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BIBLIOGRÁFICAS

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ASOCIACIÓN DE ONCÓLOGOS CLÍNICOS DE CÓRDOBA

Centro: Hospital Oncológico de Córdoba

Título: 1.“Randomized phase III study to evaluate the impact of secondary cytoreductive surgery in recurrent ovarian cancer: Final analysis of AGO DESKTOP III/ENGOT-ov20”.

2.”A randomized phase III trial of secondary cytoreductive surgery in later recurrent ovarian cancer: SOC1/SGOG-OV2".

Tissera, María Agustina

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Randomized controlled phase III study evaluating the impact of secondary cytoreductive surgery in recurrent ovarian cancer: the final analysis of AGO DESKTOP III / ENGOT ov20

Resultados preliminares en 2017

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P. Jensen (NSGO, Scandinavia), F. Selle (GINECO), F. Guyon (GINECO),
C. Pomel (GINECO), F. Lecuru (GINECO), R. Zang (SGOG, China),
E. Avall-Lundqvist (NSGO), JW Kim (KGOG, Korea), J. Ponce (GEICO, Spain),
F. Raspagliesi (MITO), S. Ghaem-Maghami (NCRI, UK),
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ENGOT
European Network of Gynaecological Oncological Trial groups

GYNECOLOGIC CANCER INTERGROUP

AGO Study Group

ANTECEDENTES:

DESKTOP I : Estudio retrospectivo, observacional basado en datos de Veinticinco instituciones miembros del Comité Ovárico AGO OC y OVAR, que recopilaron datos sobre 267 pacientes con cirugía citorreductora por cáncer epitelial de ovario invasivo recurrente realizado entre 2000-2003.

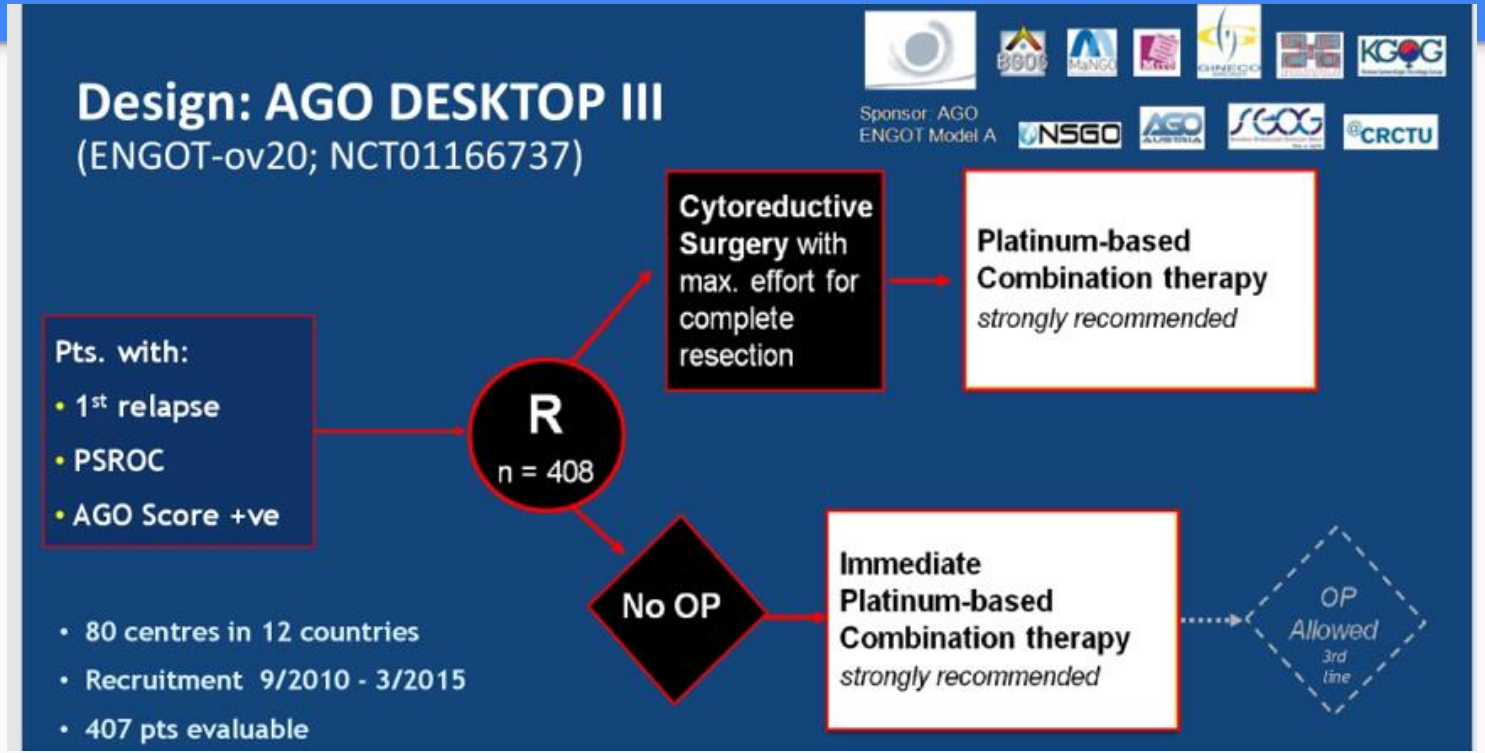
R*: Sólo la resección completa se asoció con una supervivencia prolongada en el cáncer de ovario recurrente*. Por lo cual surge la necesidad de identificar los criterios que debían cumplir las pacientes sometidas a rescate Qx, estableciendo el SCORE AGO.

SCORE:

- PS/ECOG 0
- Resección R0 en 1er intervención QX.
- Ascitis <500ml en recaída

DESKTOP II: se diseño para verificar esta hipótesis de forma prospectiva y multicentrica, se randomizaron 516 pacientes con recurrencia de CEO sensibles a platino en un periodo de 19 meses. Se aplico el score analizado a todas las pacientes, logrando una tasa de resección completa del 76% en aquellas con score favorable, lo que confirma la validez de esta puntuación con respecto a la predicción positiva de resecabilidad completa.

DESKTOP III


Design: AGO DESKTOP III
(ENGOT-ov20; NCT01166737)
Sponsor: AGO
ENGOT Model A
Pts. with:
• 1st relapse
• PSROC
• AGO Score +ve
R
n = 408
Cytoreductive Surgery with max. effort for complete resection
Platinum-based Combination therapy
strongly recommended
No OP
Immediate Platinum-based Combination therapy
strongly recommended
OP Allowed
3rd line
• 80 centres in 12 countries
• Recruitment 9/2010 - 3/2015
• 407 pts evaluable

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AGO DESKTOP III: Patients' Characteristics

(AGO–OVAR OP.4; ENGOT-ov20; NCT01166737)

	No surgery	Surgery	P-value
Pts. (n)	**201**	**206**	
Age (median, yrs)	62.2	60.8	0.37
Initial FIGO stage IIIB-IV	147 (73.1%)	155 (75.6%)	0.57
Histology G2/3 serous	155 (77.1%)	173 (84.0%)	0.08
Prior platinum	**199 (99.0%)**	**204 (99.0%)**	**0.98**
Prior taxane	180 (89.6%)	193 (93.7%)	0.13
Pt-free-Int. > 12 months	**151 (75.1%)**	**155 (75.2%)**	**0.99**
Median Pt-free-Interval	**18.7 months**	**21.1 months**	**0.40**

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PRESENTED BY: Andreas du Bois
AGO & KEM Essen, Germany

AGO DESKTOP III: Therapy after Randomisation

(AGO–OVAR OP.4; ENGOT-ov20; NCT01166737)

	No surgery	Surgery	P-value
Non compliant with random arm	8 (4.0%) with OP	14 (6.8%) w/o OP	0.21
	193	192	
Post-random chemotherapy:			
Platinum containing therapy	181 (90.0%)	183 (88.8%)	0.25
Non-platinum	9 (4.5%)	5 (2.4%)	
None / missing data	11 (5.5%)	18 (8.7%)	
Bevacizumab	47 (23.4%)	47 (22.8%)	0.89
PARP Inhibitors (or placebo in PARP-studies)	12 (6.0%)	8 (3.9%)	0.33

AGO DESKTOP III: Surgery arm

(AGO–OVAR OP.4; ENGOT-ov20; NCT01166737)

Duration of surgery (minutes; median / quartiles)	222 (150 – 300)
GI-tract resection	35.8%
Stoma diversion temporary / permanent	3.7% / 4.2%
Blood loss (ml; median / quartiles)	250 (50 – 500)
RBC transfusion	17.6%
post-OP fever > 38°C	4.8%
Antibiotics (mainly for urinary tract infections)	19.7%
Re-laparotomy rate	3.7%
30-/90- days mortality	0 / 1 pat. (0.5%)
Macroscopic complete resection rate	**74.2%**

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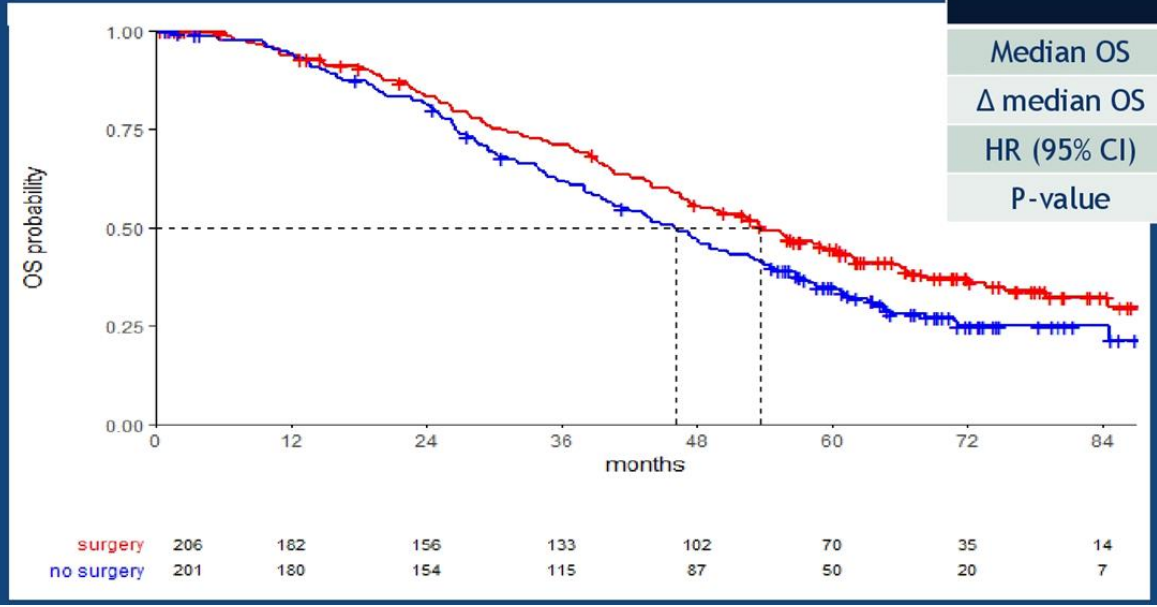
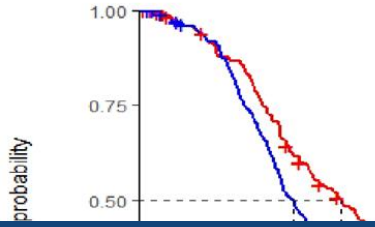
AGO DESKTOP III: Outcome 1 (OS, ITT population)

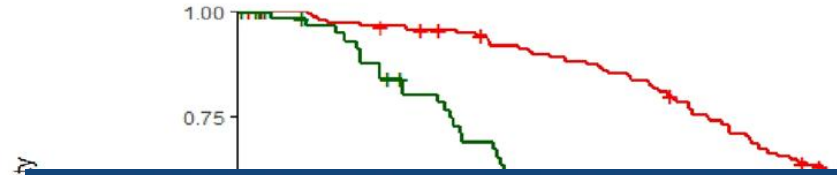
(AGO–OVAR OP.4; ENGOT-ov20; NCT01166737)



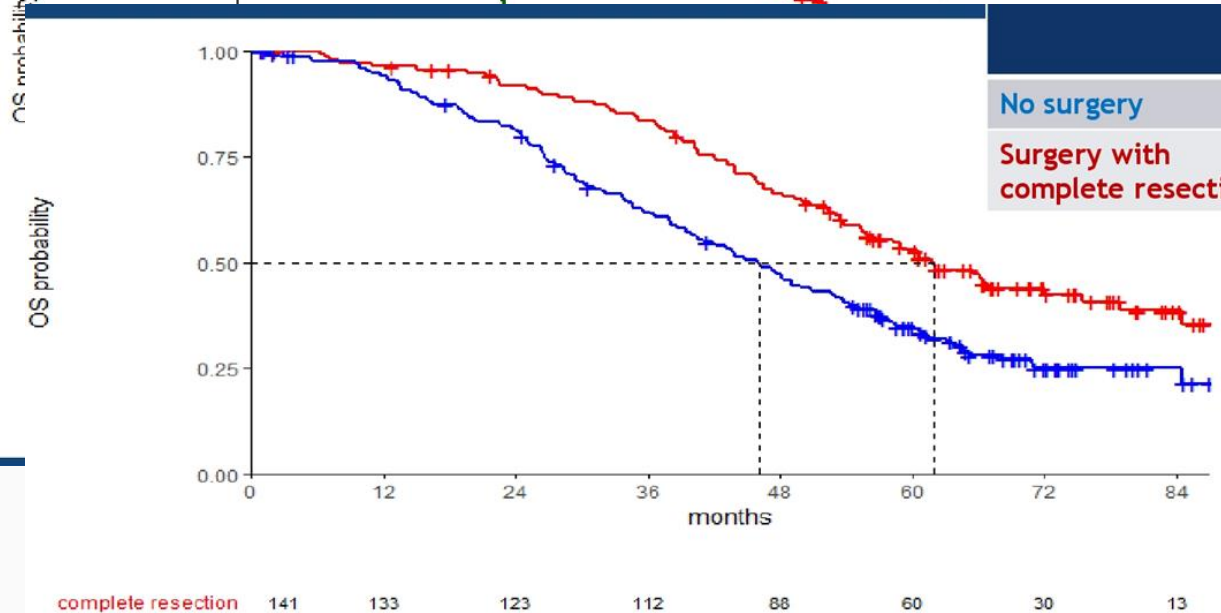
	surgery	no surgery
Median OS	53.7 mos	46.0 mos
Δ median OS	**7.7 mos**	
HR (95% CI)	**0.75** (0.58 - 0.96)	
P-value	**0.02**	



	surgery	no surgery
Median PFS	18.4 mos	14.0 mos
Δ median PFS	**4.4 mos**	
HR (95% CI)	**0.66** (0.54 - 0.82)	
P-value	**< 0.001**	



post-OP status	Median OS [mos]	Δ OS [mos]	HR (95% CI)
with residual tumor	28.8		1
complete resection	61.9	+33.1	0.40 (0.28-0.59)



	Median OS [mos]	Δ OS [mos]	HR (95% CI)
No surgery	46.0		1
Surgery with complete resection	61.9	+ 15.9	0.57 (0.43-0.76)

p-value $_{\text{Wald-Test}}$ **< 0.001**

Conclusiones

DESKTOP III es en primer ensayo en demostrar beneficio en SG en pacientes con CEO sensible a platinos sometidas a cirugía de citorreducción.

La cirugía de citoreducción para pacientes con Progresión de enfermedad posterior a los 6 meses y seleccionadas por el Score AGO prolongo significativamente la PFS.

El beneficio de SG fue alto y exclusivamente visto en la cohorte con resección completa, lo que indica la importancia en la adecuada selección de pacientes.

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Abs.6001- A Randomized Phase 3 Trial of Secondary Cytoreduction in Late Recurrent Ovarian Cancer: A Shanghai Gynecologic Oncologic Group Study

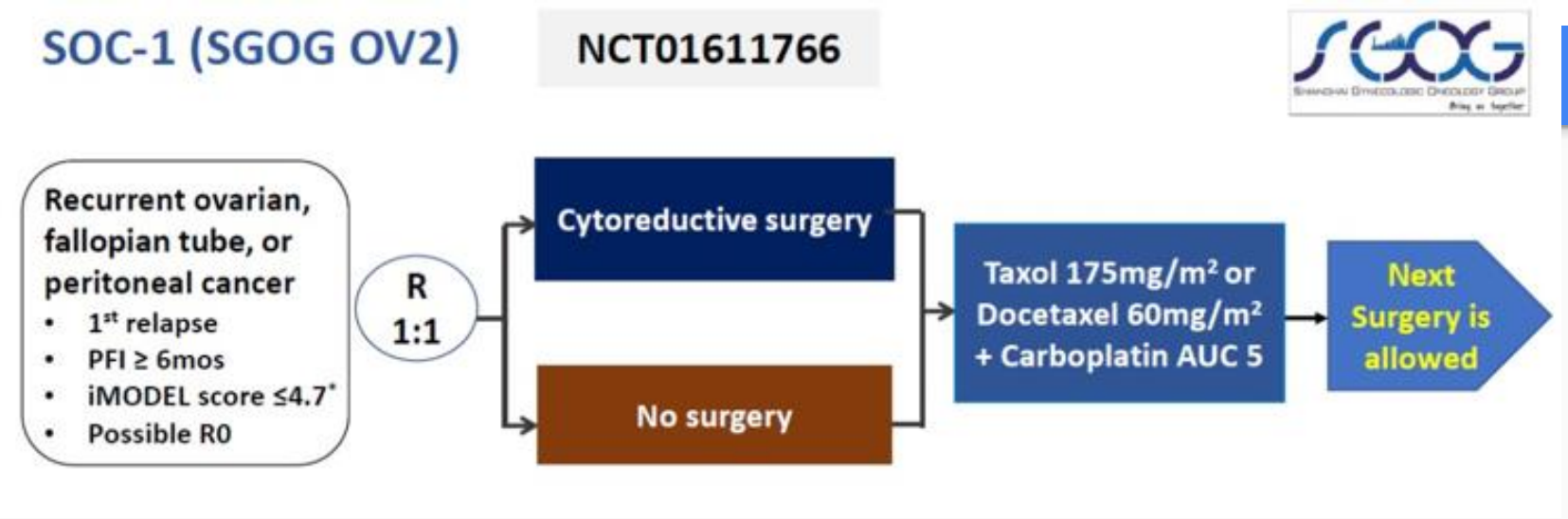
Rongyu Zang[1], Jianqing Zhu[2], Tingyan Shi[1], Jihong Liu[3], Dongsheng Tu[4], Sheng Yin[1], Ping Zhang[2], Yuqin Zhang[1], Huixun Jia[5], Xiao Huang[6], Yunlang Cai[7], Rong Jiang[1], Wenjuan Tian[6], Yuting Luan[1], Wen Gao[2], Yanling Feng[3], Huijuan Yang[6], Xi Cheng[6]

[1]Ovarian Cancer Program, Division of Gynecology Oncology, Department of Obstetrics and Gynecology, Zhongshan Hospital, Fudan University, Shanghai, China; [2]Department of Gynecologic Oncology, Zhejiang Cancer Hospital, Hangzhou, China; [3]Gynecologic Oncology Department of Sun Yat-sen University Cancer Center, Guangzhou, China; [4]Department of Mathematics and Statistics, Queen's University, Kingston, Canada; [5]Clinical Statistics Center, Shanghai General Hospital, Shanghai, China; [6]Department of Gynecologic Oncology, Fudan University Cancer Hospital; [7]Department of Obstetrics and Gynecology, Zhongda Hospital Southeast University, Nanjing, China

ANTECEDENTES:

Citorredución quirúrgica secundaria es una practica standard pero controversial para recurrencia de CEO platino sensible.

La citorreducción secundaria ha sido el estándar de tratamiento para estas pacientes en CHINA e incluso es el preferido por las pacientes.



Participaron 4 centros con 200/800 cirugías anuales, desde julio 2012 hasta junio 2019, se randomizaron 356 pacientes.

Selección de pacientes

- Intervalo libre de platino >6 meses

Impact factors	Scoring					
	0	0.8	1.5	1.8	2.4	3.0
FIGO stage	I/II	III/IV				
RD after primary surgery	0		>0			
PFI (months)	≥16				<16	
ECOG performance status	0-1				2-3	
CA125 at recurrence (U/ml)	≤105			>105		
Ascites at recurrence	Absent					Present

- iMODEL score <4,7.
- Si PI y Co-PI llegan a un consenso de que el tumor estadificado por PET TC podría resecarse por completo, el índice de CA125 podría puntuarse como 0 independiente de su valor real.
- Posibilidad de resección R0 evaluado por el cirujano interviniente.

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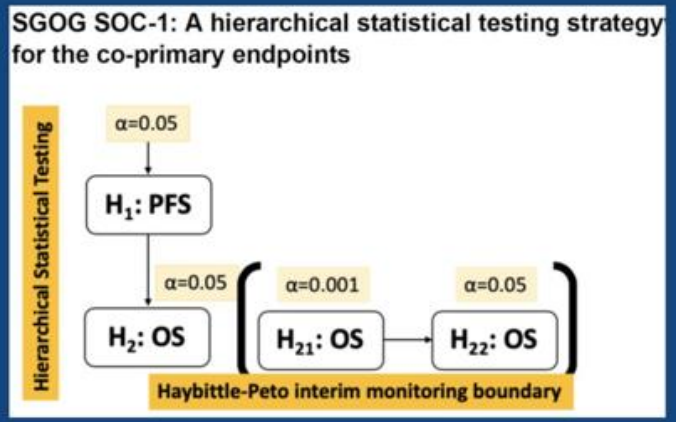
Co-Primary Endpoints: PFS and OS

- Sample size: 356 pts
- Median F/UP: 36.0m
- Interim analysis: 105 events/deaths, *P*-value < 0.001



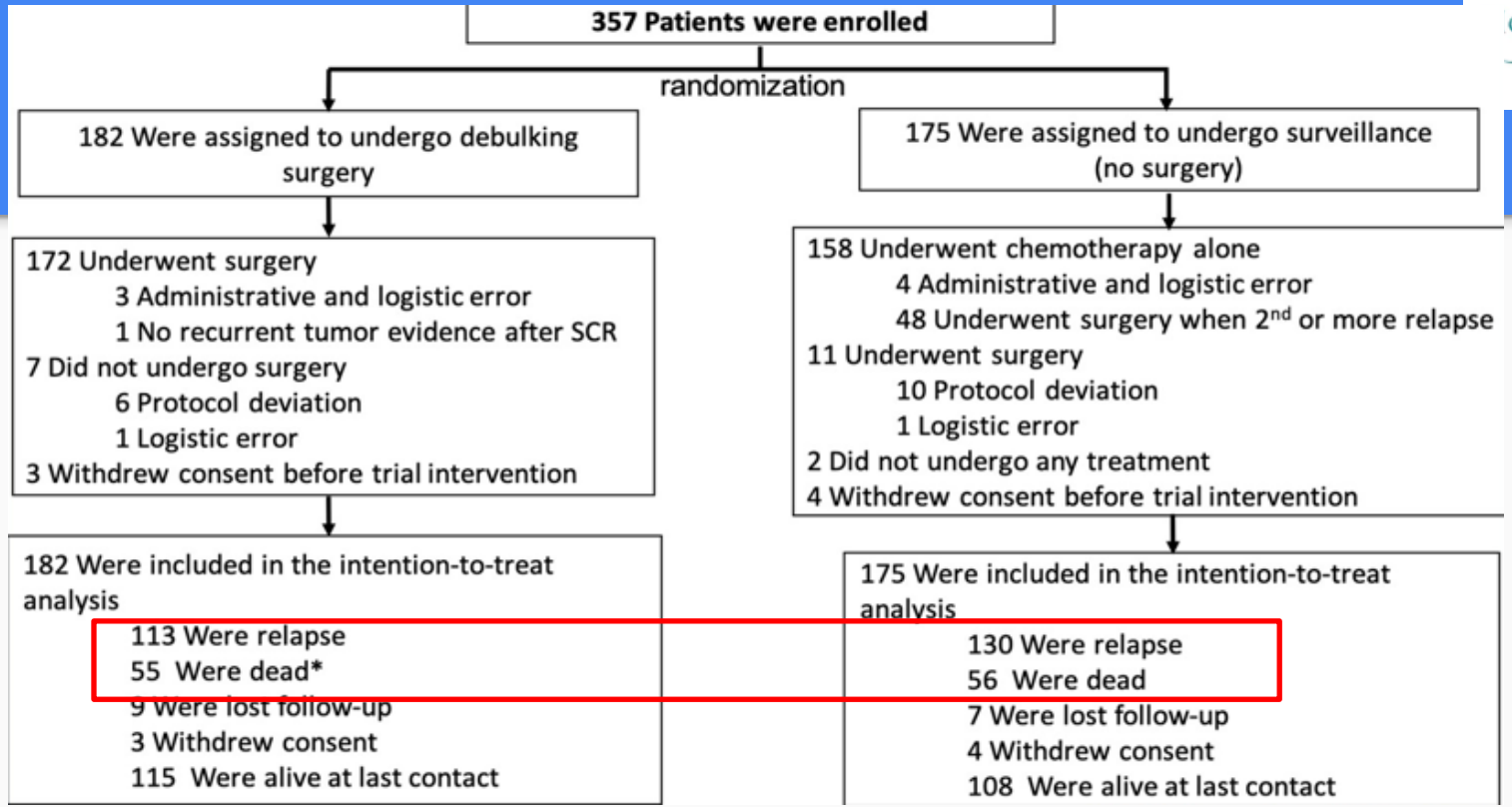
Objetivos Secundarios:

-TFSa: Supervivencia libre de tratamiento acumulativo: SG menos el tiempo de tratamiento incluyendo CX y QMT después de la aleatorización, independientemente de la terapia dirigida.

-OS modificada por Cross Over de pacientes.

- Seguridad de tratamiento

-Calidad de vida

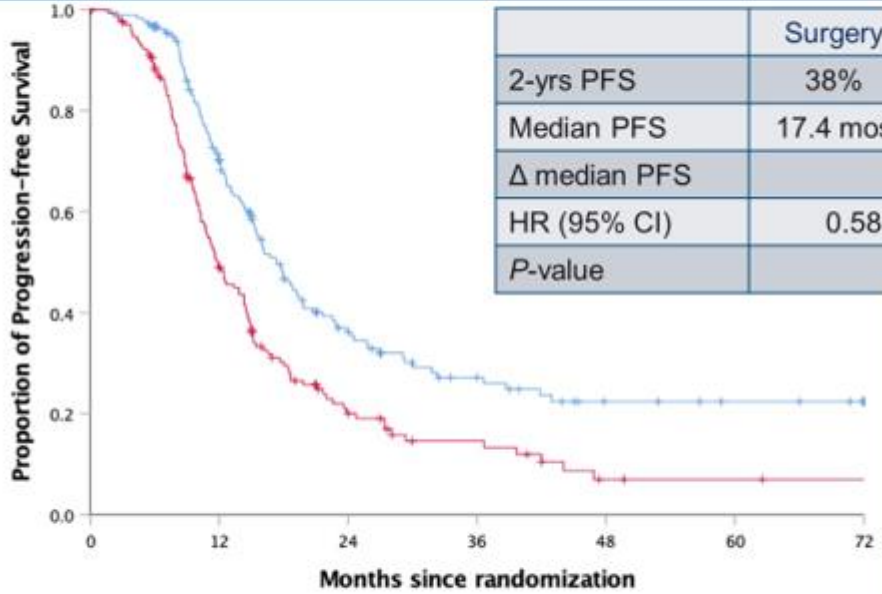

357 Patients were enrolled
randomization
182 Were assigned to undergo debulking surgery
175 Were assigned to undergo surveillance (no surgery)
172 Underwent surgery
3 Administrative and logistic error
1 No recurrent tumor evidence after SCR
7 Did not undergo surgery
6 Protocol deviation
1 Logistic error
3 Withdrew consent before trial intervention
158 Underwent chemotherapy alone
4 Administrative and logistic error
48 Underwent surgery when 2nd or more relapse
11 Underwent surgery
10 Protocol deviation
1 Logistic error
2 Did not undergo any treatment
4 Withdrew consent before trial intervention
182 Were included in the intention-to-treat analysis
113 Were relapse
55 Were dead*
9 Were lost follow-up
3 Withdrew consent
115 Were alive at last contact
175 Were included in the intention-to-treat analysis
130 Were relapse
56 Were dead
7 Were lost follow-up
4 Withdrew consent
108 Were alive at last contact

Características de Población

	Surgery	No-surgery	*P*-value
Age, median, yrs	55.2	53.1	0.011
Patients' pref			0
FIGO III-IV			6
Histology, ser			7
iMODEL scor			7
Median PFI, m			7
1-3 recurrent			6
gBRCA patho			6

Number of recurrent lesions, PP population	By image	During operation
1-3 (Localized)	59 (34.3)	45 (26.2)
4-19 (Localized)	40 (23.3)	53 (30.8)
≥ 20 (Carcinomatosis)	73 (42.4)	73 (42.4)
No evidence of tumor	NA	1 (0.6)

SGOG SOC-1 : Co-Primary Endpoint -PFS

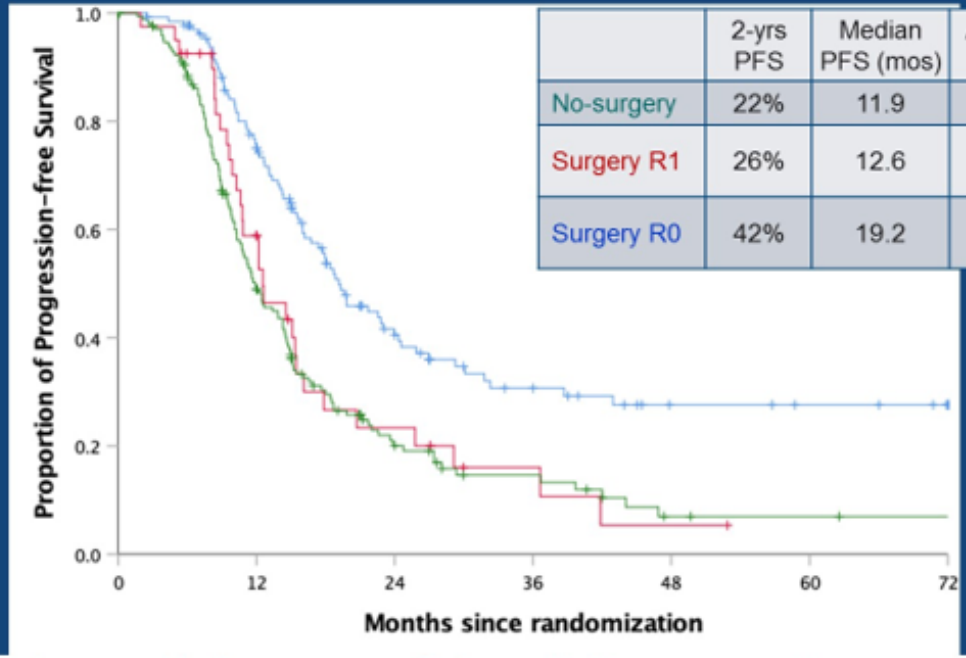


	Surgery	No-surgery
2-yrs PFS	38%	22%
Median PFS	17.4 mos	11.9 mos
Δ median PFS	5.5 mos	
HR (95% CI)	0.58 (0.45 – 0.74)	
P-value	< 0.001	

No. at risk

Surgery	182	115	45	25	14	11	8
No-surgery	175	75	21	11	3	2	1

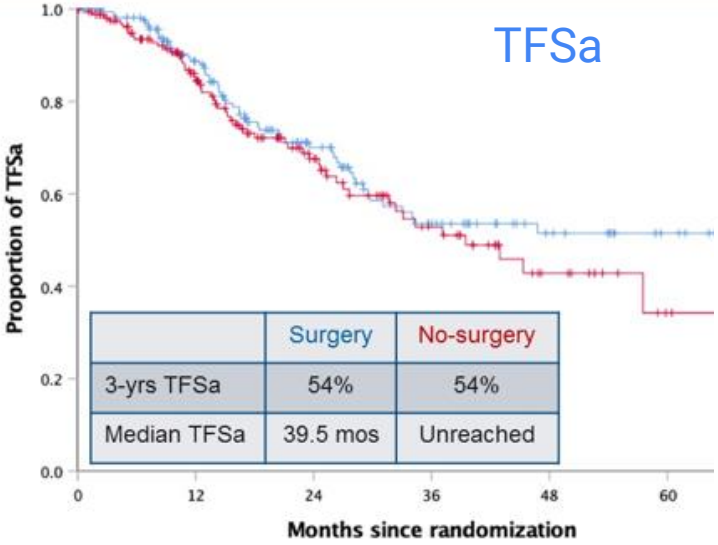
Exploratory Endpoint of PFS: R0 vs. R1 or No-Surgery



	2-yrs PFS	Median PFS (mos)	Δ PFS (mos)	HR (95% CI)	*P*-value
No-surgery	22%	11.9	-	1	-
Surgery R1	26%	12.6	+ 0.7	1.10 (0.74 – 1.63)	0.650
Surgery R0	42%	19.2	+ 7.3	0. 50 (0. 37– 0.66)	< 0.001

R0, No gross residual in surgery group; R1, Gross residual in surgery group; No-surgery group.

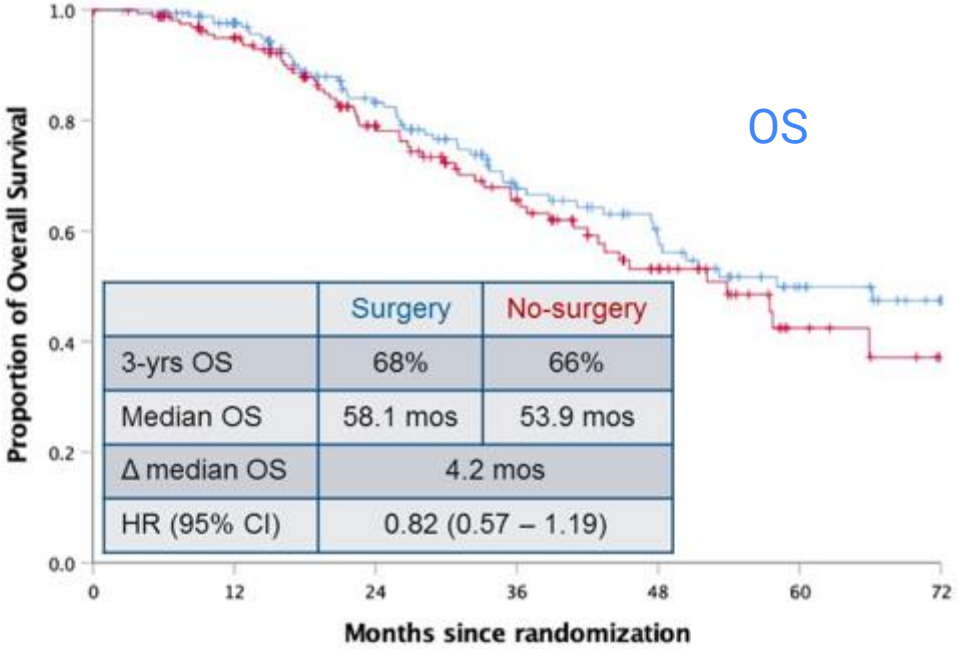
TFSa



	Surgery	No-surgery
3-yrs TFSa	54%	54%
Median TFSa	39.5 mos	Unreached

No. at risk						
Surgery	179	120	68	40	24	15
No-surgery	167	107	56	29	11	2

OS



	Surgery	No-surgery
3-yrs OS	68%	66%
Median OS	58.1 mos	53.9 mos
Δ median OS	4.2 mos	
HR (95% CI)	0.82 (0.57 – 1.19)	

No. at risk							
Surgery	182	157	105	64	42	24	13
No-surgery	175	145	89	56	31	10	3

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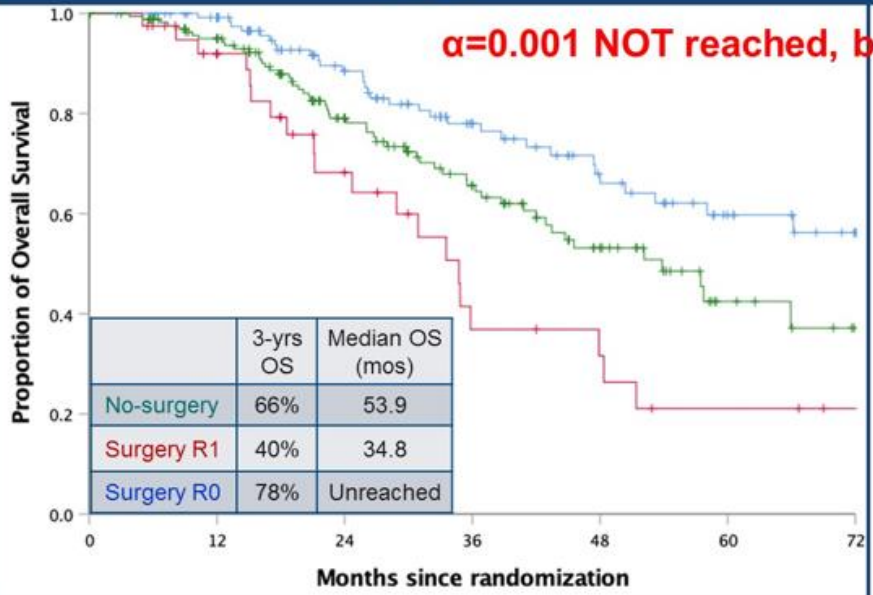
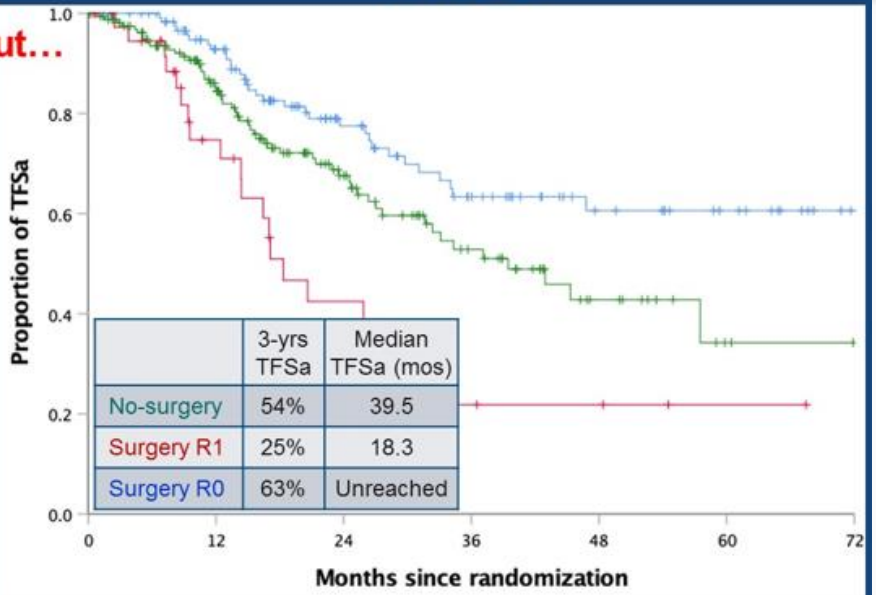
OS

α=0.001 NOT reached, but…



	3-yrs OS	Median OS (mos)
No-surgery	66%	53.9
Surgery R1	40%	34.8
Surgery R0	78%	Unreached

TFSa



	3-yrs TFSa	Median TFSa (mos)
No-surgery	54%	39.5
Surgery R1	25%	18.3
Surgery R0	63%	Unreached

Surgery R0, no gross residual; R1, gross residual

Conclusiones:

- La citorreducción secundaria brinda una ventaja en 5,5m en PFS comparado sin cirugía.
- el análisis interino de TFSa indica que cirugía puede contribuir potencialmente a prolongar los términos de sobrevida en comparación con quimioterapia sola. La evidencia en beneficio en OS y TFSa necesita mayor seguimiento.
- En las pacientes sometidas a cirugía se encontró en un 32,5% aumento de visualización de lesiones en comparación con la estadificacion inicial por imágenes.
- Incluso para pacientes con carcinomatosis que presentaban >20 lesiones se logro llegar a una cirugía R0 en un 60,3% dados los esfuerzos quirúrgicos.

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	SGOG SOC-1	GOG-0213	AGO Desktop III
Period of enrollment	2012-2019	2007-2017	2010-2014
Primary endpoint(s)	PFS & OS	OS	OS
Selection criteria	iMODEL +PET-CT	By investigator	AGO model
Series of SCR related research	Yes	No	Yes
Local clinical practice/patient's prefer	Surgery	NA	NA
With 1-3 recurrent lesions	29.7%	>50% with1-2	NA
Decline surgery in surgery arm	3.8%	6.3%	6.9%
SCR in no-surgery arm	6.3%	2.0%	8.9%
SCR in no-surgery arm at the 2nd+ relapses	36.9%	NA	11.0%
Rate of R0, PP	76.7%	67.0%	72.5%
Median PFS (surgery vs. no surgery)	17.4m vs 11.9m	18.9m vs 16.2m	19.6m vs 14.0m
The 2nd line beva maintenance	1.1%	84.1%	20.4%
The 2nd line PARPi maintenance	10.1%	NA	0.2%

Gracias

- Randomized phase III study to evaluate the impact of secondary cytoreductive surgery in recurrent ovarian cancer: Final analysis of AGO DESKTOP III/ENGOT-ov20

https://meetinglibrary.asco.org/record/185438/abstract

- A randomized phase III trial of secondary cytoreductive surgery in later recurrent ovarian cancer: SOC1/SGOG-OV2.

https://meetinglibrary.asco.org/record/185438/abstract