16.30-18.00 **MESA DE DEBATE**

Título: Qué operar y que no operar en carcinomatosis peritoneal. Indicaciones y límites.

PEDRO ANTONIO CASCALES CAMPOS

UNIDAD DE CIRUGÍA DE LA CARCIOMATOSIS PERITONEAL

SERVICIO DE CIRUGÍA GENERAL Y DEL APARATO DIGESTIVO

HOSPITAL CLÍNICO UNIVERSITARIO VIRGEN DE LA ARRIXACA. IMIB-ARRIXACA

- CP: DISEMINACIÓN PERITONEAL DE UN TUMOR MALIGNO

- NO SIEMPRE ES UNA CONDICIÓN FINAL
  - UN PEQUEÑO % DE PACIENTES CURARÁ

- TIENE UN TRATAMIENTO ESPECÍFICO
  - CCR + HIPEC

El control de la enfermedad peritoneal es el RETO ACTUAL MAS IMPORTANTE

↓

CAMBIO DE MENTALIDAD

CAMBIO DE MENTALIDAD

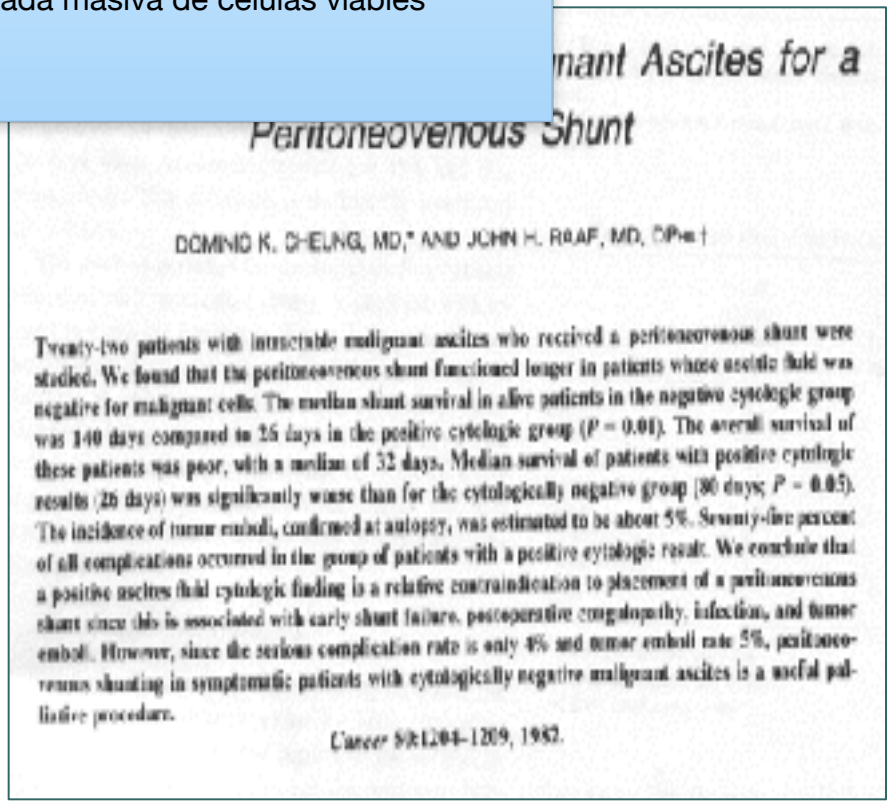
Fase terminal de un tumor abdominal

↓

ENFERMEDAD LOCORREGIONAL

En los estudios de los años 80 sobre el tratamiento de la ascitis carcinomatosa mediante shunt peritoneovenosos, se demostró que ni cuando se produce la entrada masiva de células viables

ACIENTES SE MUEREN POR LA CP

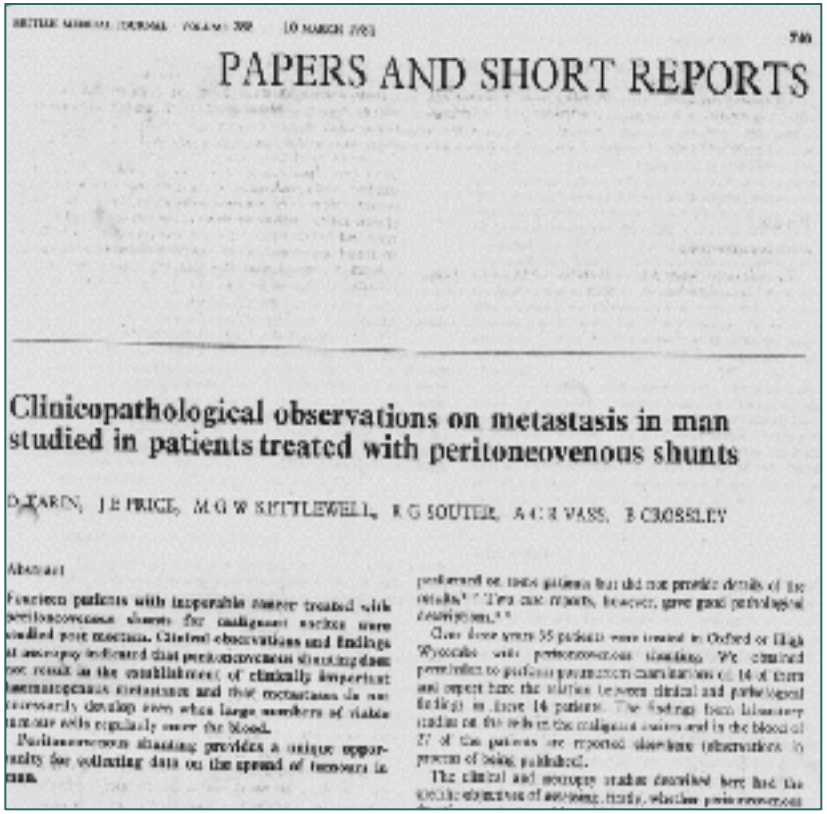


nant Ascites for a Peritoneovenous Shunt

DOMINIC K. CHEUNG, MD,* AND JOHN H. RAAF, MD, DPhil †

Twenty-two patients with intractable malignant ascites who received a peritoneovenous shunt were studied. We found that the peritoneovenous shunt functioned longer in patients whose ascitic fluid was negative for malignant cells. The median shunt survival in alive patients in the negative cytologic group was 140 days compared to 26 days in the positive cytologic group ($P = 0.01$). The overall survival of these patients was poor, with a median of 32 days. Median survival of patients with positive cytologic results (26 days) was significantly worse than for the cytologically negative group (80 days; $P = 0.05$). The incidence of tumor emboli, confirmed at autopsy, was estimated to be about 5%. Seventy-five percent of all complications occurred in the group of patients with a positive cytologic result. We conclude that a positive ascites fluid cytologic finding is a relative contraindication to placement of a peritoneovenous shunt since this is associated with early shunt failure, postoperative coagulopathy, infection, and tumor emboli. However, since the serious complication rate is only 4% and tumor emboli rate 5%, peritoneovenous shunting in symptomatic patients with cytologically negative malignant ascites is a useful palliative procedure.

Cancer 50:1204–1209, 1982.



BRITISH MEDICAL JOURNAL VOLUME 282 10 MARCH 1981 740

PAPERS AND SHORT REPORTS

Clinicopathological observations on metastasis in man studied in patients treated with peritoneovenous shunts

D TARIN, J E PRICE, M G W KETTLEWELL, R G SOUTER, A C R VASS, B CROSSLEY

Abstract

Fourteen patients with inoperable cancer treated with peritoneovenous shunts for malignant ascites were studied post mortem. Clinical observations and findings at autopsy indicated that peritoneovenous shunting does not result in the establishment of clinically important haematogenous metastases and that metastases do not necessarily develop even when large numbers of viable tumour cells regularly enter the blood.

Peritoneovenous shunting provides a unique opportunity for collecting data on the spread of tumours in man.

Los hallazgos en necrospia demostraron que el shunt Peritoneo-venoso no se traduce en metástasis hematógenas.

Goldmann E. Proc R Soc Med **1897**; 1: 1-13.

Alta eficiencia de las células tumorales en la cavidad peritoneal

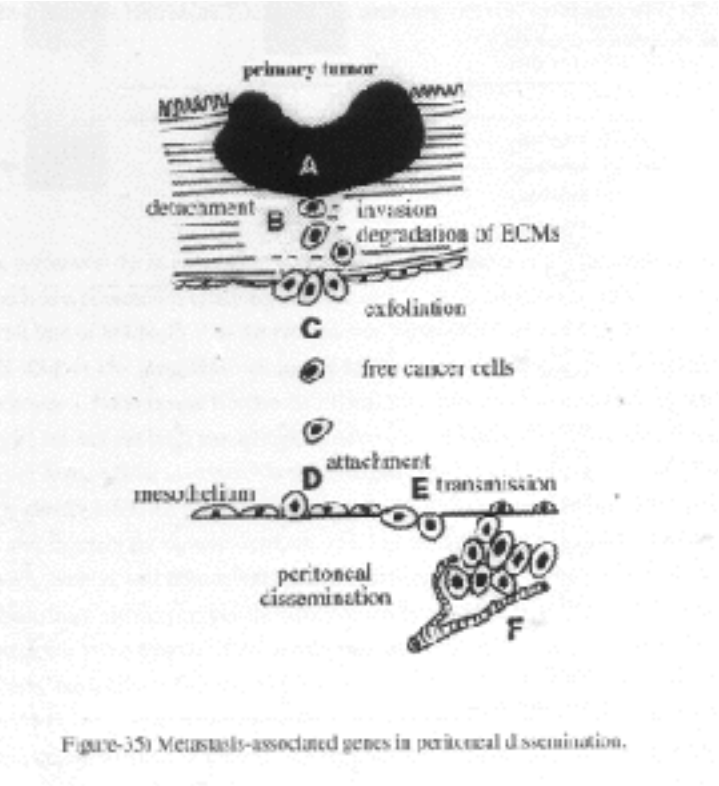


Figure-35) Metastasis-associated genes in peritoneal dissemination.

¿QUE LO PROVOCA?

ESPONTANEAMENTE

MANIPULACION TUMORAL

¿QUE LO FAVORECE?

AREAS DE FIBRINA-CICATRICES

ZONAS MAL VASCULARIZADAS

RESISTENCIA TUMORAL A QT

ADVANCES IN SURGICAL TECHNIQUE

ANNALS OF SURGERY
Vol. 221, No. 1, 25–42
© 1995 J. B. Lippincott Company

Peritonectomy Procedures

Paul H. Sugarbaker, M.D.

From The Cancer Institute, Washington Hospital Center, Washington, District of Columbia

LA CIRUGÍA NO SIEMPRE PERMITE EL R-0

ENTRE LOS "RADICALMENTE" OPERADOS DE CP HASTA UN 70% RECAEN DENTRO DE LOS 2 PRIMEROS AÑOS

↓

ENFERMEDAD MICROSCÓPICA

↓

"…lo que el ojo del cirujano no ve es lo que mata al paciente…"

↓

QUIMIOTERAPIA INTRAPERITONEAL HIPERTÉRMICA

CITORREDUCCIÓN + HIPEC (CALOR)

DESPUÉS DE MUCHO RECORRIDO

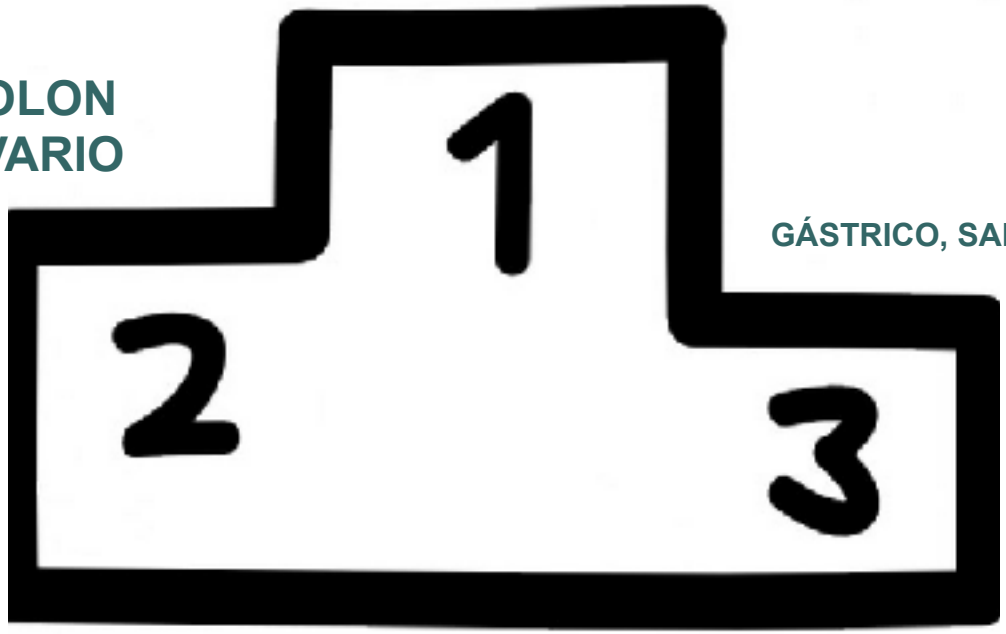
- LÍMITES DE LA CITORREDUCCIÓN:
  - INTESTINO DELGADO (<1.5m)
  - HILIO HEPÁTICO
  - MARCO DUODENOPANCREÁTICO (no cola pancreática)
  - CITORREDUCCIONES QUE CONLLEVEN UNA MALA CALIDAD DE VIDA
  - ADENOPATÍAS PATOLÓGICAS

- HIPEC: CC-0/CC-1

- NO TODAS LAS CP SE BENEFICIAN DE UNA CCR + HIPEC
  - NO EN PROGRESIÓN
  - NO SIN POSIBILIDAD DE UN TRATAMIENTO INTEGRAL DE LA ENFERMEDAD
  - HEMOS DE SER PRUDENTES CON LAS HISTOLOGÍAS
    - CELULAS EN ANILLO DE SELLO

PSEUDOMIXOMA
MESOTELIOMA MALIGNO

COLON
OVARIO



GÁSTRICO, SARCOMA, etc

Indicaciones

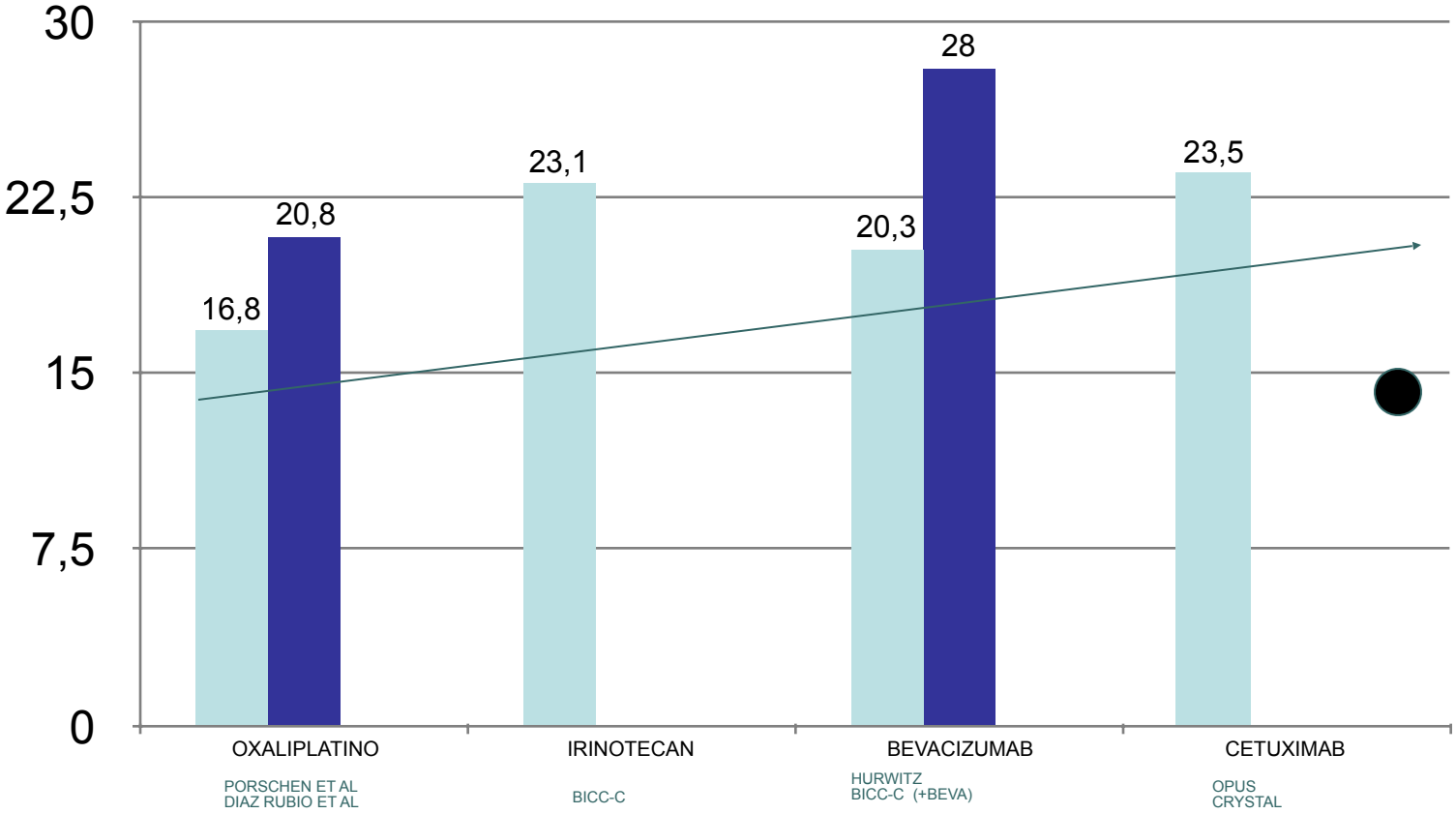
ACTITUD PROACTIVA-HIPEC

- NEOPLASIAS PERFORADAS
- ROTURA TUMOR DURANTE LA CIRUGÍA
- NEOPLASIAS CON AFECTACIÓN DE ESTRUCTURAS ADYACENTES
- NEOPLASIAS CON AFECTACIÓN DEL OVARIO
- ASCITIS CON CITOLOGIA POSITIVA

CARCINOMATOSIS PERITONEAL

CCR

QUIMIOTERAPIA SISTÉMICA



Annals of Surgical Oncology 1969:2426–2432
DOI: 10.1245/s10438-008-0066-2

8-Year Follow-up of Randomized Trial: Cytoreduction and Hyperthermic Intraperitoneal Chemotherapy Versus Systemic Chemotherapy in Patients with Peritoneal Carcinomatosis of Colorectal Cancer

Vic J. Verwaal, MD, PhD,[1] Sjoerd Bruin, MD,[1] Henk Boot, MD, PhD,[2] Gooike van Slooten, MD,[1] and Hanna van Tinteren, ScM[3]

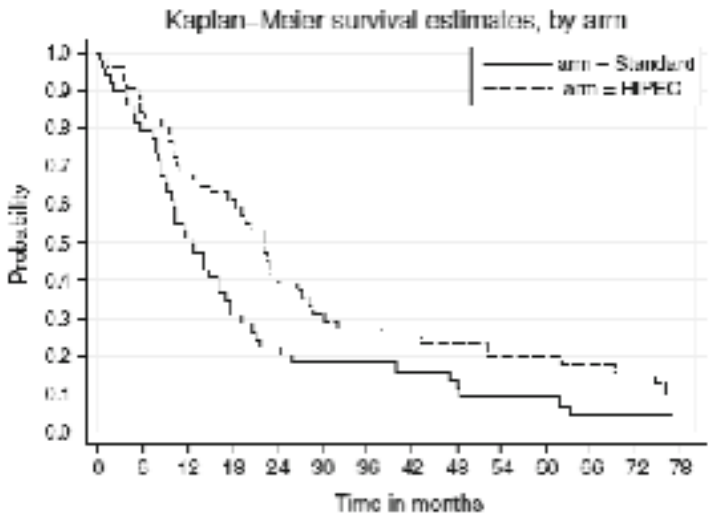


FIG. 2. Disease-specific survival of patients treated for peritoneal carcinomatosis, divided by treatment.

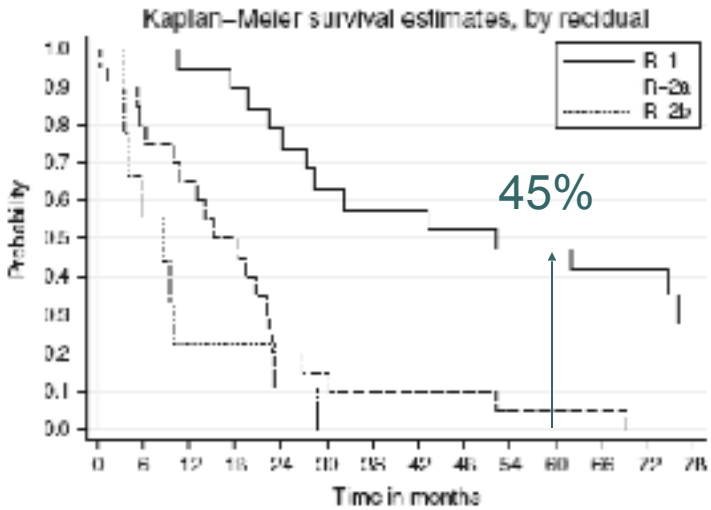
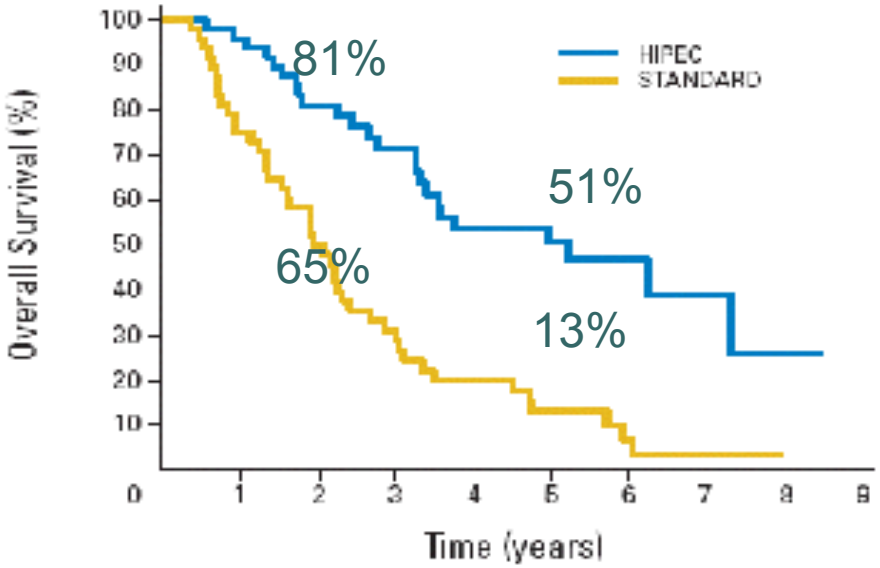


FIG. 3. Long-term results of cytoreduction followed by HIPEC in peritoneal carcinomatosis, divided to completeness of cytoreduction.

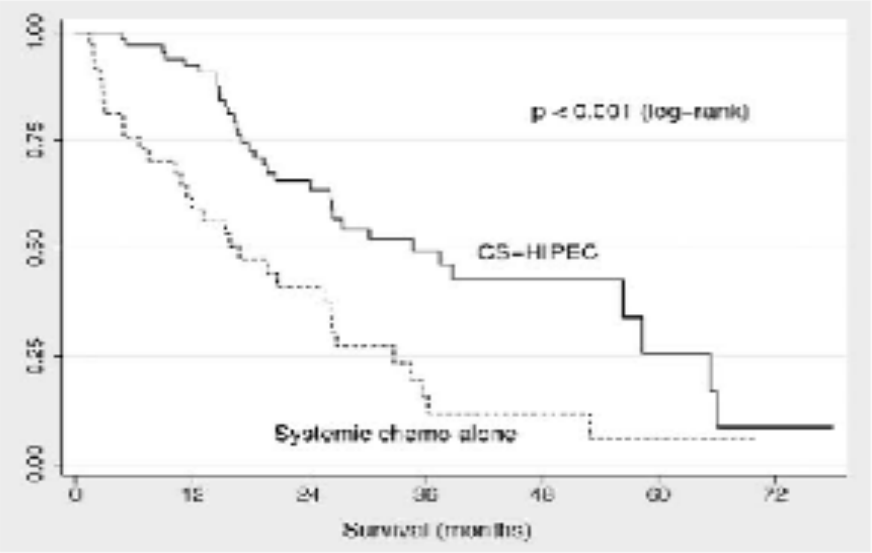
JOURNAL OF CLINICAL ONCOLOGY
ORIGINAL REPORT

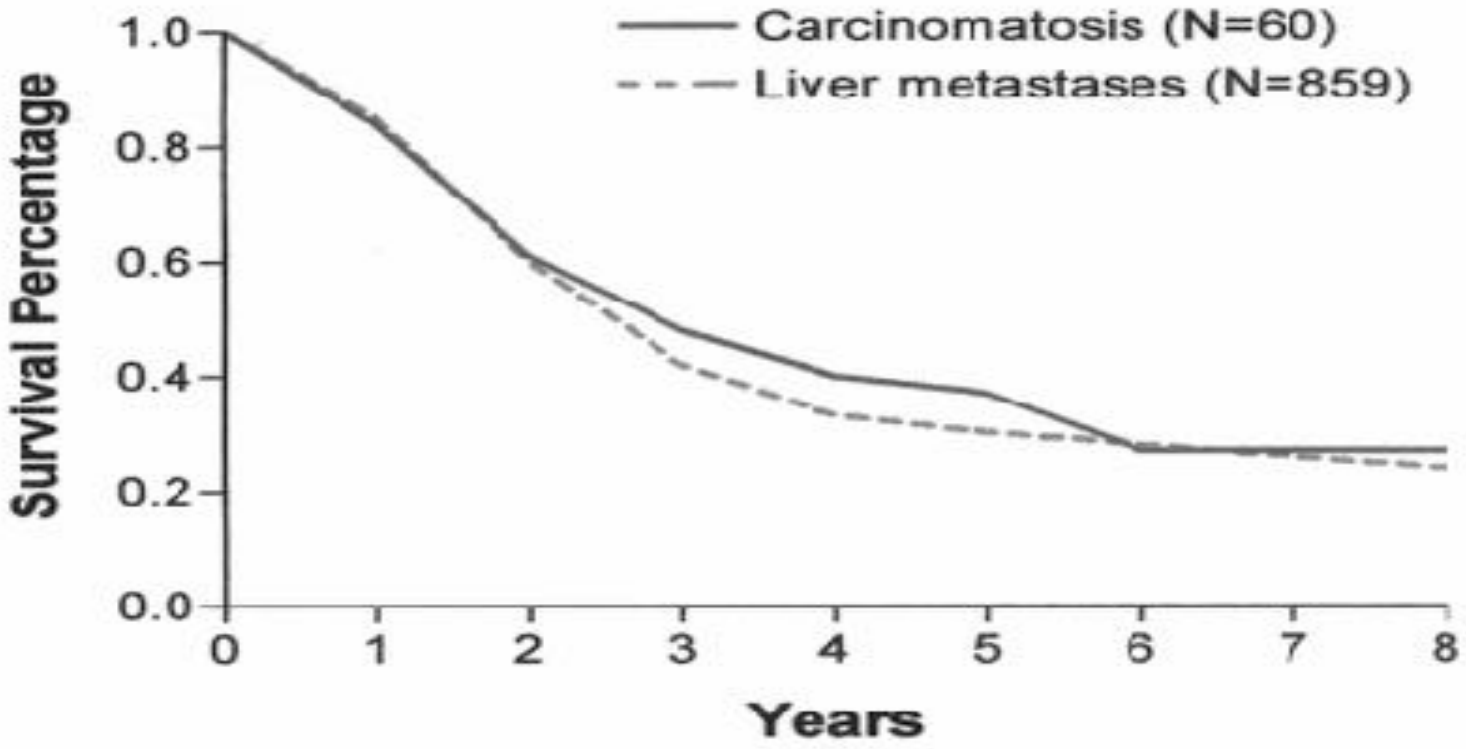
Complete Cytoreductive Surgery Plus Intraperitoneal Chemohyperthermia With Oxaliplatin for Peritoneal Carcinomatosis of Colorectal Origin



Original Article

Cytoreductive Surgery and Hyperthermic Intraperitoneal Chemoperfusion Versus Systemic Chemotherapy Alone for Colorectal Peritoneal Carcinomatosis




Carcinomatosis (N=60)
Liver metastases (N=859)
Survival Percentage
1.0
0.8
0.6
0.4
0.2
0.0
0
1
2
3
4
5
6
7
8
Years

CARCINOMATOSIS PERITONEAL

OVARIO

ESCENARIOS CLÍNICOS

1. CIRUGÍA PRIMARIA
2. CIRUGÍA DE INTERVALO
3. CIRUGÍA DE RESCATE
4. CIRUGÍA DE LAS RECURRENCIAS
   - PLATINO SENSIBLES
   - PLATINO RESISTENTES

European Journal of Obstetrics & Gynecology and Reproductive Biology

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journal homepage: www.elsevier.com/locate/ejogrb

LETTERS TO THE EDITOR—BRIEF COMMUNICATION

Heterogeneity in patients and methods. A problem for hyperthermic intraperitoneal chemotherapy (HIPEC) in ovarian carcinoma

Ann Surg Oncol (2015) 22:1570–1575
DOI 10.1245/s10434-014-4157-9

Annals of
SURGICAL ONCOLOGY
OFFICIAL JOURNAL OF THE SOCIETY OF SURGICAL ONCOLOGY

ORIGINAL ARTICLE GYNECOLOGIC ONCOLOGY

Cytoreductive Surgery and HIPEC in Recurrent Epithelial Ovarian Cancer: A Prospective Randomized Phase III Study

J. Spiliotis, MD, PhD[1], E. Halkia, MD, PhD[1,2], E. Lianos, MD[3], N. Kalantzi, MD[4], A. Grivas, MD[3], E. Efstathiou, MD[1], and S. Giassas, MD[2]

[1]First Department of Surgical Oncology, Metaxa Cancer Hospital, Piraeus, Greece; [2]Peritoneal Surface Malignancy Unit, IASO General Hospital, Athens, Greece; [3]Department of Medical Oncology, Metaxa Cancer Hospital, Piraeus, Greece; [4]Department of Anesthesiology, Metaxa Cancer Hospital, Piraeus, Greece

TABLE 1 Characteristics of 120 patients

Characteristic	HIPEC	Non HIPEC
n	60	60
Mean age, years	58.3	58.1
Mean no. of cycles of adjuvant chemotherapy	5	5
Mean preoperative CA-125 value (U/ml)	83.7	80.5

Characteristic	HIPEC		Non-HIPEC	
	n	%	*n*	%
Stage				
III_c	41	68.3	35	58.3
IV	19	31.7	25	41.7
Platinum responsiveness				
Sensitive	38	63.3	36	60
Resistant	22	36.7	24	40
Ascites				
Yes	18	30	16	26.7
No	42	70	44	73.3
Optimal cytoreduction at primary surgery	51	85	46	76.6
PCI				
PCI < 5	7	11.7	8	13.3
5 ≤ PCI < 10	24	40	22	36.7
PCI ≥ 10	29	48.3	30	50
CC				
CC-0	39	65	33	55
CC-1	12	20	20	33.3
CC-2	9	15	7	11.7

HIPEC hyperthermic intraperitoneal chemotherapy, *PCI* peritoneal carcinomatosis index, *CC* completeness of cytoreduction

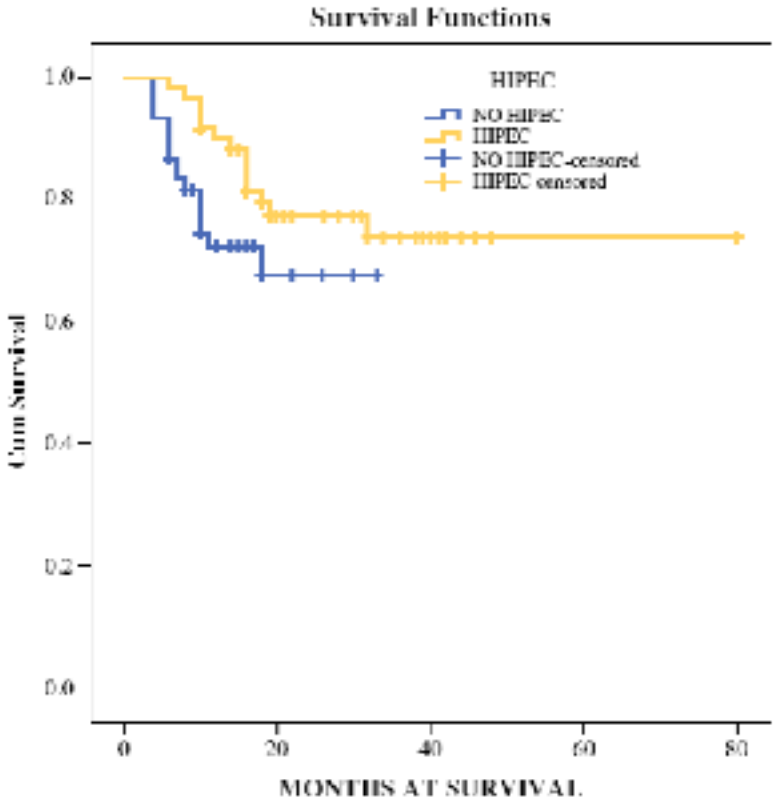
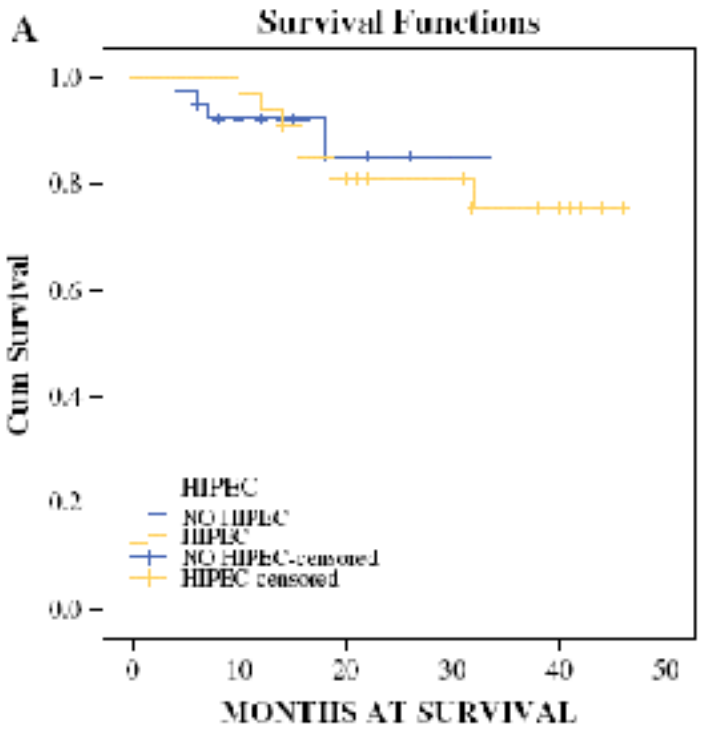
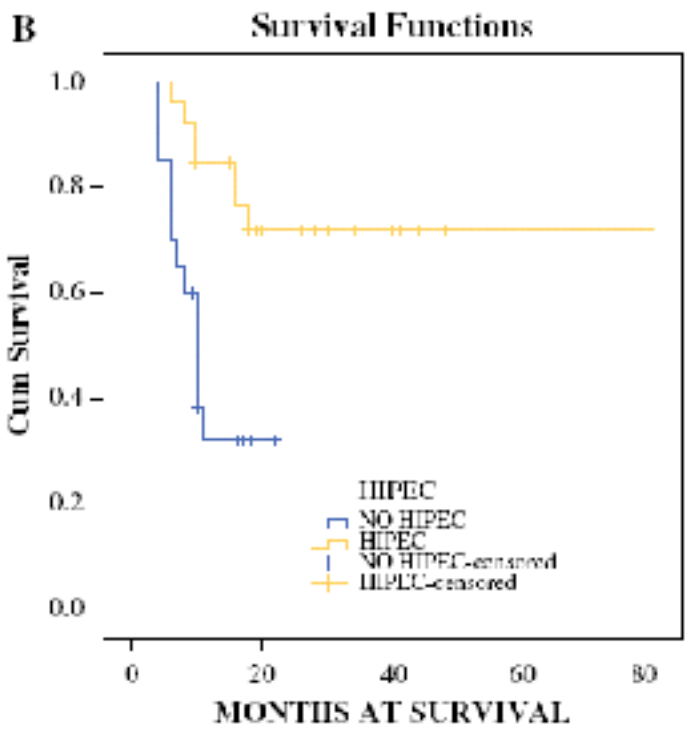


FIG. 1 Kaplan–Meier survival plot, HIPEC versus no HIPEC, $p = 0.006$


A
Survival Functions
Cum Survival
1.0
0.8
0.6
0.4
0.2
0.0
0
10
20
30
40
50
MONTHS AT SURVIVAL
HIPEC
NO HIPEC
HIPEC
NO HIPEC-censored
HIPEC censored

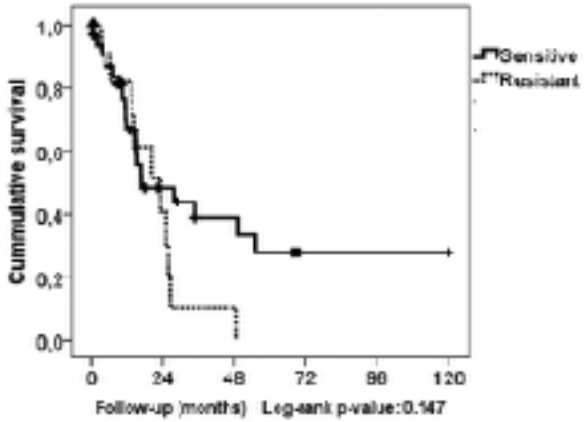

B
Survival Functions
Cum Survival
1.0
0.8
0.6
0.4
0.2
0.0
0
20
40
60
80
MONTHS AT SURVIVAL
HIPEC
NO HIPEC
HIPEC
NO HIPEC-censored
HIPEC-censored

¿REVIERTE QUIMIORESISTENCIA?

Gynaecological oncology

Secondary cytoreductive surgery and hyperthermic intraperitoneal chemotherapy for recurrent epithelial ovarian cancer: a multi-institutional study

M Deraco,[a] S Virzi,[b] DB Iusco,[b] F Puccio,[c] A Macri,[c] C Famulari,[d] M Solazzo,[c] S Bonomi,[b] A Grassi,[b] D Baratti,[a] S Kusamura,[a]



	N of events		N of patients at risk				
Sensitive	19	33	11	9	7	1	0
Resistant	10	13	4	0	0	0	0

Figure S2a Overall survival according to platin resistance in recurrent ovarian cancer treated with CRS +HIPEC

Ann Surg Oncol (2012) 19:4092–4098
DOI 10.1245/s10434-012-2510-4

Annals of SURGICAL ONCOLOGY
OFFICIAL JOURNAL OF THE SOCIETY OF SURGICAL ONCOLOGY

ORIGINAL ARTICLE – GYNECOLOGIC ONCOLOGY

Cytoreductive Surgery and Hyperthermic Intraperitoneal Chemotherapy (HIPEC) for Persistent and Recurrent Advanced Ovarian Carcinoma: A Multicenter, Prospective Study of 246 Patients

N. Bakrin, MD[1], E. Cotte, MD[1], E. Gollier, MD, PhD[2], F. N. Gilly, MD, PhD[1], G. Freyer, MD, PhD[3], W. Helm, MD, PhD[4], O. Glehen, MD, PhD[1], and J. M. Bereder, MD[5]

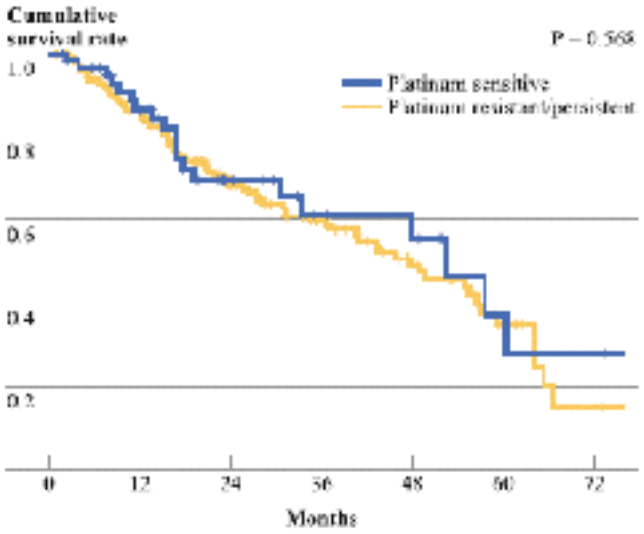


FIG. 4 Overall survival of platinum-resistant/persistent group versus platinum-sensitive group

ESTUDIOS CON GRUPOS CONTROL

AUTOR	TIME POINT	n	CONTROL	HIPEC	HIPEC DRUG	DFS	OS
BAE (39)	SECONDARY	96	29	67	PACLITAXEL or CARBOPLATIN	3y Control: 16.7% 3y HIPEC: 56.3%	5y Control: 18.8% 5y Carboplatin: 69.6% 5y Paclitaxel: 83.3%
FAGOTTI (40)	RECURRENT	67	37	30	OXALIPLATIN	Median Control: 15 months Median HIPEC: 26 months	5y Control: 42.7% 5y HIPEC: 68.4%
KIM (41)	CONSOLIDATION	43	24	19	PACLITAXEL	5y Control: 63.16% 5y HIPEC: 29.17%	5y Control: 41.67% 5y HIPEC: 84.21%
MUÑOZ- CASARES (42)	RECURRENT	26	12	14	PACLITAXEL	NOT RELATED	5y Control: 17% 5y HIPEC: 57%
LE BRUN (43)	RECURRENT	42	19	23	CISPLATIN or ELOXATIN or MITOMYCIN C	NOT RELATED	4y Control: 19.4% 4y HIPEC: 75.6%
RYU(44)*	ADVANCED	117	60	57	CARBOPLATIN + α-INTERFERON	NOT RELATED	5y Control: 40% 5y HIPEC: 65.6%
SAFRA (45)	RECURRENT	111	84	27	CISPLATIN + DOXORRUBICIN or CISPLATIN + MITOMICIN C or CARBOPLATIN + PACLITAXEL	Median Control: 6 months Median HIPEC: 15 months	5y Control: 79% 5y HIPEC: 45%
CASCALES-CAMPOS (37)	PRIMARY-ADVANCED	87	35	52	PACLITAXEL	3y Control: 18% 3y HIPEC: 63%	NOT RELATED**
CASCALES-CAMPOS (47)	RECURRENT	54	22	32	PACLITAXEL	3y Control: 23% 3y HIPEC: 45%	NOT RELATED**

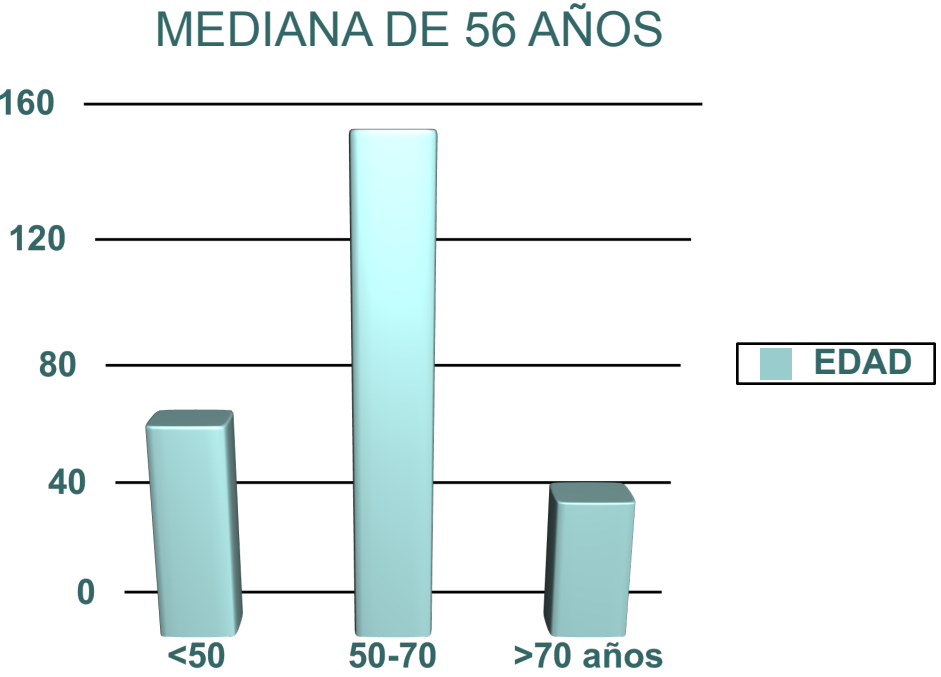
LA CITORREDUCCIÓN + HIPEC

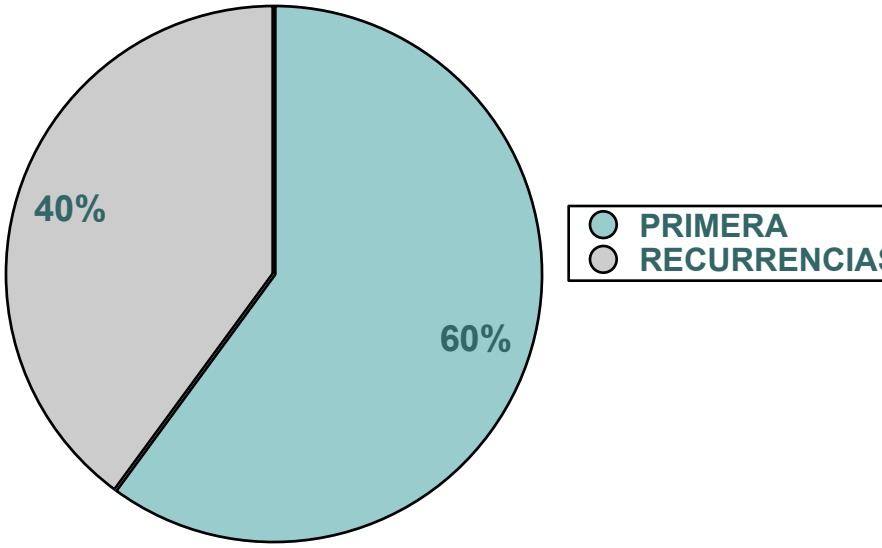
EN PACIENTES SELECCIONADOS

GENERA UN IMPACTO + SOBRE LA SV

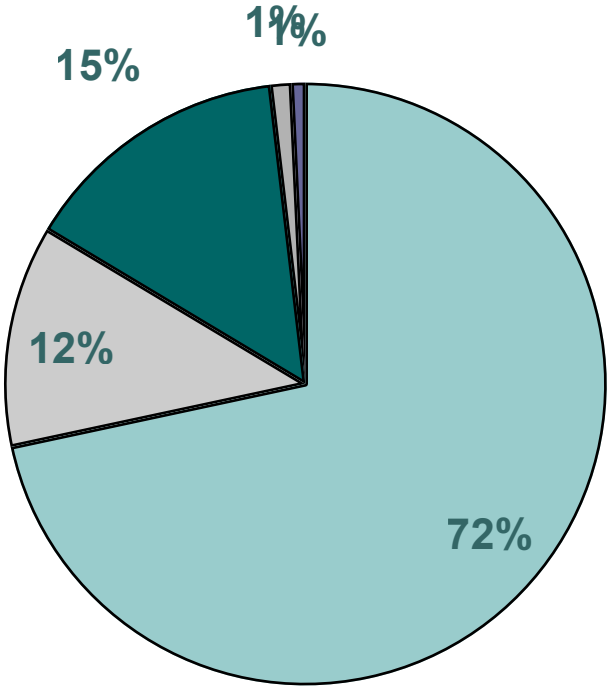
EXPERIENCIA HCUVA

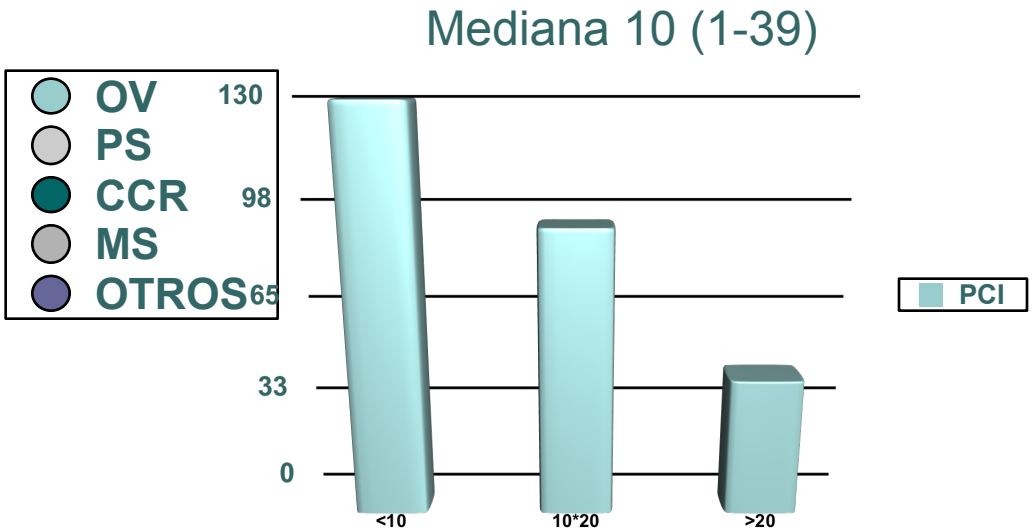
- ENERO 2008 A DICIEMBRE 2015
  - 301 PACIENTES (268 RESECABLES)



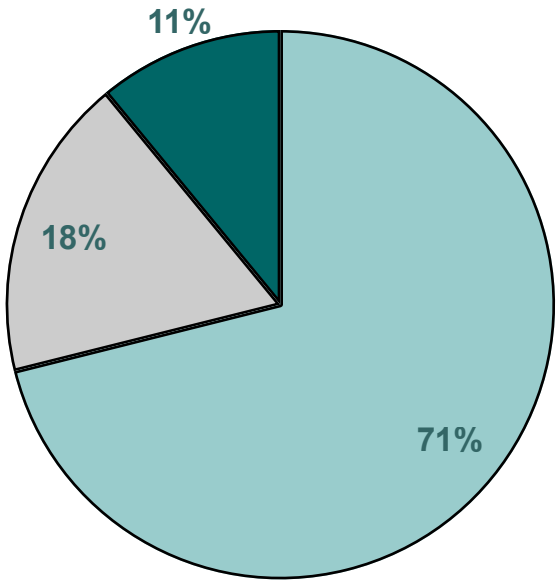


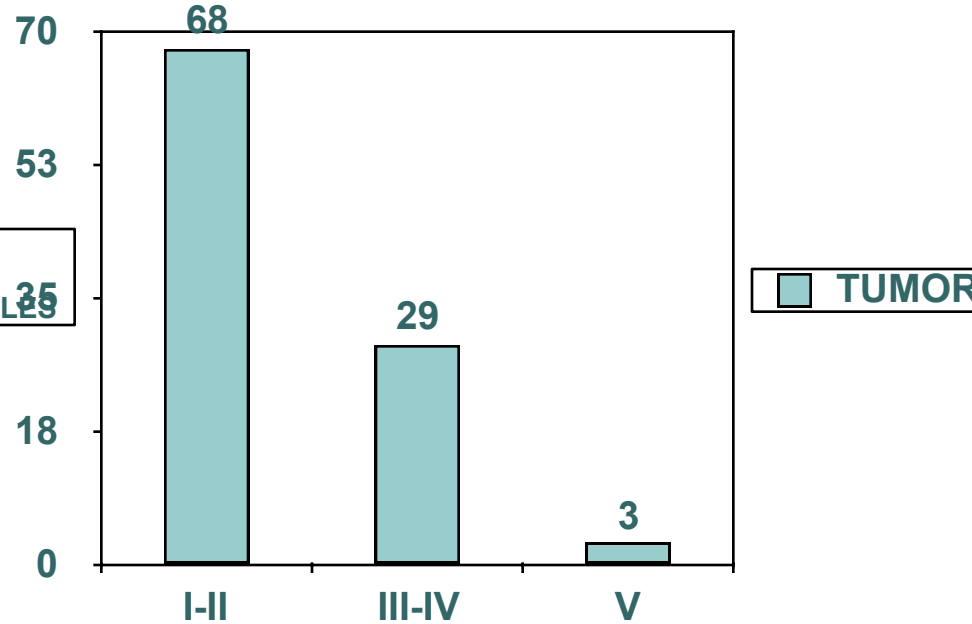
- ENERO 2008 A DICIEMBRE 2015
  - 301 PACIENTES (268 RESECABLES)



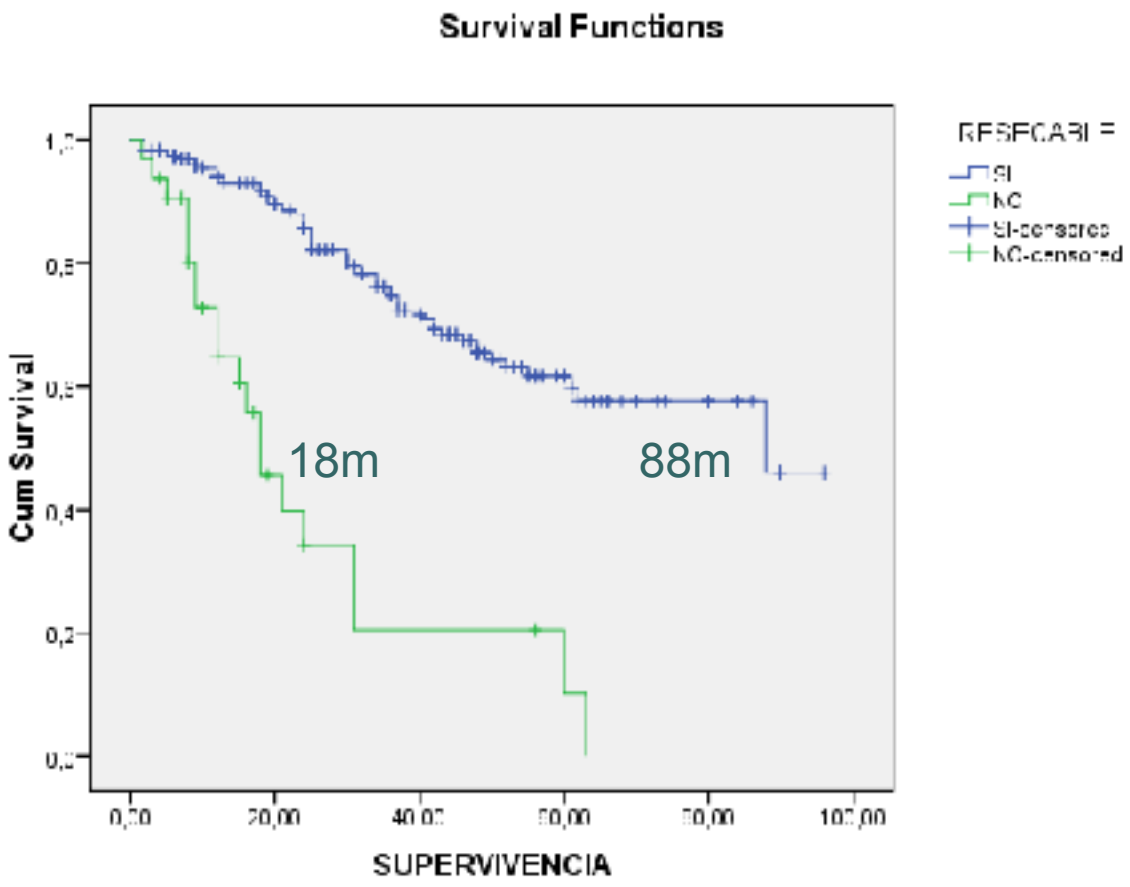


- MORBILIDAD: 31%, GRAVE III-IV: 12%
- MORTALIDAD: 3 PACIENTES: 1.1%





QUÉ IMPORTANTE ES LA SELECCIÓN DE LOS PACIENTES



- NOS CENTRAREMOS EN EL OV.
  - CIRUGÍA PRIMARIA
  - CIRUGÍA INTERVALO
  - RECURRENCIAS PLATINOSENSIBLES

NUESTRA MENTALIDAD

MORBIMORTALIDAD

↓

SUPERVIVENCIA

↓

CASE-CONTROL

↓

Ann Surg Oncol (2014) 21:2553–2561
DOI: 10.1245/s10434-014-3599-4

Annals of
SURGICAL ONCOLOGY
OFFICIAL JOURNAL OF THE SOCIETY OF SURGICAL ONCOLOGY

ORIGINAL ARTICLE – GYNECOLOGIC ONCOLOGY

Treatment of Microscopic Disease with Hyperthermic Intraoperative Intraperitoneal Chemotherapy After Complete Cytoreduction Improves Disease-Free Survival in Patients with Stage IIIC/IV Ovarian Cancer

Pedro Antonio Cascales-Campos, MD, PhD[1], J. Gil, MD, PhD[1], E. Gil, MD[1], E. Feliciangeli, MD[2], A. González-Gil, MD[1], J. J. Parrilla, MD, PhD[3], and P. Parrilla, MD, PhD[1]

[1]Departamento De Cirugía General, Unidad De Cirugía De La Carcinomatosis Peritoneal, Virgen De La Arrixaca University Hospital, Murcia, Spain; [2]Departamento De Oncología Médica, Virgen De La Arrixaca University Hospital, Murcia, Spain; [3]Servicio De Ginecología y Obstetricia, Unidad De Ginecología Oncológica, Virgen De La Arrixaca University Hospital, Murcia, Spain

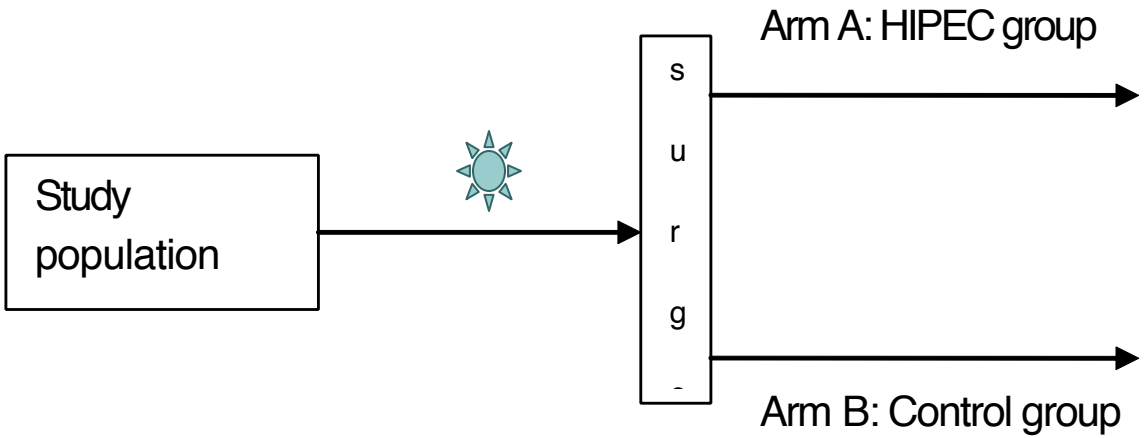
ENSAYO CLÍNICO FASE III

ENSAYO CLÍNICO

Citorreducción inicial CON ó SIN HIPEC en pacientes con carcinomatosis peritoneal de origen ovárico, tubárico y peritoneal primario.

NCT02328716

NCT02328716



	V_1	V_2	V_{end}
Days	0	30	
Months			60

EC PROSPECTIVO, RANDOMIZADO, SIMPLE CIEGO

CRITERIOS DE INCLUSIÓN
NCT02328716

- Carcinomatosis peritoneal por carcinoma epitelial de ovario, carcinoma de la trompa de Falopio y Carcinoma Peritoneal Primario de reciente diagnóstico y en estadios IIIB/C-IV.
- Edad < 75 años
- Tumor residual < 2.5 mm a la finalización de una citorreducción quirúrgica.
- Adecuada situación basal, ECOG 0-1 (Eastern Cooperative Oncologic Group)
- Adecuada función de la médula ósea con hemoglobina ≥ 8 g / dl (tras la corrección en caso de anemia por deficiencia de hierro) recuento leucocitario con ≥ 3,000 / mm3 , plaquetas ≥ 100,000 / mm3.
- Adecuada la función renal con cifras de creatinina ≤ 1,5 mg / dl
- Adecuada función hepática con cifras de bilirrubina ≤ 1,5 mg / dl y AST y ALT ≤ 80 UI / L
- Óptima función cardiopulmonar.
- En pacientes con neoadyuvancia sistémica, se contemplará la realización de la citorreducción con o sin HIPEC tras el tercer ciclo de quimioterapia, con un total de 6 ciclos de quimioterapia sistémica: Carboplatino (AUC 5) + Paclitaxel 175 mgr/m2.
- Participación voluntaria y firma del consentimiento informado por escrito.

NCT02328716

- <u>OBJETIVO PRINCIPAL</u>
  - INTERVALO LIBRE DE ENFERMEDAD (meses)

- <u>OBJETIVOS SECUNDARIOS</u>
  - SUPERVIVENCIA GLOBAL (meses)
  - MORBIMORTALIDAD (NCI-CTC v.3)
  - CALIDAD DE VIDA (AGO-OVAR 16 esp, EQ-5D3)
  - CORRELACIÓN EX-VIVO IN-VITRO

Teniendo el cuenta la población a estudio, siendo la frecuencia esperada del fenómeno de 0.025, asumiendo un error de 0.01 para un intervalo de confianza del 95%, el tamaño muestral implicaría el reclutamiento de **63 pacientes en cada brazo (n=126).**

NCT02328716

- DESDE MARZO DE 2012:
  - EVALUADOS: 51 pacientes
    - 5 no cumplían criterios de inclusión
  - SELECCIONADOS: 46 pacientes cumplían criterios de inclusión
  - DATOS INCLUIDOS: 36 pacientes
  - EXLUIDOS: 10 pacientes
    - ALERGIA QUIMIOTERAPIA POSTQX: 1 paciente
    - IRRESECABLES: 3 pacientes
    - NO QUERER PARTICIPAR POR HIPEC: 3 pacientes
    - NO QUERER PARTICIPAR POR NO HIPEC: 3 pacientes

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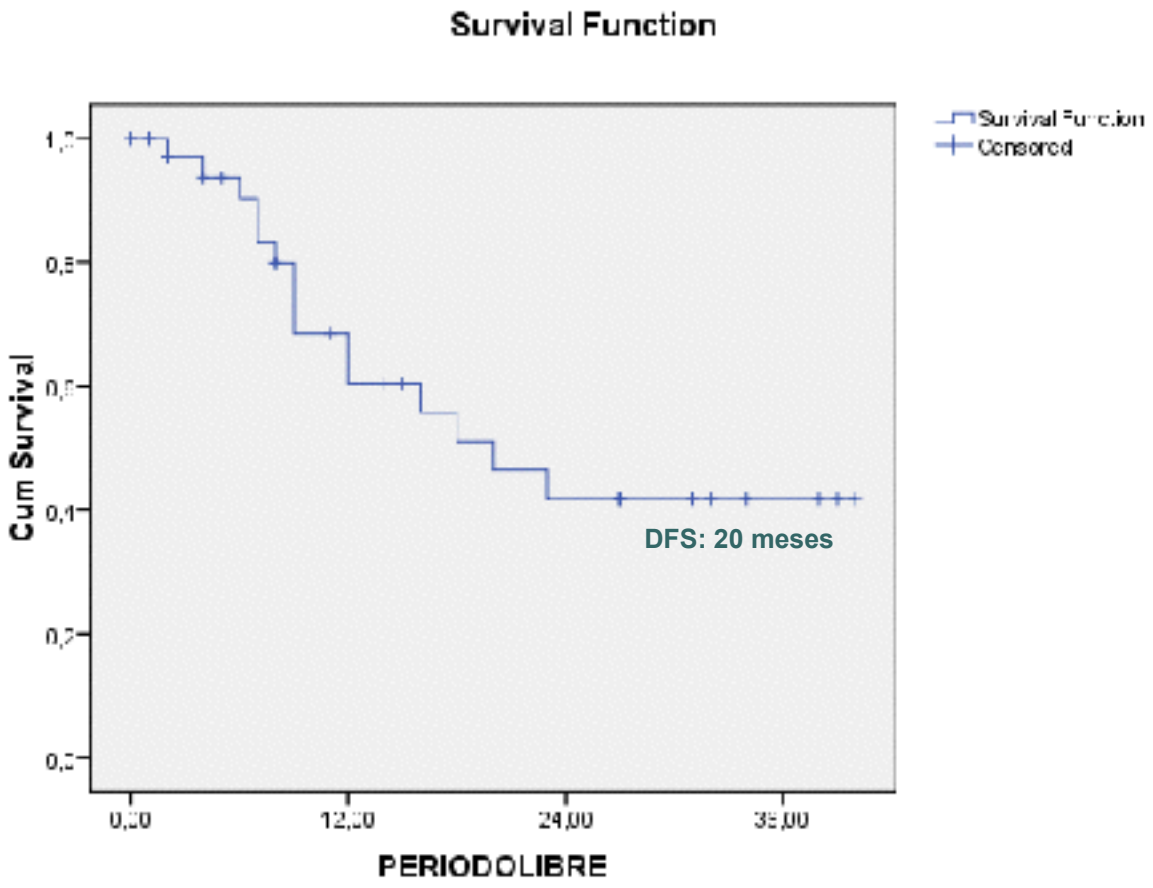

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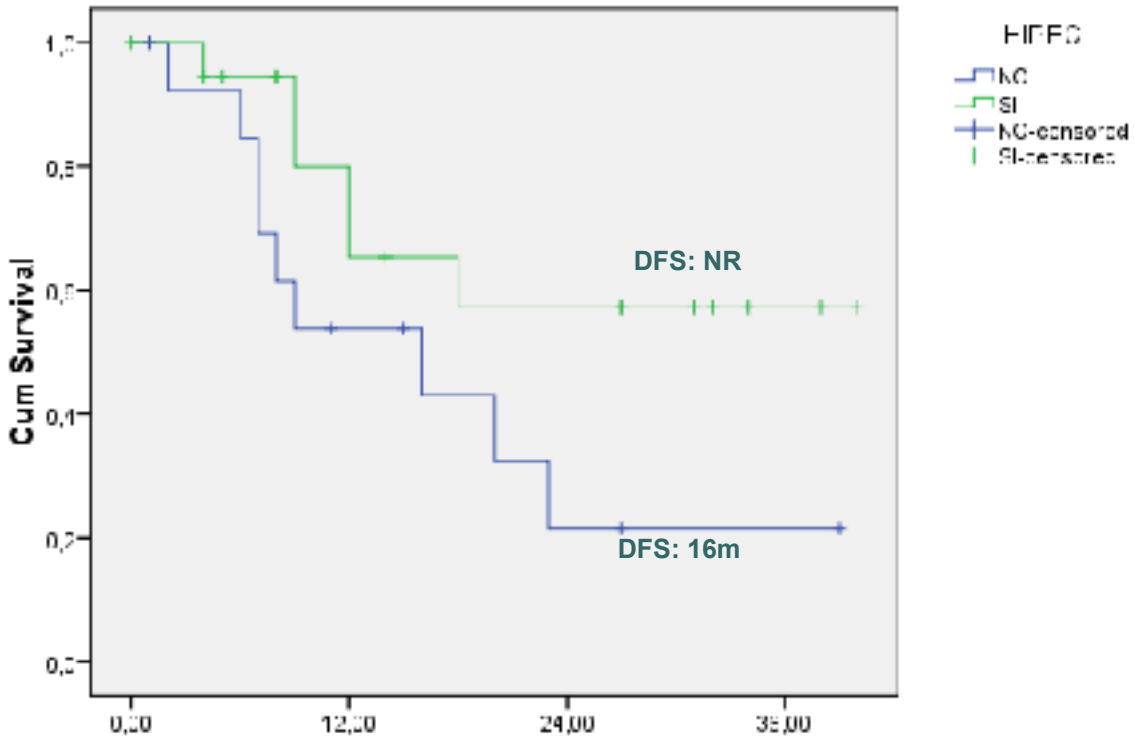

Means and Medians for Survival Time

HIPEC	Mean[a]				Median			
			95% Confidence Interval				95% Confidence Interval	
	Estimate	Std. Error	Lower Bound	Upper Bound	Estimate	Std. Error	Lower Bound	Upper Bound
NO	17,754	3,745	10,417	25,091	19,000	6,356	5,549	28,467
SI	27,629	3,084	9,881	35,261				
Overall	23,712	2,814	7,706	29,118	23,000	5,002	10,000	28,970

a. Estimation is limited to the largest survival time if it is censored.

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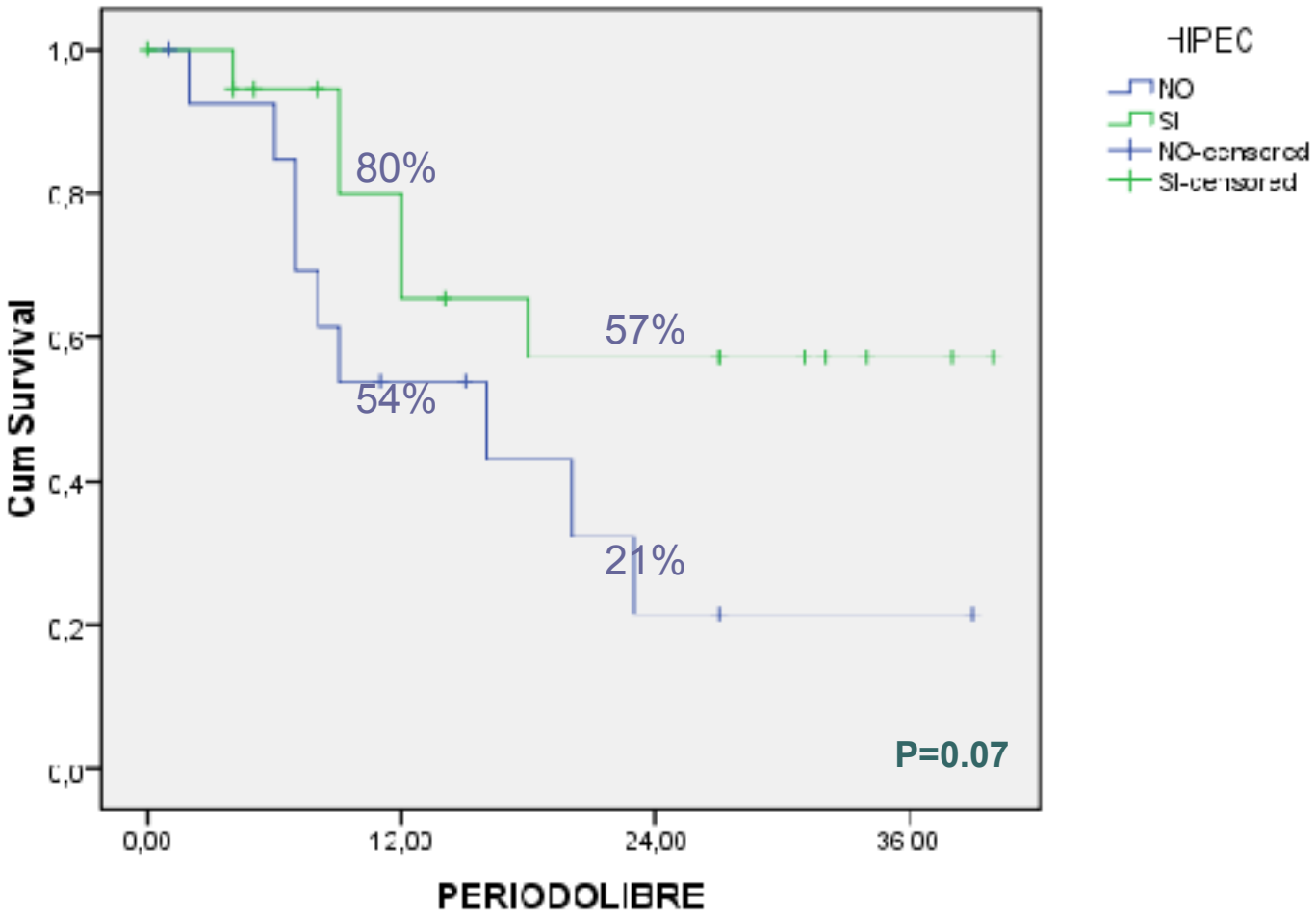

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