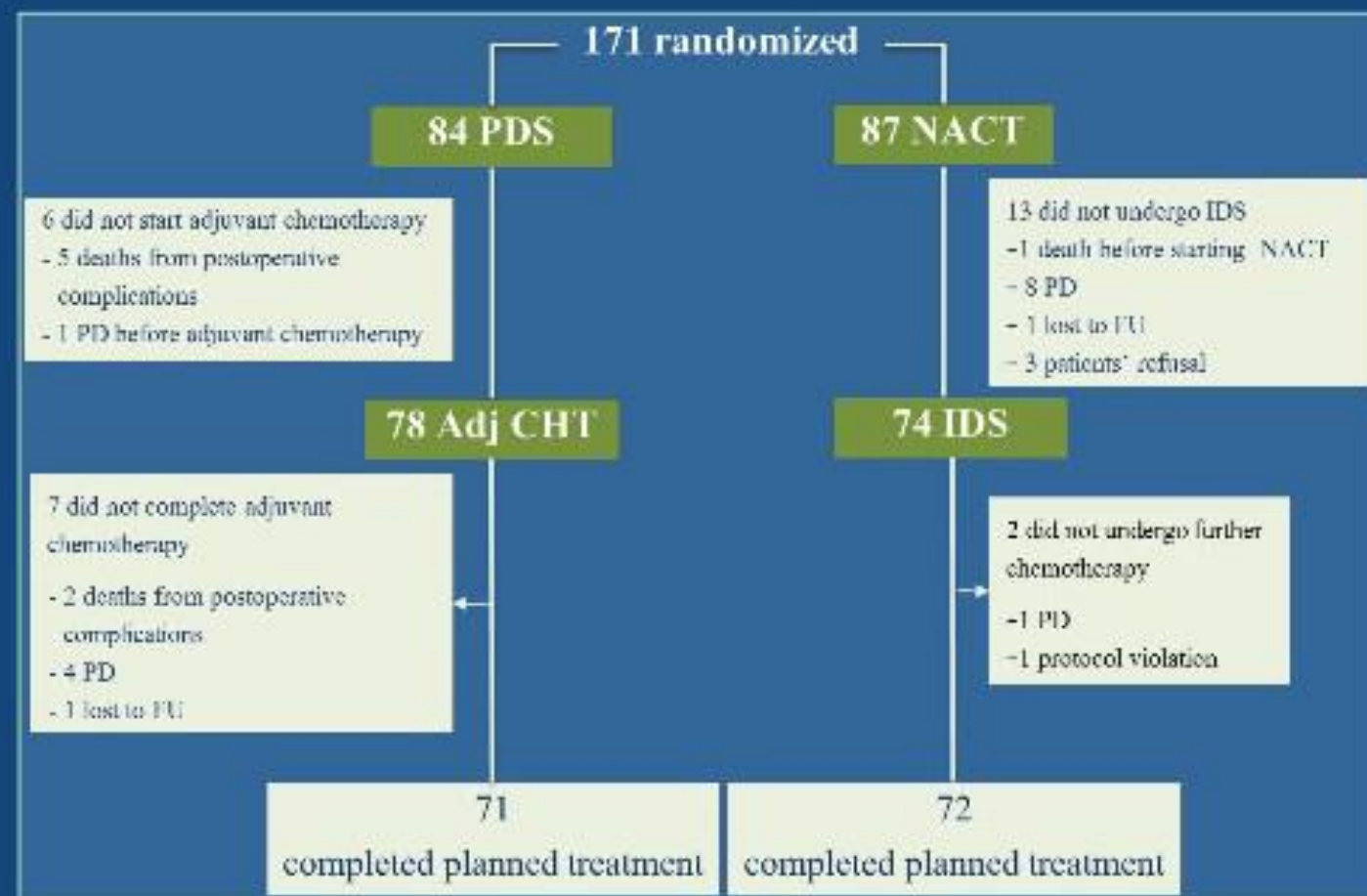
Fagotti A, Ferrandina G, Vizzielli G, Fanfani F, Gallotta V, Chiantera V, Costantini B, Margariti PA, Gueli Alletti S, Cosentino F, Tortorella L, Scambia G.

*Fondazione Policlinico Universitario A. Gemelli, IRCCS
Università Cattolica del Sacro Cuore, Rome, Italy*

Abs #5516

#5516: SCORPION Trial (NACT-IDS v PDS for patients with high tumor load)

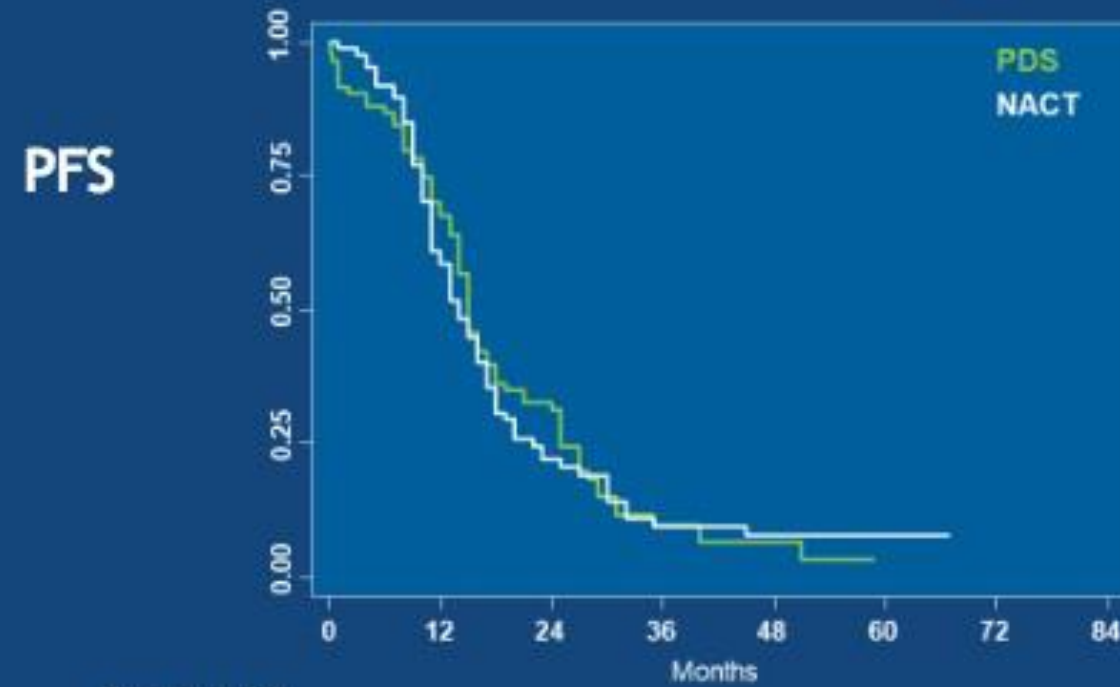
CONSORT Diagram and Patient Characteristics



Variable	Arm A PDS N. (%)	Arm B NACT N. (%)
All cases	84	87
FIGO surgical stage		
IIIc	71 (84.5)	79 (90.8)
IV	13 (15.5)	8 (9.2)
LPS score at diagnosis		
8	46 (54.8)	34 (39.1)
10	28 (33.3)	43 (49.4)
12	10 (11.9)	10 (11.5)

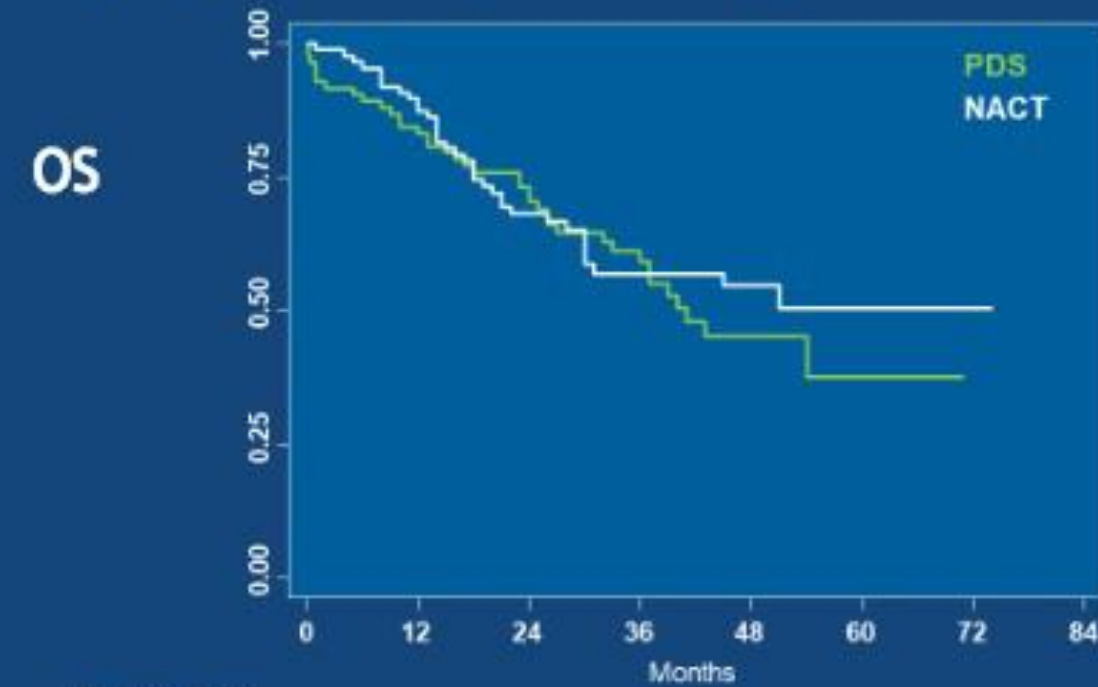
#5516: SCORPION Trial (NACT-IDS v PDS for patients with high tumor load)

Survival Analyses (ITT population, N=171)



Number at risk		0	12	24	36	48	60	72	84
PDS	84	58	24	4	2	0	0	0	0
NACT	87	53	16	6	4	1	0	0	0

	PDS	NACT	HR (95% CI) P value
Recurrences	65 (77.4)	72 (82.4)	0.378
Median PFS (mths)	14	15	1.06 (0.77-1.46) 0.729



Number at risk		0	12	24	36	48	60	72	84
PDS	84	70	53	31	11	2	0	0	0
NACT	87	78	49	31	18	5	1	0	0

	PDS	NACT	HR (95% CI) P value
Deaths	38 (45.2)	36 (41.4)	0.611
Median OS (mths)	41	NR	0.88 (0.56-1.39) 0.593

Waiting for the AGO TRUST trial...

% NEO ADJUVANT CHEMOTHERAPY (NAC)

50 à 70 % IN « EXPERTS CENTRES »... ! (Luyckx et al.)

ALSO...

>20% of patients treated by NAC will have close to complete response

Why to perform a medial xypho-pubic laparotomy for this selected group of patients ?

CILOVE STUDY

Laparoscopic management of advanced epithelial ovarian cancer after neoadjuvant chemotherapy: a phase II prospective multicenter non-randomized trial (CILOVE study)

Pomel c et al IJGC 2021 31(12) pp1272-78

■ Primary objective:

→ Rate of conversion to laparotomy

Secondary objectives:

Rate of trocars metastases

→ clinical exam, CA125, CTscan every 6 month, RECIST 1.1.

Morbidity

→ Death, per and post-op complications (Clavien-Dindo)

Pain

→ Pre-op EVA, during hospitalisation, 1 week post-op, 1 month, 3 months and 6 months post-op.

QOL

→ QLQ-C30 inclusion, 1 week, 1 month, 3 and 6 months,

Economic evaluation

→ Surgical cost, per and post op

- Prospective non randomized multi centre study

- 1 step fleming

n=47 patients

15% minimum rate of laparotomy

35% maximum rate

Positive if 37 patients with no conversion

■ Inclusion criteria

- Consent form signed.
- Age \geq 18 yo
- PS : OMS $<$ 2
- Unresectable Epithelial ovarian, tubal or primary peritoneal cancer :
 - Stage IV FIGO by imaging (CT scan ou PET CT)
 - Unresectable stage IIIc disease I
 - patients uneligible for primary debulking
- No primary debulking.
- A minimum of 3 cycles of neoadjuvant chemotherapy.

■ Inclusion criteria

- Patients sensitive to first line chemotherapy CT SCAN
 - No residual supra colic peritoneal carcinosis
 - Less than 10 cm residual pelvic disease
 - Less than 1 cm retroperitoneal nodes

■ Non inclusion criteria

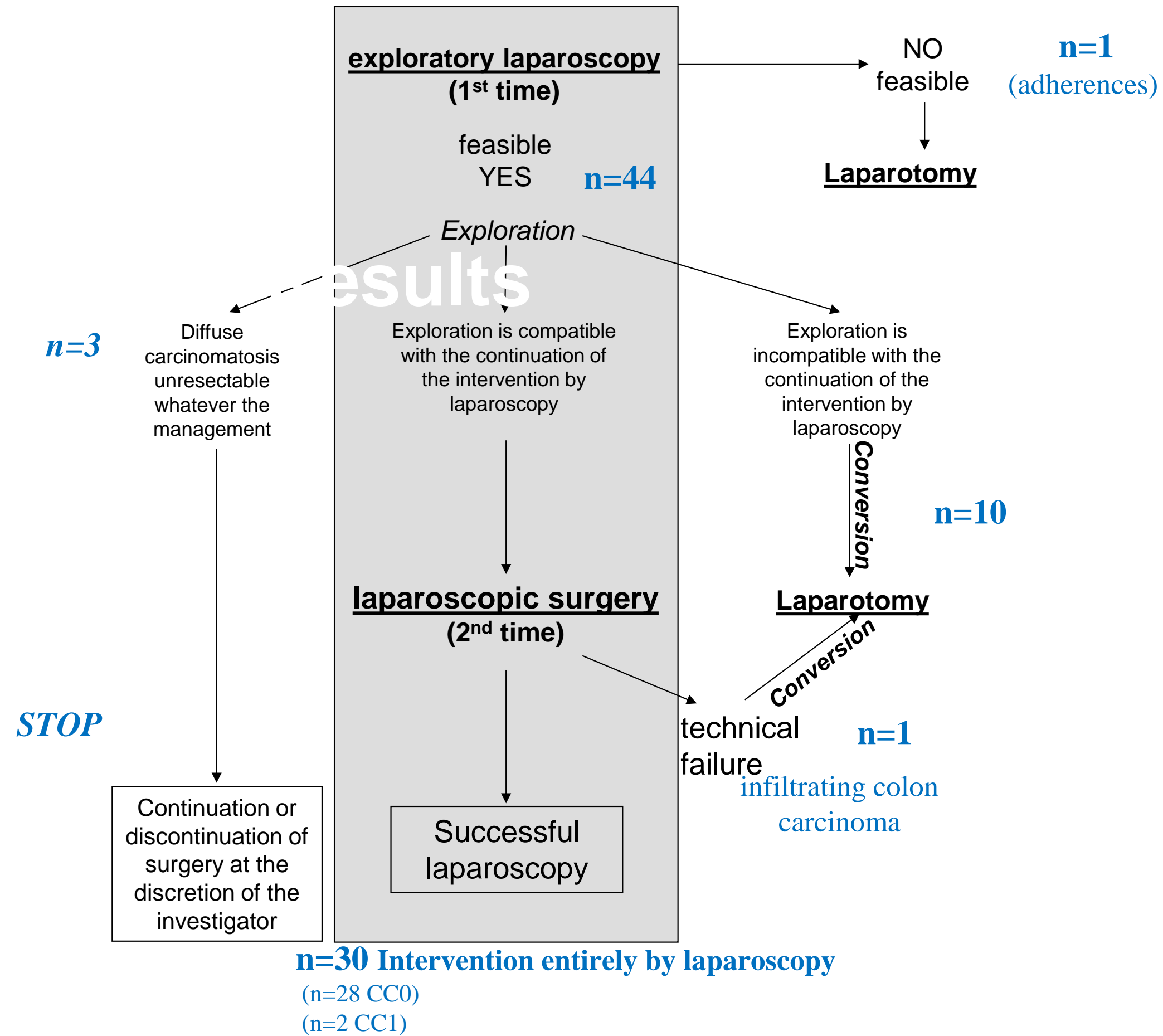
- Patients unsuitable for laparoscopy
- Psychiatric disorders.
- Patients enrolled in a surgical trial

- Minimum surgical requirements:

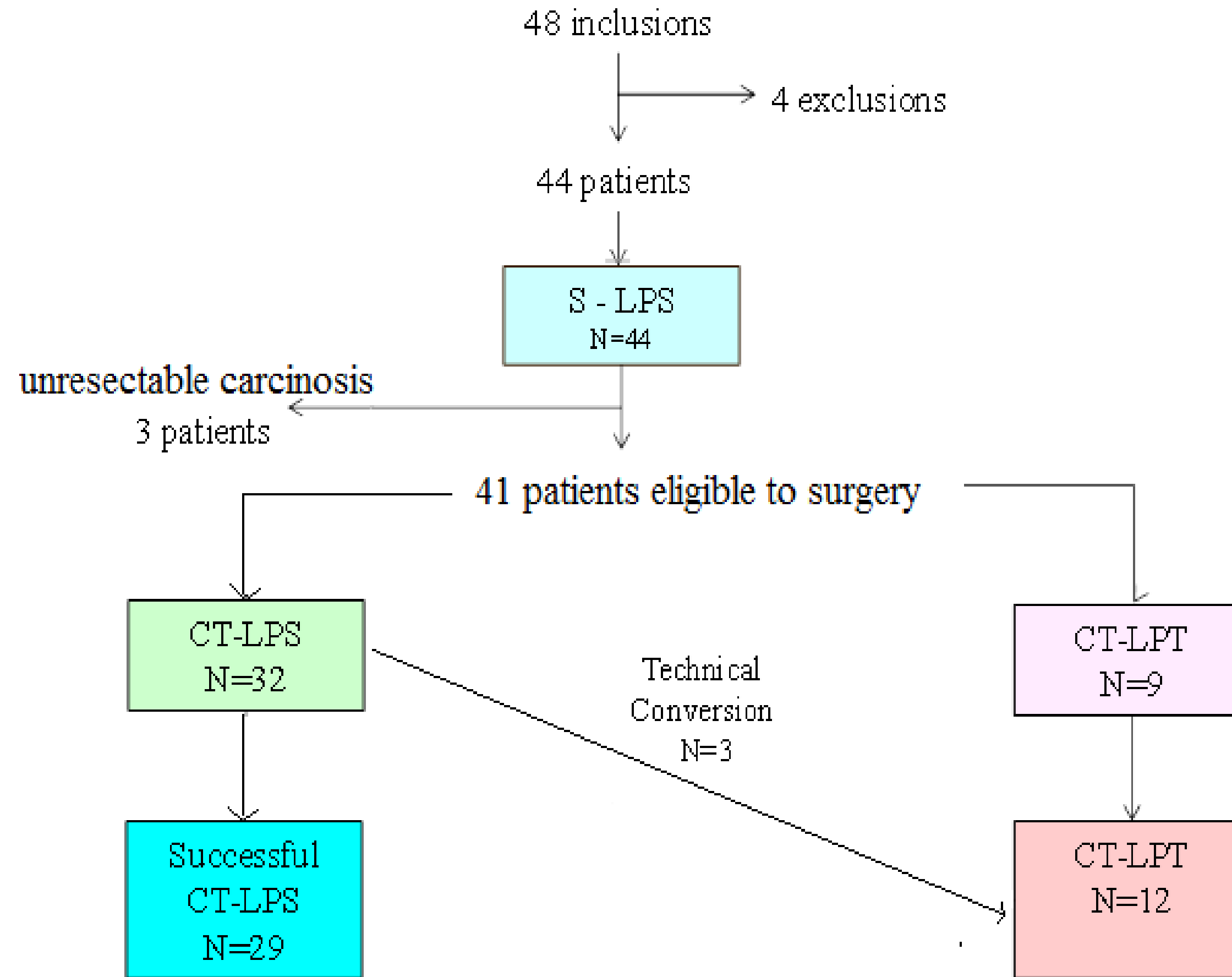
- Peritoneal cytology
- TAH BSO
- Appendicectomy
- Total infragastric omentectomy
- Lymphadenectomy to the discretion of the surgeons

A minimum of 3 peritoneal biopsies in case of complete response.

▪intervention (n=45)



Results



LPS laparoscopy, S-LPS staging laparoscopy, LPT laparotomy, CT cytoreductive surgery

Results

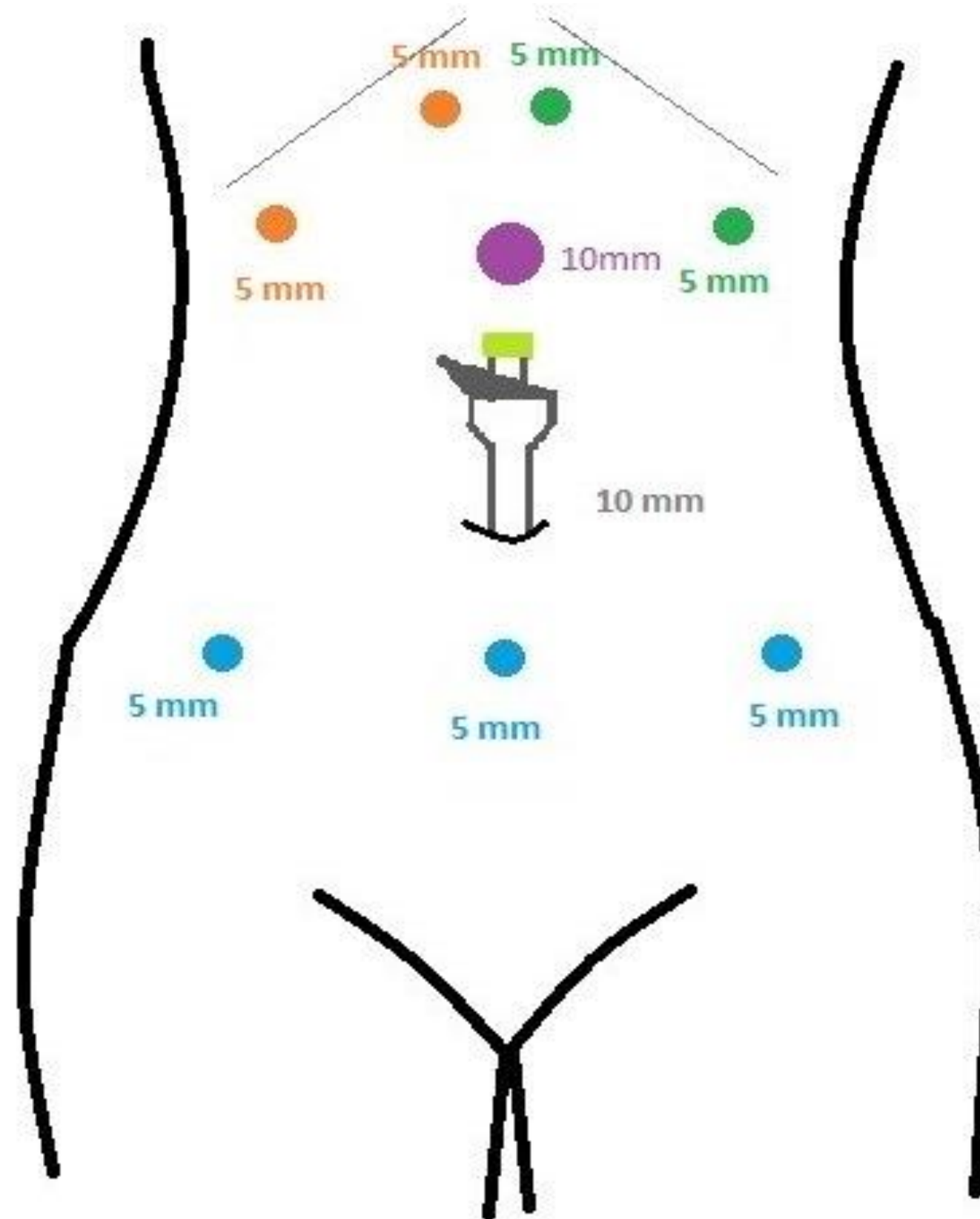
Patient number	PCI during intervention	PCI CT scan proofreading	Residual mass	
Patients not eligible for laparoscopy				
1	19	3	Left ovary 32 mm	carcinomatosis of the right diaphragm dome and mesentery
2	17	11		Carcinomatosis of the right diaphragmatic dome and the small omentum.
3	4	8		carcinomatosis of the right and left diaphragmatic domes and unexplorable pelvis
4	10	8		carcinomatosis of the right and left diaphragmatic domes
5	10	3		
6	12	5	Right ovary 27 mm	supra mesocolic carcinomatosis
7	15	5	Right ovary 30mm	mesentery carcinomatosis
8	3	5	Right ovary 37mm / left ovary 32 mm	
9	3	3		dense adhesions between the omentum and parietal meshes
Patients eligible to laparoscopy but for whom a conversion was necessary				
10	5	5		conversion for carcinomatosis and adhesion
11	0	3	Right ovary 20mm	conversion for multiple dense adhesions
12	N/A	N/A		conversion for poor laparoscopic evaluation of transverse colon involvement

Results

	Eligible to CT-LPS (n=32)	successful CT-LPS (n=29)	technical conversion (n=3)
PCI (median, range)	2 [0-13]	2 [0-13]	0 [0-3]
Median Operative time (mn)	274	264	222
Estimated blood loss (ml)	172	176	125
Blood transfusion (%)	5 (16)	5 (18)	0
Residual tumor			
- CC-0	31	28	3
- CC-1	1	1	0
Median length of stay	6.9	6.6	10
MedianTime (day) to start chemotherapy	36.8	37.4	52

Results

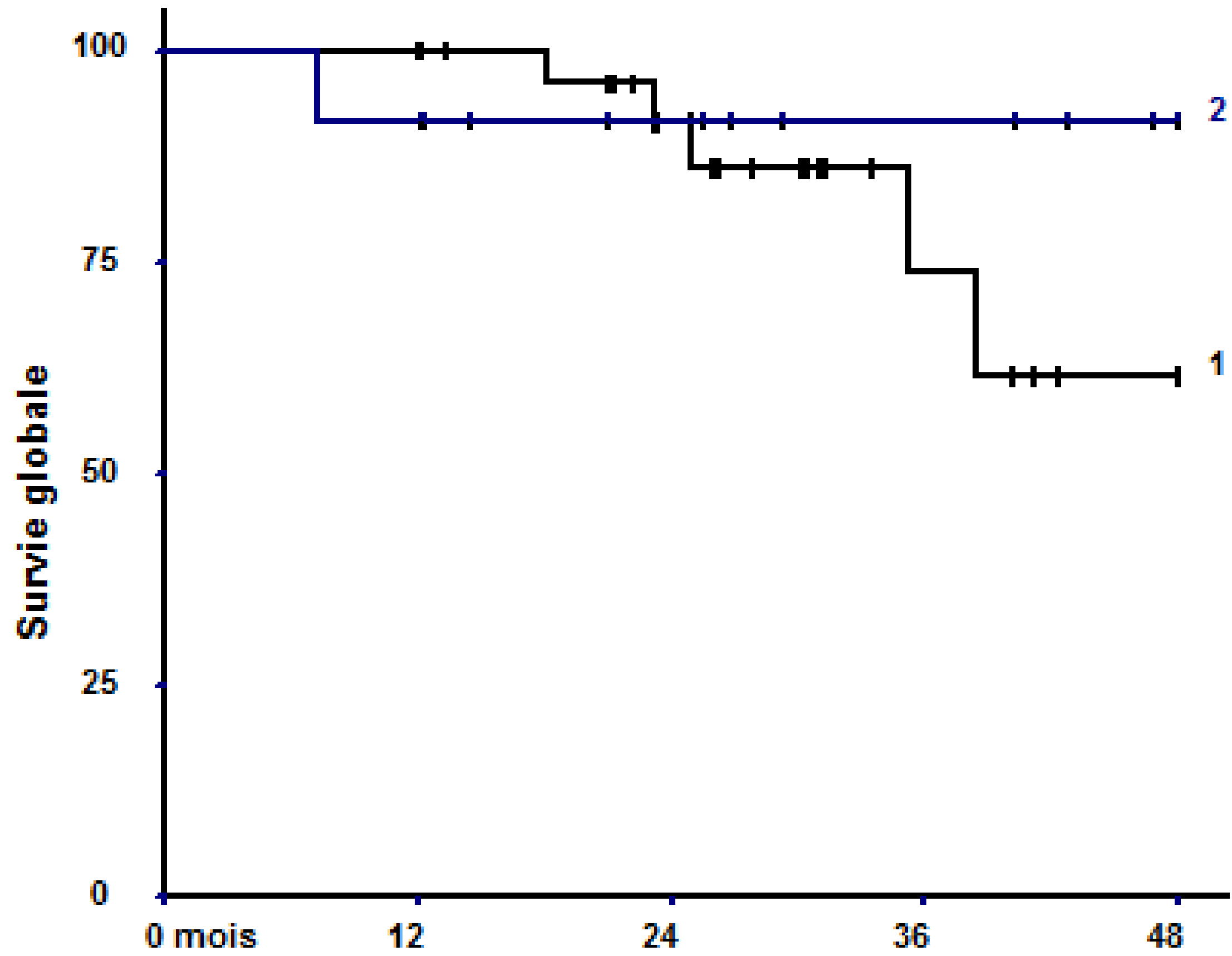
Trocars number: 4 to 9



Results

	Eligible to CT-LPS (n=32)	Successful CT-LPS (n=29)	Technical conversion (n=3)
Intraoperative complication	2 (6%)		
Medical incident	1 (3%)	1 (3%) bradycardia	
Surgical incident	1 (3%)	1 (3%) diaphragmatic hernia	
Major Post-operative complication grade 3-4* (< 1 month)	0	0%	0%
Re-admission	2 (grade 2: intervention du to dura mater breach)	2	0
Re-intervention	1 paracentesis	1	0
Major Complication delayed (grade 3-4*)	4	5	
Thromboembolic	1	1	0
Occlusion	1	1	0
lymphocyst	1	4	0
hematoma	2	2	0
sphincterial trouble	1		1 cementoplasty
other	4	7	0
Rehospitalization	1	1	0

Résultats

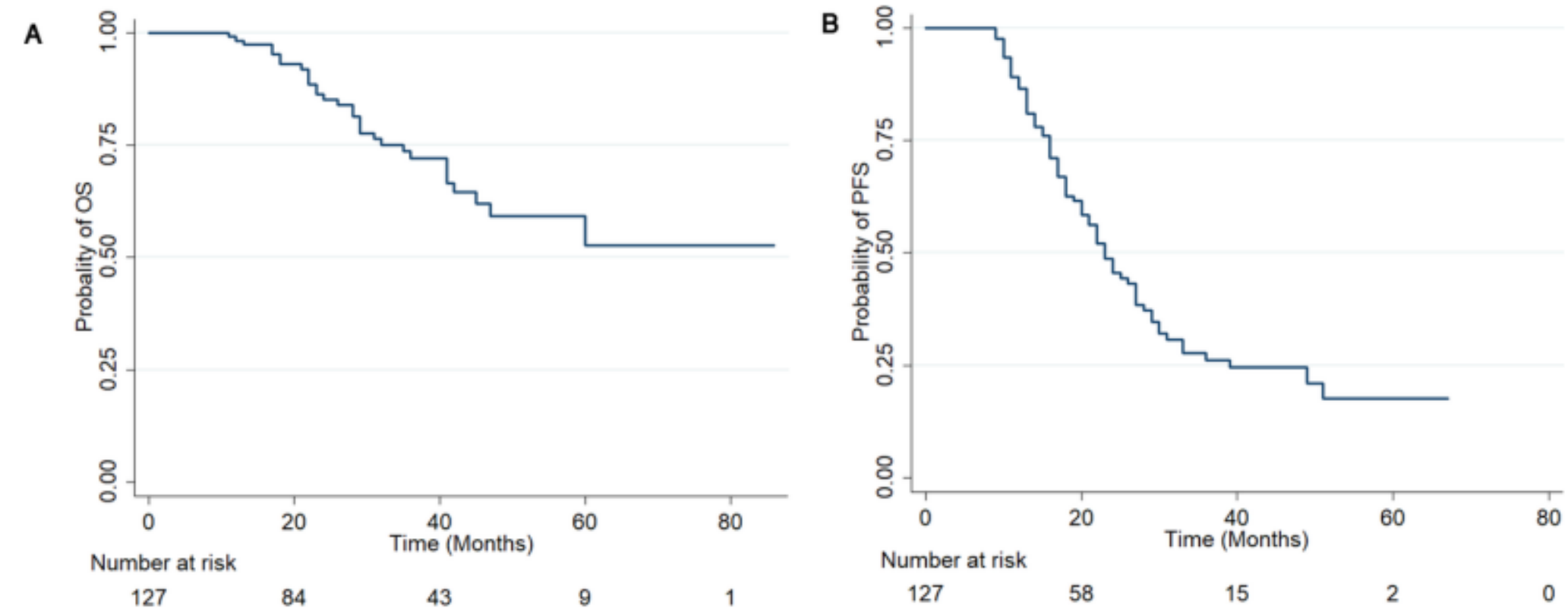


The INTERNATIONAL MISSION study: minimally invasive surgery in ovarian neoplasms after neoadjuvant chemotherapy

A Fagotti,^{1,2} S Gueli Alletti,¹ G Corrado,³ E Cola,² E Vizza,³ M Vieira,⁴ C E Andrade,⁴ A Tsunoda,⁴ G Favero,⁵ I Zapardiel,⁶ T Pasciuto,⁷ G Scambia^{1,2}

Table 3 Surgical data

Surgical data	
Variable	No. (%) [*]
All cases	127
Type of surgery:	
Hysterectomy +/-BSO†	122 (96.1)
Omentectomy	111 (87.4)
Regional peritonectomy	50 (39.4)
Pelvic/aortic lymphadenectomy	38 (29.9)
Appendectomy	8 (6.3)
Diaphragmatic stripping	6 (4.7)
Bowel resection	3 (2.4)
Residual tumor:	
0	122 (96.1)
<1	5 (3.9)
Median OT (range)	225 (60–600)
Median discharge time, d (range)	2 (1–33)
Intra-operative blood transfusion	2 (1.6)
Median EBL, ml (range)	100 (70–1320)
Estimated median TTC, d (range)‡	20 (15–60)



National Cancer Database

3,071 women

450 (15%) underwent surgery initiated laparoscopically after NAC.

There was no difference in 3-year survival between patients undergoing laparoscopy [47.5%; 95% confidence interval (CI) 41.4-53.5] and laparotomy (52.6%; 95% CI 50.3-55.0; P=.12).

Survival did not differ after adjustment for demographic characteristics, facility type, presence of comorbidities, and stage (adjusted hazard ratio, 1.09; 95% CI 0.93-1.28; P=.26).

Laparoscopy Compared With Laparotomy for Debulking Ovarian Cancer After Neoadjuvant
Chemotherapy

Alexander Melamed 1, Roni Nitecki, David M Boruta 2nd, Marcela G Del Carmen, Rachel M Clark,
Whitfield B Growdon, Annekathryn Goodman, John O Schorge, J Alejandro Rauh-Hain

FIRST RCT !



Laparoscopic cytoreduction After Neoadjuvant ChEmotherapy (LANCE)

Roni Nitecki ¹, Jose Alejandro Rauh-Hain, ¹ Alexander Melamed, ² Giovanni Scambia, ^{3,4} Rene Pareja, ⁵ Robert L Coleman, ⁶ Pedro T Ramirez, ¹ Anna Fagotti ^{3,4}

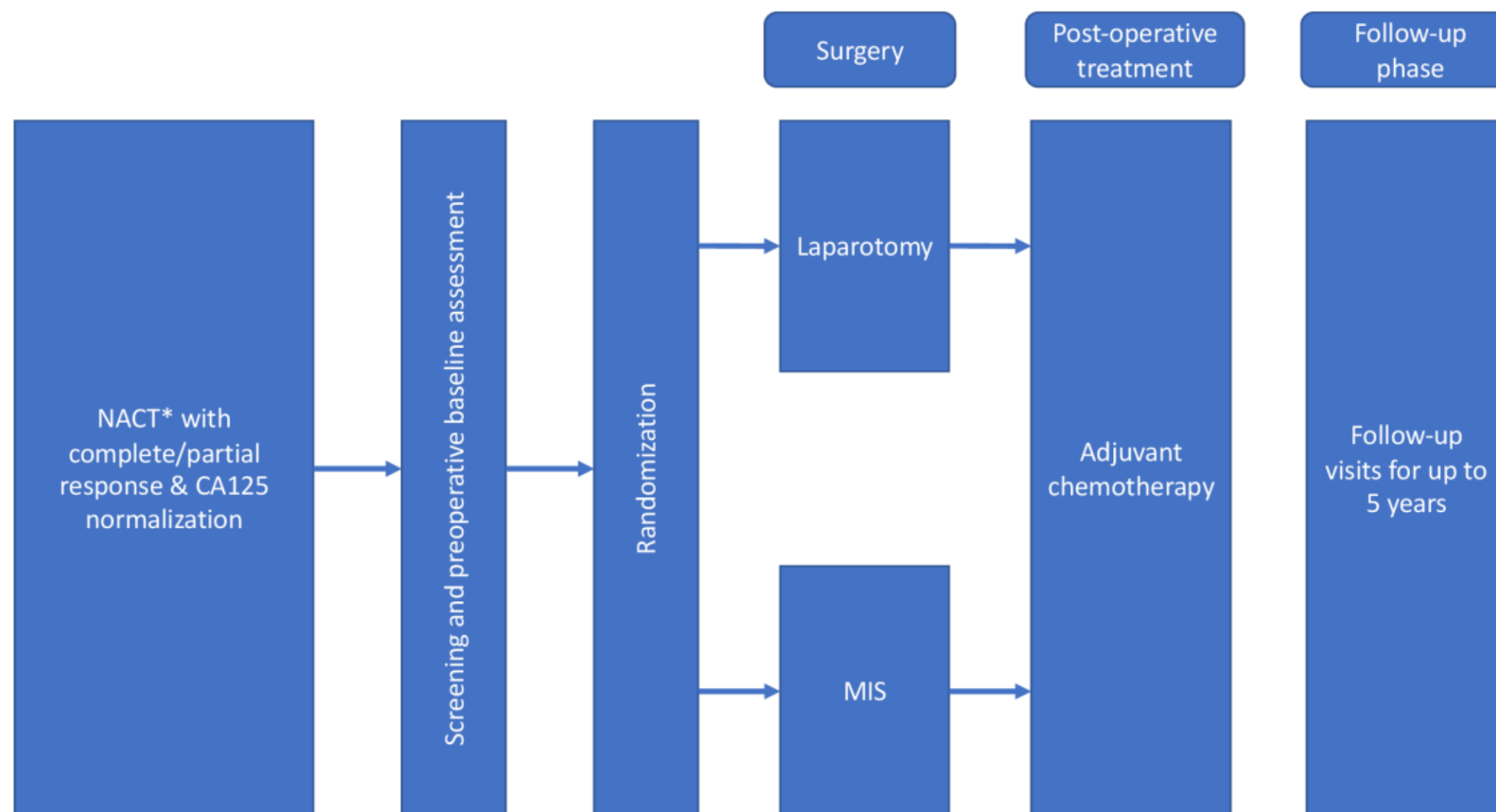


Figure 1. Study scheme. NACT: neoadjuvant chemotherapy; *Chemotherapy regimen will be documented before randomization.

Laparoscopy and ovarian cancer; How far can we go?

Take-home messages

- ✓ **The oncologic safety of laparoscopy in ovarian cancer is uncertain**
 - ✓ *Highly controversial* in Advanced stage (No RCT level A)
 - ✓ Uncertain in early stage (No RCT level A)
- ✓ **A good tool to select patients eligible for complete debulking**

THANK YOU



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