Carcinoma de Endometrio

Tratamiento Sistémico de Enfermedad Recurrente y Metastásica

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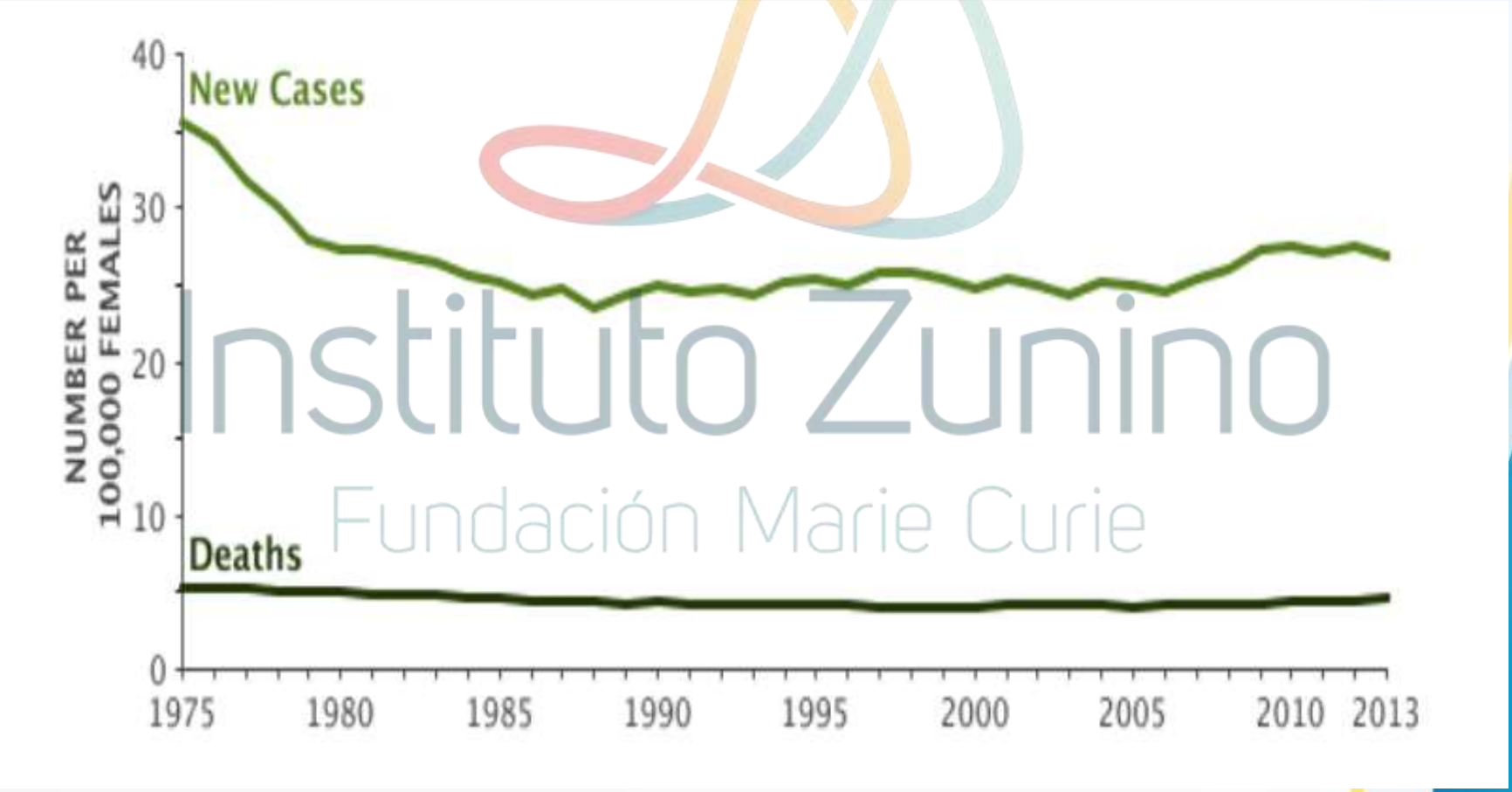
Carcinoma de Endometrio



Uterine Corpus

	2013	2018
Estimated New Cases U.S.	49,560	63,230
Estimated Deaths	8,190 (#8)	11,350 (#6)
5-year relative survival All stages	82%	81%

Carcinoma de Endometrio

- Recurrencia vaginal aislada
- Recurrencia Pelviana
- Enfermedad diseminada

- Rol de Citoreducción
- Criterios Recist
- Rol de Ca 125
- RE y RP

Hormonoterapia en Carcinoma de Endometrio

Study	Agent	Patients, no.	RR, %	Median PFS (months)	Median OS (months)
Thigpen et al. [29]	MPA 200 mg/day	331	18	4	10.5
Thigpen et al. [30]	MPA 200 mg/day	145	25	3.2	11.1
	MPA 1,000 mg/day	154	15	2.5	7
Thigpen et al. [31]	Tamoxifen 20 mg b.i.d.	68	10	1.9	10.1
McMeekin et al. [32][b]	Arzoxifene 20 mg/day	34	31	3.7	NA
Rose et al. [33]	Anastrazole 1 mg/day	23	9	1	6
Ma et al. [28]	Letrozole 2.5 mg/day	28	9	NA	NA
Covens et al. [34]	Fulvestrant 250 mg q4w	22 ER−	0	2	3
		31 ER+	16	10	26
Emons et al. [35][b]	Fulvestrant 250 mg q4w	35	11	2.3	13.2
Gallagher et al. [36]; Jeyarajah et al. [37]	Goserelin acetate 3.6 mg monthly, subcutaneously	32	28	19	NA
Lhommé et al. [38]	Triptorelin 3.75 mg q4w, subcutaneously	24	9	4.2	7.2
Asbury et al. [39]	Goserelin acetate 3.6 mg monthly, subcutaneously	40	12	1.9	7.3
Pandya et al. [40]	MGA	20	20	NA	12
	MGA and tamoxifen	42	19	NA	8.6
Whitney et al. [41]	MPA qow, tamoxifen continuously	61	33	3	13
Fiorica et al. [42]	MGA, tamoxifen alternating q3w	56	27	2.7	14

Bestvina et al. TheOncologist2016;21:1–10

Carcinoma de Endometrio
Hormonoterapia

- G1 G2
- Expresión de RH
- Asintomáticos
- Mínima invasión y citoreducción óptima
- No dosis dependencia
- Estudios Fase II
- TR: 11-56 %
- SLP 2.5 - 14 meses

Carcinoma de Endometrio
Poliquimioterapia

	Tasa de respuestas	SG
A vs AC [1]	22 vs 30	6.7 vs 7.3 (P=0.48)
A vs AP[2]	25 vs 42	9.2 vs 9 (NA)
A vs AP [3]	17 vs 43	7 vs 9 (p=0.65)

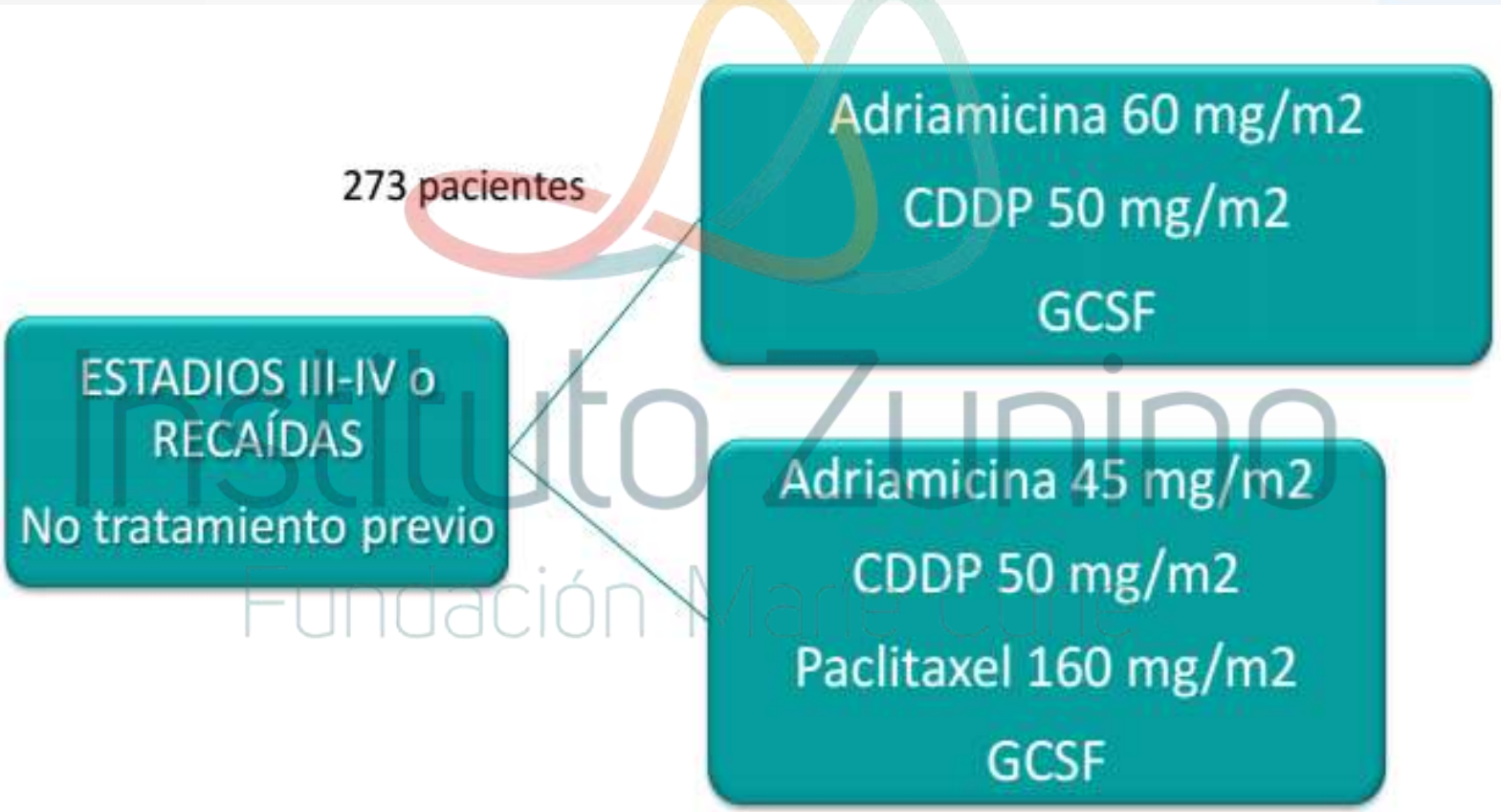
MAYOR INCIDENCIA DE MIELOTOXICIDAD Y EMESIS GRADO 3-4 CON LA COMBINACIÓN

Carcinoma de Endometrio
Poliquimioterapia

Esquema	Tasa de respuestas	SLP (meses)	SG (meses)
Adriamicina/cisplatino (AP)	40	7.2	12.6
Adriamicina-paclitaxel (AT)[1]	43	6	13.6
Adriamicina/cisplatino (AP)	27	6.7	–
carboplatino-paclitaxel (CP)[2]	35	7.7	

1. 5. Fleming GF, et al. Ann Oncol. 2004;15(8):1173- 1178.
2. Weber B, et al. Proc Am Soc Clin Oncol. 2003;22(Supplement): Abstract 1819.

Carcinoma de Endometrio
GOC 177



Fleming GF, et al. J Clin Oncol. 2004;22(11):2159-2166.

Carcinoma de Endometrio
GOC 177

	TR	SLP	SG
AP	34%	5 meses	12.3 meses
TAP	57%	8 meses	15.3 meses

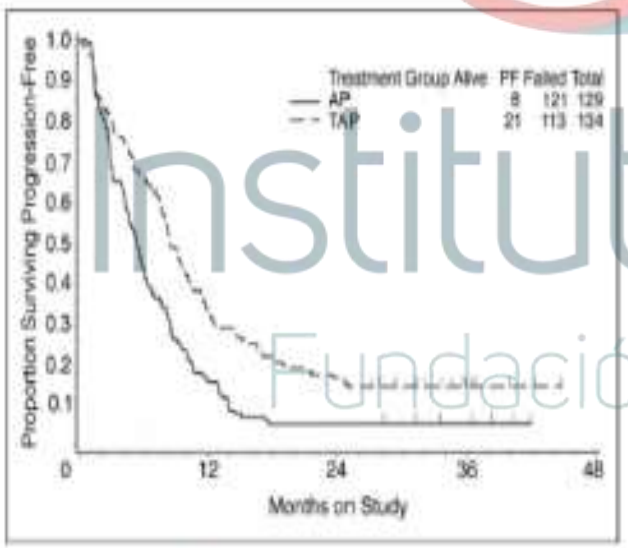


Fig 1. Progression-free (PF) survival by randomized treatment. AP, doxorubicin + cisplatin; TAP, doxorubicin + cisplatin + paclitaxel.

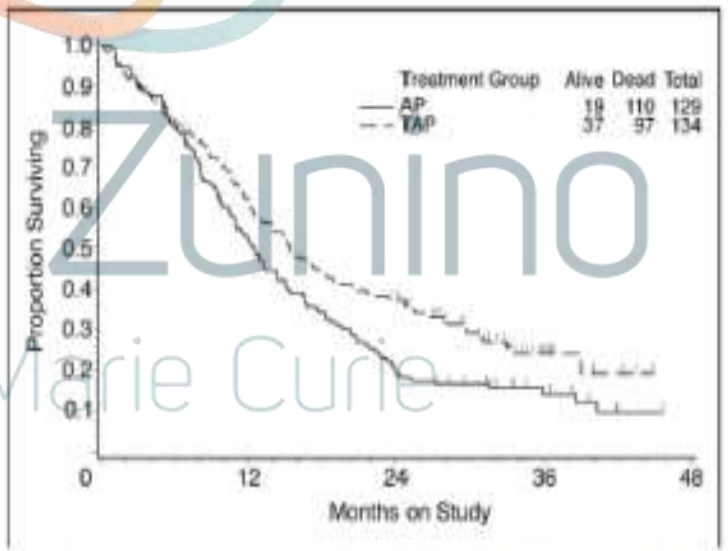
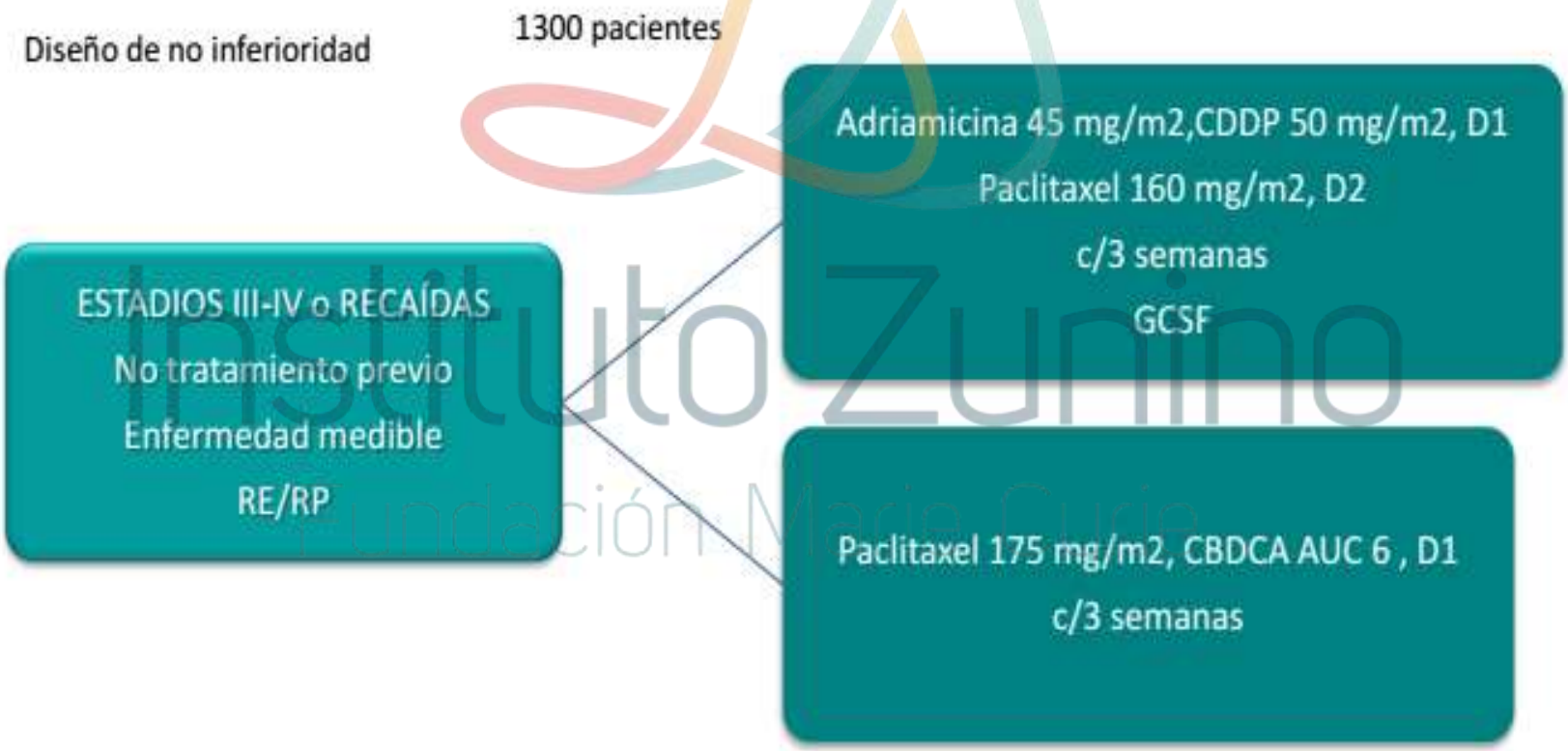


Fig 2. Survival by randomized treatment. AP, doxorubicin + cisplatin; TAP, doxorubicin + cisplatin + paclitaxel.

Mayor neurotoxicidad grado 3 con el triplete (12% v s 1%

Carcinoma de Endometrio
GOC 209



Miller D, et al. Gyn Oncol. 2012;125(3): Abstract LBA1

Carcinoma de Endometrio
GOC 209

	Tasa de respuestas (%)	SLP (meses)	SG (meses)
TC	51	13	37
TAP	51	13	40

HR:1.01

Menor incidencia de toxicidad mayor o igual a grado 2 con TC: neuropatía (19 vs 26%), trombocitopenia (12 vs 23%), emesis (4 vs 7%), diarrea (2 vs 6%) y alteraciones metabólicas (8 vs 14%)

Nuevo standard primera línea: CARBOPLATINO-PACLITAXEL

Carcinoma de Endometrio
Rol de Bevacizumab

RAMA CONTROL: CARBOPLATINO-PACLITAXEL (GOG 209)

	SLP	SG (meses)
CARBOPLATINO-PACLITAXEL-TEMSIROLIMUS	HR: 1.22 (92% 0.9- 1.5)	25
CARBOPLATINO-PACLITAXEL-BEVACIZUMAB	HR:0.85 (92% 0.6-1.02)	34
CARBOPLATINO-IXABEPILONA-BEVACIZUMAB	HR: 0.87 (92% 0.6-1.07)	25.2

Aghajanian C, et al.J Clin Oncol 2015;abstr 5500

SG rama control: 22.7

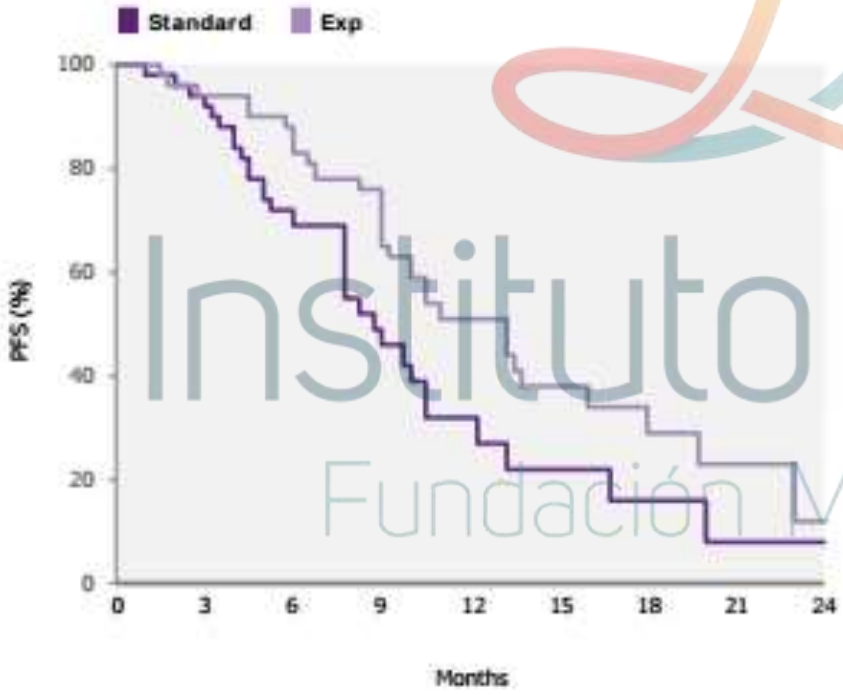
RANDOMIZED PHASE II TRIAL OF CARBOPLATIN- PACLITAXEL (CP) COMPARED TO CARBOPLATIN- PACLITAXEL-BEVACIZUMAB (CP-B) IN ADVANCED (STAGE III-IV) OR RECURRENT ENDOMETRIAL CANCER: THE MITO END-2 TRIAL

Clinical response	CP N=46 (%) (CI 95%)	CP-B N=46 (%) (CI 95%)	P value
Objective response (CR+PR)	25 (54.3) (39.9-98.7)	33 (71.7) (58.7-84.7)	0.065
SD	20 (43.5) (29.2-57.8)	10 (21.7) (9.8-33.6)	
6-months non PD (%)	69%	83%	0.09
PD	1 (2.2) (-2.0-6.4)	3 (6.5) (-0.6-13.6)	

Recurrent	*36 (59)*	*34 (55)*
Serous/Clear cell	*11 (20.3)*	*13 (24)*

Lorusso D, et al. J Clin Oncol. 2015;33(suppl): Abstract 5502

RANDOMIZED PHASE II TRIAL OF CARBOPLATIN- PACLITAXEL (CP) COMPARED TO CARBOPLATIN- PACLITAXEL-BEVACIZUMAB (CP-B) IN ADVANCED (STAGE III-IV) OR RECURRENT ENDOMETRIAL CANCER: THE MITO END-2 TRIAL



	CT (N=54)	CT-B (N=54)
Events, n	34	32
Median PFS, months (95% CI)	8.7 (6.3-11.2)	13 (9.2-16.8)
HR (stratified) (95% CI) 2-sided log-rank p-value	0.59 (0.35–0.98) 0.036	

Lorusso D, et al. J Clin Oncol. 2015;33(suppl): Abstract

Endometrial Carcinoma
Selected Second-Line Phase II cytotoxic trials

Agent	Response Rate
Liposomal Doxorubicin	9.5%
Topotecan	9%
Ixabepilone	12%
Pemetrexed	4%
Gemcitabine	4%

Carcinoma de Endometrio
Quimioterapia 2 Línea

¿INTERVALO LIBRE DE PLATINO?

TASA DE RESPUESTAS

- ILP < 6 meses: 25%
- ILP > 24 meses: 65%

Nagao S, et al.Gynecol Oncol 2013; 131:567–573.

Carcinoma de Endometrio
Quimioterapia 2 Línea

Study	Agent	Patients, no.	RR, %
Pawinski et al. [62]	Cyclophosphamide	15	0
Rose et al. [61]	Etoposide PO	22	0
Tait et al. [64]	Gemcitabine	23	4
Sutton et al. [65]	Ifosfamide	40	15
Pawinski et al. [62]	Ifosfamide	16	0
Dizon et al. [66]	Ixabepilone	50	12
McMeekin et al. [67][a]	Ixabepilone	223	15
Muggia et al. [60]	Liposomal doxorubicin	42	9.5
Fracasso et al. [57]	Oxaliplatin	52	13.5
Lissoni et al. [55]	Paclitaxel	19	37
Lincoln et al. [54]	Paclitaxel	44	27
Markman et al. [56]	Paclitaxel	48	20.9
Homesley et al. [53]	Paclitaxel	15	26.7
Miller et al. [63]	Pemetrexed	25	4
Miller et al. [59]	Topotecan	22	9

[a]All trials were phase II, with the exception of the McMeekin et al. study [67], which was one arm of a phase III trial.

Bestvina et al. TheOncologist2016;21:1–10

Carcinoma de Endometrio
Quimioterapia 2 Línea

- Fase III: Rama control (adriamicina o paclitaxel) vs ixabepilona
- Rama control: 69% pacientes recibieron adriamicina
- QT previas: 50% adyuvancia o neoadyuvancia

	Tasa de respuestas (%)	SG
Control	15.2	12.3 P=0.04)
Ixabepilona	15.7	10.9

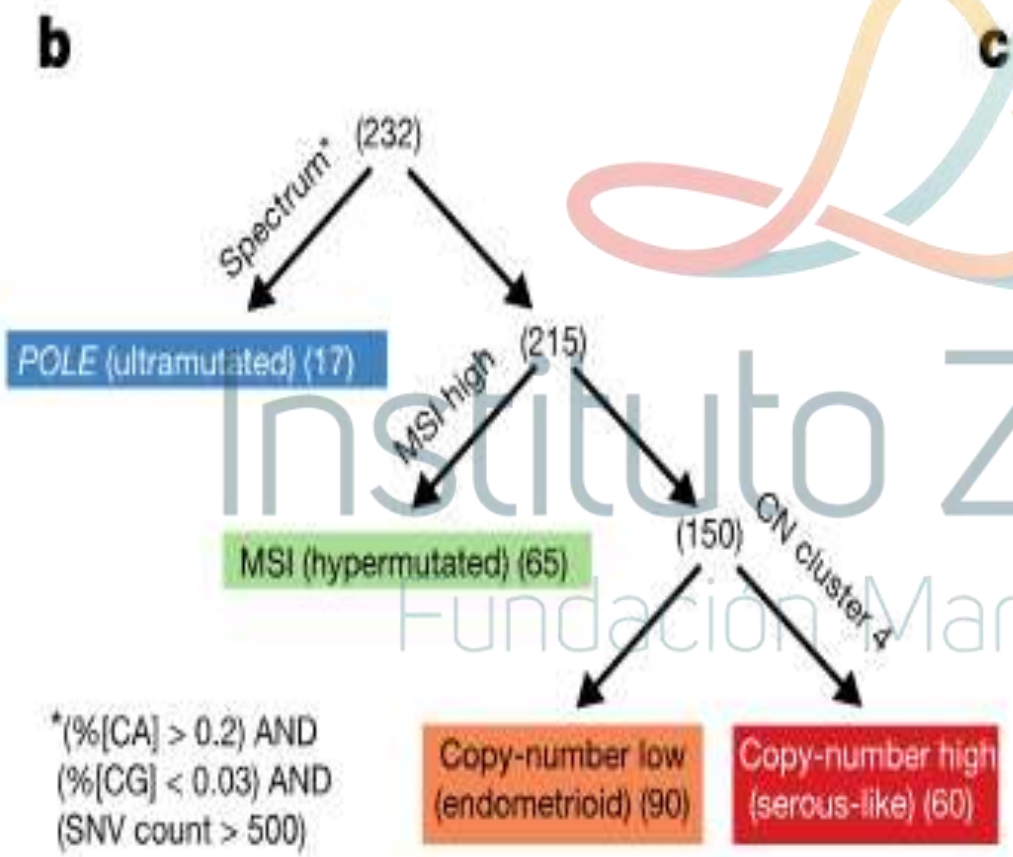
McMeekin S, et al. Gynecol Oncol 2015;138:18–23

Carcinoma de Endometrio
Quimioterapia 2 línea

- No candidatos a htp - Inmunoterapia
- Tiempo libre de enfermedad
- Mono o poliquimioterapia
- SV próximas al año

Integrated genomic characterization of endometrial carcinoma

The Cancer Genome Atlas Research Network*



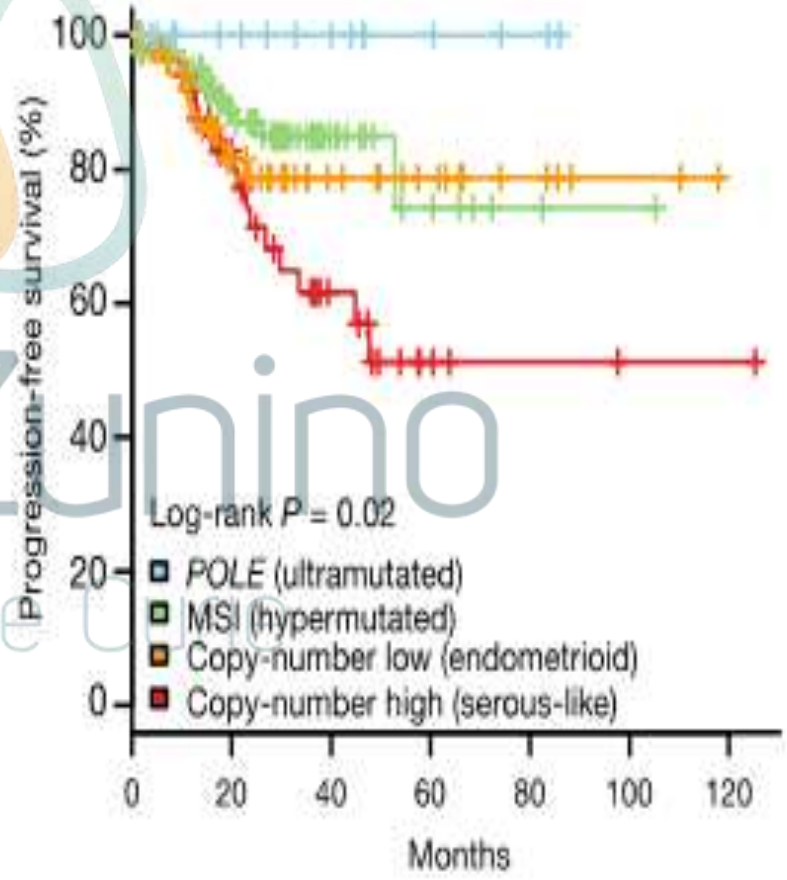
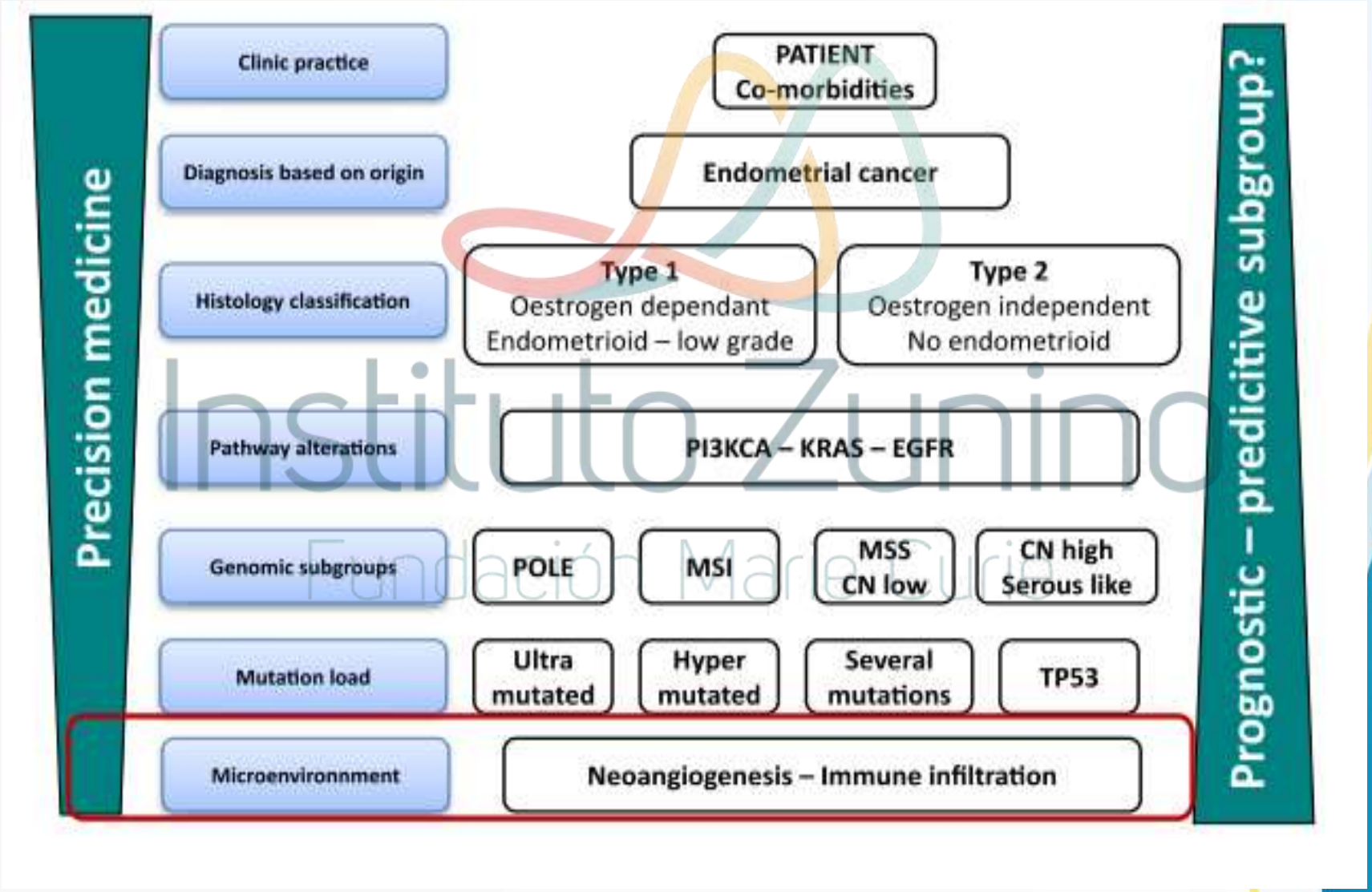


Table 1 Characteristics of four genomic classes of endometrioid and serous carcinomas defined by the TGCA

	POLE (ultramutated)	MSI (hypermutated)	Copy-number low (endometriod)	Copy-number high (serous-like)
Copy-number alterations	Low	Low	Low	High
MSI/MLH1 methylation	Mixed MSI high, low, stable	MSI high	MSI stable	MSI stable
Mutation rate	Very high (232×10^{-4} mutations/Mb)	High (18×10^{-4} mutations/Mb)	Low (2.09×10^{-4} mutations/Mb)	Low (2.3×10^{-4} mutations/Mb)
Molecular profile	POLE (100 %) PTEN (94 %) PIK3CA (71 % PIK3R1 (65 %) FBXW7 (82 %) ARID1A (76 % KRAS (53 %) ARID5b (47 %) PD1/PD-L1 overexpression	PTEN (88 % RPL22 (37 %) KRAS (35) PIK3CA (54 % PIK3R1 (40 %) ARID1A (37 %) PD1/PD-L1 overexpression	PTEN (77 %) CTNNB1 (52 % PIK3CA (53 %) PIK3R1 (33 %) ARID1A (42 %) FGFR2 (10.9 %	TP53 (92 % PPP2R1A (22 %) FBXW7 (22 %) PIK3CA (47 % PTEN (11 %) FGFR amplifications and mutations (7 %) HER2 amplified 25 %
Histological type	Endometrioid	Endometrioid	Endometrioid	Serous, Endometrioid, and mixed serous and endometrioid
Tumor grade	Mixed (grades 1–3)	Mixed (grades 1–3)	Grade 1–2	Grade 3
Prognostic	Good	Intermediate	Intermediate	Poor
Potential drugs	PI3K/PTEN/AKT/mTOR pathway inhibitors PARP inhibitors Anti-PD1/PD-L1 inhibitors HDAC inhibitors (against FBXW7 mutations) Hormonal therapies	PI3K/PTEN/AKT/mTOR pathway inhibitors PARP inhibitors Anti-PD1/PD-L1 inhibitors Hormonal therapies	PI3K/PTEN/AKT/mTOR pathway inhibitors PARP inhibitors Hormonal therapies FGFR inhibitors	HER2 targeted inhibitors PI3K inhibitors PARP inhibitors Wee-1 inhibitors HDAC inhibitors (against FBXW7 mutations) FGFR inhibitors

Mb megabase, *MSI* microsatellite instability, *HDAC* Histone deacetylases

Carcinoma de Endometrio



VOLUME 36 · NUMBER 20 · JULY 10, 2018

JOURNAL OF CLINICAL ONCOLOGY

ORIGINAL REPORT

Randomized Phase II Trial of Carboplatin-Paclitaxel Versus Carboplatin-Paclitaxel-Trastuzumab in Uterine Serous Carcinomas That Overexpress Human Epidermal Growth Factor Receptor 2/neu

Amanda N. Fader, Dana M. Roque, Eric Siegel, Natalia Buza, Pei Hui, Osama Abdelghany, Setsuko K. Chambers, Angeles Alvarez Secord, Laura Havrilesky, David M. O'Malley, Floor Backes, Nicole Nevadunsky, Babak Edraki, Dirk Pikaart, William Lowery, Karim S. ElSahwi, Paul Celano, Stefania Bellone, Masoud Azodi, Babak Litkouhi, Elena Ratner, Dan-Arin Silasi, Peter E. Schwartz, and Alessandro D. Santin

Carcinoma de Endometrio Seroso

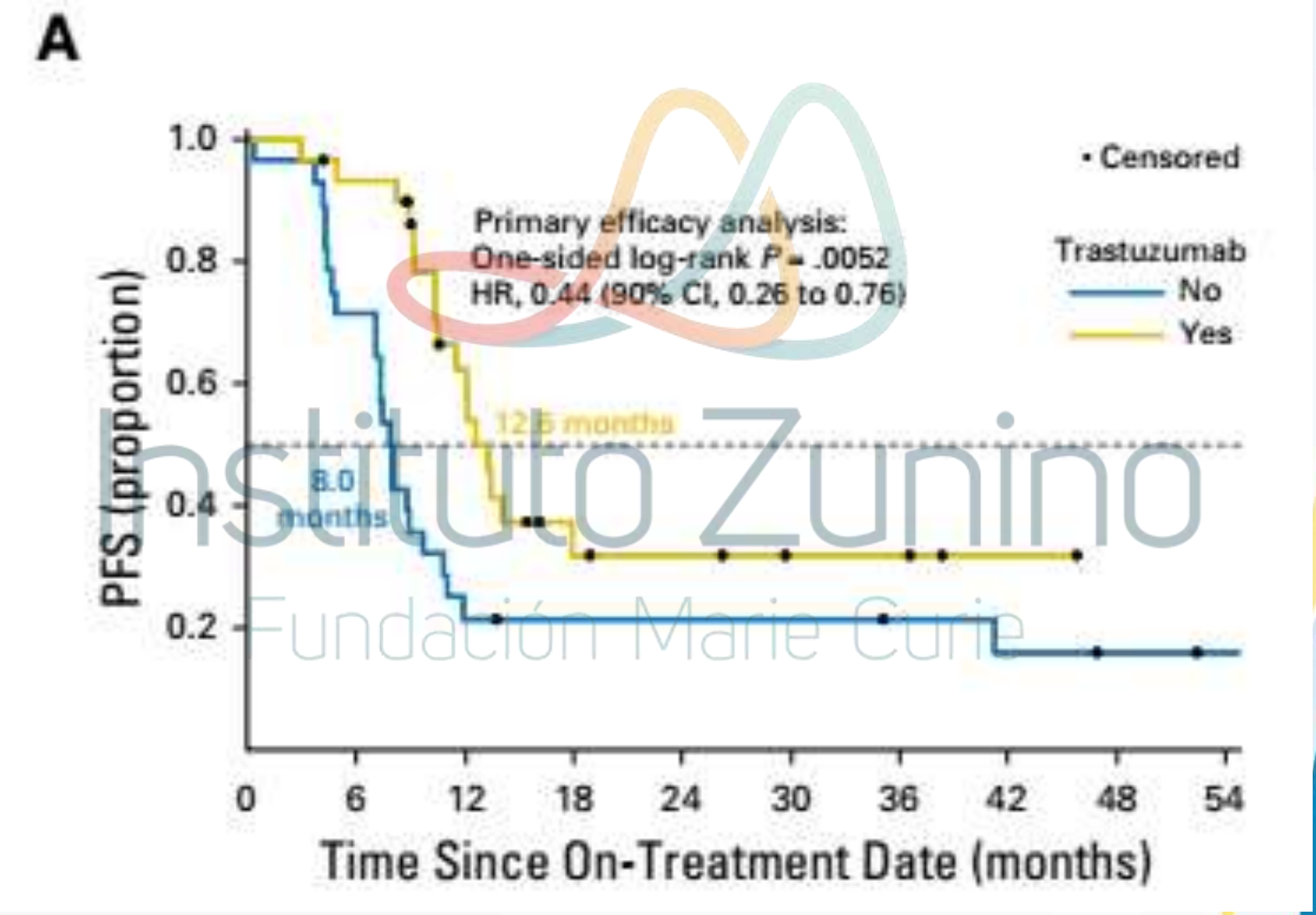
- Representa 10% de los casos
- Responsable del 40% de la mortalidad de carcinoma de endometrio
- Her2 expresa en 25% de los casos
- SLP end point

Table 1. Patient and Disease Characteristics

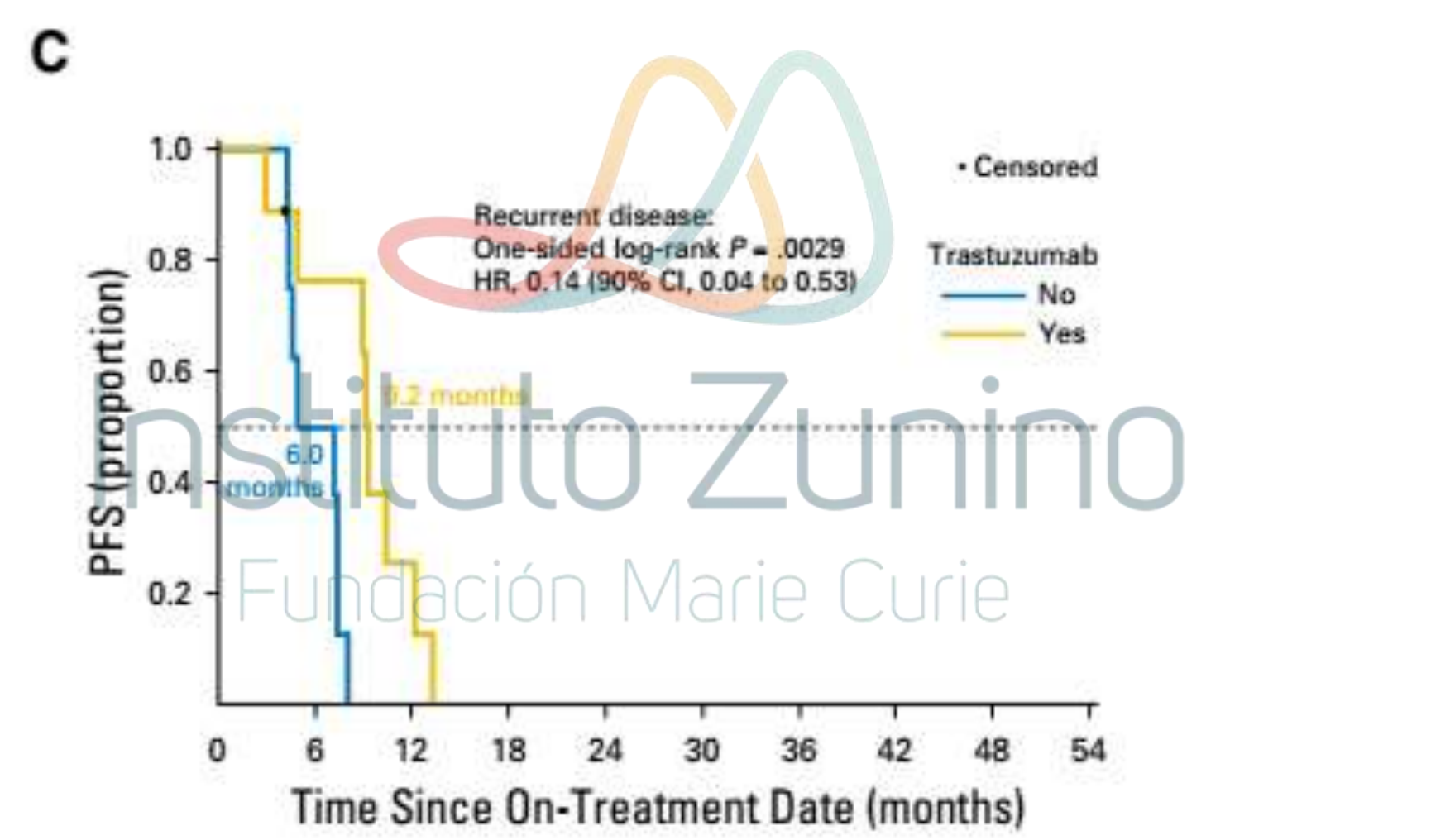
Characteristic	Control Arm		Experimental Arm		Both Arms	
	No.	%	No.	%	No.	%
All patients	(n = 28)		(n = 30)		(n = 58)	
Age,* years						
Median	73		67		69	
Quartiles	68-78		64-69		65-73	
Range	45-88		57-85		45-88	
Race						
White	17	61	20	67	37	64
Black or African American	8	29	10	33	18	31
Asian	1	4	0	0	1	2
American Indian/Alaska native	1	4	0	0	1	2
Unknown	1	4	0	0	1	2
Ethnicity						
Hispanic or Latino	1	4	3	10	4	7
Non-Hispanic or Latino	26	93	26	87	52	90
Unknown	1	4	1	3	2	3
Disease status						
Advanced	20	71	21	70	41	71
Recurrent	8	29	9	30	17	29
Study site						
Duke University Medical Center	3	11	3	10	6	10
Greater Baltimore Medical Center	3	11	3	10	6	10
Jersey Shore University Medical Center	0	0	1	3	1	2
John Muir Medical Center	1	4	2	7	3	5
Montefiore Medical Center	1	4	2	7	3	5
Penrose–St Francis Medical Center	3	11	1	3	4	7
Ohio State–Wexner Medical Center	3	11	3	10	6	10
University of Arizona Cancer Center	3	11	2	7	5	9
University of Maryland	1	4	2	7	3	5
Walter Reed National Military Medical Center	1	4	1	3	2	3
Yale University	9	32	10	33	19	33
Advanced-disease subgroup	(n = 20)		(n = 21)		(n = 41)	
FIGO stage						
Stage IIIA	3	15	1	5	4	10
Stage IIIB	0	0	1	5	1	2
Stage IIIC1	5	25	3	14	8	20
Stage IIIC2	4	20	6	29	10	24
Stage IV	2	10	4	19	6	15
Stage IVB	6	30	6	29	12	29
Primary radiation						
No	9	45	10	48	19	46
Yes	11	55	11	52	22	54
Residual disease						
No	17	85	19	90	36	88
Yes	3	15	2	10	5	12
Recurrent-disease subgroup	(n = 8)		(n = 9)		(n = 17)	
Prior lines						
0	1	13	2	22	3	18
1	6	75	5	56	11	65
2	1	13	2	22	3	18

Abbreviation: FIGO, International Federation of Gynecology and Obstetrics.
*Median age was significantly lower in the experimental arm ($P = .006$). All other characteristics were not significantly different between treatment arms.

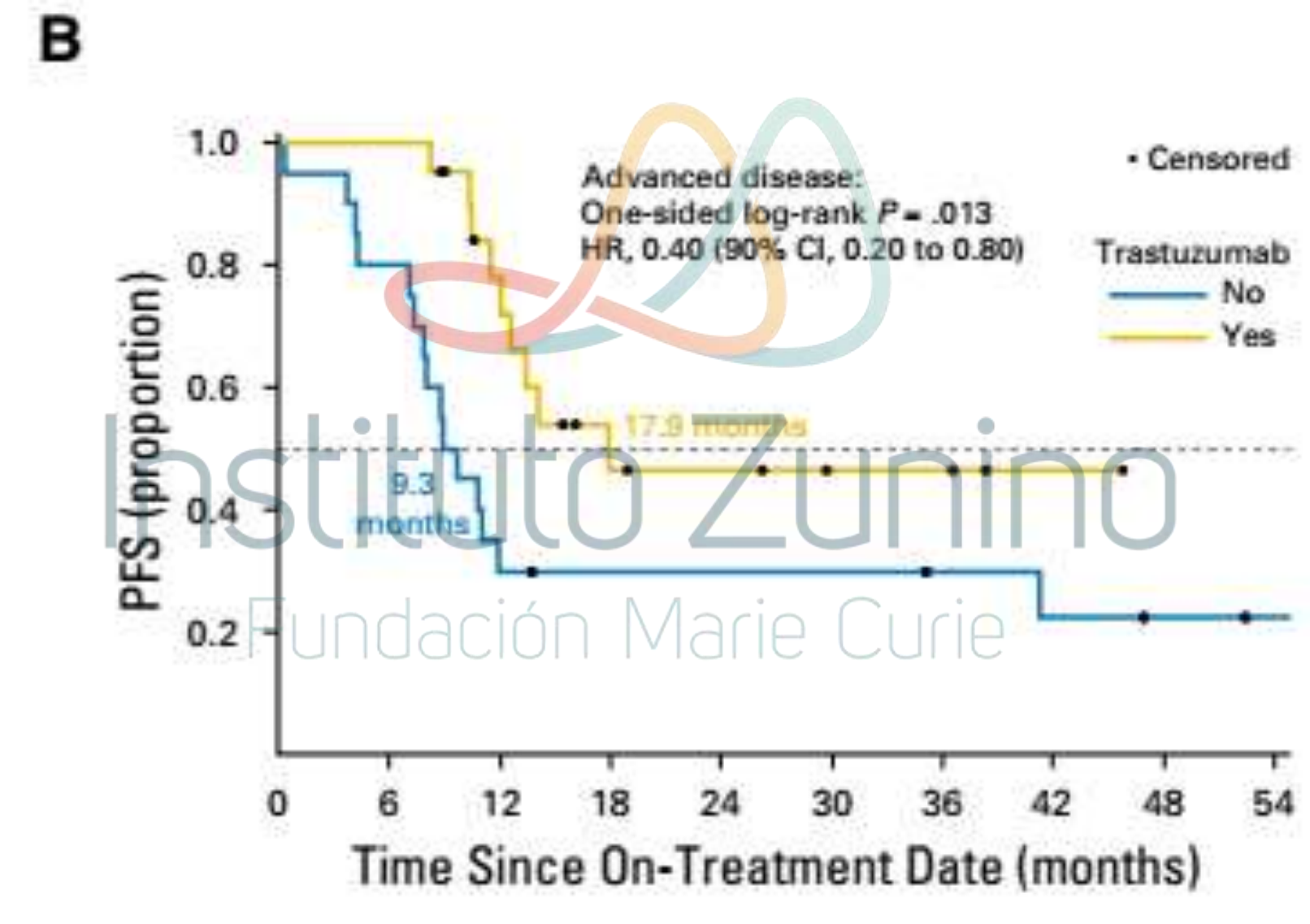
Trastuzumab en Cáncer de Endometrio



Trastuzumab en Cáncer Endometrio



Trastuzumab en Cáncer de Endometrio



Trastuzumab en Cáncer de Endometrio

- Diferencia etaria entre las ramas
- No revisión central de imágenes
- Cerrado temprano por lento enrolamiento
- No hay datos de Sobrevida

- Cambio Práctica Clínica !!!

VOLUME 35 · NUMBER 22 · AUGUST 1, 2017

JOURNAL OF CLINICAL ONCOLOGY

ORIGINAL REPORT

Safety and Antitumor Activity of Pembrolizumab in Advanced Programmed Death Ligand 1–Positive Endometrial Cancer: Results From the KEYNOTE-028 Study

Patrick A. Ott, Yung-Jue Bang, Dominique Berton-Rigaud, Elena Elez, Michael J. Pishvaian, Hope S. Rugo, Igor Puzanov, Janice M. Mehnert, Kyaw L. Aung, Juanita Lopez, Marion Carrigan, Sanatan Saraf, Mei Chen, and Jean-Charles Soria

Carcinoma de Endometrio
Keynote 028

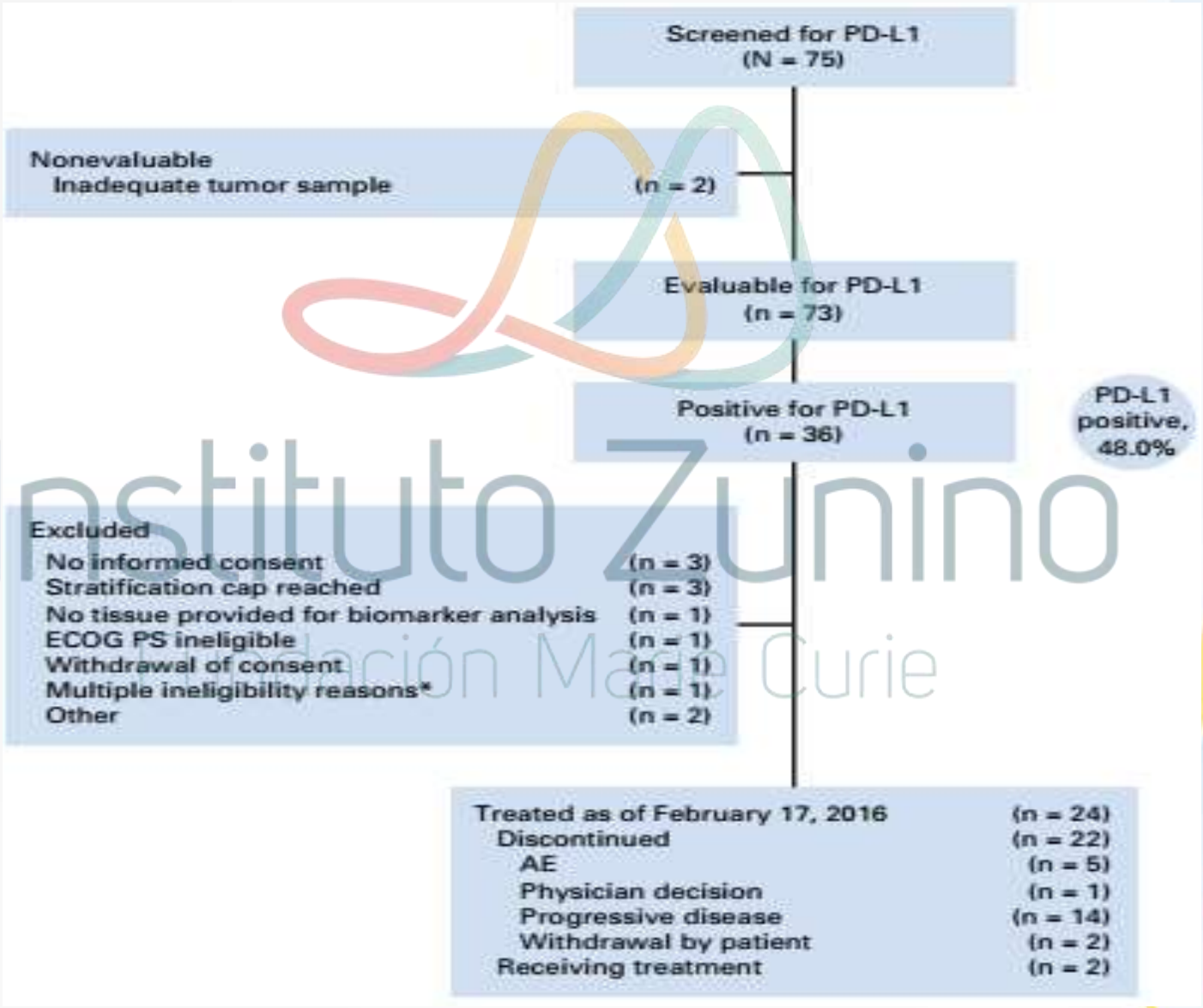


Table 1. Baseline Characteristics (N = 24)

Characteristic	No. (%)
Age, years	
Median	67
Range	34-87
Race	
White	17 (70.8)
Asian	3 (12.5)
Black or African American	1 (4.2)
Not specified	3 (12.5)
ECOG PS*	
0	7 (29.2)
1	16 (66.7)
Histology*	
Endometrioid adenocarcinoma	17 (70.8)
Adenocarcinoma other	3 (12.5)
High-grade serous carcinoma	2 (8.3)
Carcinosarcoma	1 (4.2)
Prior (neo)adjuvant therapy	12 (50.0)
No. of lines of prior therapy for advanced disease	
0	2 (8.3)
1	7 (29.2)
2	5 (20.8)
3	6 (25.0)
4	2 (8.3)
≥ 5	2 (8.3)
Previous treatments received by > two patients†	
Paclitaxel + platinum	20 (83.3)
Doxorubicin monotherapy	9 (37.5)
Doxorubicin + platinum	5 (20.8)
Paclitaxel monotherapy	4 (16.7)

Carcinoma de Endometrio
Keynote 028

Table 2. Treatment-Related AEs Observed in ≥ Two Patients (N = 24)

AE	No. (%)
Any	13 (54.2)
Fatigue	5 (20.8)
Pruritus	4 (16.7)
Pyrexia	3 (12.5)
Decreased appetite	3 (12.5)
Asthenia	2 (8.3)
Anemia	2 (8.3)
Arthralgia	2 (8.3)

Abbreviation: AE, adverse event.

Carcinoma de Endometrio
Keynote 028

Table 3. Best Objective Response Assessed per RECIST (version 1.1) by Investigator Review (n = 23)

Best Objective Response	No.	%	95% CI
Objective response rate*	3	13.0	2.8 to 33.6
PR†	3	13.0	2.8 to 33.6
Stable disease	3	13.0	2.8 to 33.6
Progressive disease‡	13	56.5	34.5 to 76.8
No assessment§	3	13.0	2.8 to 33.6
Nonevaluable‖	1	4.3	0.1 to 21.9

Carcinoma de Endometrio
Keynote 028

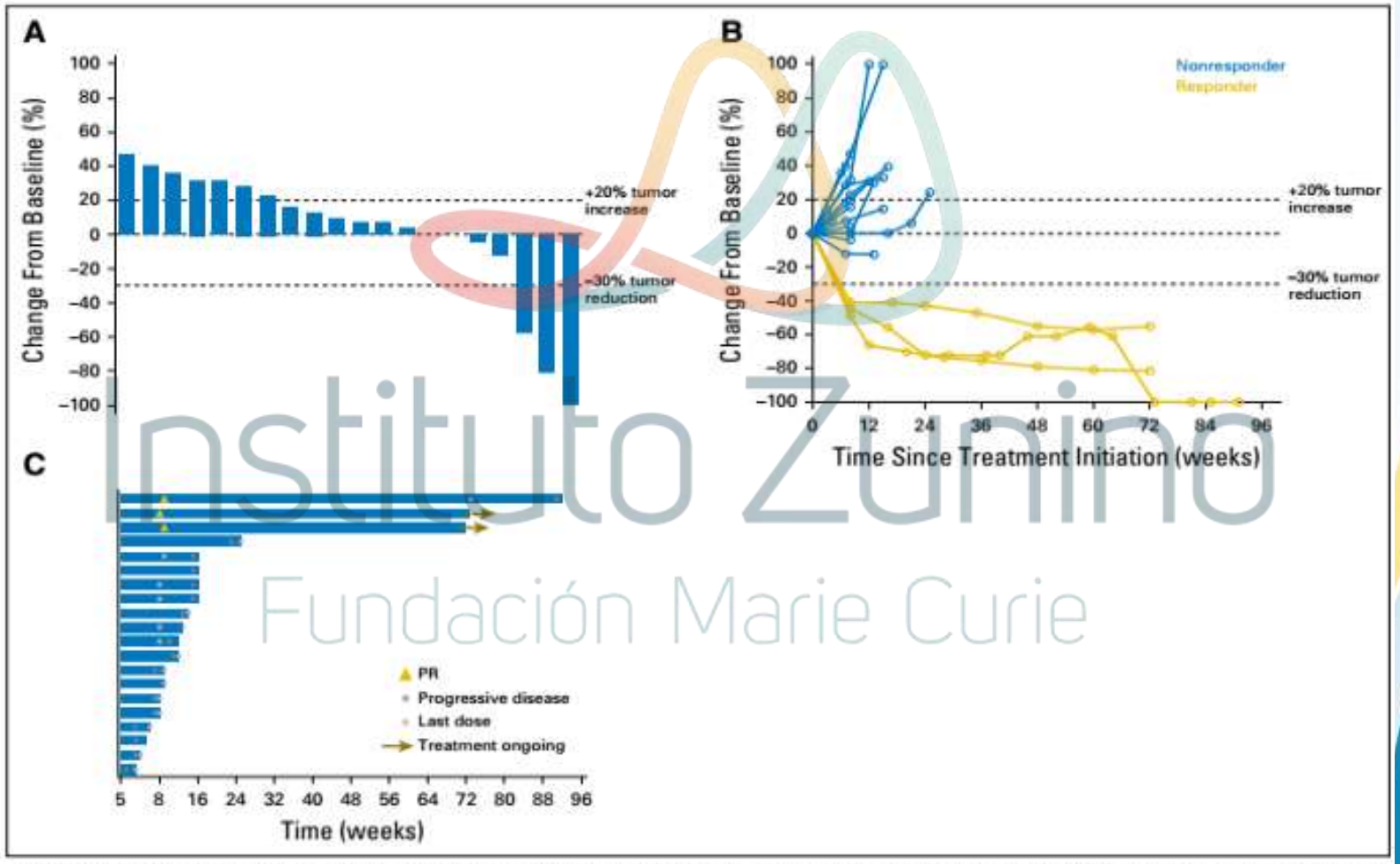


Fig 2. (A) Maximum change from baseline in tumor size (n = 20). (B) Longitudinal change from baseline in tumor size (n = 20). (C) Treatment exposure and response duration (n = 20). PR, partial response.

Carcinoma de Endometrio
Keynote 028

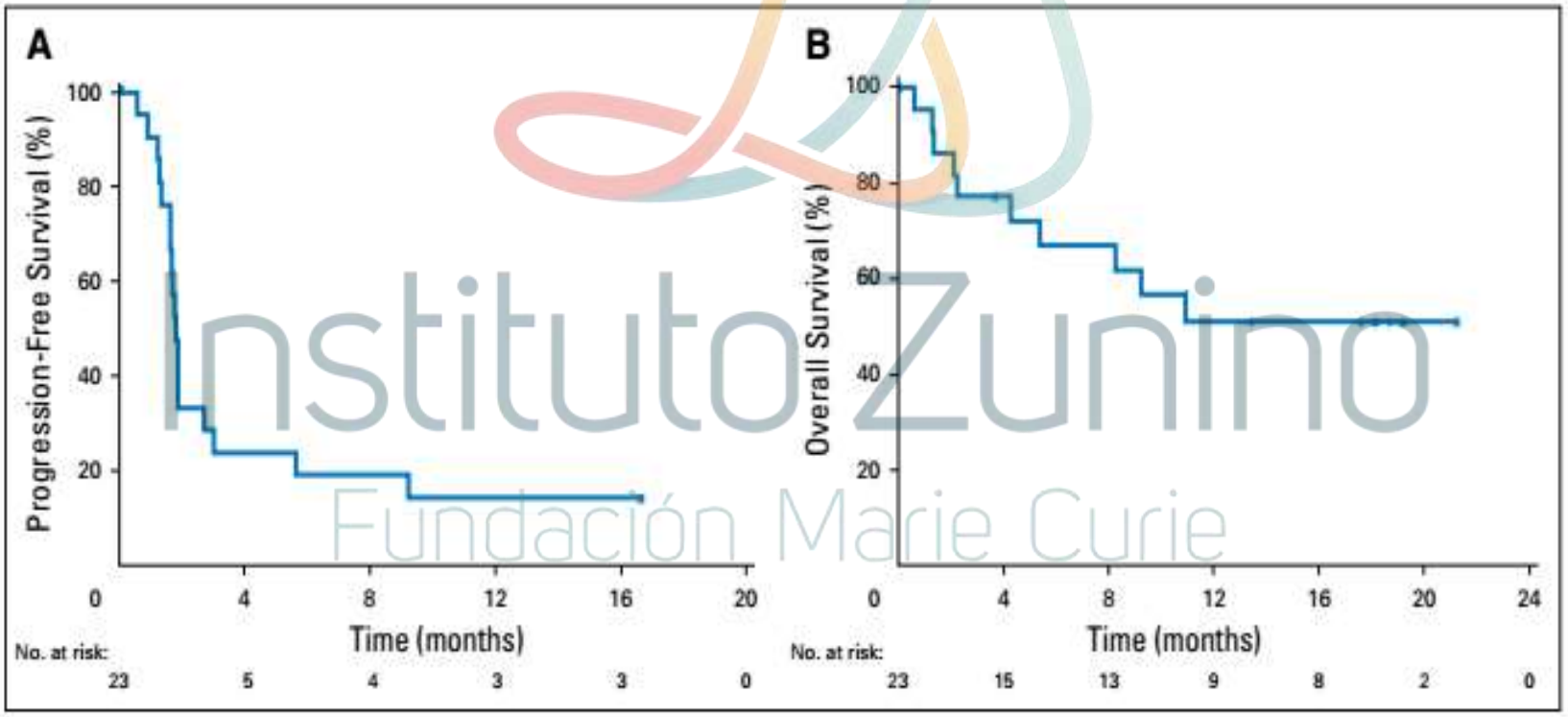


Fig 3. Kaplan-Meier estimates of (A) progression-free and (B) overall survival.

Carcinoma de Endometrio
Keynote 028

- Pembrolizumab: Pdl-1 o IMS ?
- Compite con hormonoterapia en 2 línea
- Reservado para alto riesgo
- Cambio práctica clínica!!!

ZoptEC: Phase III randomized controlled study comparing zoptarelin with doxorubicin as second line therapy for locally advanced, recurrent, or metastatic endometrial cancer (NCT01767155).

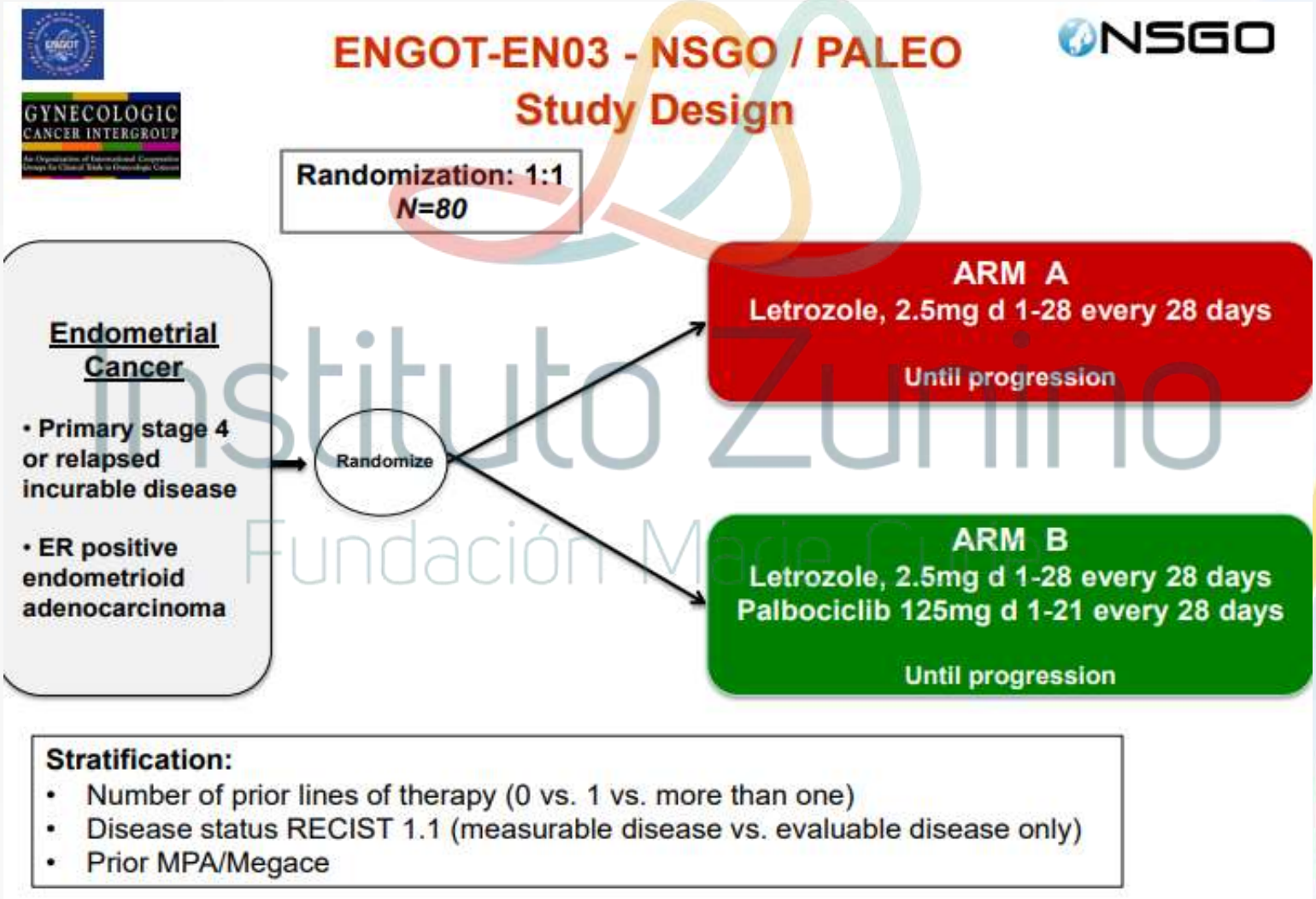
Presented Tuesday, June 5, 2018

ZoptEC trial

- Rationally designed
- Adequately powered, promptly accrued
- Phase II AGO-GYN 5 data
  - 25% RR (23% with prior chemotherapy)
- Negative
  - RR 14% for either arm
    - What was RR for doxorubicin in patients whose prior chemotherapy was in setting of metastatic disease?
  - Toxicities similar
    - Was alopecia similar?

Palbociclib versus placebo in combination with letrozole for patients with advanced or recurrent endometrial cancer: The NSGO ENGOT-EN3/PALEO trial.

Mansoor Raza Mirza, Vanda Salutari, Cesar Mendiola, Jalid Sehouli, Rene dePont Christensen, Line Bjorge, ...



Carcinoma de Endometrio

PI3K targeting agents

- AIs in breast cancer have been reported to upregulate PI3K pathway
- GOG 3007 randomized EC trial of everolimus/letrozole vs MPA/tamoxifen reported at SGO
  - 0-1 prior regimens
  - 66% endometrioid
  - RR for E/L 24%
  - No grade3/4 toxicity

GOG 3007, a randomized phase II (RP2) trial of everolimus and letrozole (EL) or hormonal therapy (medroxyprogesterone acetate/tamoxifen, PT) in women with advanced, persistent or recurrent endometrial carcinoma (EC): A GOG Foundation study

B.M. Slomovitz[a,b,*], V.L. Filiaci[c], R.L. Coleman[d], J.L. Walker[e], A.C. Fleury[f], L.L. Holman[g], D.S. Miller[h]

Regimen	N	RR-Intent-to-treat	RR-NPC	RR or Stable	PFS mos.	Overall Survival mos.	Grade 3/4 TE
EL	37	24%	53%	78%	6.4	20.0	0%
PT	36	22%	43%	69%	3.8	16.6	8.3%

Carcinoma de Endometrio

PI3K targeting agents in EC

- Tendency to excessive toxicity
- Increased response rates in genomically targeted subset difficult to show

Carcinoma de Endometrio

PARPi in EC

- Case report of decreased size of brain metastases in pt with PTEN deficient EC
- Ongoing trial of single agent niraparib (NCT03016338)

Carcinoma de Endometrio

PARPi + anti AKT/mTOR/PI3k

- Westin et al show PARPi upregulate PI3K pathway
- Other preclinical data show inhibition of PI3K-AKT-mTOR sensitizes cancers to PARPi
- Westin et al have reported (ESMO 2017) a 50% (4/8) RR in recurrent EC with olaparib + AZK5363 (AKTi)

Carcinoma de Endometrio

Olaparib + Vistusertib (mTORC1/2i)

- Promising RR in pretreated EC (27% overall) with good duration of response!
  - Responses seen in endometrioid and serous subtypes
- Combination appears moderately toxic
  - Would a more traditional mTORi work as well?
- Further development clearly warranted
  - Randomized trial will eventually be needed

Carcinoma de Endometrio
Metformina

- Fase II con 54 pacientes
- 2 o más líneas de tratamiento previo

Beneficio clínico	Tasa de respuestas
66.7%	29 %

Soliman P ,et al. J Clin Oncol 34, 2016 (suppl; abstr 5506)

Carcinoma de Endometrio Avanzado Conclusiones

- Sobrevida sin cambios signifcativos
- Htp puede ser utilizado en 1a ó 2da línea
  - Baja agresividad
  - Mínima carga tumoral
- Quimioterapia 1a Línea estándart PC
  - Enfermedad agresiva
  - Alta carga tumoral
- Bevacizumab beneficio en Slp
  - Puede ser utilizado bajo ciertas circunstancias en 2a línea...

Carcinoma de Endometrio Avanzado Conclusiones

- Caracterización Histológica - Molecular:
  - Importancia pronóstica
  - Definir terapias blanco
- Carcinoma Seroso:
  - Trastuzumab 1 línea con CP
- Inmunoterapia:
  - Compite con htp por 2 línea terapéutica
  - Definir utilidad por pdl-1 o IMS

Carcinoma de Endometrio Avanzado Conclusiones

- Quimioterapia de 2a línea en NO candidatos a hormonoterapia - imunoterapia

- Nuevas combinaciones

  Lestrozol palbociclib

  Everolimus Lestrozol

  Inhibidores de Parp +- iPI3K / imTOR

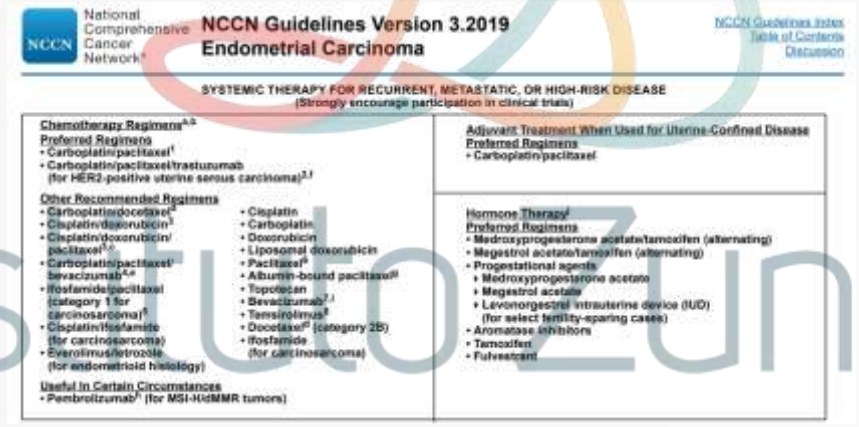
  Metformina

- Reemplazo de quimioterapia ?

- Gracias por su atención

Instituto Zunino

Fundación Marie Curie



National Comprehensive Cancer Network

NCCN Guidelines Version 3.2019
Endometrial Carcinoma

NCCN Guidelines Index
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(Strongly encourage participation in clinical trials)

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- Carboplatin/paclitaxel/trastuzumab (for HER2-positive uterine serous carcinoma)[2,f]

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Useful In Certain Circumstances
- Pembrolizumab[h] (for MSI-H/dMMR tumors)

Adjuvant Treatment When Used for Uterine-Confined Disease

Preferred Regimens
- Carboplatin/paclitaxel

Hormone Therapy[i]

Preferred Regimens
- Medroxyprogesterone acetate/tamoxifen (alternating)
- Megestrol acetate/tamoxifen (alternating)
- Progestational agents
  - Medroxyprogesterone acetate
  - Megestrol acetate
  - Levonorgestrel intrauterine device (IUD) (for select fertility-sparing cases)
- Aromatase inhibitors
- Tamoxifen
- Fulvestrant

Uterine Sarcoma

- Carcinosarcoma (metaplastic carcinoma)
- Leiomyosarcoma
- Low grade endometrial stromal sarcoma (*JAZF1-SUZ12* fusion)
- High grade ESS (*YWHAE-NUTM2A/B* fusion)
- Undifferentiated uterine sarcoma
- Fibrosarcoma-like tumors with *NTRK* fusions?

Uterine Leiomyosarcoma

- 1% of uterine malignancies
  - Somewhat over 1500 cases in US per year
- 60% with early stage disease
- 5 yr disease-specific survival stage I = 75%
  - 50+% recur
  - Stage, grade, race, prognostic

EORTC 55874

--224 patients in 13 years

--103 uLMS

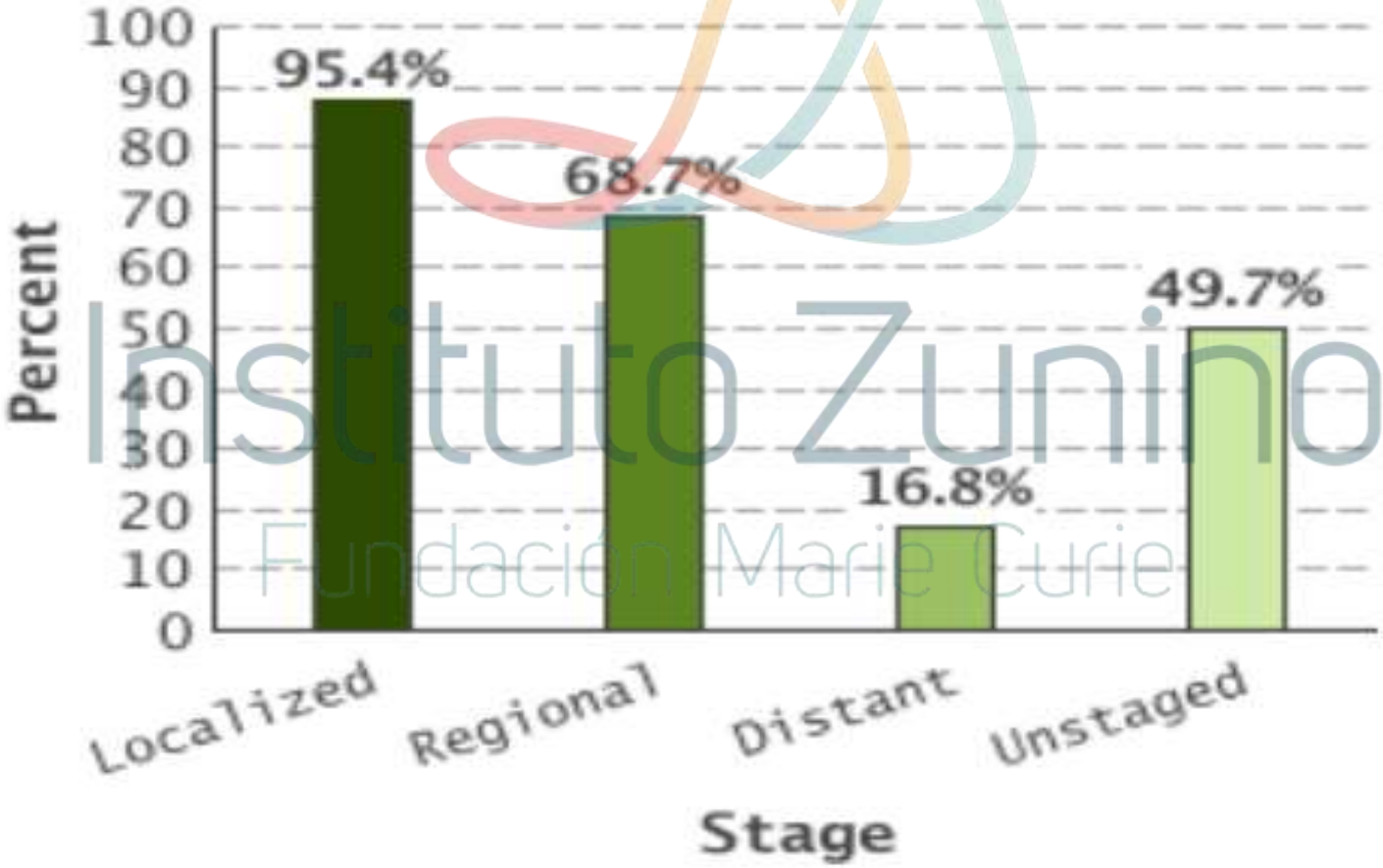
	Pelvic RT	Observation
Any local recurrence	20%	24%
Any distant recurrence	54%	33%

Adjuvant Chemotherapy Uterine LMS

- Retrospective analysis Kaiser Permanente
  - 110 stage I uLMS
  - 30% adjuvant gemcitabine/docetaxel (increasing use)
  - 70% observed
  - No difference in recurrence, DFS or OS Littell et al Gynecol Oncol 2017
- Similar data in meta-analysis and NCDB observational cohort

GOG 277	Local/pelvic rec	Distant rec	Death
Chemotherapy n=20	5	3	5
Observation n=18	1	7	1

Cáncer de Endometrio
Sobrevida



Chemotherapy for advanced, recurrent or metastatic endometrial carcinoma (Review)

Vale CL, Tierney J, Bull SJ, Symonds PR

- 9 ensayos, QT menos intensa vs más intensa
- N = 1519
- SLP 6 → 7 meses, HR 0.82, CI 0.77-0.96
- OS 9 → 10.5 meses, HR 0.86, CI 0.77-0.96
- Mayores efectos adversos (st, GI)

Randomized phase II trial of carboplatin-paclitaxel (CP) compared to carboplatin-paclitaxel-bevacizumab (CP-B) in advanced (stage III-IV) or recurrent endometrial cancer: The MITO END-2 trial.

Domenica Lorusso , Gabriella Ferrandina , Nicoletta Colombo , Sandro Pignata , Vanda Salutari , Giuseppina Maltese...

	CP (N = 48)	CP-B (N = 48)
PFS (IRC*)		
Events, n (%)	31 (35.4)	27 (43.8)
HR (95% CI)	0.57 (0.34, 0.96) Log-rank p = 0.036	
Median, mo (95% CI)	8.7 (6.3-11.2)	13.0 (9.2-16.8)
ORR (IRC), %	(54.3)§ (39.9-68.7)	(72.7)° (59.5-85.9)

§Calculated on 46 cases; ° calculated on 44 cases.

Carcinoma de Endometrio