

PDS versus IDS

criteri per la scelta

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25 Giugno 2026

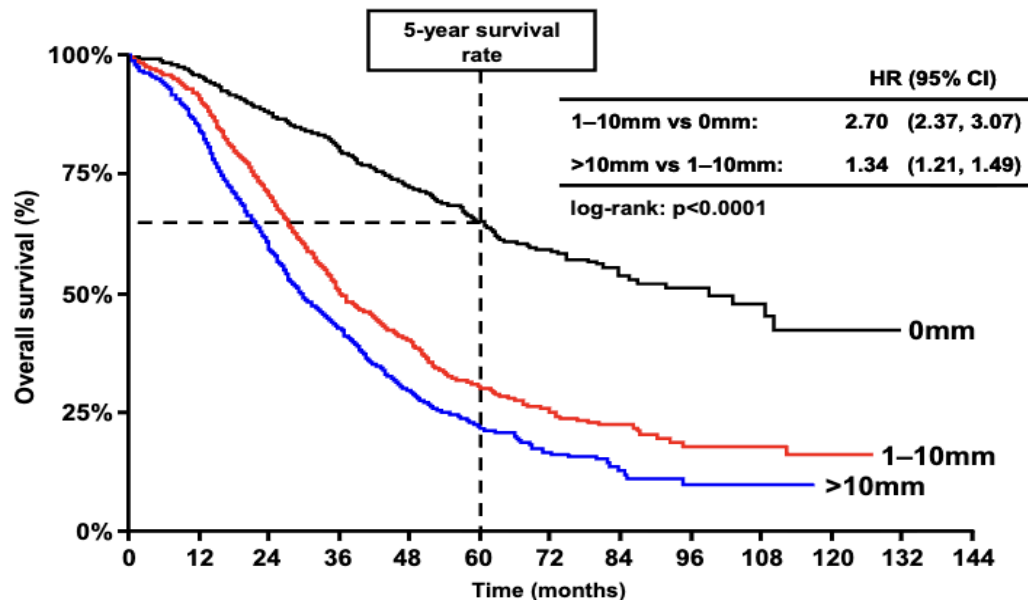
ASO S. Croce e Carle - Cuneo

La chirurgia nell'AOC, perché?

- L'obiettivo è prolungare la sopravvivenza mantenendo una buona qualità della vita.
- RT0 è associato ad outcome favorevoli.
- Il timing ottimale della chirurgia in pazienti con malattia considerata resecabile resta controverso.

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



Timing of surgery in advanced ovarian cancer. What is the published evidence?



Pre-TRUST

- **EORTC 55971** (Vergote et al. 2011)

NACT is not
inferior



The NEW ENGLAND
JOURNAL of MEDICINE

- **CHORUS** (Kehoe et al. 2015)

NACT is not
inferior

THE LANCET

- **SCORPION** (Fagotti et al. 2016)

Superiority NACT
not confirmed



- **JCOG0602** (Onda et al. Eur J Cancer 2016)

Non-inferiority NACT
not confirmed

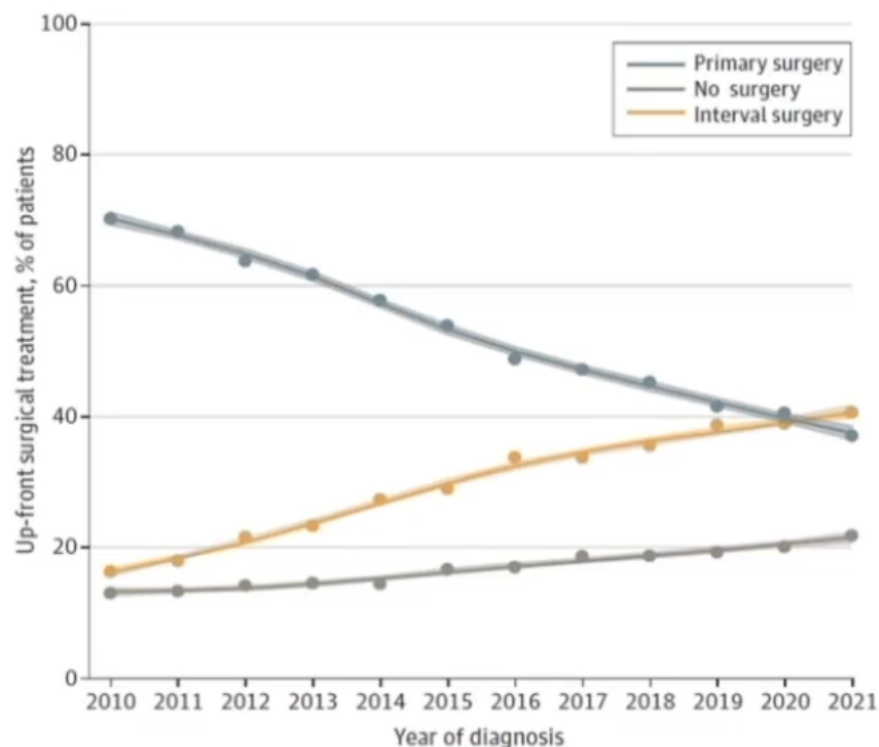




Research Letter | Obstetrics and Gynecology

Utilization of Primary Cytoreductive Surgery for Advanced-Stage Ovarian Cancer

Alexandra Bercow, MD; Taylor Stewart, MD; Amy J. Bregar, MD; Allison Gockley, MD; Varvara Mazina, MD; J. Alejandro Rauh-Hain, MD, MPH;
Alexander Melamed, MD, MPH



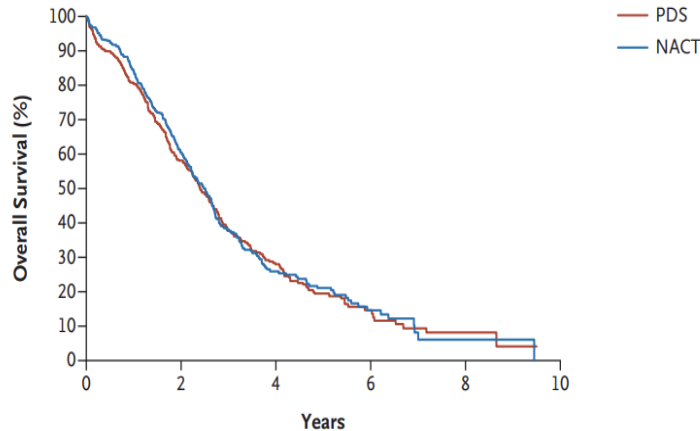
EORTC 55971(Vergote et al. NEJM 2011)

NACT Non-inferiority study



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A Intention-to-Treat Analysis



	No. of Events		No. of Patients at Risk			
Primary Debulking Surgery (PDS)	253	336	189	62	14	2
Neoadjuvant Chemotherapy (NACT)	245	334	195	46	13	2

➤ 670 pts

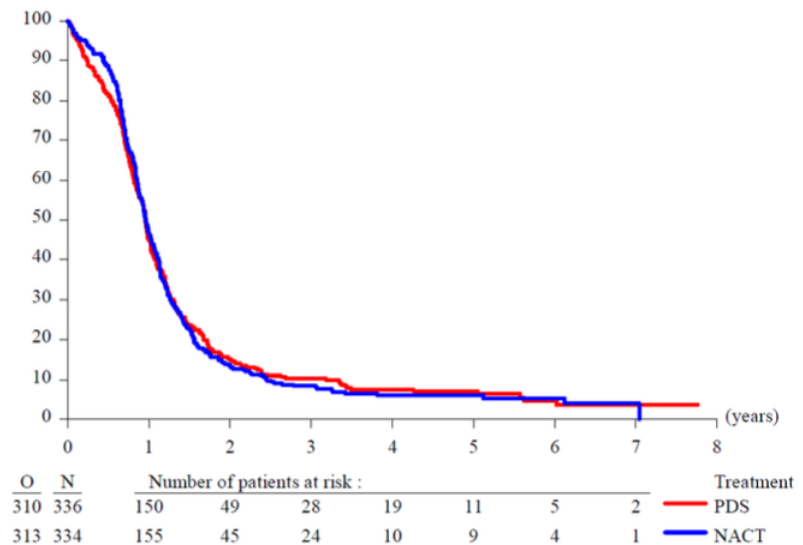
➤ FIGO IIIC/IVA/IVB

ORIGINAL ARTICLE

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

Ignace Vergote, M.D., Ph.D., Claes G. Tropé, M.D., Ph.D.,
Frédéric Amant, M.D., Ph.D., Gunnar B. Kristensen, M.D., Ph.D.,
Tom Ehlen, M.D., Nick Johnson, M.D., René H.M. Verheijen, M.D., Ph.D.,
Maria E.L. van der Burg, M.D., Ph.D., Angel J. Lacave, M.D.,
Pierluigi Benedetti Panici, M.D., Ph.D., Gemma G. Kenter, M.D., Ph.D.,
Antonio Casado, M.D., Cesar Mendiola, M.D., Ph.D., Corneel Coens, M.Sc.,
Leen Verleye, M.D., Gavin C.E. Stuart, M.D., Sergio Pecorelli, M.D., Ph.D.,
and Nick S. Reed, M.D., for the European Organization for Research and
Treatment of Cancer—Gynaecological Cancer Group and the NCIC Clinical Trials
Group* — a Gynecologic Cancer Intergroup Collaboration

Progression-free survival



➤ Median PFS

PCS 12 months - ICS 12 months

➤ Median OS

PCS 29 months - ICS 30 months

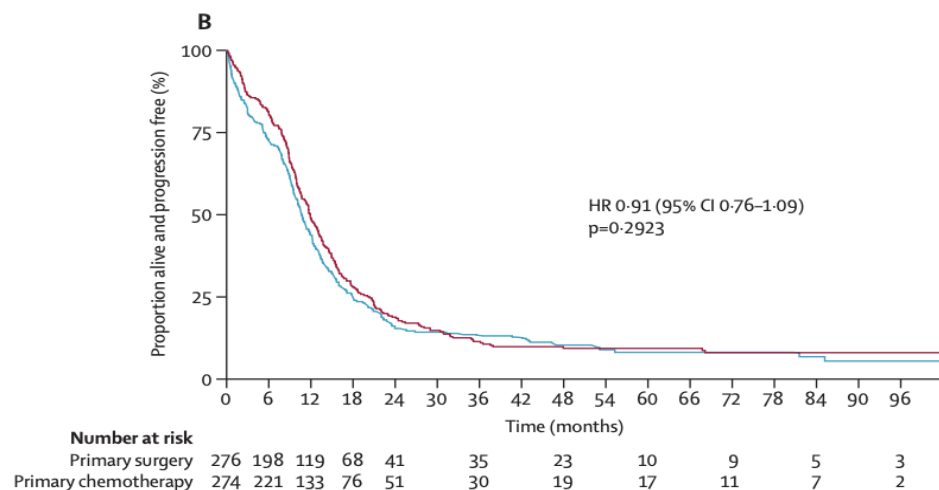
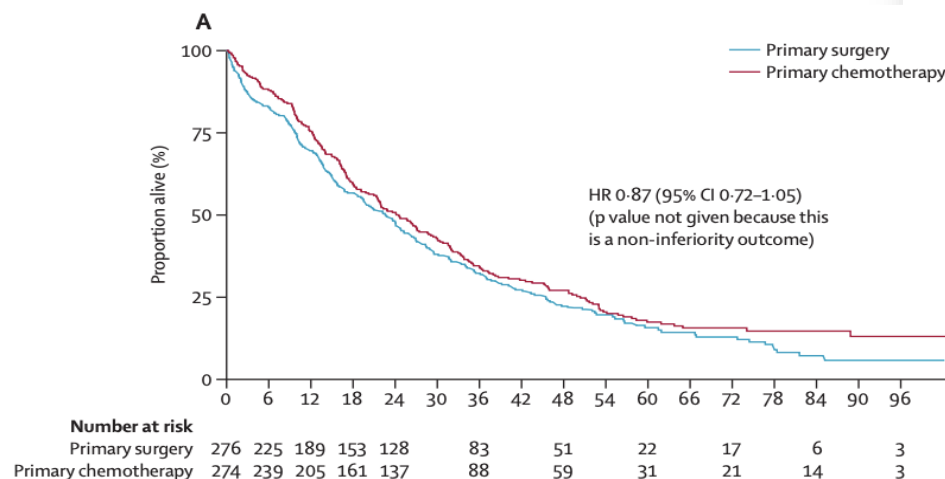
CHORUS -Kehoe et al. Lancet 2016

NACT Non-inferiority study

THE LANCET

Primary chemotherapy versus primary surgery for newly diagnosed advanced ovarian cancer (CHORUS): an open-label, randomised, controlled, non-inferiority trial

Sean Kehoe, Jane Hook, Matthew Nankivell, Gordon C Jayson, Henry Kitcheener, Tito Lopes, David Luesley, Timothy Perren, Selina Bannoo, Monica Mascarenhas, Stephen Dobbs, Sharadah Essapen, Jeremy Twigg, Jonathan Herod, Glenn McCluggage, Mahesh Parmar, Ann-Marie Swart



- 552 pts
- FIGO IIIA/IIIB/IIIC/IVA/IVB
- Median PFS
PCS 10.7 months - ICS 12 months
- Median OS
PCS 22.6 months - ICS 24.1 months



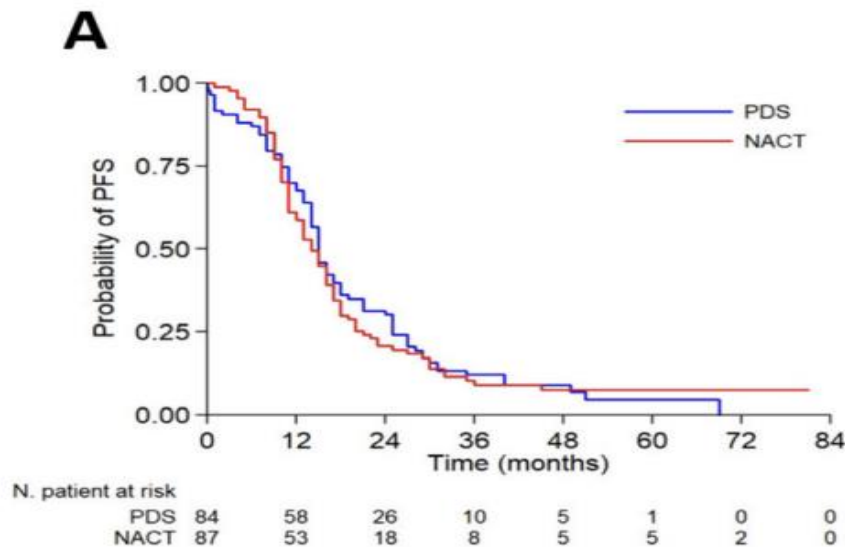
SCORPION (Fagotti et al. 2016)

Superiority NACT **not confirmed**

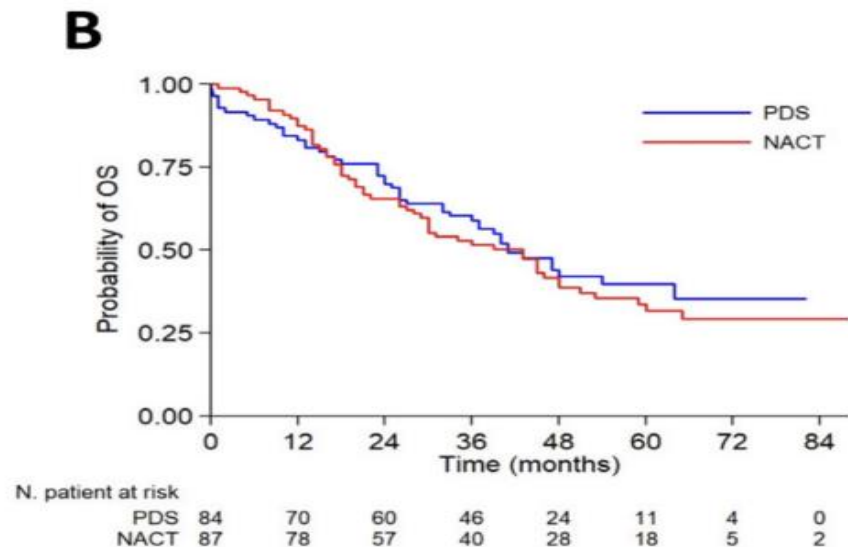
IJGC INTERNATIONAL JOURNAL OF
GYNECOLOGICAL
CANCER

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

[Anna Fagotti](#), [Giuseppe Vizzielli](#), [Gabriella Ferrandina](#), [Francesco Fanfani](#), [Valerio Gallotta](#), [Vito Chiantera](#), [Barbara Costantini](#), [Pasquale Alessandro Margariti](#), [Salvatore Gueli Alletti](#), [Francesco Cosentino](#), [Lucia Tortorella](#), [Giovanni Scambia](#)



HR 1.05 (95% CI, 0.77 to 1.44); log rank P= .733)



HR 1.12 (95% CI, 0.76 to 1.65); log rank P= .556)

- 171 pts single center
- FIGO IIIC/IVA/IVB
- «high tumor load» by laparoscopic detection

- Median PFS
PCS: 15 months - ICS: 14 months
- Median OS
PCS: 41 months - ICS: 43 months

JCOG0602 - Onda et al. 2020

NACT Non inferiority **not confirmed**

EJC

EUROPEAN JOURNAL OF CANCER

European Journal of Cancer 130 (2020) 114–125



Available online at www.sciencedirect.com

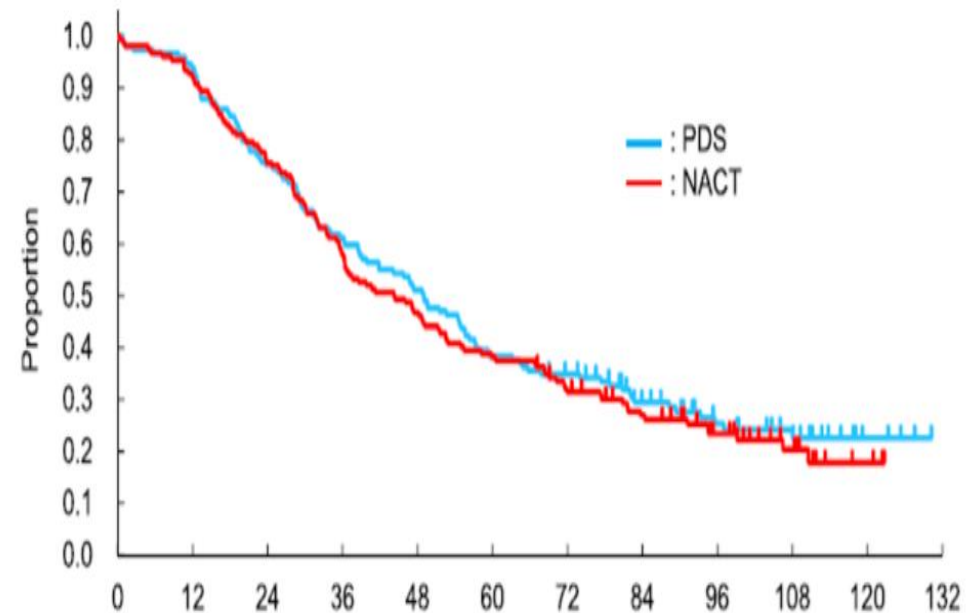
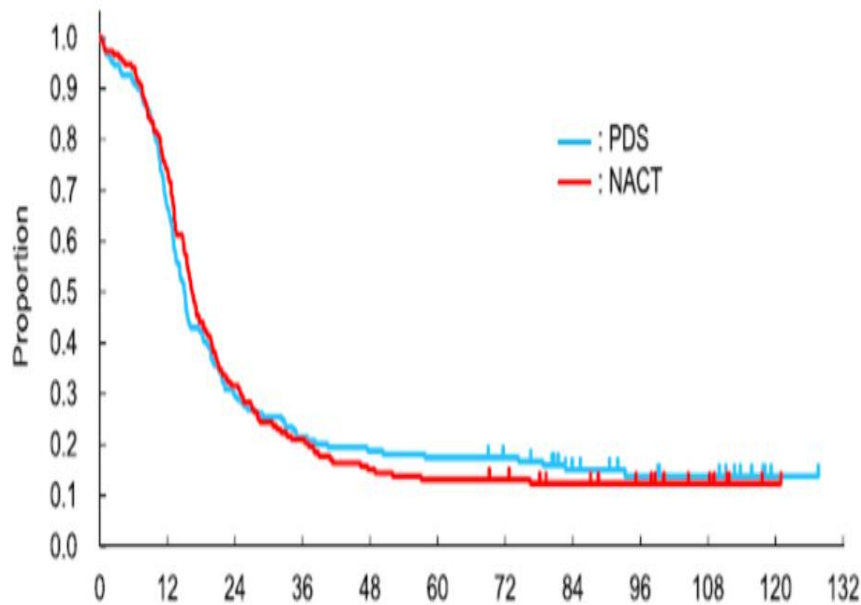
ScienceDirect

journal homepage: www.ejccancer.com



Clinical Trial

Comparison of survival between primary debulking surgery and neoadjuvant chemotherapy for stage III/IV ovarian, tubal and peritoneal cancers in phase III randomised trial



➤ 301 pts

➤ FIGO III/IV

➤ Median PFS

PCS: 15.1 months - ICS: 16.4 months

➤ Median OS

PCS: 49 months - ICS: 44.3 months

PUBLISHED EVIDENCE

		EORTC	CHORUS	SCORPION	JCOG0602
No of pts		670 pts	550 pts	171 pts	301 pts
Median age		62y	65y	55y	60y
FIGO Stage IV	PCS	23%	25%	15%	32%
	ICS	24%	25%	9%	30%
Operative time	PCS	180 min	120 min	451 min	240 min
	ICS	165 min	120 min	253 min	302 min
Complete gross resection	PCS	19%	17%	48%	31%
	ICS	51%	33%	77%	64%
PFS	PCS	12 months	10.7 months	15 months	15.1 months
	ICS	12 months	12 months	14 months	16.4 months
OS	PCS	29 months	22.6 months	41 months	49 months
	ICS	30 months	24.1 months	43 months	44.3 months

Vergote et al. N Engl J Med 2011; Kehoe et al. Lancet 2016; Fagotti et al. Int J Gynecol Cancer 2020; Onda et al. Eur J Cancer 2020

Can we answer the question of optimal timing in this patient population?



Red: percentage of pts with successful surgery in PCS in EORTC/CHORUS study

Green: proposed minimal percentage of pts with successful surgery in PCS to allow valid evaluation of surgical impact

TRUST: Trial of Radical Upfront Surgical Therapy in Advanced Ovarian Cancer (ENGOT ov33 / AGO-OVAR OP.7)

Sven Mahner¹, Florian Heitz², Sahar Salehi³, Alexander Reuss⁴, Frederic Guyon⁵, Andreas du Bois², Philipp Harter²,
Christina Fotopoulou⁶, Denis Querleu⁷, Berit Jul Mosgard⁸, Bernhard Krämer⁹, Francesco Raspagliesi¹⁰, Björn Lampe¹¹,
Alexander Burges¹, Barbara Schmalfeldt¹², Pauline Wimberger¹³, Holger Bronger¹⁴, Dennis Chi¹⁵, Jalid Sehouli¹⁶, Giovanni Aletti¹⁷
and the TRUST investigators

¹AGO Study Group & Department of Obstetrics and Gynecology, LMU University Hospital, Munich, Germany; ²AGO Study Group & Department for Gynecology and Gynecologic Oncology; Kliniken Essen Mitte, Essen, Germany; ³NSGO & Department of Women's and Children's Health, Karolinska Institutet and Department of Pelvic Cancer, Theme Cancer, Karolinska University Hospital, Stockholm, Sweden; ⁴AGO Study Group & KKS Marburg, Marburg, Germany; ⁵GINECO & Institut Bergonié Bordeaux, Bordeaux, France; ⁶AGO Study Group & Division of Cancer, Department of Surgery and Cancer, Imperial College London, London, UK; ⁷GINECO & UOC ginecologia oncologica, dipartimento di scienze della donna, del bambino e di sanità pubblica, Fondazione Policlinico Universitario A. Gemelli, IRCCS, Rome, Italy; ⁸NSGO & Copenhagen University Hospital Rigshospitalet, Copenhagen, Denmark; ⁹AGO Study Group & University Hospital Tuebingen, Tuebingen, Germany; ¹⁰MaNGO & Istituto Tumori di Milano, Milano, Italy; ¹¹AGO Study Group & Kaiserswerther Diakonie, Duesseldorf, current address: Staedtische Kliniken, Moenchengladbach, Germany; ¹²AGO Study Group & University Medical Center Hamburg Eppendorf, Hamburg, Germany; ¹³AGO Study Group & Dresden University Hospital, Dresden, Germany; ¹⁴AGO Study Group & TUM School of Medicine and Health, Technical University of Munich (TUM), Munich, Germany; ¹⁵AGO Study Group & MSKCC, New York, USA; ¹⁶AGO Study Group & Charite University Hospital, Berlin, Germany; ¹⁷MaNGO & Istituto Europeo di Oncologia, IRCCS, Milano, Italy

TRUST Rationale

TRUST was designed to evaluate the optimal timing of maximal effort cytoreductive surgery in patients with advanced ovarian cancer

- considered resectable
- fit enough to tolerate radical surgery
- treated in gynecologic cancer centers with defined surgical quality assurance criteria.

TRUST Quality Assurance

- Centers were required to obtain accreditation for the trial including onsite quality assurance review.¹
- Quality criteria were based on ESGO certification² and extended for TRUST including
 - evaluation of cytoreductive surgery in the operating room
 - assessment of surgical proficiency and infrastructure
 - complete resection rates ($\geq 50\%$ in upfront surgery for FIGO IIIB-IVB pts)
 - surgical volume (≥ 36 cytoreductive surgeries/year).

¹Reuss et al. Int J Gynecol Cancer 2019, ²Fotopoulou et al. Int J Gynecol Cancer 2020
ESGO: European Society of Gynecologic Oncology

TRUST Study Design



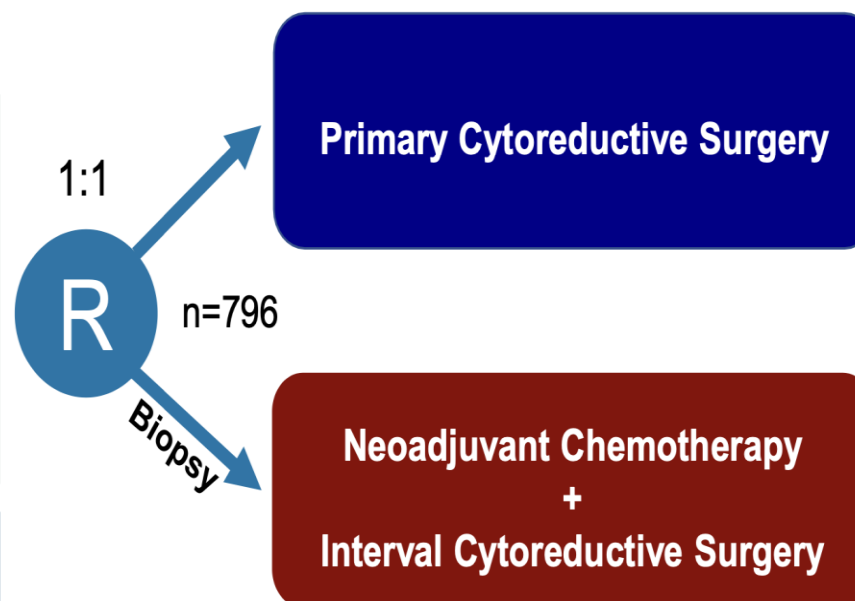
Main Inclusion Criteria

- Epithelial ovarian, fallopian tube or peritoneal cancer
 - FIGO stage IIIB/C, IVA/B
 - Considered resectable
- Fit enough to tolerate radical surgery

Stratification factors

- Center
- Age-ECOG-combination
ECOG0 and age ≤65y vs.
ECOG>0 or age >65y

Qualification process for participating centers to ensure surgical quality



Primary endpoint

- Overall survival

Key secondary endpoints

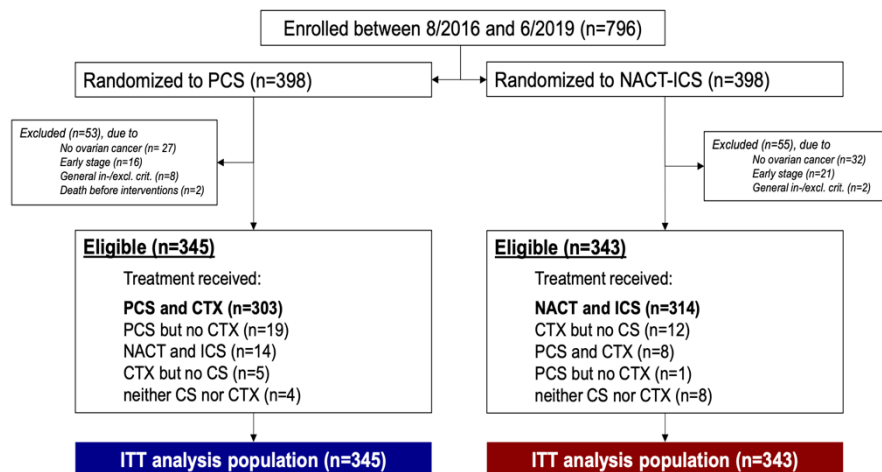
- Progression-free survival
- Complete resection rate
- Surgical procedures
- Surgical morbidity
- Quality of life

Predefined exploratory and translational endpoints

Recommended systemic treatment:

- Carboplatin AUC5, Paclitaxel 175mg/m² q3w
- Bevacizumab 15mg/kg q3w as indicated
- PARPi as indicated
- Study participation or any other treatment as long as applicable for both study arms

TRUST Patient Disposition



CS: Cytoreductive surgery; CTX: Chemotherapy; ITT: Intention-to-treat

TRUST Baseline Characteristics



	PCS (n=345)	NACT-ICS (n=343)	Total (n=688)
Median age, years (range)	63 (34-83)	64 (32-83)	63.5 (32-83)
Median BMI, kg/m ² (range)	24.6 (15.6-50.1)	24.9 (15.9-47.2)	24.8 (15.6-50.1)
ECOG, n (%)			
0	267 (77%)	263 (77%)	530 (77%)
1	78 (23%)	80 (23%)	158 (23%)
Confirmed FIGO stage (highest), n (%)			
IIIB	30 (8.7%)	18 (5.3%)	48 (7.0%)
IIIC	203 (59%)	217 (63%)	420 (61%)
IVA	31 (9.0%)	35 (10%)	66 (9.6%)
IVB	79 (23%)	68 (20%)	147 (21%)
Not reported	2 (0.6%)	5 (1.5%)	7 (1.0%)
Histological subtype, n (%)			
High grade serous	320 (93%)	312 (91%)	632 (92%)
Low grade serous	18 (5.2%)	23 (6.7%)	41 (6.0%)
Other*	4 (1.2%)	4 (1.2%)	8 (1.2%)
Not reported	3 (0.9%)	4 (1.2%)	7 (1.0%)

*Other: PCS: 3 endometrioid, 1 seromucinous; NACT-ICS: 2 clearcell, 1 seromucinous, 1 mucinous.

TRUST Results: Surgical Effort and Procedures



Procedure, n* (%)	PCS (n=331)	NACT-ICS (n=328)
Median duration of surgery, minutes (IQR)	331 (253-432)	284 (213-360)
Median blood loss, mL (IQR)	500 (300-800)	400 (200-600)
Mean number of RBC units transfused (SD)	0.9 (1.5)	0.6 (1.1)
Upper abdominal procedures	263 (79%)	221 (67%)
Splenectomy	91 (27%)	42 (13%)
Intestinal resections	224 (68%)	123 (38%)
Colorectal resection	187 (56%)	95 (29%)
Large bowel resection	135 (41%)	74 (23%)
Small bowel resection	70 (21%)	33 (10%)
Stoma formation	66 (20%)	27 (8.2%)
Lymph node dissection	197 (60%)	156 (48%)
Pelvic nodes	166 (50%)	135 (41%)
Paraortic nodes	172 (52%)	134 (41%)
Chest procedures	63 (19%)	35 (11%)
Pericardiophrenic nodes	33 (10%)	15 (4.6%)
Open assessment of the pleura	47 (14%)	23 (7.0%)
Pleurectomy	15 (4.5%)	5 (1.5%)

TRUST Results: Surgical Outcome



	PCS (n=345)	NACT-ICS (n=343)	Total (n=688)
Residual disease, n (%)			
complete gross resection	235 (68%)	271 (79%)	506 (74%)
macroscopic residual disease	99 (29%)	49 (14%)	148 (22%)
0.1-0.5 cm	39 (11%)	29 (8.5%)	68 (9.9%)
0.6-1 cm	25 (7.3%)	7 (2.0%)	32 (4.7%)
> 1 cm	35 (10%)	13 (3.8%)	48 (7.0%)
not operated / not reported	11 (3.2%)	23 (6.7%)	34 (4.9%)
Documented complete resections in operated patients, n (%)	235/334 (70%)	271/320 (85%)	506/654 (77%)

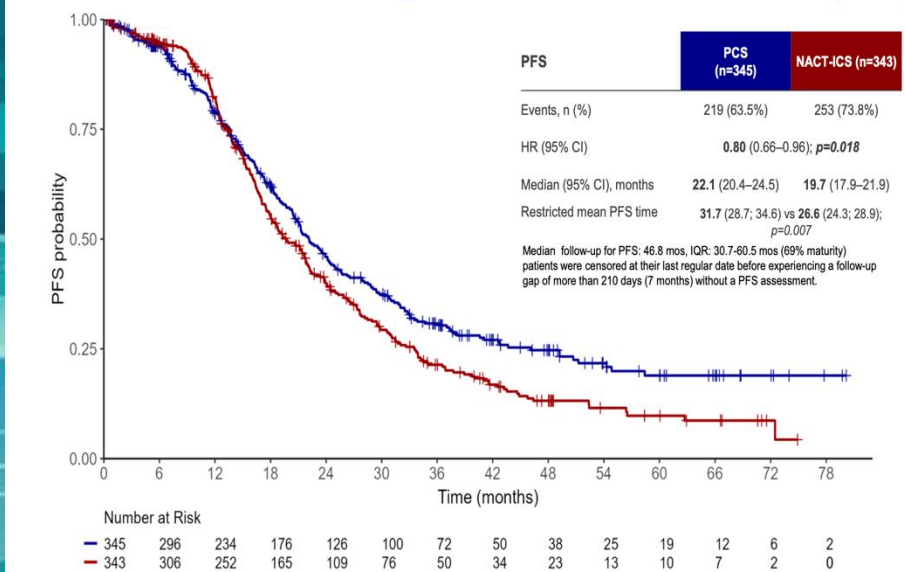
TRUST results – complete resection at PCS



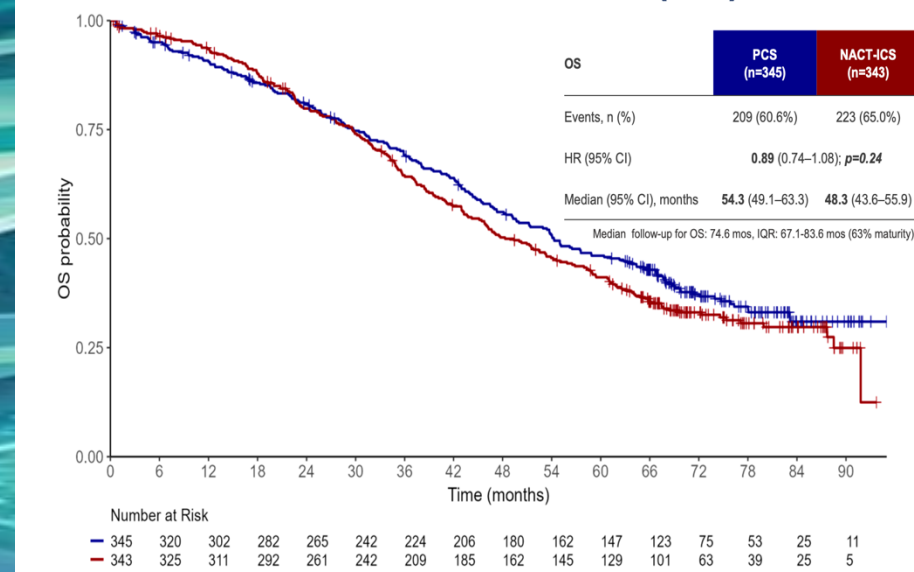
Green: minimal percentage of pts with successful surgery in PCS aimed for in the TRUST design

Blue: additional percentage achieved in TRUST

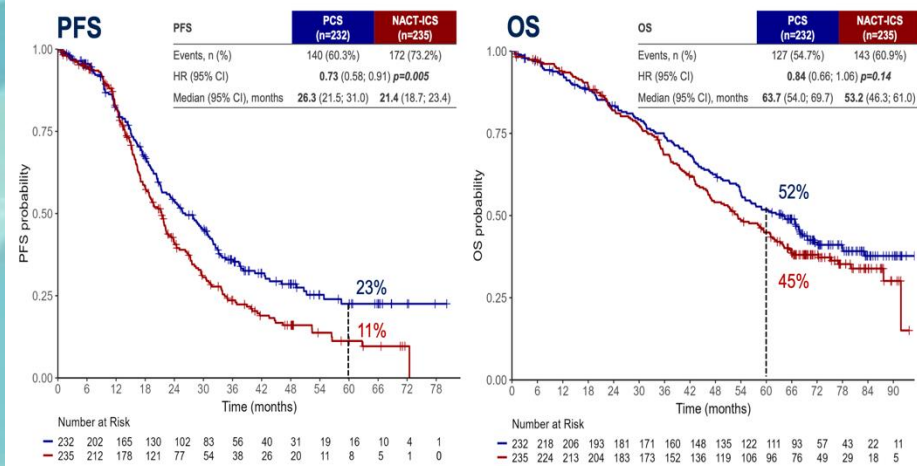
TRUST Results: Progression-free Survival (ITT)



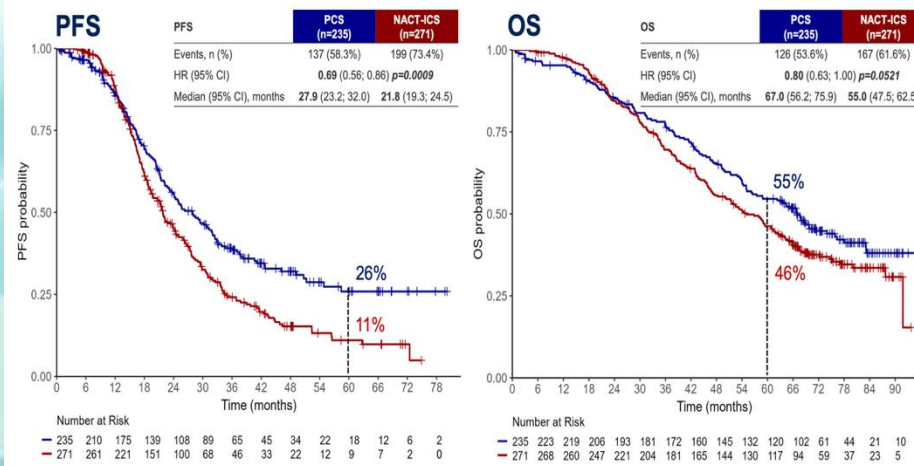
TRUST Results: Overall Survival (ITT)



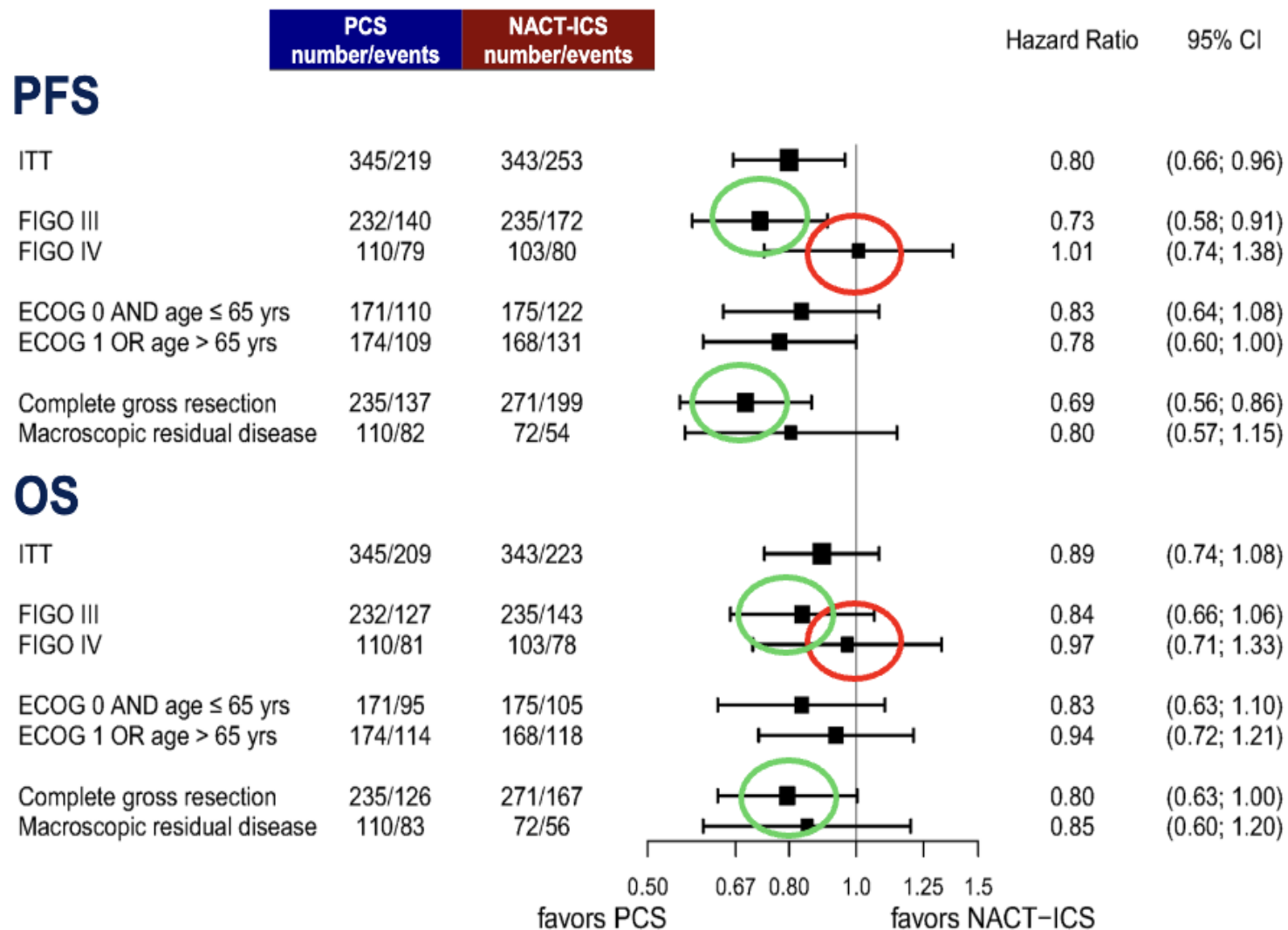
TRUST Results: Prespecified Exploratory Subgroup Analysis AGO FIGO Stage III



TRUST Results: Prespecified Exploratory Subgroup Analysis AGO Complete Gross Resection in All FIGO Stages



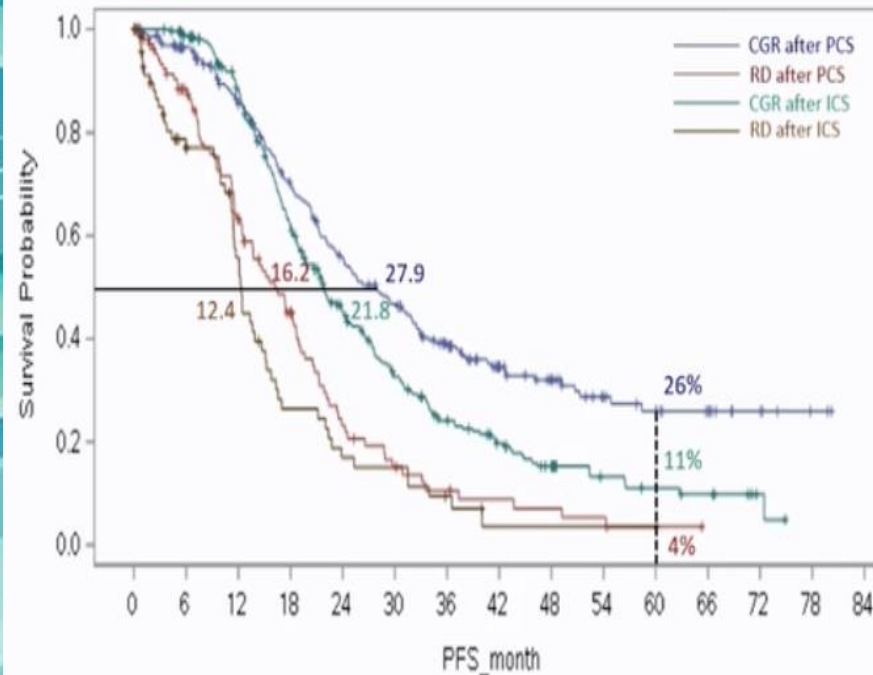
TRUST Results: Treatment Effects According to Subgroups



TRUST Results: Prespecified Exploratory Subgroup Analysis by Residual Disease

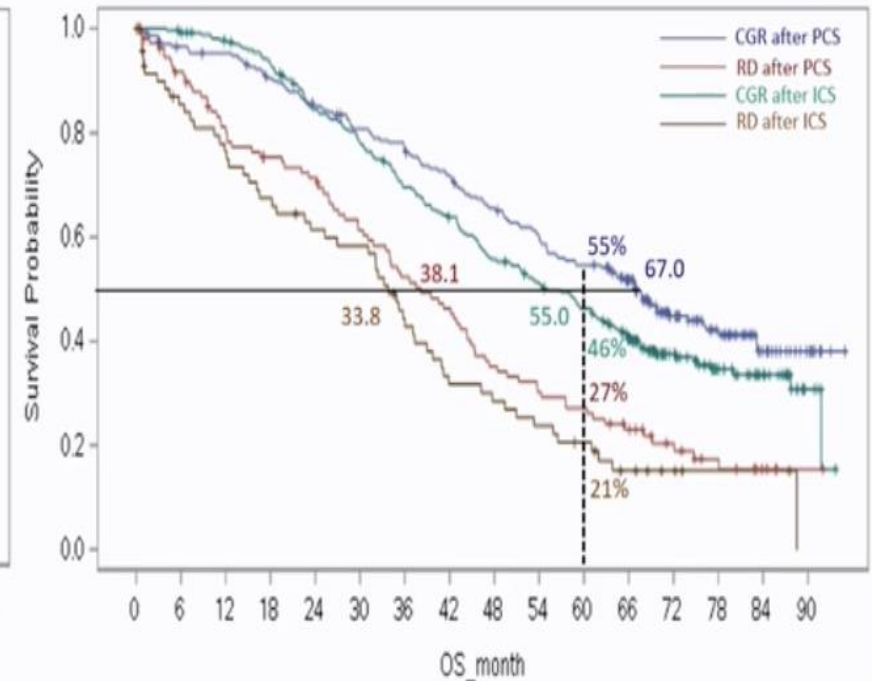


PFS



1	235	210	175	139	108	89	65	45	34	22	18	12	6	2	0
2	110	86	59	37	18	11	7	5	4	3	1	0			
3	271	261	221	151	100	68	46	33	22	12	9	7	2	0	
4	72	45	31	14	9	8	4	1	1	1	1	0			

OS



1	235	223	219	206	193	181	172	160	145	132	120	102	61	44	21	10
2	110	97	83	76	72	61	52	46	35	30	27	21	14	9	4	1
3	271	268	260	247	221	204	181	165	144	130	117	94	59	37	23	5
4	72	57	51	45	40	38	28	20	18	15	12	7	4	2	2	0

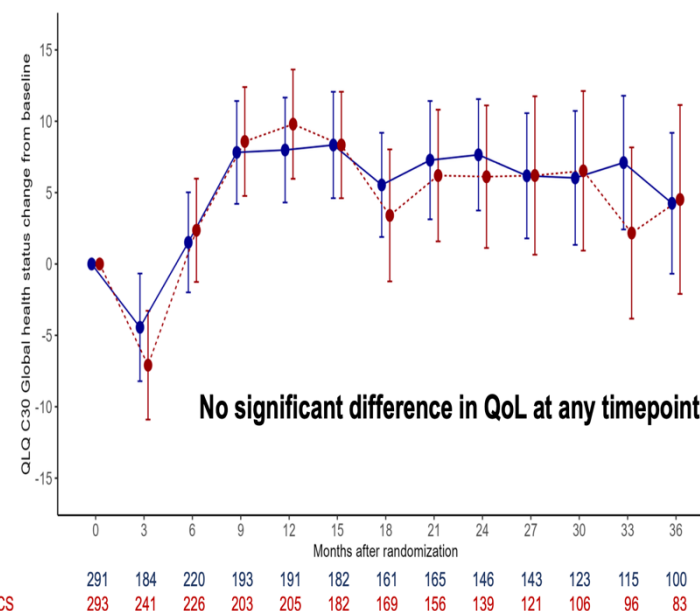
TRUST Results: Surgical Morbidity



Complication, n* (%)	PCS (n=331)	NACT-ICS (n=328)
Any complication	60 (18%)	39 (12%)
>10 packed red blood cells within 24h	0	0
30-day post-op mortality	3 (0.9%)	2 (0.6%)
Re-laparotomy	21 (6.3%)	12 (3.7%)
Wound breakdown	11 (3.3%)	11 (3.4%)
Deep venous thrombosis	3 (0.9%)	1 (0.3%)
Pulmonary embolism	5 (1.5%)	3 (0.9%)
Sepsis	6 (1.8%)	4 (1.2%)
Anastomotic leak / fistula	11 (3.3%)	7 (2.1%)
Intraabdominal abscess	2 (0.6%)	1 (0.3%)
Nerve damage	1 (0.3%)	3 (0.9%)
Liver/renal failure	6 (1.8%)	2 (0.6%)
Serious cardiovascular event	8 (2.4%)	1 (0.3%)
Readmittance b/o any other complication	11 (3.3%)	5 (1.5%)

* patients with documented cytoreductive surgery; analyzed as treated; complications that occurred within 28 days of debulking surgery

TRUST Results: Overall Quality of Life



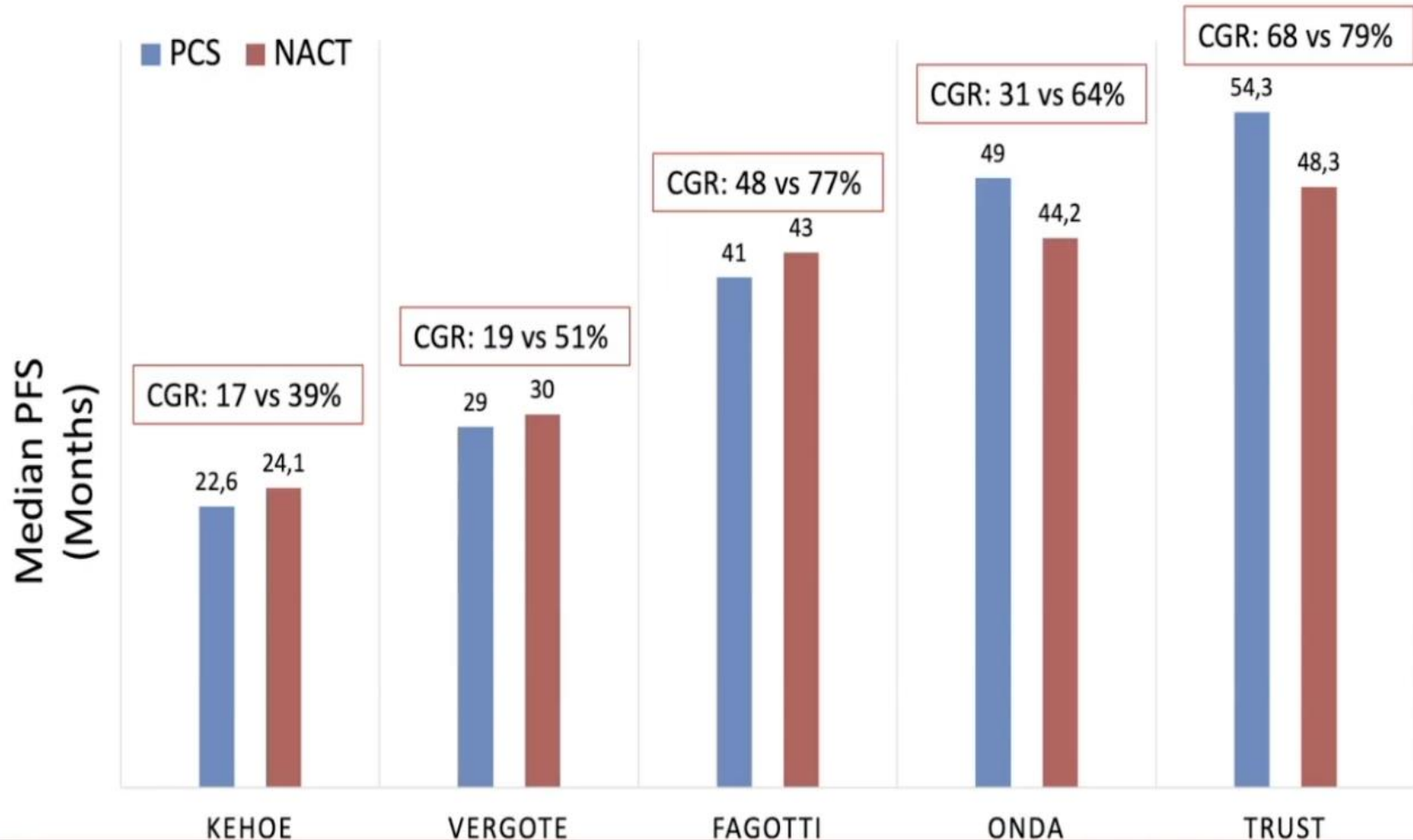
TRUST and EORTC/CHORUS in comparison

		TRUST	EORTC	CHORUS	SCORPION	JCOG0602
No of pts		688 pts	670 pts	550 pts	171 pts	301 pts
Median age		64y	62y	65y	55y	60y
FIGO Stage IV	PCS	32%	23%	25%	15%	32%
	ICS	30%	24%	25%	9%	30%
Duration of surgery	PCS	331 min	180 min	120 min	451 min	240 min
	ICS	284 min	165 min	120 min	253 min	302 min
Complete gross resection	PCS	70%	19%	17%	48%	31%
	ICS	84%	51%	39%	77%	64%
PFS	PCS	31.7 months*	12 months	10.7 months	15 months	15.1 months
	ICS	26.6 months*	12 months	12 months	14 months	16.4 months
OS	PCS	54.3 months	29 months	22.6 months	41 months	49 months
	ICS	48.3 months	30 months	24.1 months	43 months	44.3 months

*Restricted mean PFS time

Vergote et al. N Engl J Med 2011; Kehoe et al. Lancet 2016; Fagotti et al. Int J Gynecol Cancer 2020; Onda et al. Eur J Cancer 2020

Good Surgery (whenever) is Good for Patients



Trust Trial Summary

One key question:

What is the **optimal timing** of maximal-effort cytoreductive surgery in **fit patients** with AOC **considered resectable** and treated in **high quality centres**?

Designed in a different biological era:

BRCA/HRD status was not a stratification factor – the study predates SOLO-1, PRIMA, PAOLA-1 and ATHENA.

NACT-ICS improved surgical feasibility:

Higher complete resection rates (85% vs 70%) without clinically meaningful differences in complication rates (18% PCS vs 12% NACT-ICS).

Primary endpoint (OS) not met – but the signal matters:

- First randomized phase III trial showing **median PFS advantage for PCS vs ICS**.
- **Complete gross resection** remains the key driver of benefit across **ALL FIGO stages**
PFS HR 0.69 and OS HR 0.80.
- **Surgical quality assurance is not optional** – it is central to outcomes.

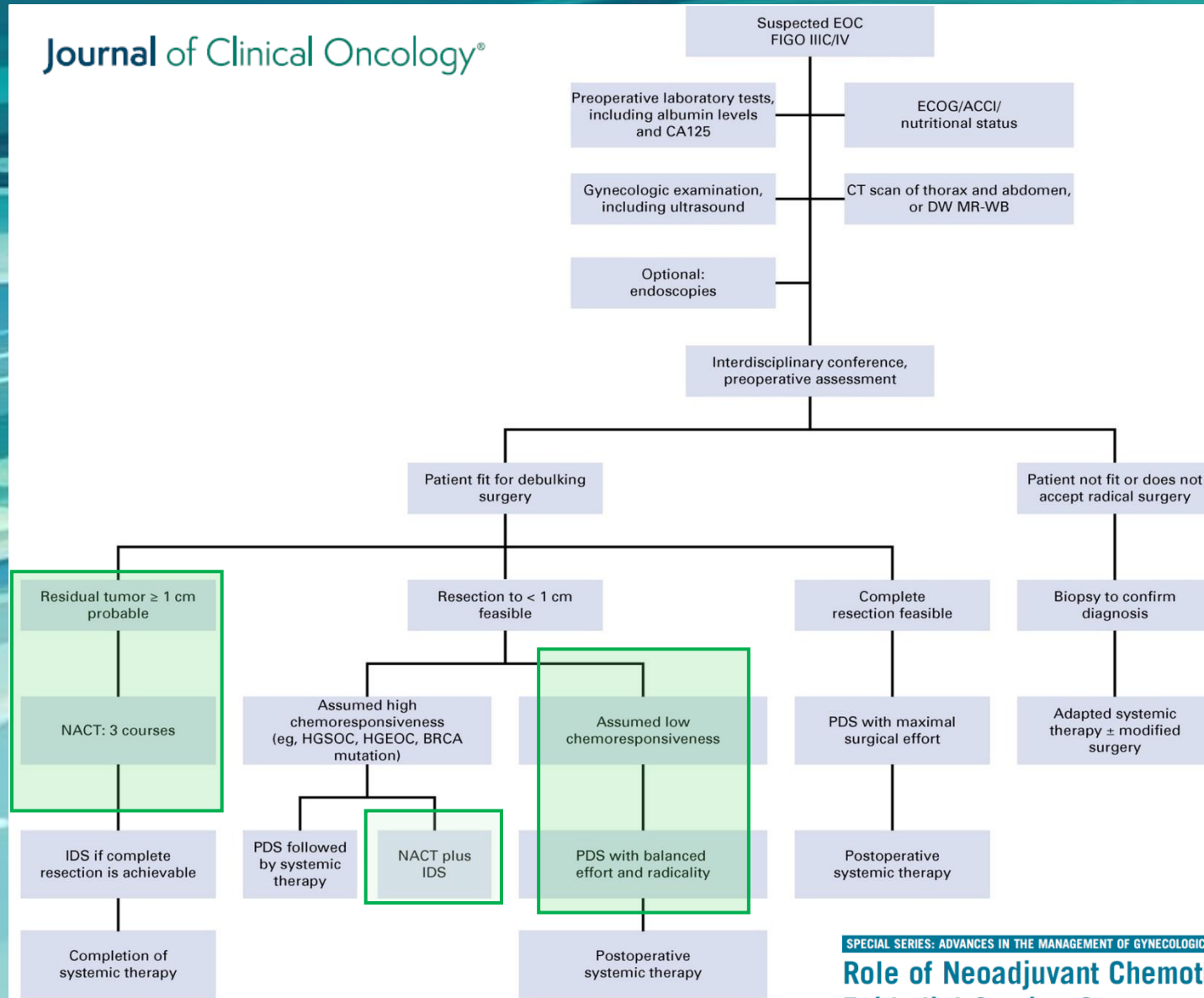
How does Trust Trial fit into the new **ESGO 2026 OC GL?**

Patients with a suspicion of primary or recurrent tubo-ovarian carcinoma should be referred to a centre specialized in a gynecologic oncology in a timely manner and be informed if the centre is certified or accredited either nationally or internationally, such as the ESGO accreditation [III,A].

- PCS is recommended for fit patients with potentially completely resectable disease and acceptable morbidity profile [I, A].
- NACT is the preferred option for patients with performance/nutritional status and/or when CR is not possible and/or when resectability is expected to be associated with High surgical morbidity [I, A]

Clinical algorithm for identifying pts for NACT

Journal of Clinical Oncology®



SPECIAL SERIES: ADVANCES IN THE MANAGEMENT OF GYNECOLOGIC CANCERS

Role of Neoadjuvant Chemotherapy in Advanced Epithelial Ovarian Cancer

Andreas du Bois, MD, PhD¹; Thais Baert, MD, PhD^{1,2}; and Ignace Vergote, MD, PhD^{2,3}

Indications for primary cytoreductive surgery in stage III disease

	Fit patient without significant comorbidities (ECOG 0-1) (regardless of age)	Poor performance/nutritional status (ECOG >1) (regardless of age)
High-grade tubo-ovarian carcinoma presumed to achieve complete cytoreduction	Green	Red
Clear cell or mucinous carcinoma presumed to achieve complete cytoreduction	Green	Red
Low-grade tubo-ovarian carcinomas with complete cytoreduction or with residual disease <1cm	Green	Red
High-grade tubo-ovarian carcinomas with expected macroscopic residual disease	Red	Red
Clear cell or mucinous carcinoma with expected residual disease ≤1cm	Yellow	Red
Unresectable tumour dissemination patterns leaving bulky (>1cm) residual disease (all histologies)	Red	Red
Ultraradical procedures required to achieve clearance ¹ (any histology)	Red	Red

¹ Example: Total gastrectomy, complete vaginectomy, extensive short bowel resections resulting in short bowel syndrome, pancreatic head resection/Whipples

Legend

- = primary cytoreductive surgery is the preferred option [I, A]; for low-grade tubo-carcinoma presumed to achieve complete cytoreduction [III, B]
- = both options can be considered [III, B]
- = NACT is the preferred option [I, A]



Indications for primary cytoreductive surgery in stage IV disease

	Fit patient without significant comorbidities (ECOG 0-1) (regardless of age)	Poor performance/nutritional status (ECOG >1) (regardless of age)
Stage IVA presumed to achieve complete cytoreduction (regardless of histology)	*	
Stage IVA with expected residual disease <1 cm (regardless of histology)		
Stage IVB due to inguinal lymph nodes, or trocar/umbilical metastases, presumed to achieve complete cytoreduction (regardless of histology)	*	
Stage IVB due to visceral/parenchymal metastases, presumed to achieve complete cytoreduction regardless of histology	*	
Stage IVB due to visceral/parenchymal metastases, with expected residual disease <1cm when low-grade histology	*	
Unresectable tumour dissemination patterns leaving bulky (>1cm) residual disease (all histologies)		
Ultraradical procedures required to achieve clearance ¹ (any histology)		

* Depending on the extent of disease/number of procedures needed to achieve complete gross resection

¹ Example: Total gastrectomy, complete vaginectomy, extensive short bowel resections resulting in short bowel syndrome, pancreatic head resection/Whipples, lung resection, apical pleura resection, high mediastinal LND

Legend



= both options can be considered [I, A]



= NACT is the preferred option [I, A]



Highlights

- The aim of surgery in advanced ovarian cancer is to prolong patients' remission and improve overall survival while sustaining quality of life.
- We now have evidence from a randomized phase III trial showing a significant benefit in PFS and a long-term benefit in OS for primary over interval surgery without compromising short- or long-term quality of life.
- Benefits in outcome are linked to high complete resection rates, reinforcing the value of radical upfront surgery in patients with resectable advanced ovarian cancer.
- The high rate of complete cytoreduction with low morbidity and mortality along with encouraging PFS and OS observed in the TRUST study emphasize the importance of surgical quality assurance programs and the treatment of patients in specialized centers.



Cura, Innovazione e Futuro in Ginecologia Oncologica



**GRAZIE PER
L'ATTENZIONE**

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ASO S. Croce e Carle - Cuneo

