BASURTUKO UNIBERTSITATE OSPITALEA
HOSPITAL UNIVERSITARIO BASURTO

DESESCALANDO **TIEMPO** EN EL TRATAMIENTO ADYUVANTE DEL CÁNCER DE **COLON**

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25 ONKOLOGIA MEDIKOAREN URTEURRENA
ANIVERSARIO ONCOLOGÍA MÉDICA

Etorkizunari begira
Mirando al futuro

DECLARACIÓN DE POTENCIALES CONFLICTOS DE INTERESES

Título de la presentación: “DESESCALANDO tiempo en el tratamiento adyuvante del cáncer de colon”

Autor: JAIRO LEGASPI FOLGUEIRA

Declaro **NO** tener ningún **conflicto de interés**

DESESCALANDO **TIEMPO** EN EL TRATAMIENTO ADYUVANTE DEL CÁNCER DE COLON

1. **INTRODUCCIÓN a la Adyuvancia del CC**
2. **Estudios INICIALES**
3. **Metaanálisis IDEA**
4. **Controversias**
5. **CONCLUSIONES**

INTRODUCCIÓN

- España: 41441 personas dx de CCR

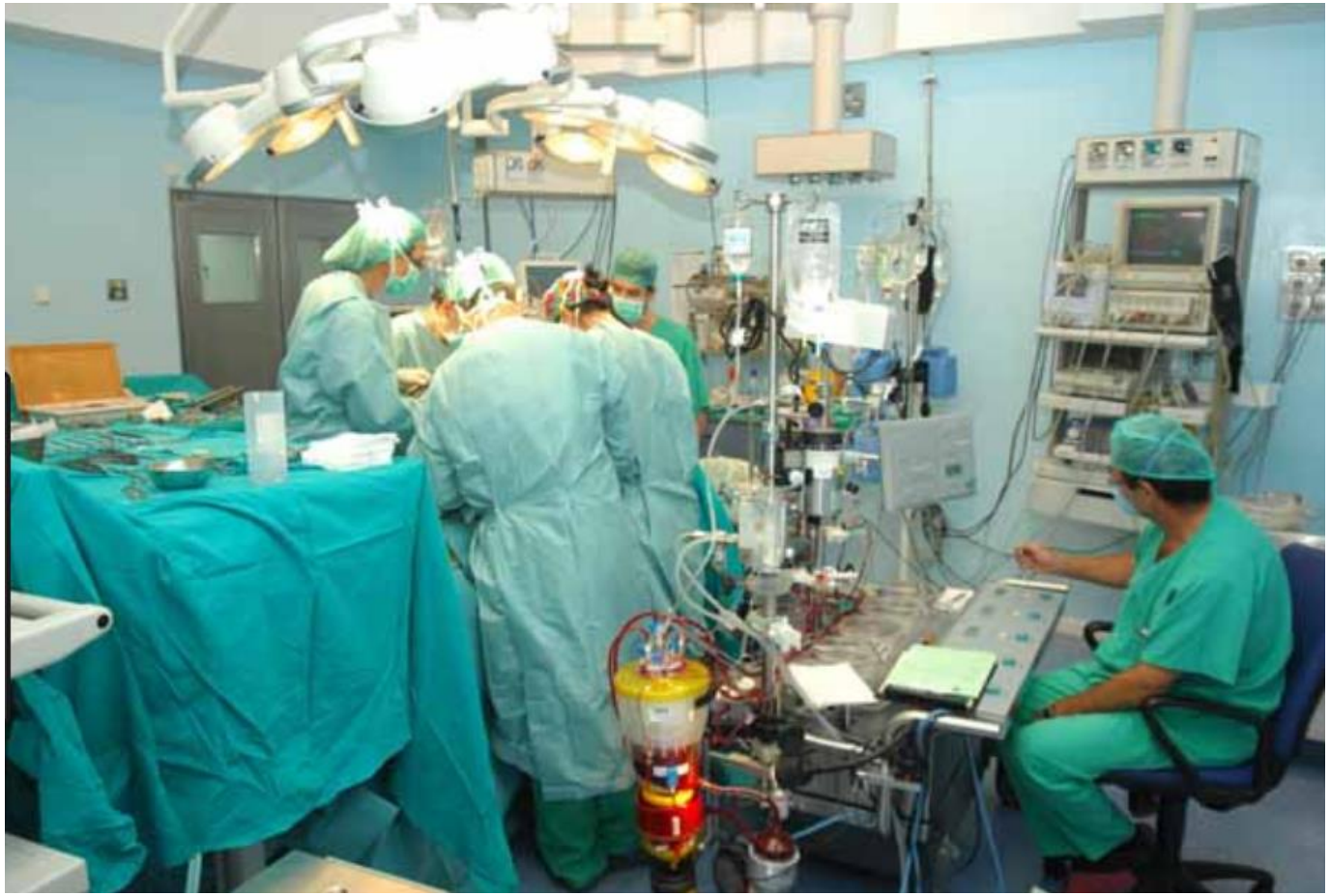
  13706 recto

- Edad media: 70 años
- Factores de Riesgo: IMC, Dieta, tóxicos

  DM2, enfermedad de Crohn / Colitis Ulcerosa

- Síndromes hereditarios: S^{d} Polipoide Familiar, S^{d} LYNCH

CÁNCER DE COLON LOCALMENTE AVANZADO



RECAÍDA TRAS CIRUGÍA

Riesgo de recurrencia de cáncer de colon en estadio II y III

Table II. Five-year disease-free survival in colon cancer stratified according to stage and adjuvant treatment.

Stage	Patients (n)	DFS (%), 95% CI[1]	Included studies
Without adjuvant therapy			
II	2250	81.4 (75.4–87.4)	[11,31–34,43,46,51]
III	312	49.0 (23.2–74.8)	[11,43]
With adjuvant therapy			
II	2655	79.3 (75.6–83.1)	[11,24,25,43,46,58]
III	8624	63.6 (59.3–67.9)	[11,24–26,32,33,35,38,43,44,48,50,54,58,59]
Adjuvant status unclear[2]			
II	10 654	81.1 (77.3–84.8)	[27,37,45,49,56]
III	9489	58.7 (50.0–67.5)	[26,27,41,45,56]

[1]Meta-analysis was done with the random effects model; [2] Adjuvant status unclear refers to studies where adjuvant chemotherapy was given only to a proportion of patients or was not clearly described.
CI, confidence interval; DFS, disease-free survival; n, number.

Camilla Böckelman, *Acta Oncologica* 2014

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Camilla Böckelman, *Acta Oncologica* 2014

TRATAMIENTO ADYUVANTE
¿POR QUÉ?

- ↓ CARGA tumoral
- ↓ *Tumor burden*

Annals of Oncology 2013; 24 (sup6) JCO 2009; 27: 3109

ADYUVANCIA /5fu

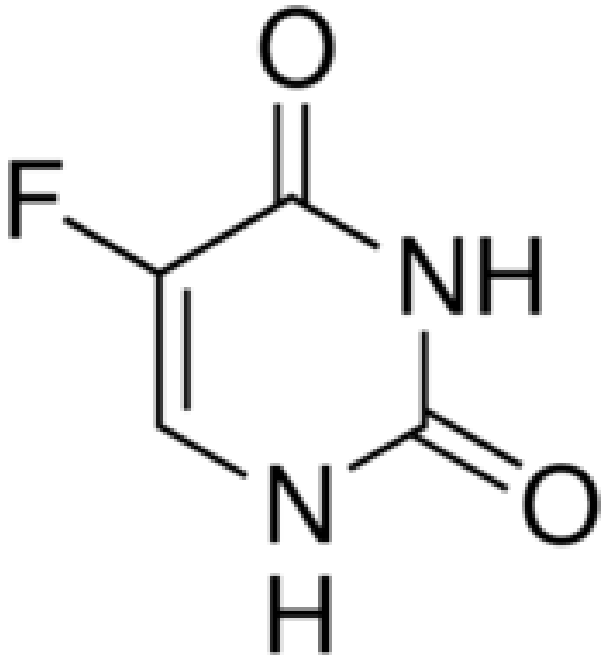
- INICIOS
- IMPACT

PLATINO

- MOSAICO
- NSABP C-07
- XELOXA

TERAPIAS DIANA

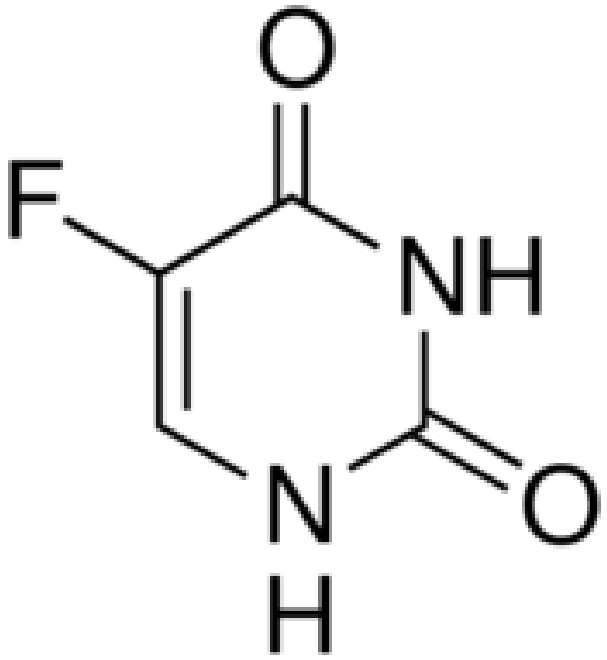
- AVANT
- PETACC



$C_4H_3FN_2O_2$

2,4-Dihydroxy-5-fluoropyrimidine, 5-FU, 5-Fluoro-2,4(1*H*,3*H*)-pyrimidinedione

5-FLUORURACILO



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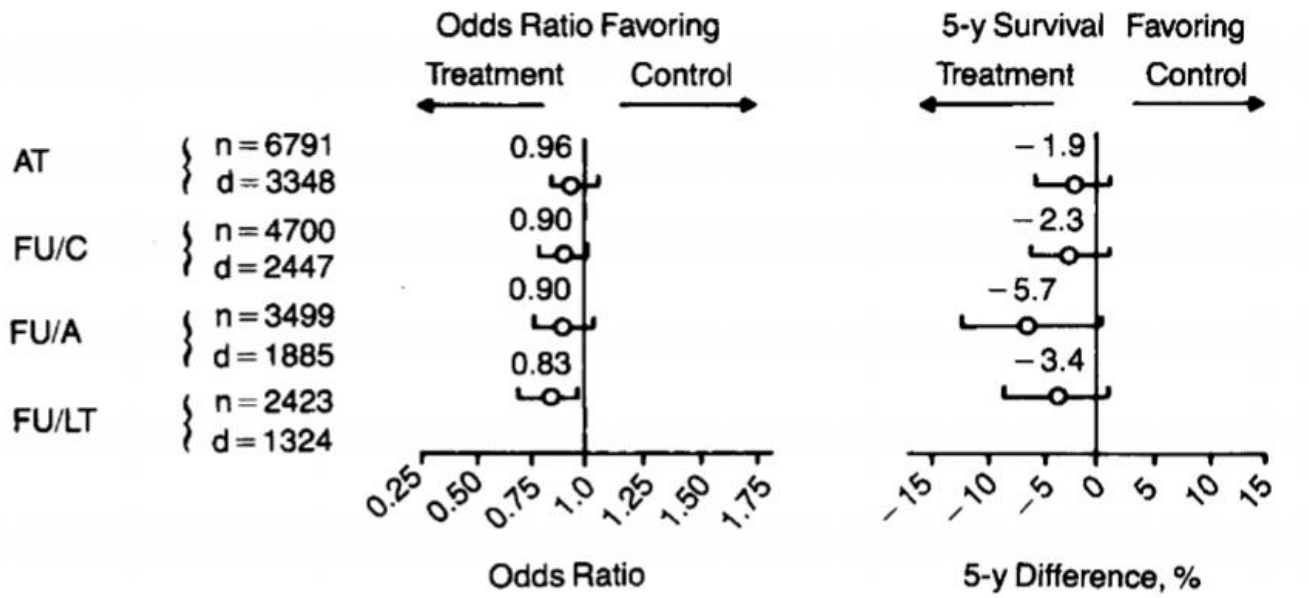
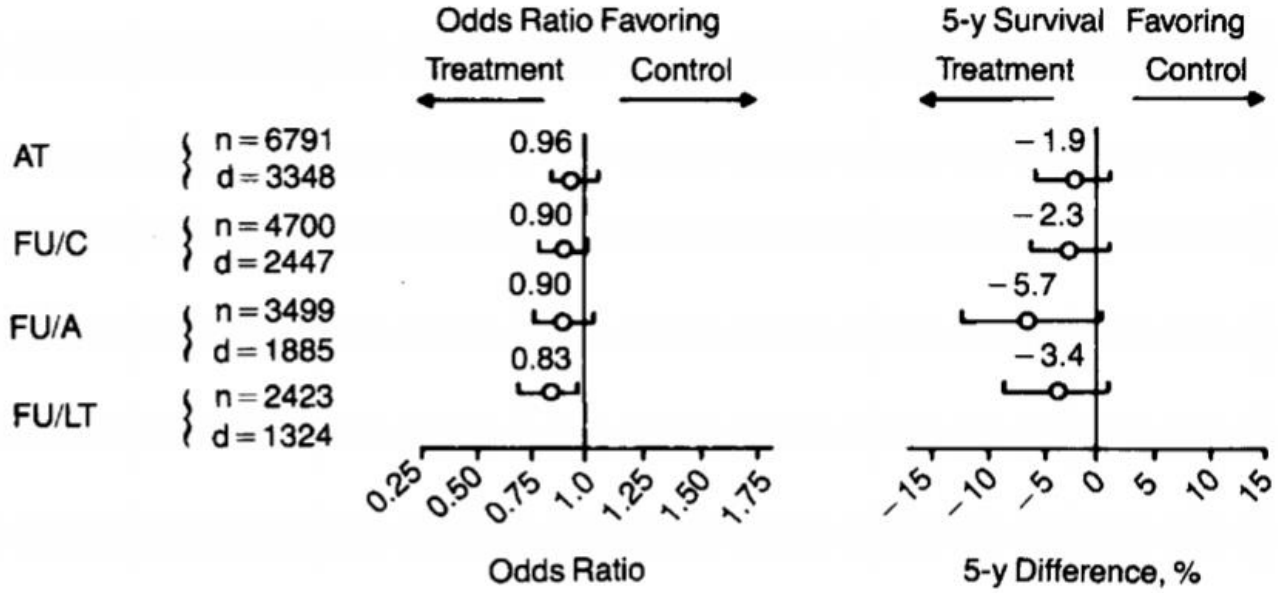
BUYSE ET AL JAMA 1988



- 5FU:
  - RR: 10%
  - SPG a 5ª de un 2,3%

  (incluso mayor si tto > 1ª)

BUYSE ET AL JAMA 1988



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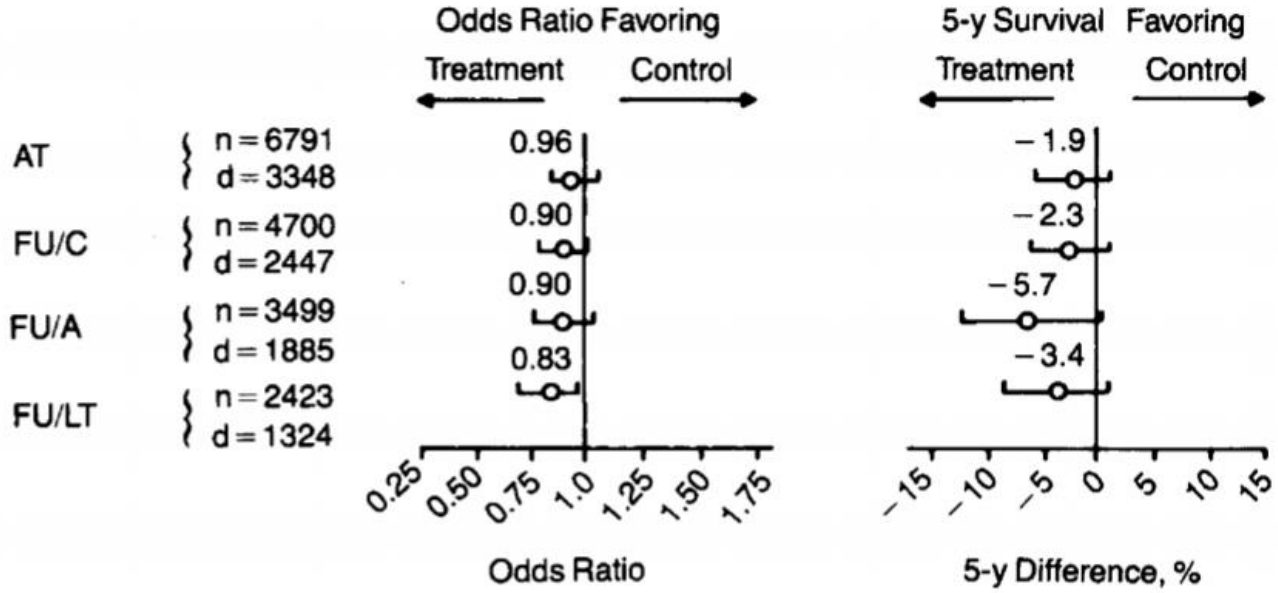
IMPACT

THE INTERNATIONAL MULTICENTER POOLED ANALISIS OF COLON CANCER TRIALS

- 5-FU 370-400 mg/m^2 + FA 200 mg/m^2
- Dukes B y C operados
- RRm: 22% (95% CI 3-38; p=0·029)

BUYSE ET AL JAMA 1988



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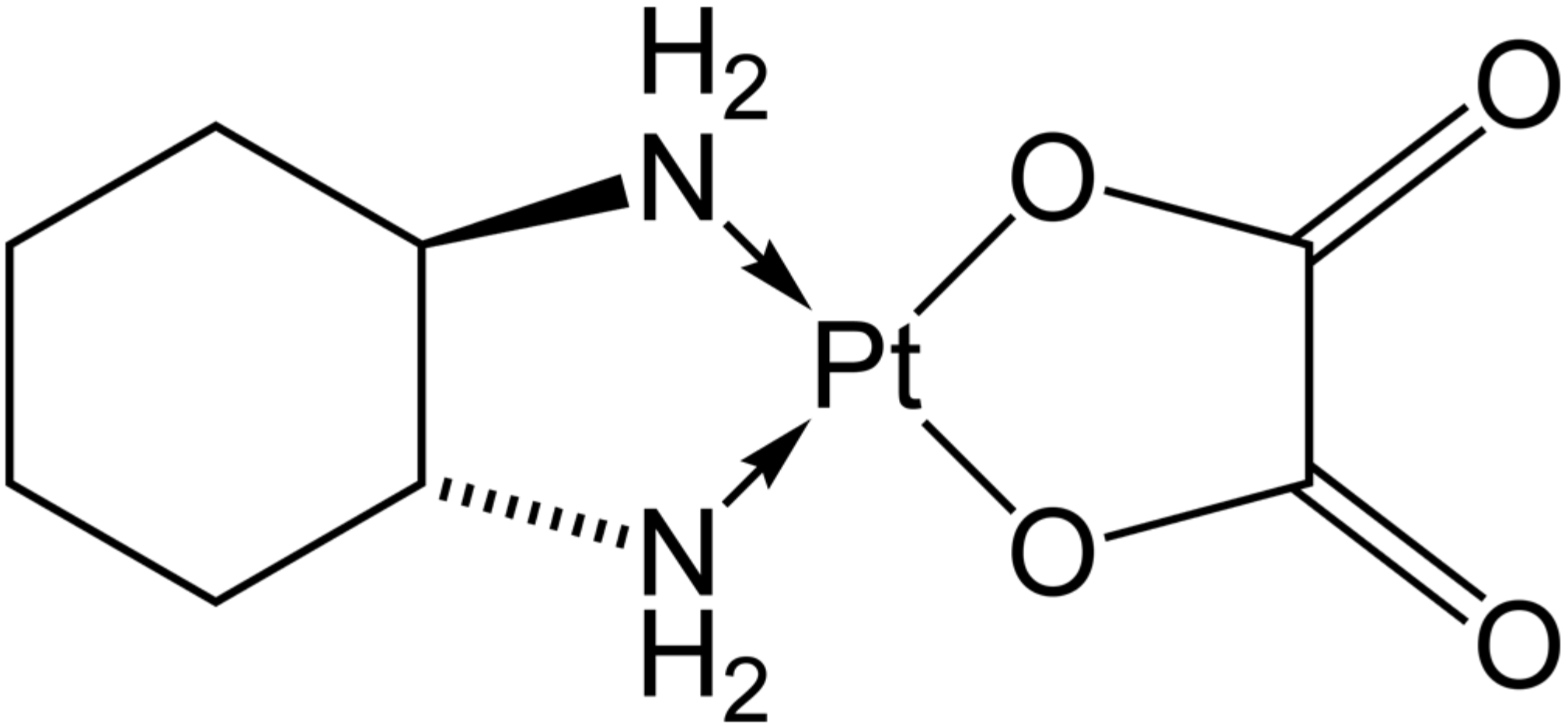
- ESTADIO B2 de DUKE--→ HR a 5 a: 0.83 (90% CI, 0.72 to 1.07)


H2
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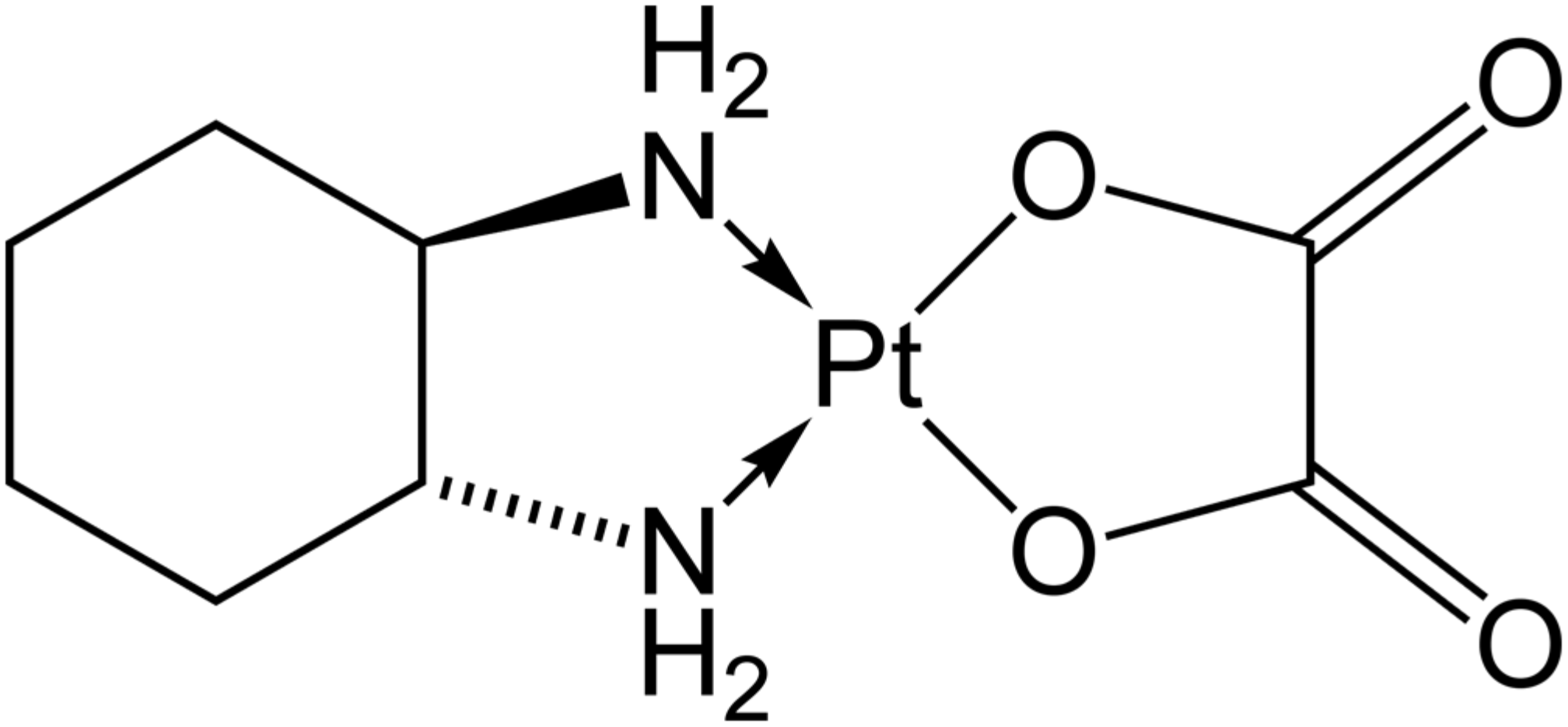
H2

OXALIPLATINO



ADYUVANCIA /5fu

- INICIOS
- IMPACT

PLATINO

- **MOSAICO**
- **NSABP C-07**
- **XELOXA**

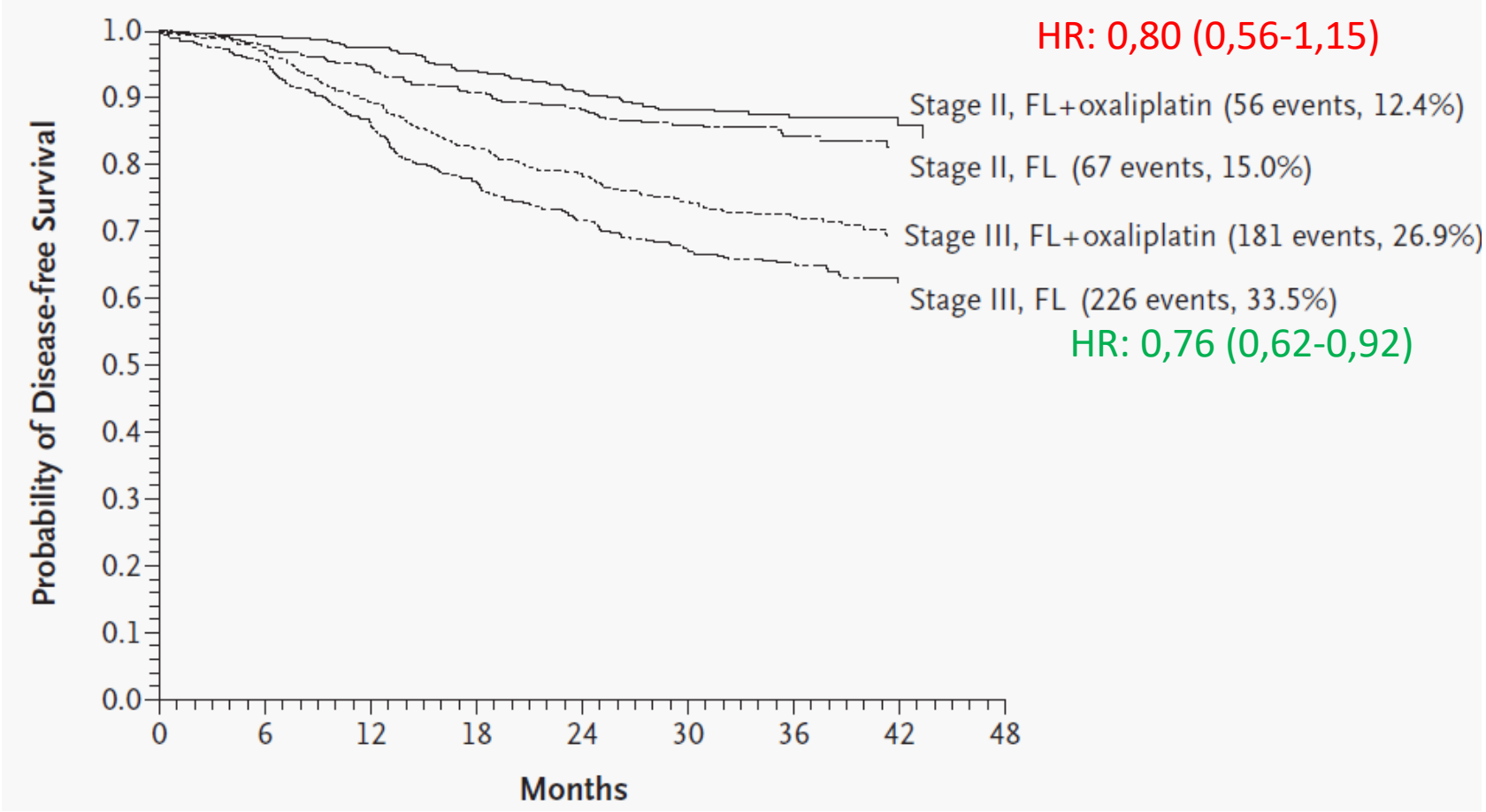
TERASPIAS DIANA

- AVANT
- PETACC

MOSAIC

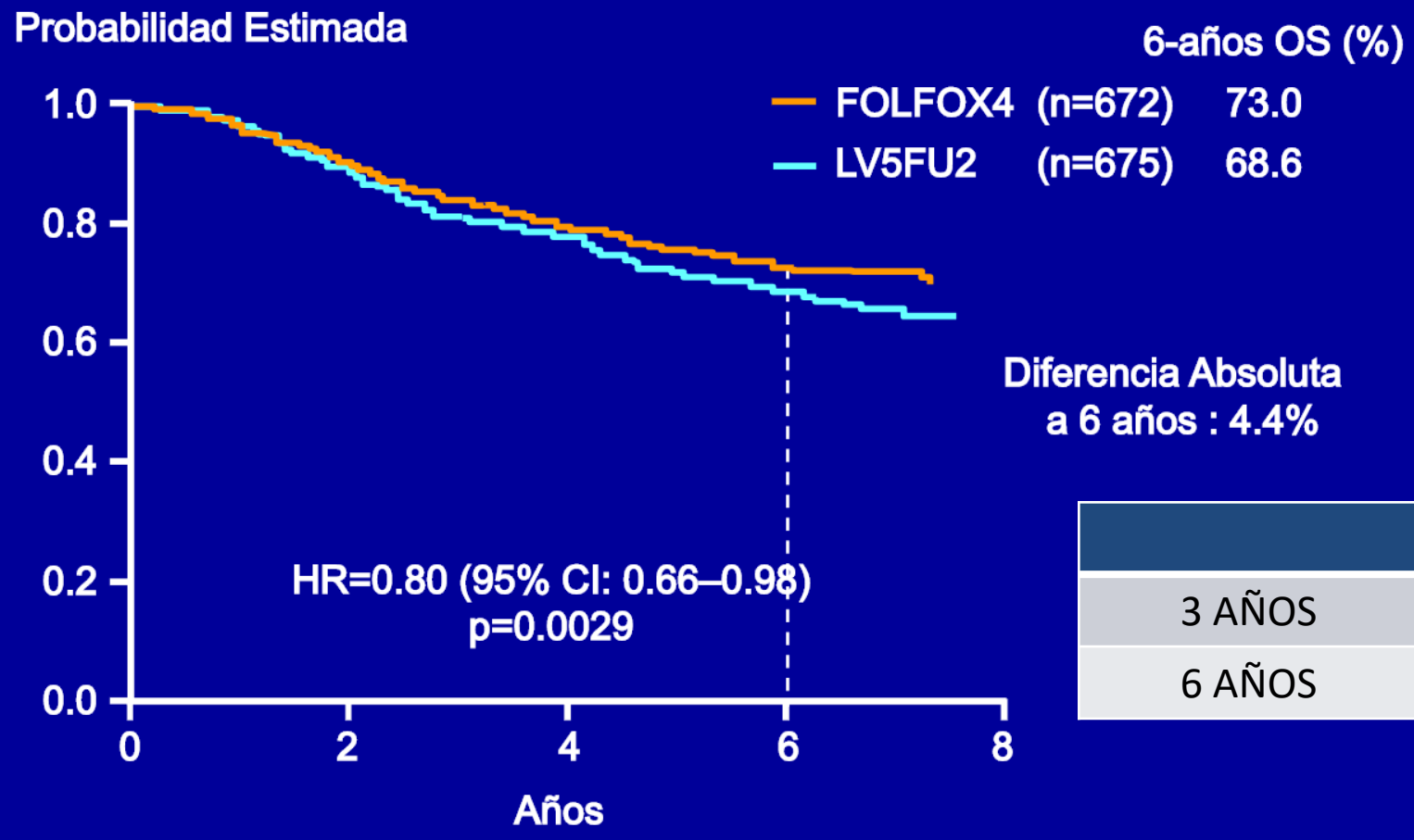
MULTICENTER INTERNATIONAL STUDY OF OXALIPLATIN/5-FLUOROURACIL/LEUCOVORIN IN THE ADJUVANT TREATMENT OF COLON CANCER

- FOLFOX vs 5Fu+L
- PFS/SLE A 3 AÑOS
- HR : 0.77 (P=0.002)



T. André, N Engl J Med 2004

MOSAIC – S Global superior Oxaliplatino adyuvante Estadío III



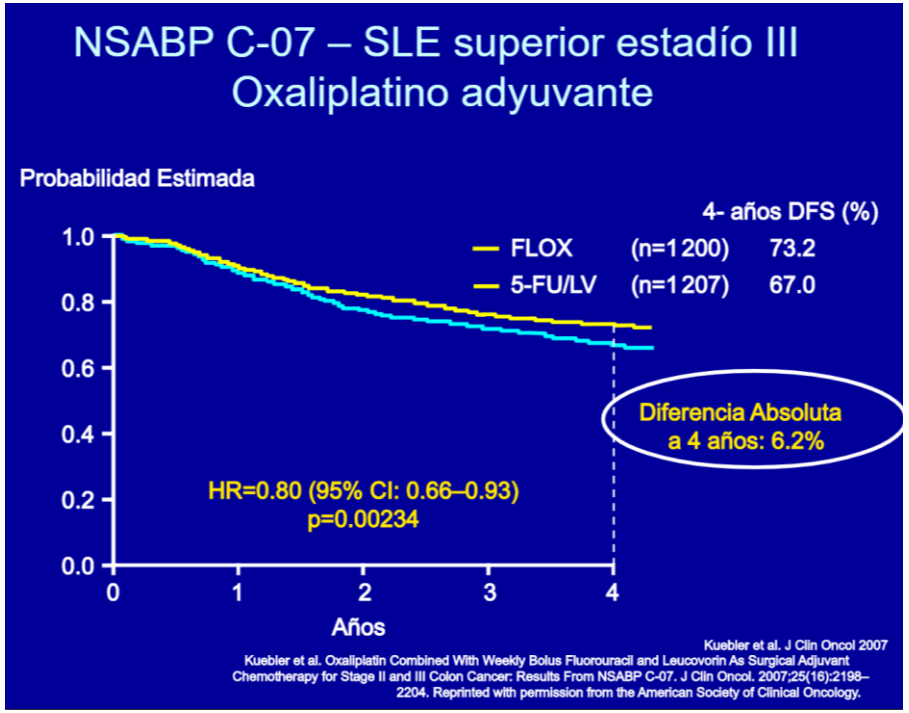
de Gramont et al. ASCO 2007

	FOLFOX	5FU-LV
3 AÑOS	78,2%	72,9%
6 AÑOS	73 %	68,6%

NSABP C-07

NSABP, NATIONAL SURGICAL ADJUVANT BREAST AND BOWEL PROJECT

HR SLE: 0,8 (p= 0,002)



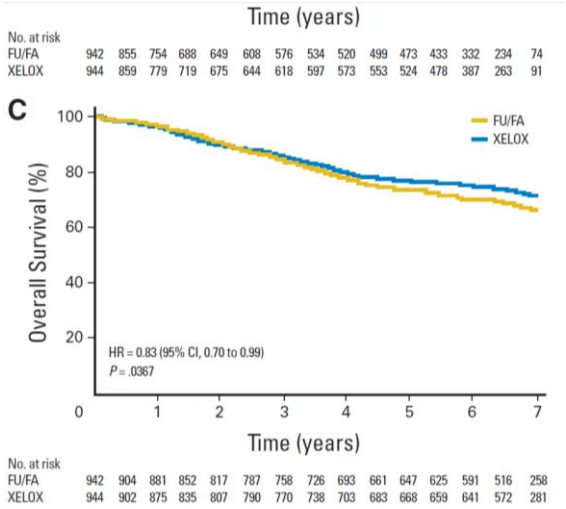
XELOXA

XELODA-OXALIPLATINO

XELODA OXALI

5FU en 24h FA semanal

HR: 0,83 (p= 0,034)



Schmoll et al, *J Clin Oncol 2015*

ADYUVANCIA /5fu

- INICIOS
- IMPACT

PLATINO

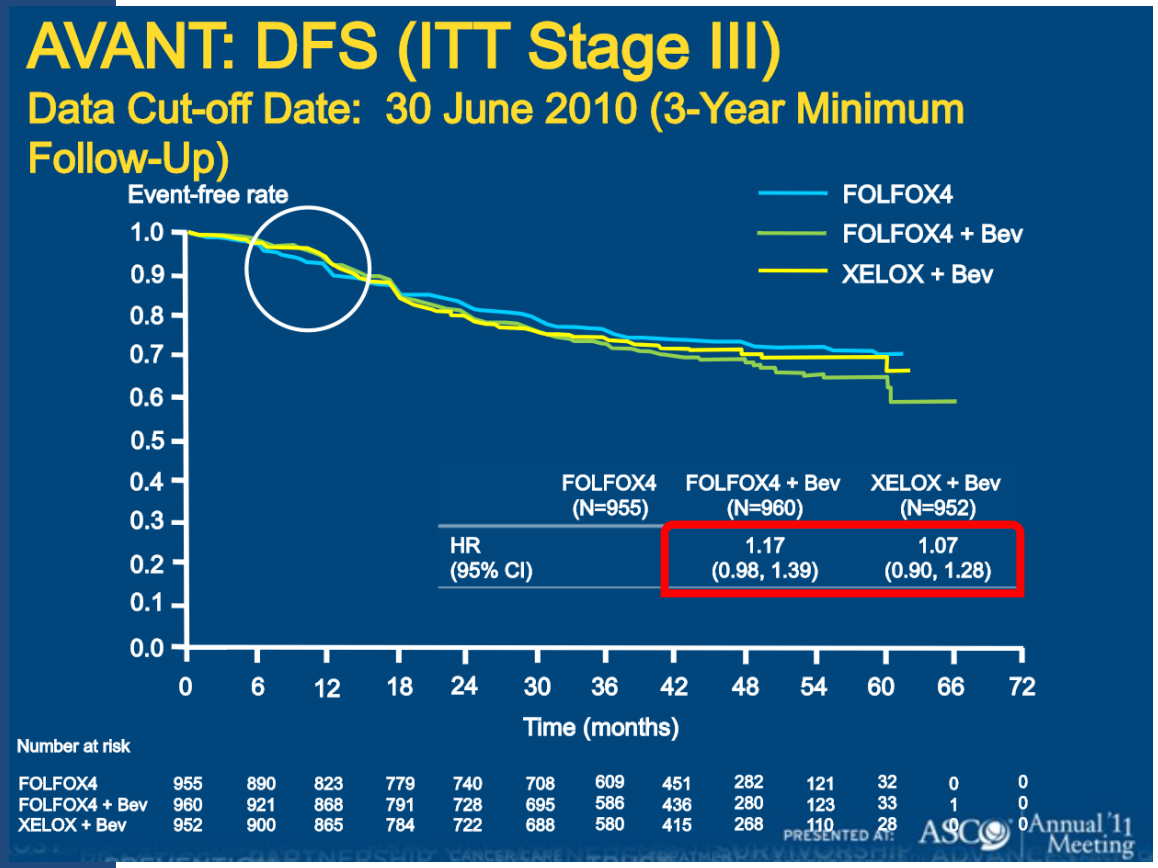
- MOSAICO
- NSABP C-07
- XELOXA

TERASPIAS DIANA

- **AVANT** VEGFR
- **PETACC** EGFR

AVANT

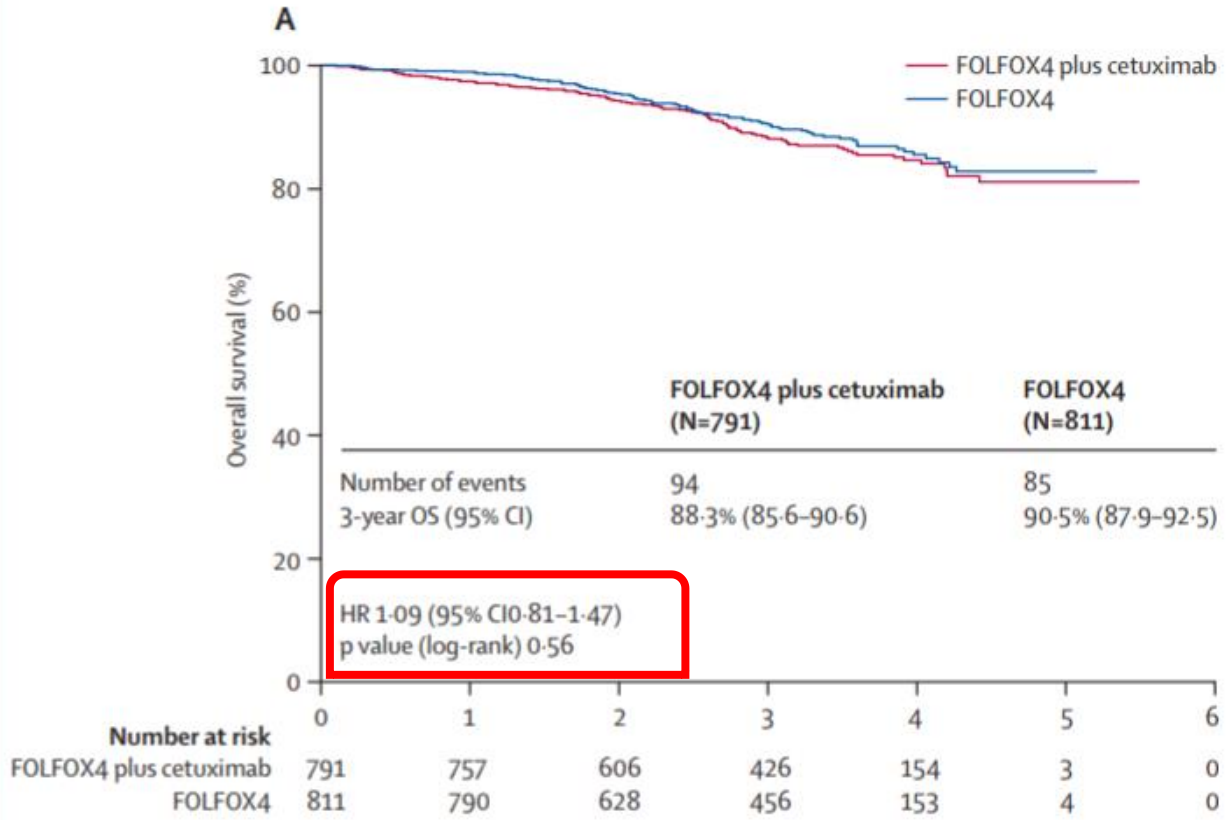
"AVASTIN"



Aimery de Gramont, Eric Van Cutsem
Lancet Oncol 2012; 13: 1225–33

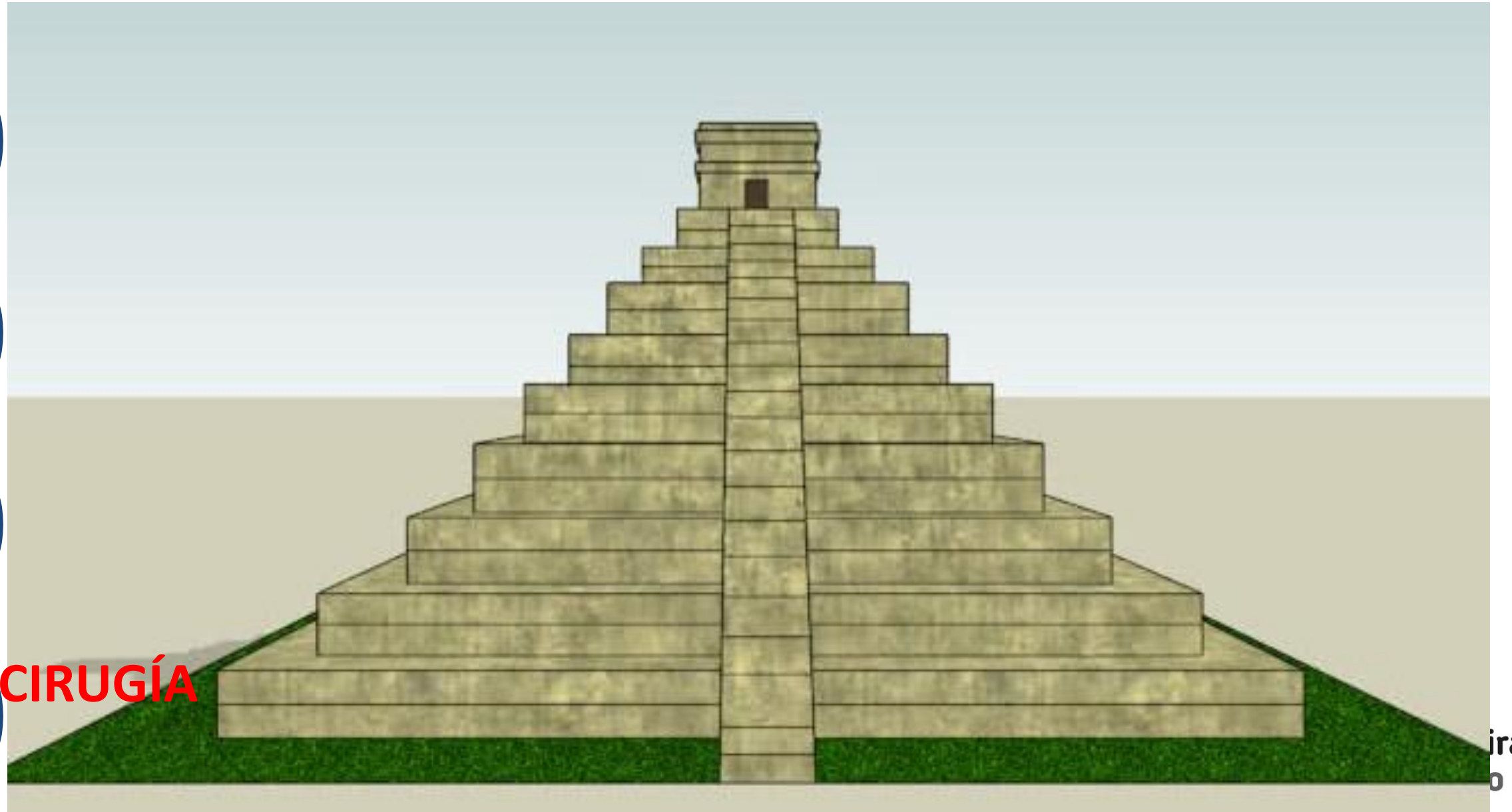
PETTAC

CETUXIMAB



Julien Taieb, *Lancet Oncol* 2014; 15: 862–73

ESTADIO III



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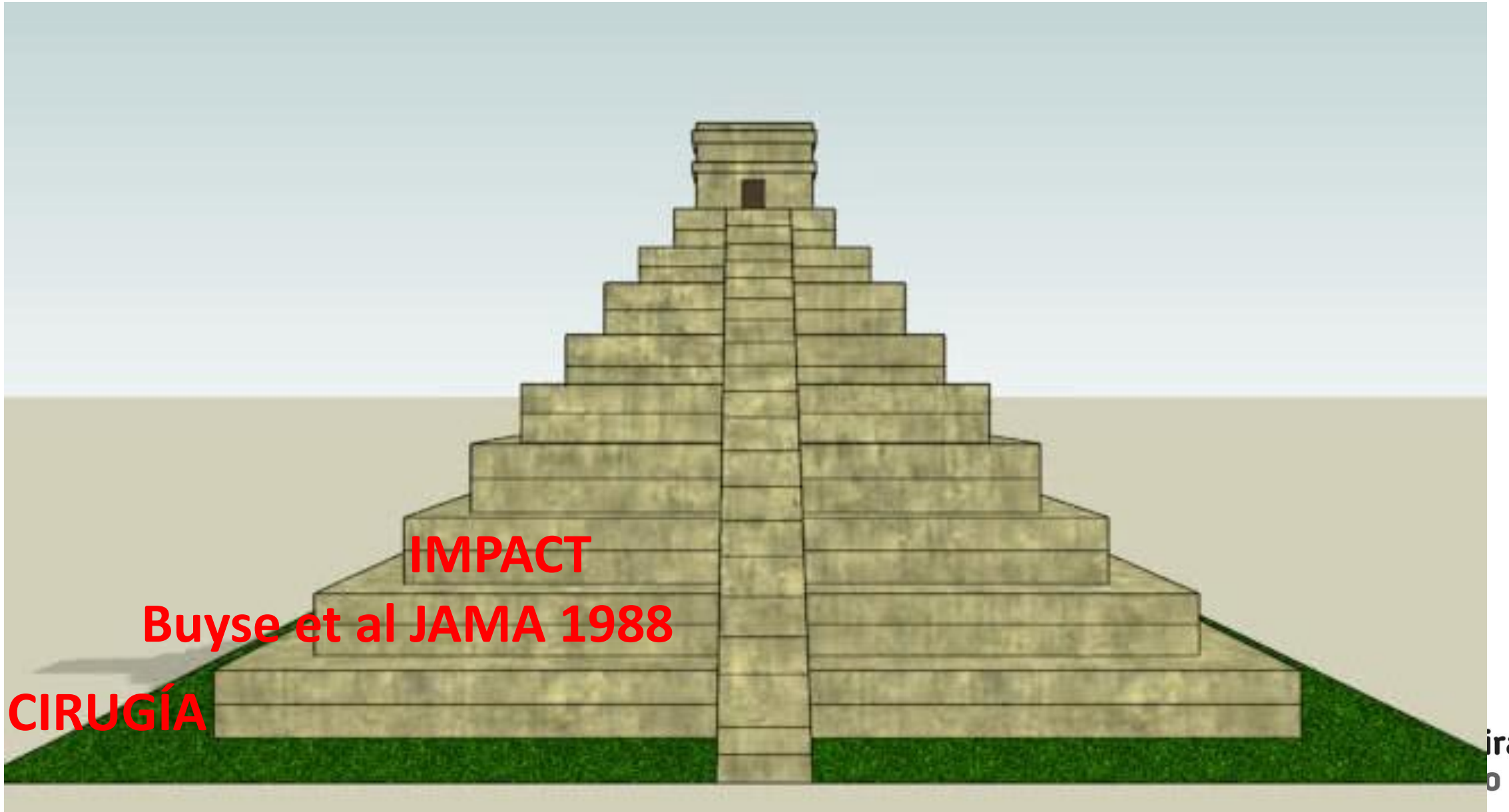

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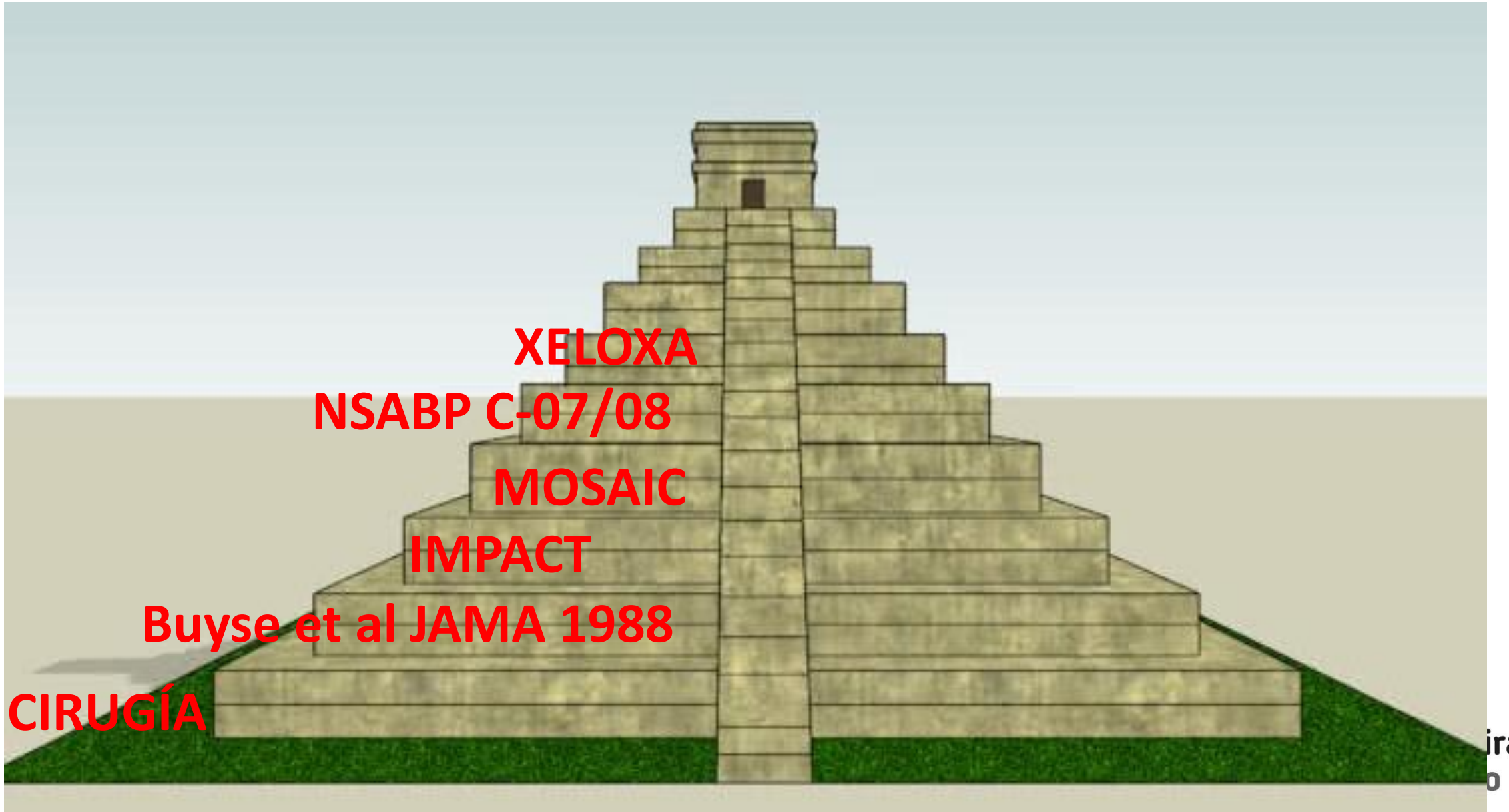
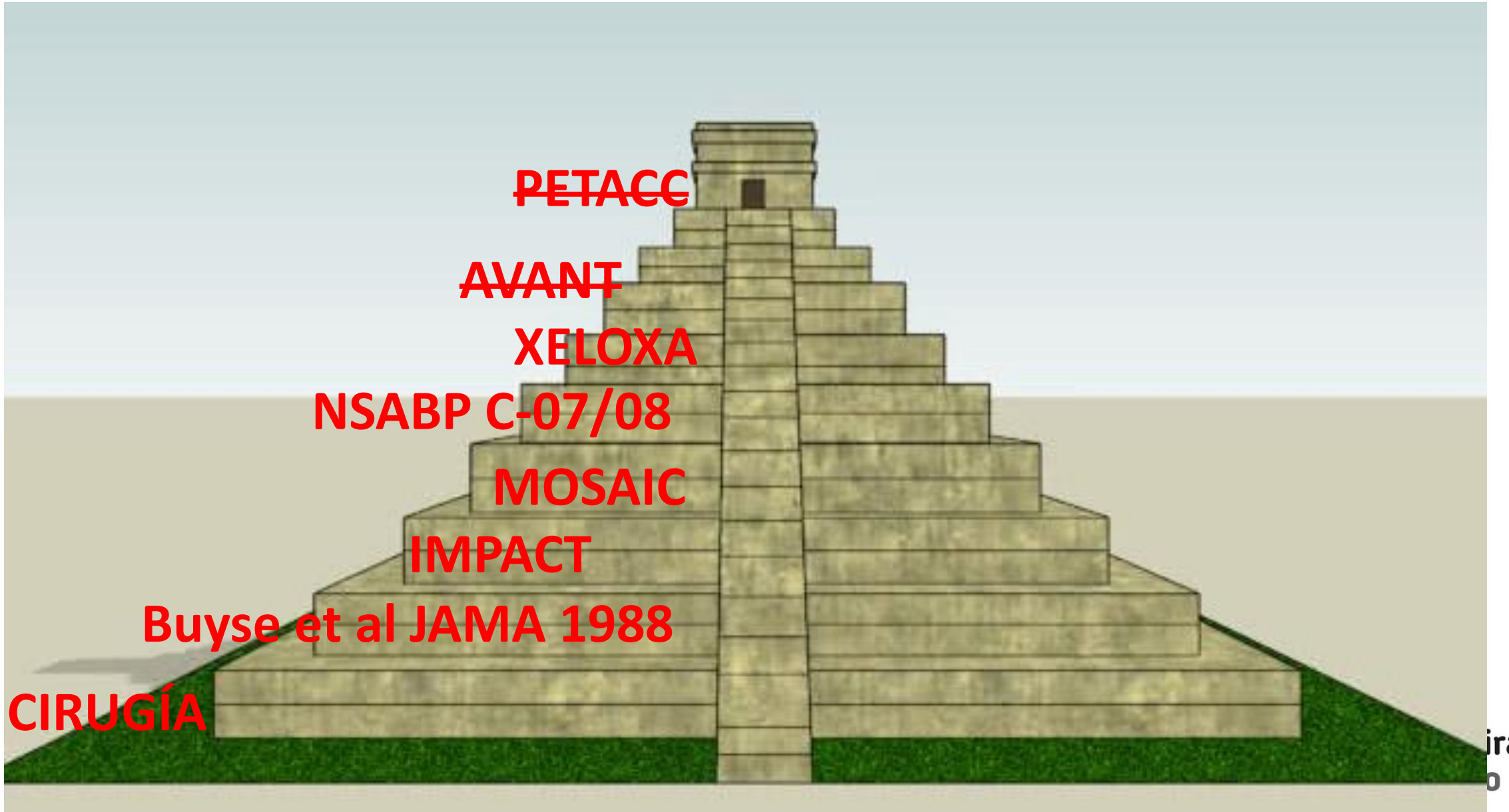

XELOXA
NSABP C-07/08
MOSAIC
IMPACT
Buyse et al JAMA 1988
CIRUGÍA

ESTADIO III


~~PETACC~~
~~AVANT~~
XELOXA
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TRATAMIENTO ADYUVANTE

XELOX O FOLFOX POR 6 MESES

*ESTADIO II CON FR

- DEBÚT: obstrucción o perforación
- Invasión linfovascular/perineural:
- G3 (sin MSI)
- T4
- Márgenes afectos
- Linfadenectomía incompleta

*ESTADIO III

TRATAMIENTO ADYUVANTE

-¿CUANDO EMPEZAR?

EJC
EUROPEAN JOURNAL OF CANCER

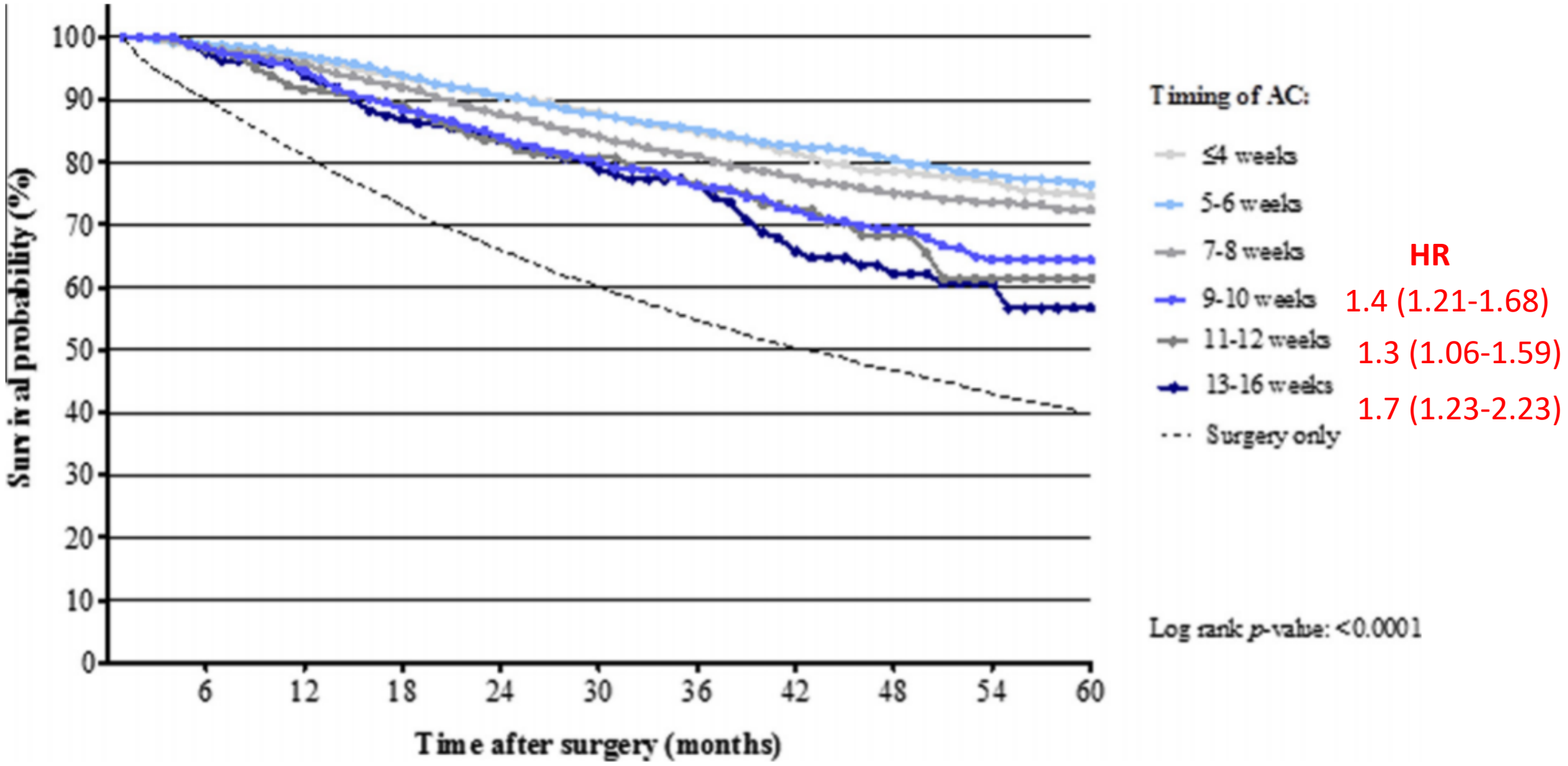
Timing of adjuvant chemotherapy and its relation to survival among patients with stage III colon cancer

A.C.R.K Bos, EJC 2015

Table 1
Demographic and clinical variables according to timing of adjuvant chemotherapy for patients diagnosed with stage III colon cancer in the Netherlands, 2008–2013 ($n = 6620$).

Variable	Timing of adjuvant chemotherapy						p-value*
	⩽4 weeks	5–6 weeks	7–8 weeks	9–10 weeks	11–12 weeks	13–16 weeks	
	1106 (17)	2950 (45)	1562 (24)	611 (9)	226 (3)	165 (2	
	n (%)	*n* (%)	*n* (%)	*n* (%)	*n* (%)	*n* (%)	
Gender							0.979
Male	587 (53)	1564 (53)	841 (54)	327 (53)	125 (55)	86 (52)	
Female	519 (47)	1386 (47)	721 (46)	284 (47)	101 (45)	79 (48)	
Age							0.001*
<65 years	493 (45)	1449 (49)	682 (44)	264 (43)	88 (39)	72 (43)	
65–74 years	432 (39)	1139 (39)	657 (42)	254 (42)	94 (42)	70 (43)	
⩾75 years	181 (16)	362 (12)	223 (14)	93 (15)	44 (19)	23 (14)	
Period of diagnosis							0.001*
2008–2009	261 (24)	697 (24)	454 (29)	168 (28)	62 (28)	46 (28)	
2010–2011	371 (33)	1075 (36)	558 (36)	199 (33)	80 (35)	65 (40)	
2012–2013	474 (43)	1178 (40)	550 (35)	244 (39)	84 (37)	54 (32)	
T stage							0.022*
T1	16 (2)	62 (2)	36 (2)	8 (1)	3 (1)	2 (1)	
T2	103 (9)	256 (9)	123 (8)	46 (8)	18 (8)	12 (7)	
T3	788 (71)	2083 (70)	1070 (69)	423 (69)	145 (64)	105 (63)	
T4	199 (18)	549 (19)	333 (21)	134 (22)	60 (27)	46 (29)	
N stage							0.440
N1	686 (62)	1894 (64)	976 (62)	381 (62)	135 (60)	111 (67)	
N2	420 (38)	1056 (36)	586 (38)	230 (38)	91 (40)	54 (33)	

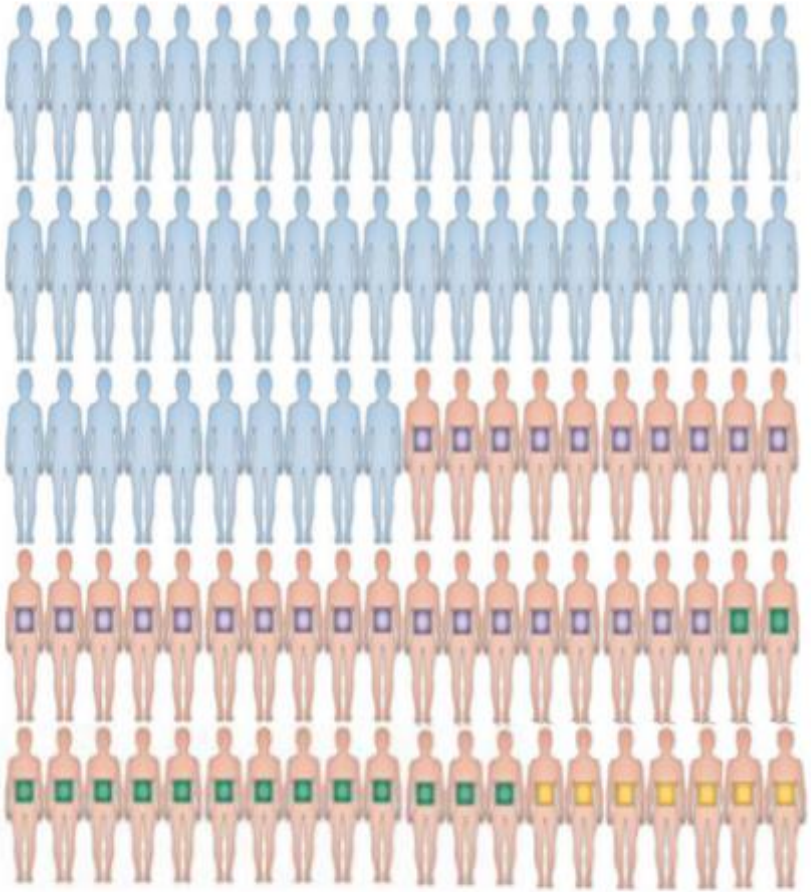
≤8S

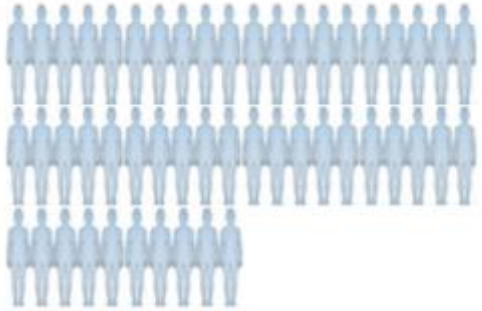


SPG 5ª: 39%

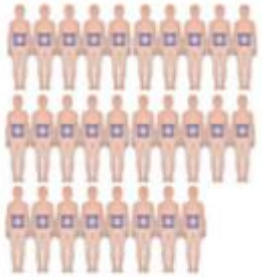
A.C.R.K Bos, EJC 2015

Stage III colon cancer

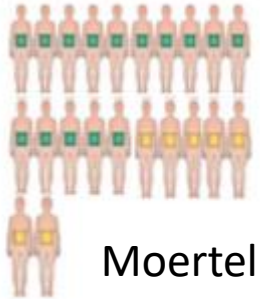




50%
Cured with surgery alone
No added value from chemo



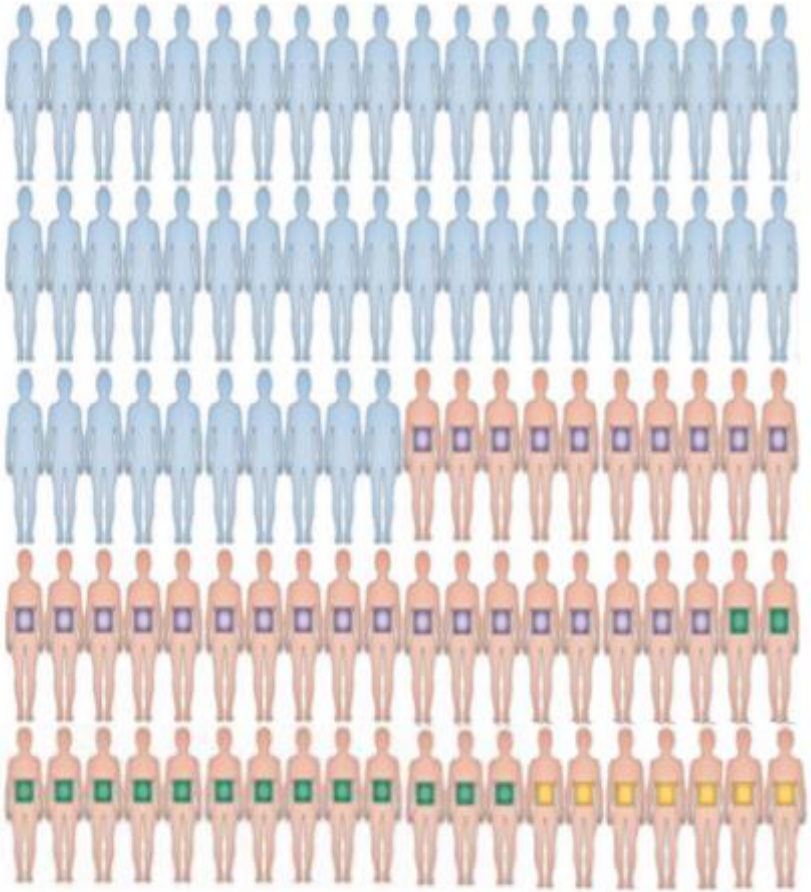
28%
Recur after adj chemo
Chemo did not help

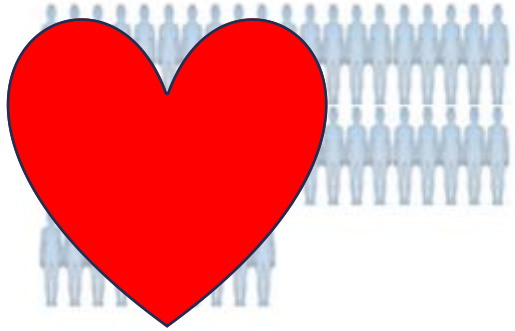


22%
Cured because they received chemo

Moertel CG, N Engl J Med 1990; IMPACT investigators, Lancet 1995; Andre´ T, J Clin Oncol. 2009; Yothers G, J Clin Oncol 2011; Haller D, J Clin Oncol 2011

Stage III colon cancer





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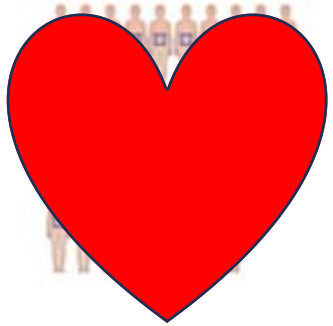

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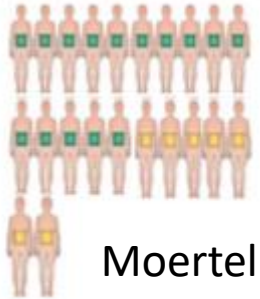

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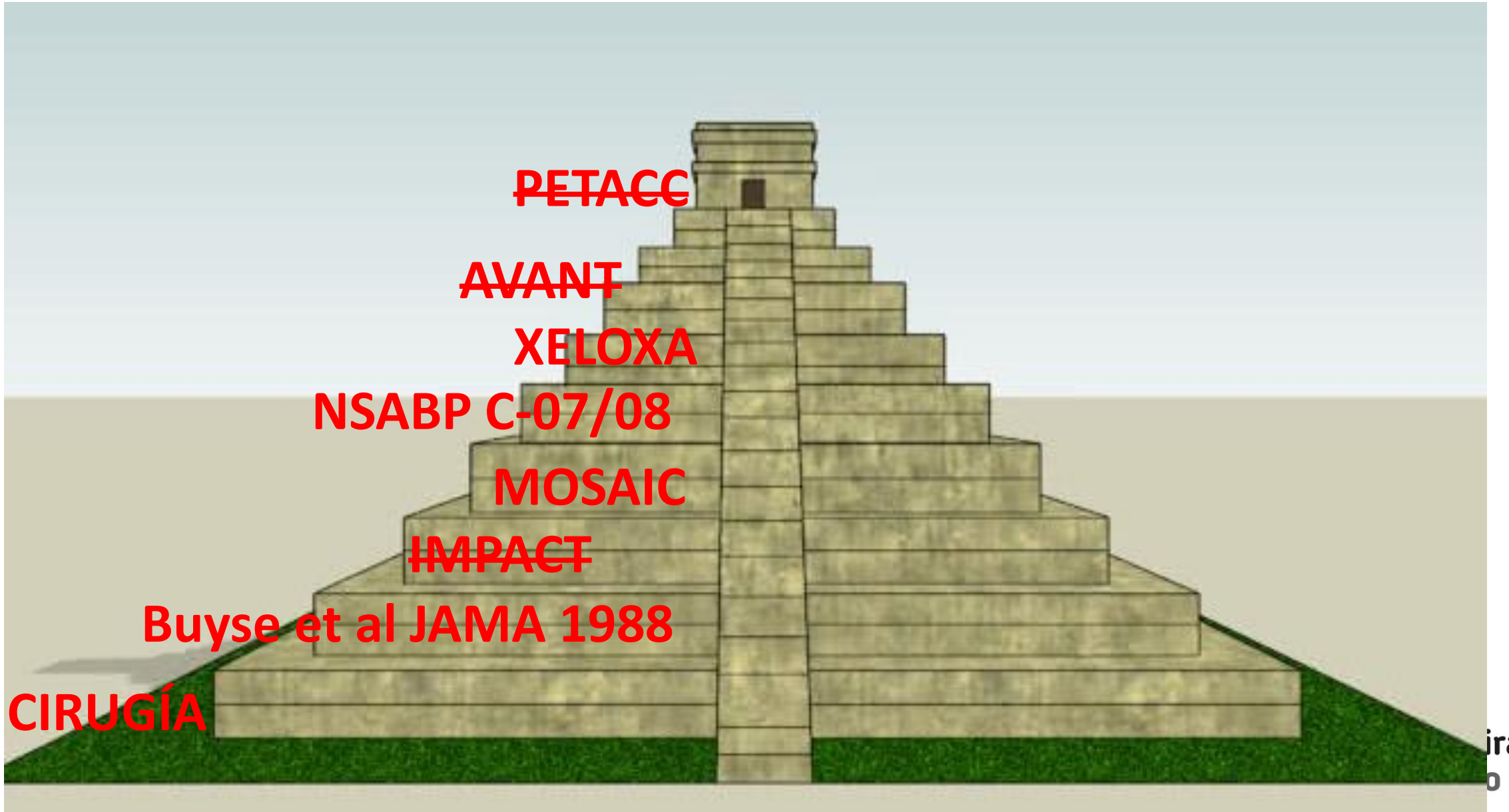
ESTADIO III


~~PETACC~~
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MOSAIC
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ESTADIO III

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ESTADIO III

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IDEA

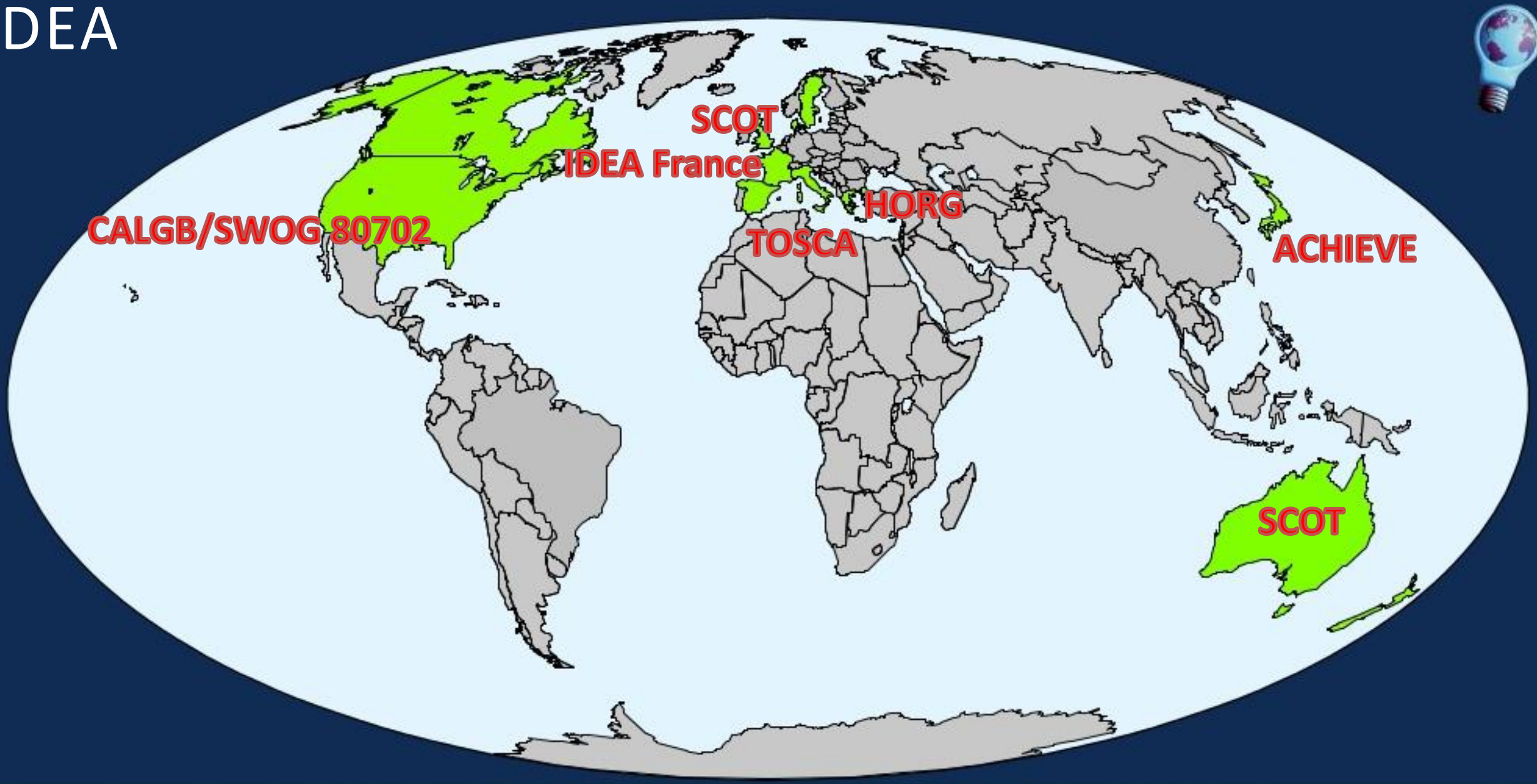
THE INTERNATIONAL DURATION EVALUATION OF ADJUVANT CHEMOTHERAPY

- En 2006
- Metanálisis con 6 estudios simultáneos
- OBJETIVO:

  NO INFERIORIDAD de 3 meses vs 6 meses

- CAPOX o FOLFOX

IDEA



IDEA

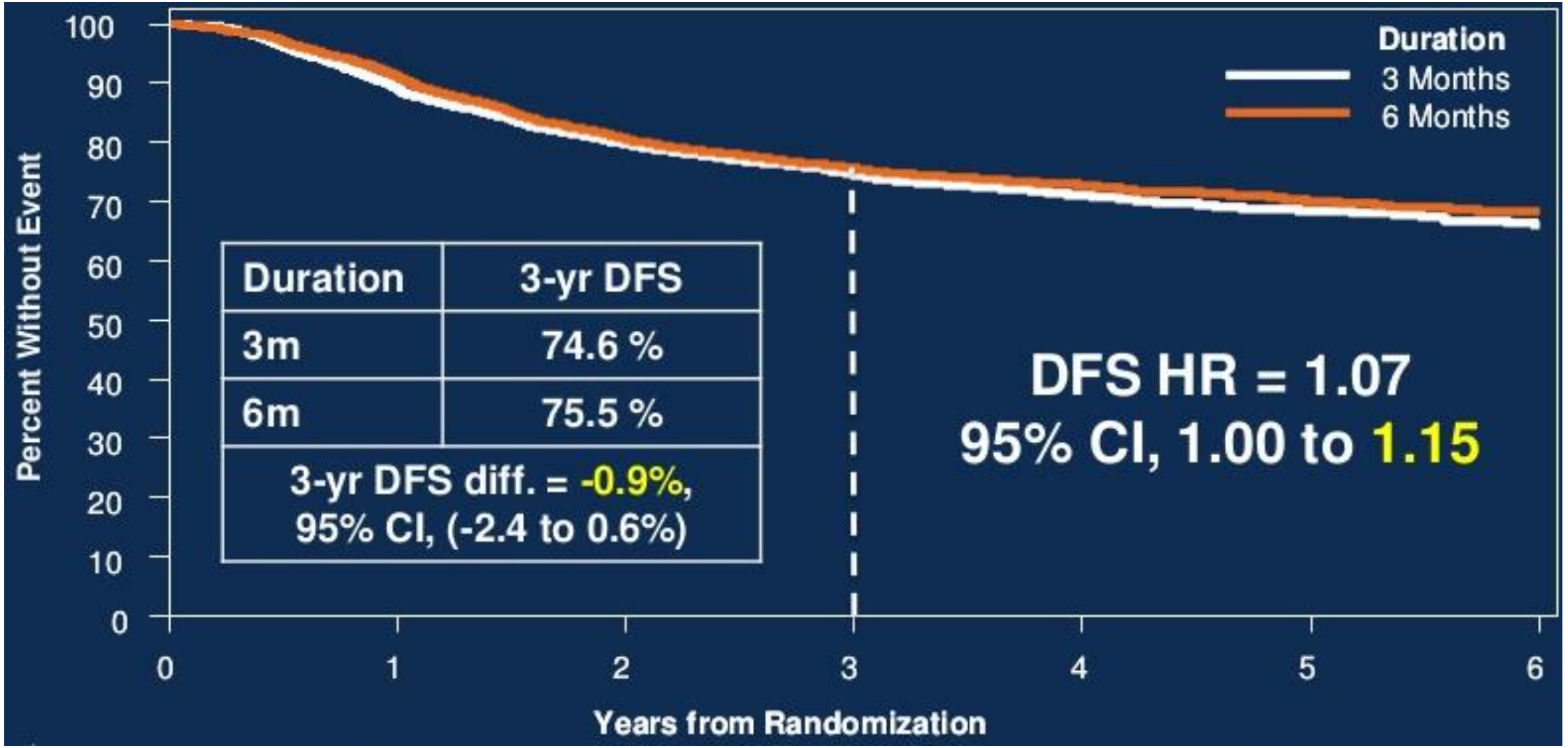
THE INTERNATIONAL DURATION EVALUATION OF ADJUVANT CHEMOTHERAPY

- E-III
- **NO-Inferioridad**
- **Potencia = 90% (**n>10500 pacientes)

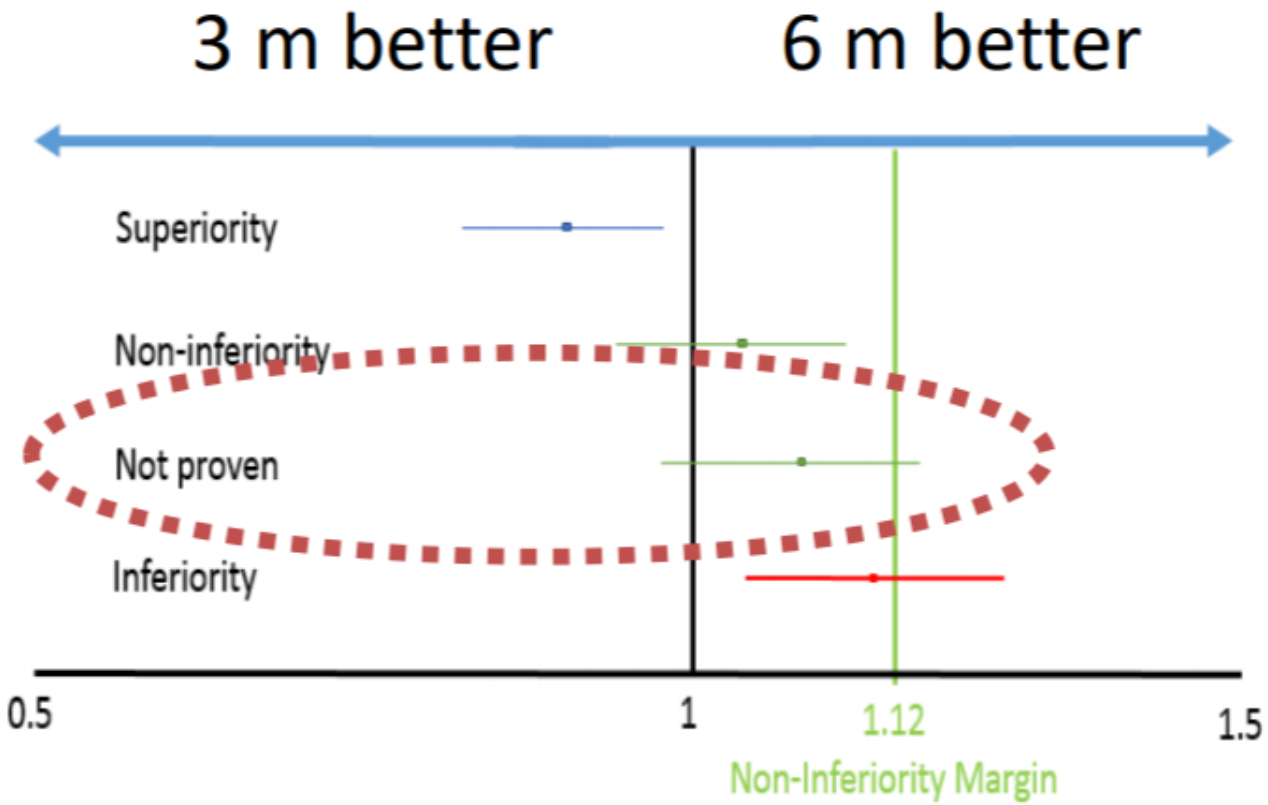
- Objetivos:
  - DFS/SLE a 3 años = **HR no superior a 1,12**
  - Subgrupos T/N y esquema de QT
  - Resultado por ITT modificado (1 ciclo)

	FOLFOX		CAPOX	
Patient characteristics	**3m (n=3870)**	**6m (n=3893)**	**3m (n=2554)**	**6m (n=2517)**
Median Agne, years	64	64	65	65
ECOG PS*				
0	77%	77%	82%	81%
1	22%	22%	18%	19%
T stage				
T1-2	13%	14%	13%	12%
T3	68%	67%	63%	63%
T4	19%	19%	24%	25%
N Stage				
N1	72%	73%	71%	71%
N2	28%	27%	29%	29%

Qian Shi, ASCO 2017

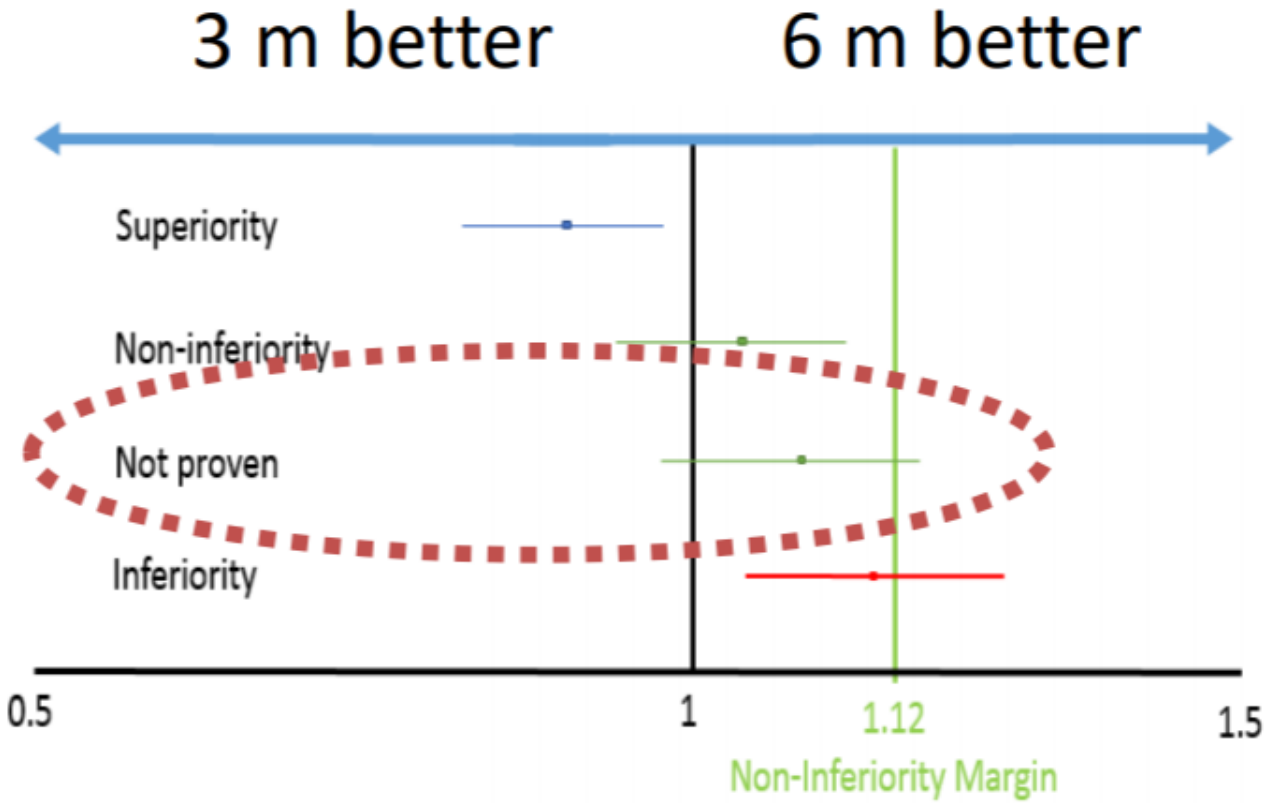


Qian Shi,PhD ASCO MEETING 2017



Resultado de TODOS los pacientes: 1.07 (1-1.15) p= 0,045

Piaggio et al. Jama 2006 and 2012



NO SE DEMUESTRA
NO-INFERIORIDAD

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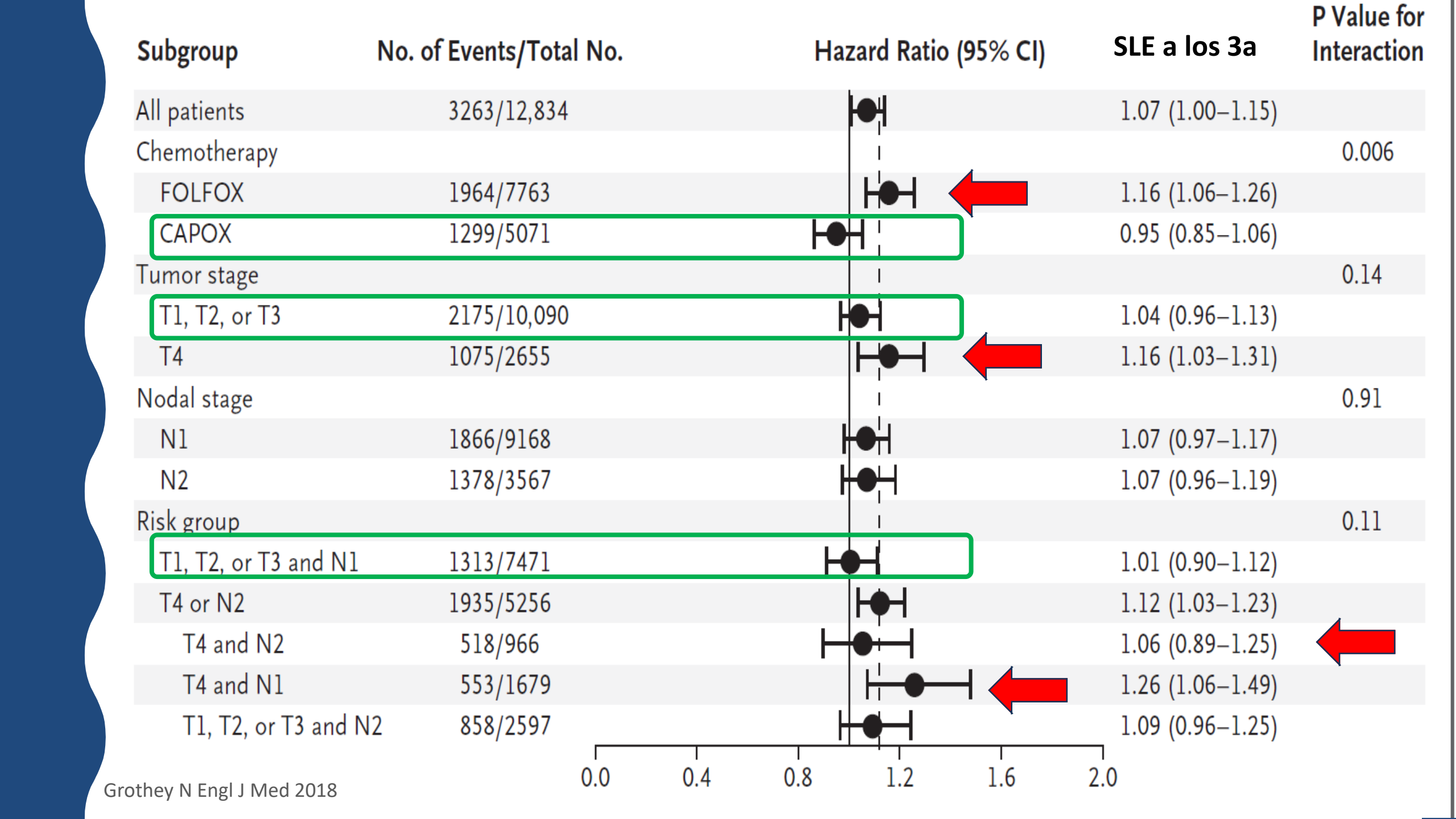
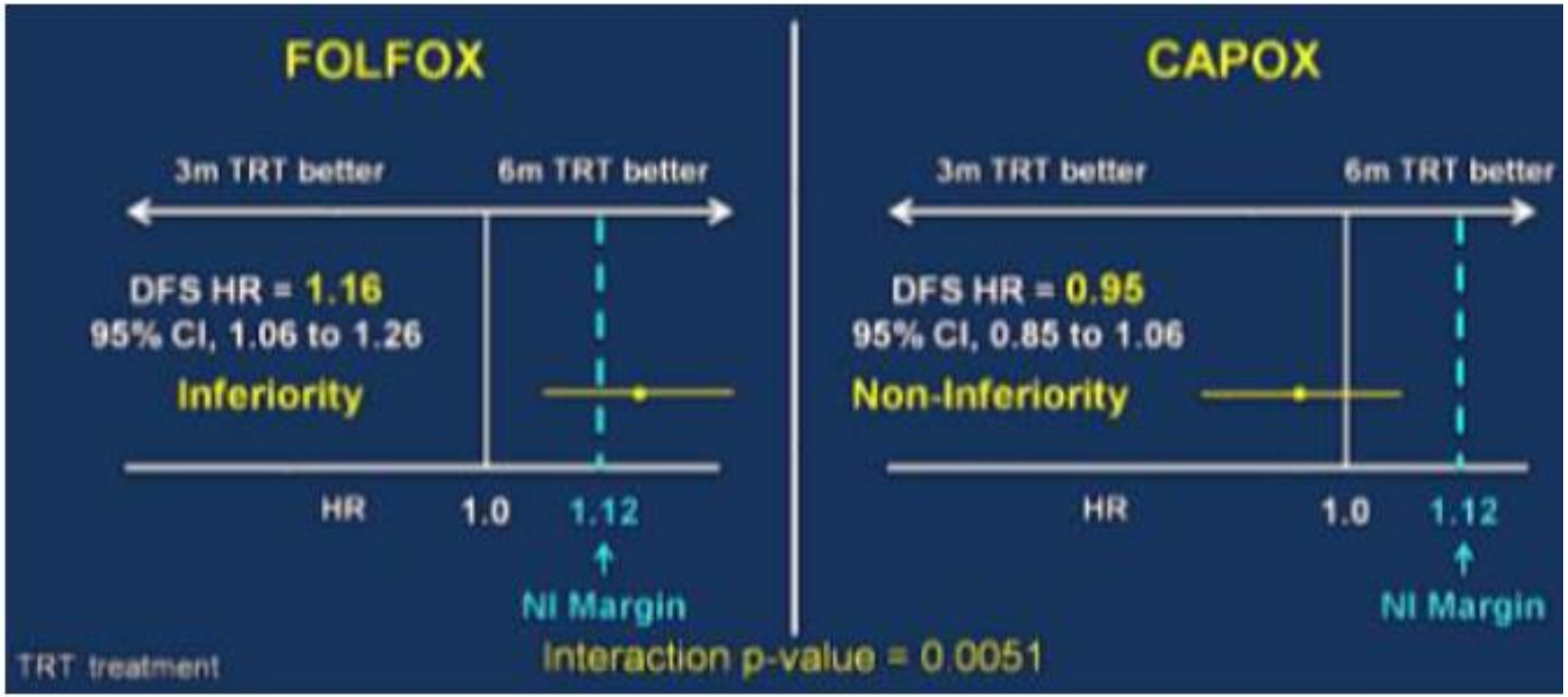
Piaggio et al. Jama 2006 and 2012



Grothey N Engl J Med 2018

IDEA
SEGÚN TRATAMIENTO



Qian Shi et al. J Clin Oncol 35, 2017 (suppl; abstr LBA1)

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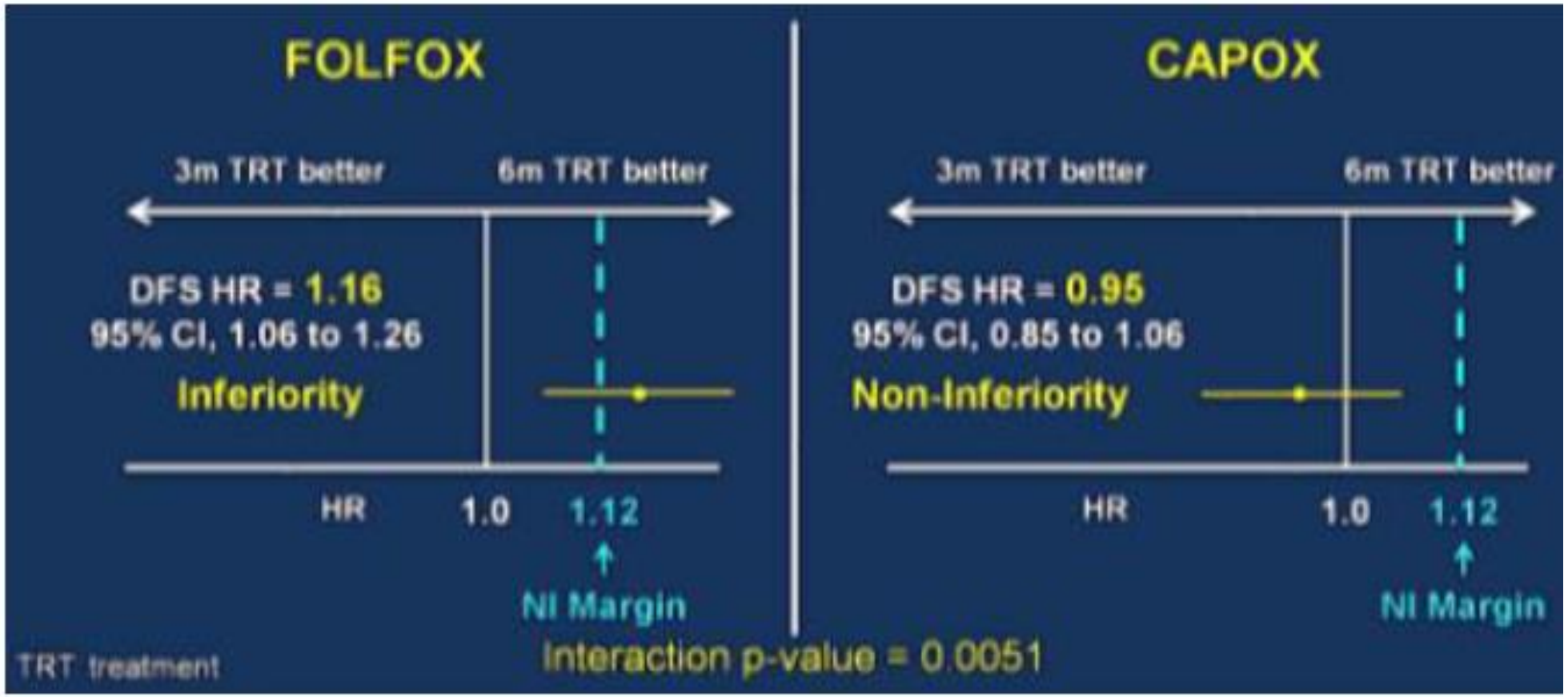

Qian Shi et al. J Clin Oncol 35, 2017 (suppl; abstr LBA1)

NO INFERIORIDAD PARA SUBGRUPO DE 3m vs 6m con CAPOX

IDEA
SEGÚN ESTADIO

BAJO RIESGO **ALTO RIESGO**

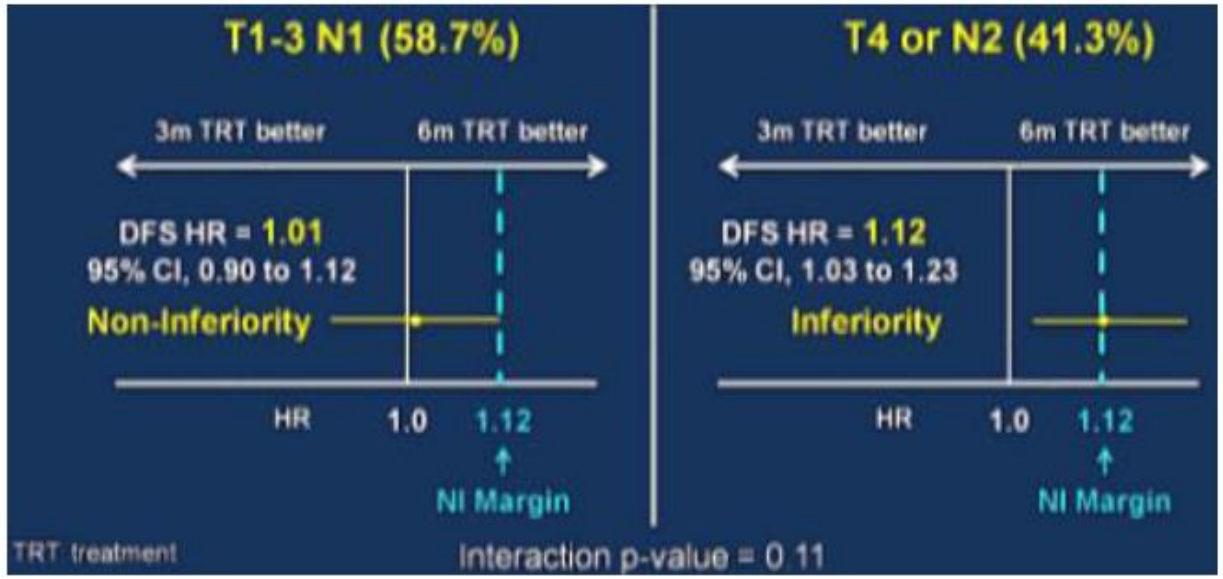

Table 2 3 *vs.* 6 months of FOLFOX or CAPOX in low-risk and high-risk colon cancer

Tumor stage	HR DFS (CI)	
	FOLFOX (3 m) *vs.* FOLFOX (6 m)	CAPOX (3 m) *vs.* CAPOX (6 m)
T1-3 N1	1.10 (0.96–1.26)	0.85 (0.71–1.01)
T4 or N2	1.20 (1.07–1.35)	1.02 (0.90–1.17)
All patients	1.16 (1.06–1.26)	0.95 (0.85–1.06)

HR, hazard ratio; CI, confidence interval; FOLFOX, folinic acid, 5-FU, oxaliplatin; CAPOX, capecitabine, oxaliplatin; DFS, disease free survival.

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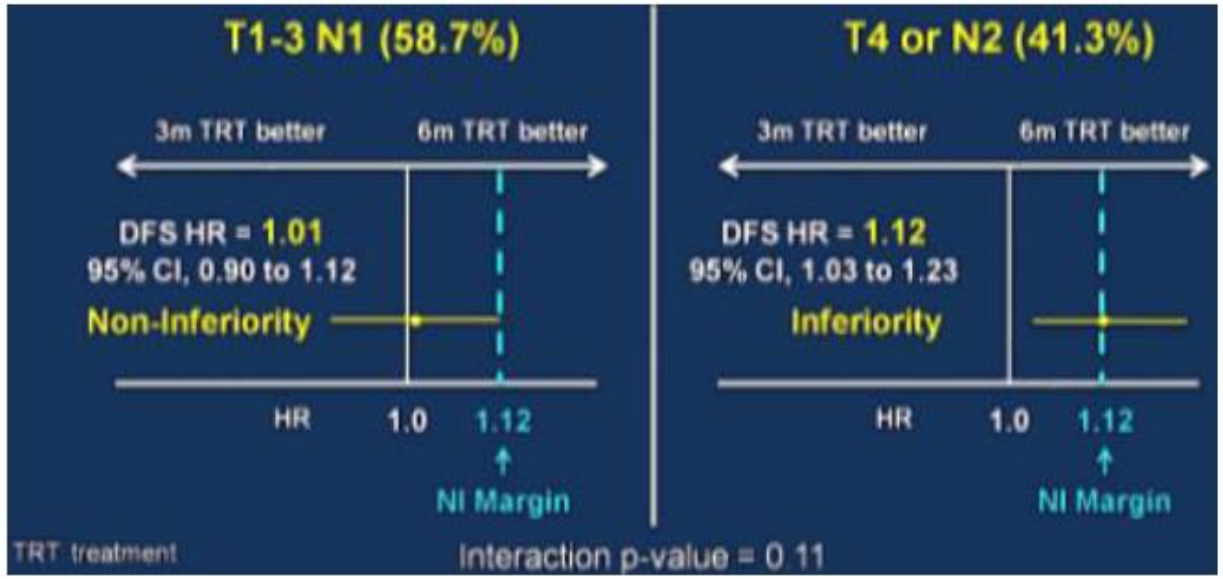
IDEA
SEGÚN ESTADIO

BAJO RIESGO **ALTO RIESGO**



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HR, hazard ratio; CI, confidence interval; FOLFOX, folinic acid, 5-FU, oxaliplatin; CAPOX, capecitabine, oxaliplatin; DFS, disease free survival.

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NO INFERIORIDAD PARA SUBGRUPO de Bajo Riesgo de 3 vs 6 meses con CAPOX

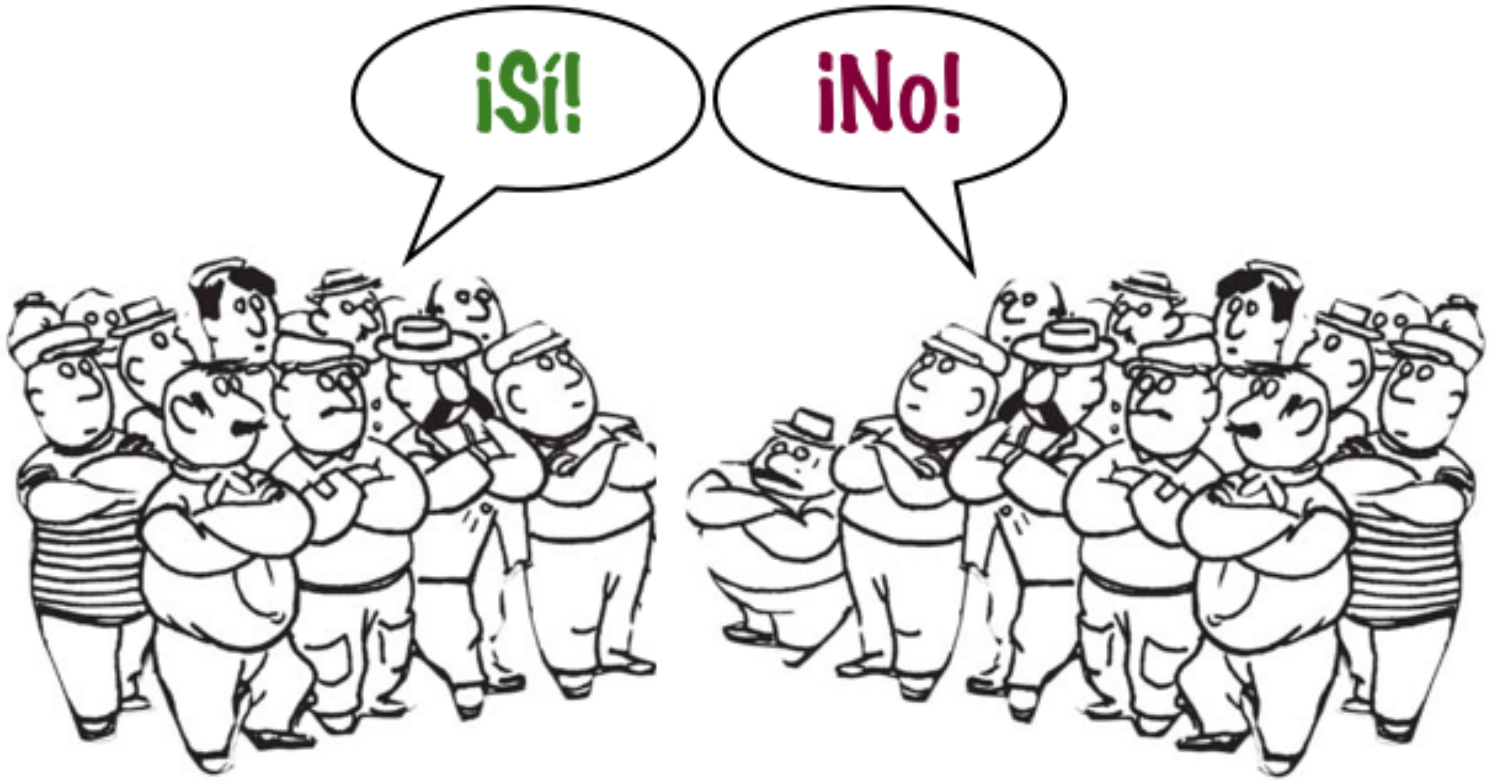
IDEA
CONCLUSIONES

- Estadio-III de BAJO riesgo (pT1-3,N1)
  - CAPOX 3 meses es no inferior a 6 meses para SLE
  - FOLFOX no ha demostrado la no inferioridad con 3 meses frente a 6 meses para SLE

IDEA
CONCLUSIONES

- Estadio-III de BAJO riesgo (pT1-3,N1)
  - CAPOX 3 meses es no inferior a 6 meses para SLE
  - FOLFOX no ha demostrado la no inferioridad con 3 meses frente a 6 meses para SLE

- Estadio-III de ALTO riesgo (pT4,N1-2 o pTany,N2)
  - CAPOX no ha demostrado la no inferioridad con 3 meses frente a 6 meses para SLE
  - FOLFOX es INFERIOR con 3 meses frente a 6 meses para SLE


¡Sí!
¡No!

CONTROVERSIAS - IDEA

1. DIFERENCIAS INTERNAS

2. SLE vs SPG

3. DOSIS

4. COSTO-EFICACIA. CALIDAD DE VIDA

Table 1. Characteristics of the Study Patients (Modified Intention-to-Treat Population).*

Characteristic	TOSCA (N=2402)	SCOT (N=3983)	IDEA France (N=2010)	CALGB/SWOG 80702 (N=2440)	HORG (N=708)	ACHIEVE (N=1291)	All Patients (N=12,834)
Countries	Italy	U.K., Denmark, Spain, Australia, Sweden, New Zealand	France	U.S., Canada	Greece	Japan	
Median age (range) — yr	64 (20–83)	65 (20–84)	64 (18–85)	61 (19–88)	67 (20–75)	66 (28–85)	64 (18–88)
Male sex — no. (%)	1348 (56.1)	2356 (59.2)	1144 (56.9)	1348 (55.3)	398 (56.2)	649 (50.3)	7,243 (56.4)
ECOG performance status — no. (%)							
0	2268 (94.4)	2827 (71.0)	1479 (73.6)	1734 (71.1)	579 (81.8)	1245 (96.4)	10,132 (79.0)
1	130 (5.4)	1156 (29.0)	502 (25.0)	680 (27.9)	128 (18.1)	46 (3.6)	2,642 (20.6)
2	1 (<0.1)	0	29 (1.4)	26 (1.1)	1 (0.1)	0	57 (0.4)
Missing data	3 (0.1)	0	0	0	0	0	3 (<0.1)
Tumor stage — no. (%)							
T1	76 (3.2)	128 (3.2)	78 (3.9)	135 (5.5)	1 (0.1)	75 (5.8)	493 (3.8)
T2	236 (9.8)	333 (8.4)	161 (8.0)	288 (11.8)	60 (8.5)	119 (9.2)	1,197 (9.3)
T3	1773 (73.8)	2347 (58.9)	1399 (69.6)	1598 (65.5)	549 (77.5)	734 (56.9)	8,400 (65.5)
T4	291 (12.1)	1174 (29.5)	372 (18.5)	359 (14.7)	96 (13.6)	363 (28.1)	2,655 (20.7)
Missing data	26 (1.1)	1 (<0.1)	0	60 (2.5)	2 (0.3)	0	89 (0.7)
Nodal stage — no. (%)							
N1	1748 (72.8)	2749 (69.0)	1501 (74.7)	1739 (71.3)	472 (66.7)	959 (74.3)	9,168 (71.4)
N2	636 (26.5)	1233 (31.0)	506 (25.2)	630 (25.8)	230 (32.5)	332 (25.7)	3,567 (27.8)
Missing data	18 (0.7)	1 (<0.1)	3 (0.1)	71 (2.9)	6 (0.8)	0	99 (0.8)
Risk group — no. (%)							
T1, T2, or T3 N1	1553 (65.5)	2032 (51.0)	1245 (62.0)	1507 (63.6)	416 (59.1)	718 (55.6)	7,471 (58.7)
T4, N2, or both	817 (34.5)	1950 (49.0)	764 (38.0)	864 (36.4)	288 (40.9)	573 (44.4)	5,256 (41.3)
Median no. of lymph nodes examined (range)	18 (0–85)	Not recorded	20 (1–99)	20 (1–132)	18 (10–85)	21 (1–123)	19 (0–132)
Chemotherapy regimen — no. (%)							
CAPOX	840 (35.0)	2649 (66.5)	201 (10.0)	0	412 (58.2)	969 (75.1)	5,071 (39.5)
FOLFOX	1562 (65.0)†	1334 (33.5)	1809 (90.0)	2440 (100)	296 (41.8)†	322 (24.9)	7,763 (60.5)
Median follow-up time — mo	61.7	36.8	51.3	34.9	47.5	36.7	41.8

* Percentages may not total 100 because of rounding. ACHIEVE denotes Adjuvant Chemotherapy for Colon Cancer with High Evidence, CALGB/SWOG Cancer and Leukemia Group B/Southwest Oncology Group, HORG Hellenic Oncology Research Group, IDEA International Duration Evaluation of Adjuvant Therapy, SCOT Short Course Oncology Treatment, and TOSCA Three or Six Colon Adjuvant.

† Patients in this trial received FOLFOX4; those in the other trials received modified FOLFOX6.

Table 1. Characteristics of the Study Patients (Modified Intention-to-Treat Population).*

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ECOG performance status — no. (%)					
0	2268 (94.4)	2827 (71.0)	1479 (73.6)	1734 (71.1)	579 (81.8)
1	130 (5.4)	1156 (29.0)	502 (25.0)	680 (27.9)	128 (18.1)
2	1 (<0.1)	0	29 (1.4)	26 (1.1)	1 (0.1)
Missing data	3 (0.1)	0	0	0	0
Tumor stage — no. (%)					
T1	76 (3.2)	128 (3.2)	78 (3.9)	135 (5.5)	1 (0.1)
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Nodal stage — no. (%)					

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Nodal stage — no. (%)						
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N2	636 (26.5)	1233 (31.0)	506 (25.2)	630 (25.8)	230 (32.5)	332 (25.7)

CONTROVERSIAS – ESQUEMA TERAPÉUTICO –NO ALEATORIZADO

- **C A L G B / S W O G 8 0 7 0 2:** FOLFOX-6m en 100%
  Cancer and Leukemia Group B/ Southwest Oncology Group
- **IDEA FRANCE:** **FOLFOX-6m** en **90%**
- **ACHIEVE**: **CAPOX** en **75%!**

CONTROVERSIAS – ESQUEMA TERAPÉUTICO –NO ALEATORIZADO

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- **IDEA FRANCE:** **FOLFOX-6m** en **90%**
- **ACHIEVE**: **CAPOX** en **75%!**

Trials	3m	6m	HR	3 yrs DFS Δ	Non Inferiority
SCOT	76.7%	77.1%	1.006 (0.909-1.114)	-0.4%	Proven (upper margin 1.13)
TOSCA	81.1%	83%	1.14 (0.99-1.32)	-1.9%	Not proven (upper margin > 1.2)
IDEA France	72%	76%	1.24 (1.05-1.46)	4%	Inferiority

CONTROVERSIAS - IDEA

1. DIFERENCIAS INTERNAS

2. SLE vs SPG

3. DOSIS

4. COSTO-EFICACIA. CALIDAD DE VIDA

COMENTARIO II- SLE VS SPG

SLE	SPG
TIEMPO (objetivo y seguimiento)	Fácil de MEDIR
Abarata	Fácil de INTERPRETAR
Disponibilidad MÁS RÁPIDA Fármaco	Fácil de EXPLICAR
Ausencia dé recaída = eficacia	Lineas sucesivas

ACCENT

Adjuvant Colon Cancer Endpoints Group

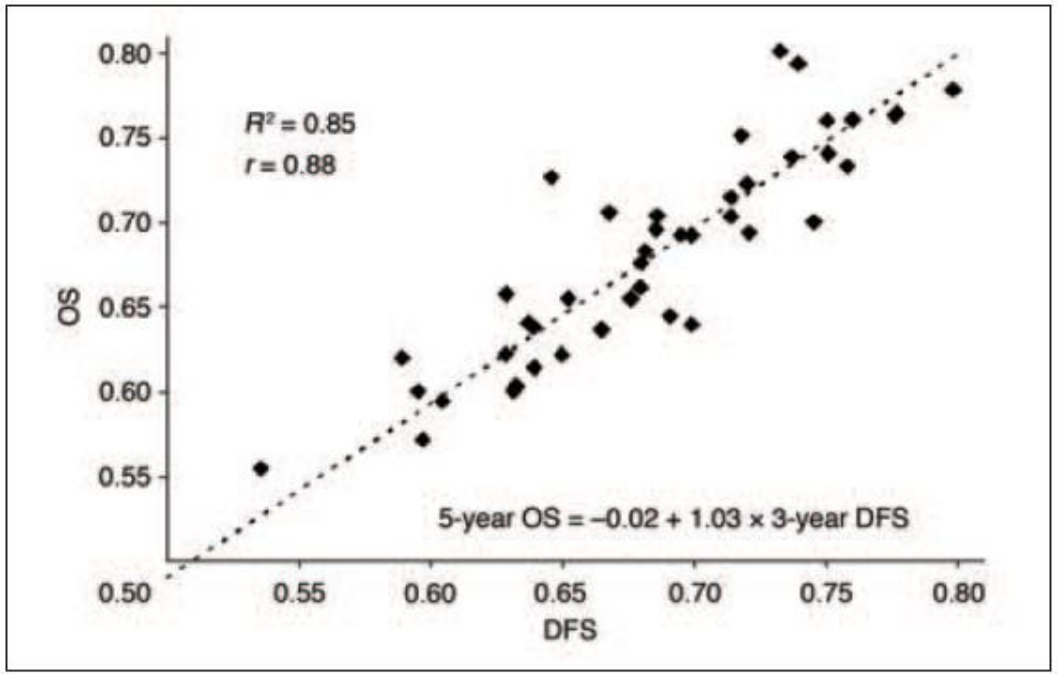


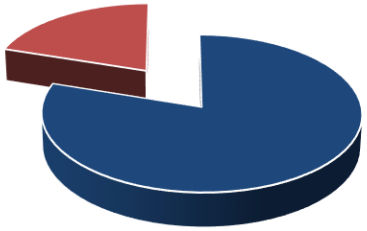
Fig 1. Three-year disease-free survival (DFS) versus 5-year overall survival (OS) by study arm.

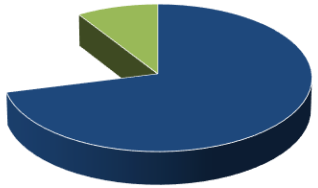
Table 2 Newer ACCENT trials

Trial	Years accrued	Treatment arms	Number (n=20,234)
NSABP C-06*	1997–1999	IFU/LV *vs.* UFT + LV	1,557
X-ACT*	1998–2001	FU/LV *vs.* Cap	1,987
MOSAIC*	1998–2001	FU/LV *vs.* FOLFOX	2,246
CALGB 89803*	1999–2001	FU/LV *vs.* FU/LV + Iri	1,264
PETACC-3*	2000–2002	FU/LV (AIO or LVFU2) *vs.* ± Iri	3,188
NSABP C-07*	2000–2002	FU/LV *vs.* FOLFOX	2,434
XELOXA	2003–2004	FU/LV *vs.* XELOX	1,793
NSABP C-08	2004–2006	mFOLFOX6 ± bevacizumab	2,612
N0147	2004–2009	mFOLFOX6 ± cetuximab	3,153

Review from Lindsay A. Renfro, Daniel J. Sargent *Chin Clin Oncol* 2016

RESULTADOS





De los que progresaron ANTES del 5 AÑO
80% lo hicieron antes del 3 AÑO

De los que progresaron ANTES del 3º AÑO,
91% fallecieron ANTES del 5º año

La mSPG tras progresión = 12 meses

CONTROVERSIAS - IDEA

1. ESQUEMA TERAPEÚTICO
2. SLE vs SPG
3. **DOSIS**

   (Adherencia, DD, tiempo de inicio de tto)

4. COSTO-EFICACIA. CALIDAD DE VIDA

CONTROVERSIAS – IDEA ADHERENCIA

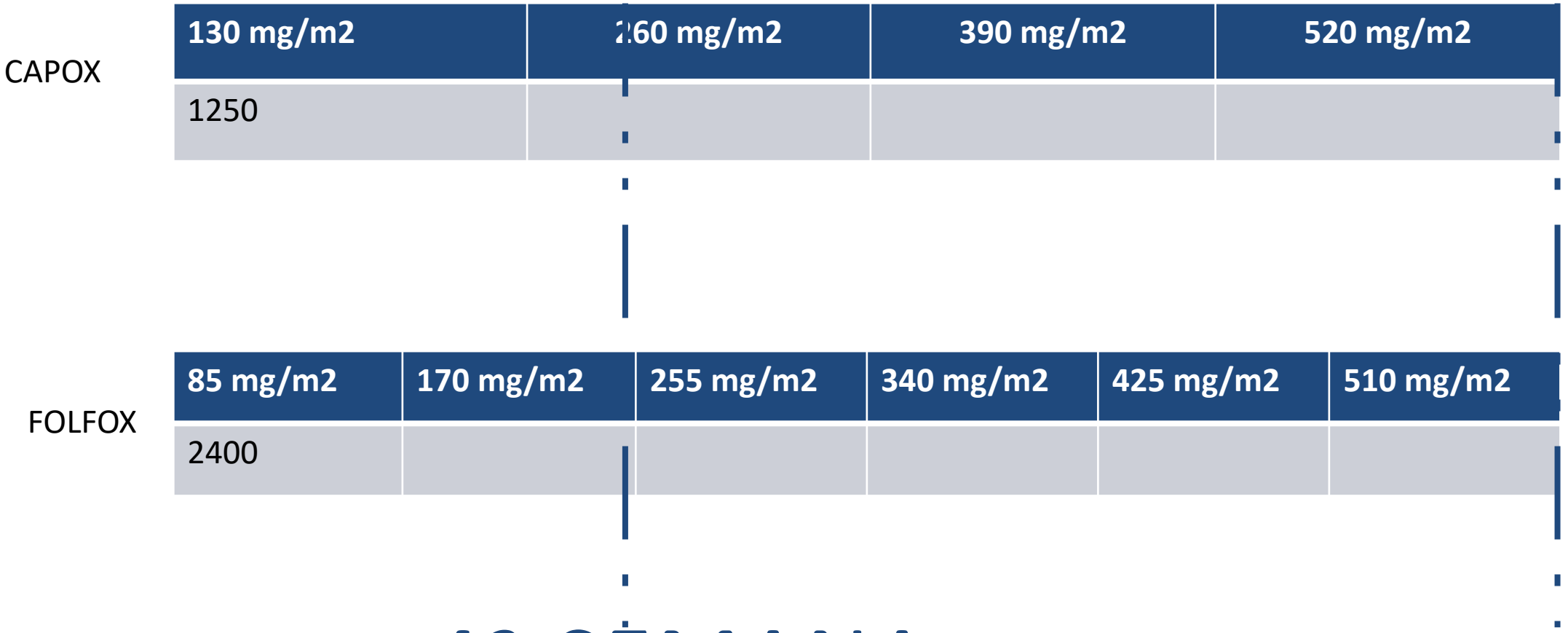
Adherencia	3 MESES		6 MESES	
5-FU	92,4 %		81,6 %	
CAPE	91,2 %		78 %	
OXALI	5-FU	91,4%	5-FU	72,8%
	CAPE	89,8%	CAPE	69,3%

Presented at ASCO 2017 by: Qian Shi, PhD on behalf of IDEA collaborators

CONTROVERSIAS – IDEA ADHERENCIA

FOLFOX		CAPOX	
3m	6m	3m	6m
12 (12-12)	24 (20-24)	12 (12-12)	24(18-24)
90%	71%	86%	65%

CONTROVERSIAS- DENSIDAD DE DOSIS

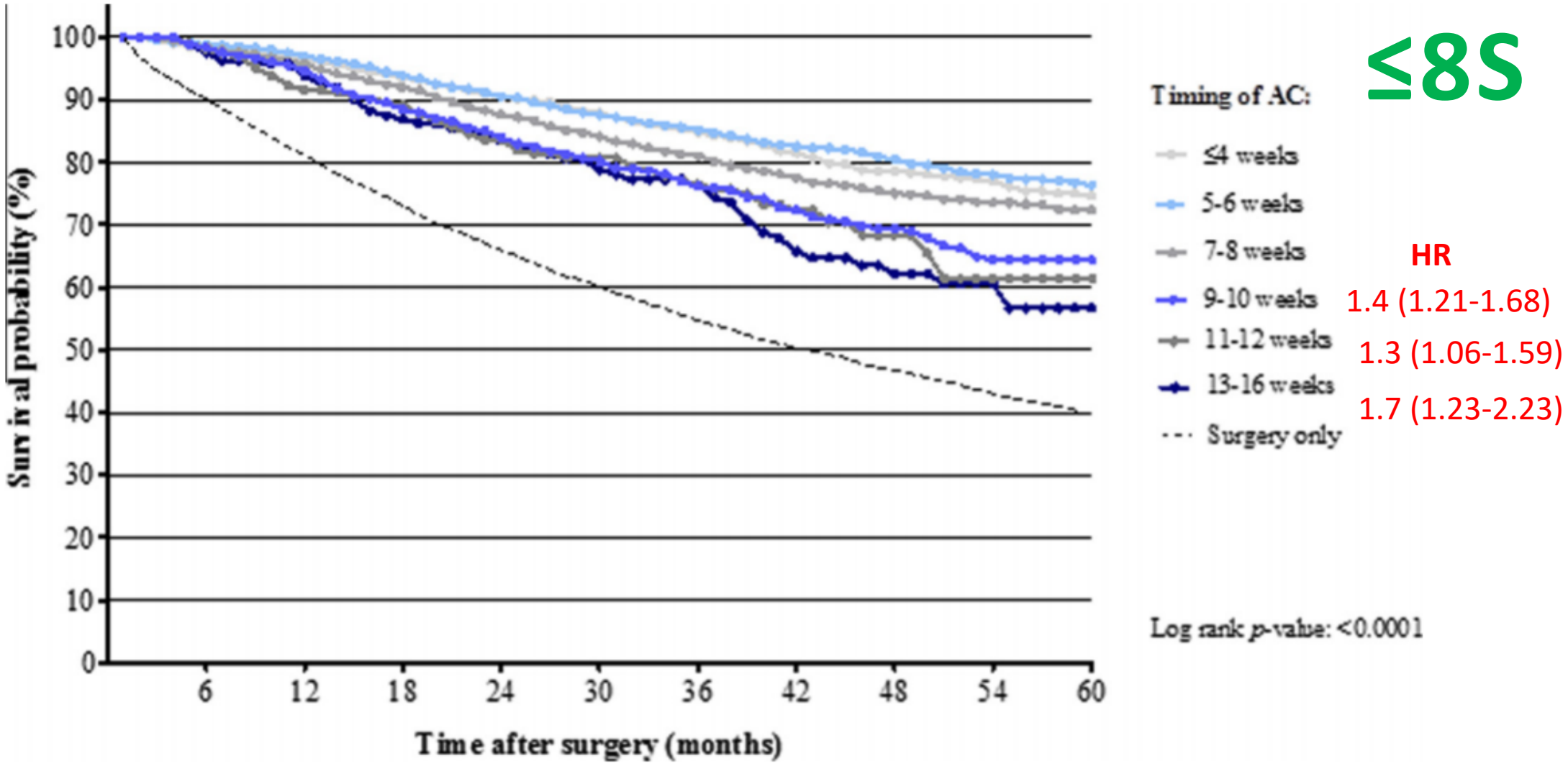


CONTR DE DOSIS

CAPOX	130 mg/m2	520 mg/m2
	1250	
FOLFOX	85 mg/m2	ng/m2 510 mg/m2
	2400	

3 VS 6 M

CONTROVERSIAS- TIEMPO AL INICIO



≤8S

SPG 5ª: 39%

A.C.R.K Bos, EJC 2015

CONTROVERSIAS - IDEA

1. ESQUEMA TERAPEÚTICO
2. SLE vs SPG
3. DENSIDAD DE DOSIS
4. **COSTO-EFICACIA. CALIDAD DE VIDA**

COSTO-EFICACIA IDEA

ESTUDIO SCOT: SHORT COURSE ONCOLOGY TREATMENT

Table 4. Estimates of costs and QALYs for the two strategies

Intervention strategies	Costs (£/patient)		LE		QALYs		NMB (£30 K/QALY)		Prob CE $\lambda = £30{,}000$
	Mean	[95% CI]	Mean	[95% CI]	Mean	[95% CI]	Mean	[95% CI]	
3 Months	18,401	[17,538; 19,328]	6.87	[6.73; 6.99]	5.30	[5.17; 5.40]	140492	[135,327; 145,658]	0.995
6 Months	23282	[22,227; 24,367]	6.90	[6.78; 7.02]	5.22	[5.10; 5.34]	133246	[129,569; 136,922]	0.005
Incremental	−4881	[−6269; −3492]	−0.03	[−0.22; 0.13]	.08	[−0.086; 0.230]	7246	[3469; 11,023]	(3 M dominates)

Health utilities conditional on survival considered
KMSA estimator and partitioned survival analysis used for costs and QALYs, respectively
CIs are computed using bootstrap sampling
Probability of cost-effectiveness calculated using 1000 bootstrap replications

J Robles-Zurita et al. BJC 2018

- 3 vs 6: **AVAC/QALY = 0.08** (95% CI: −0.086; 0.230)
- 3 meses = ahorro de -£4881 (95% CI: -£6269; -£3492)
- **FOLFOX 3 era peor que 6**

COSTO-EFICACIA (SCOT)
CALIDAD DE VIDA

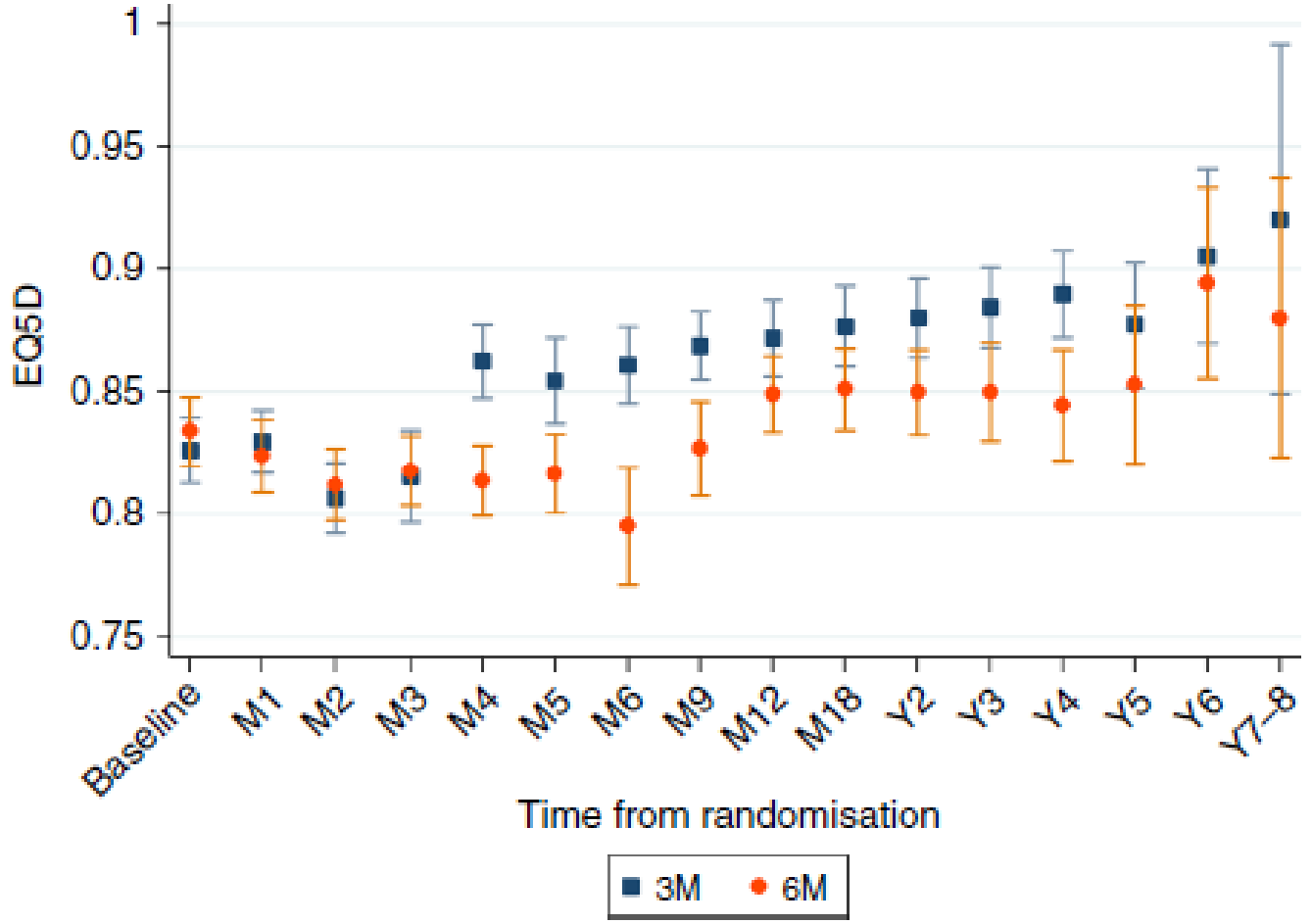
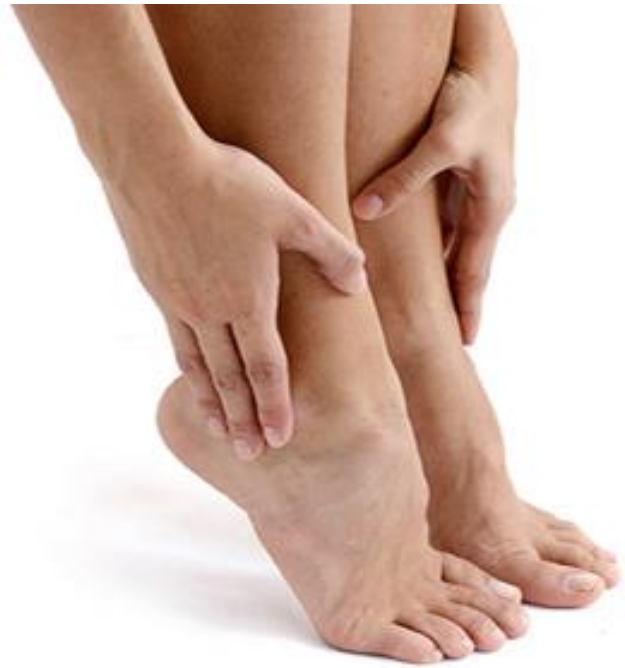


Fig. 2 Evolution of EQ-5D utilities over time by arms. Average and 95% CI

CALIDAD DE VIDA



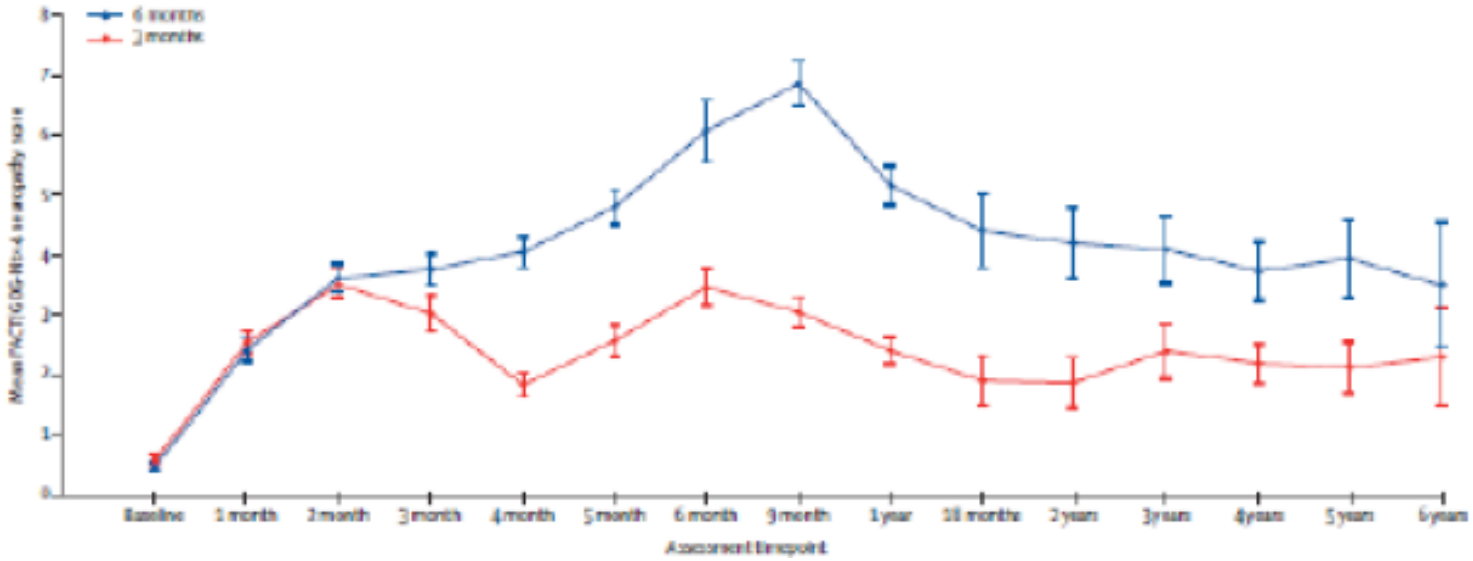
NEUROTOXIDAD G≥2

ESQUEMA	3 MESES	6 MESES
FOLFOX	17%	48%
CAPOX	15%	45%

Qian Shi et al. J Clin Oncol 35, 2017 (suppl; abstr LBA1)

NEUROTOXICIDAD

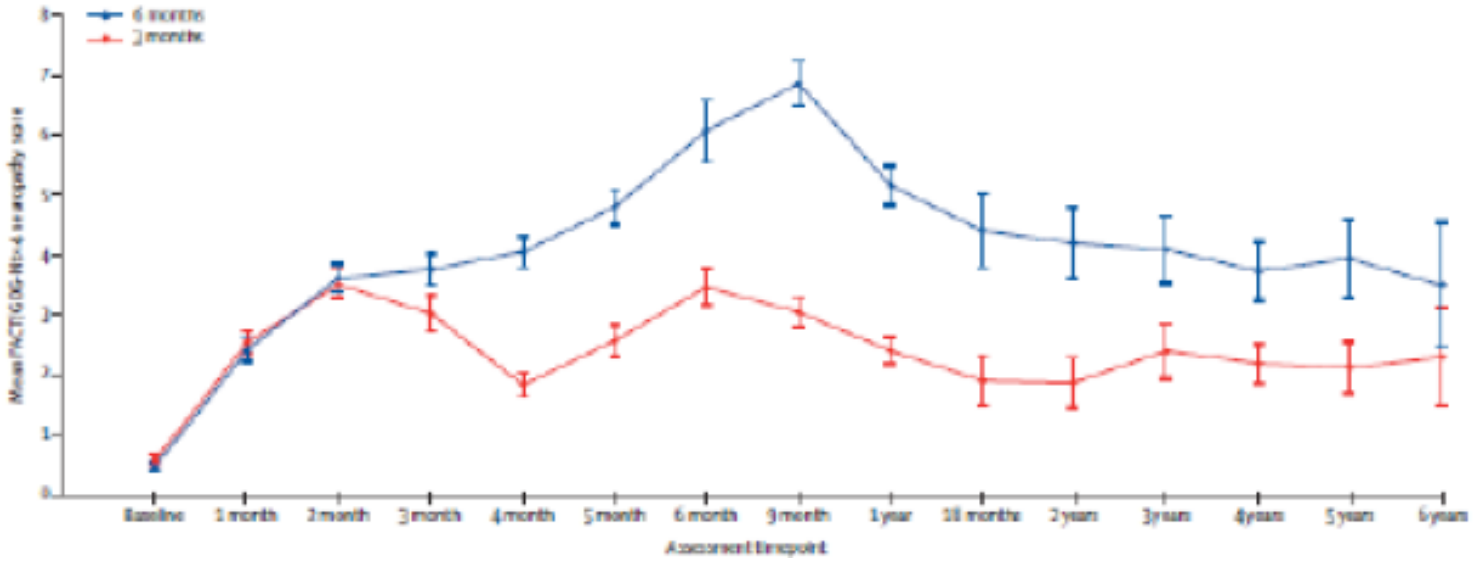
ESTUDIO SCOT: SHORT COURSE ONCOLOGY TREATMENT



Robles-Zurita, B*ritish Journal of Cancer* 2018

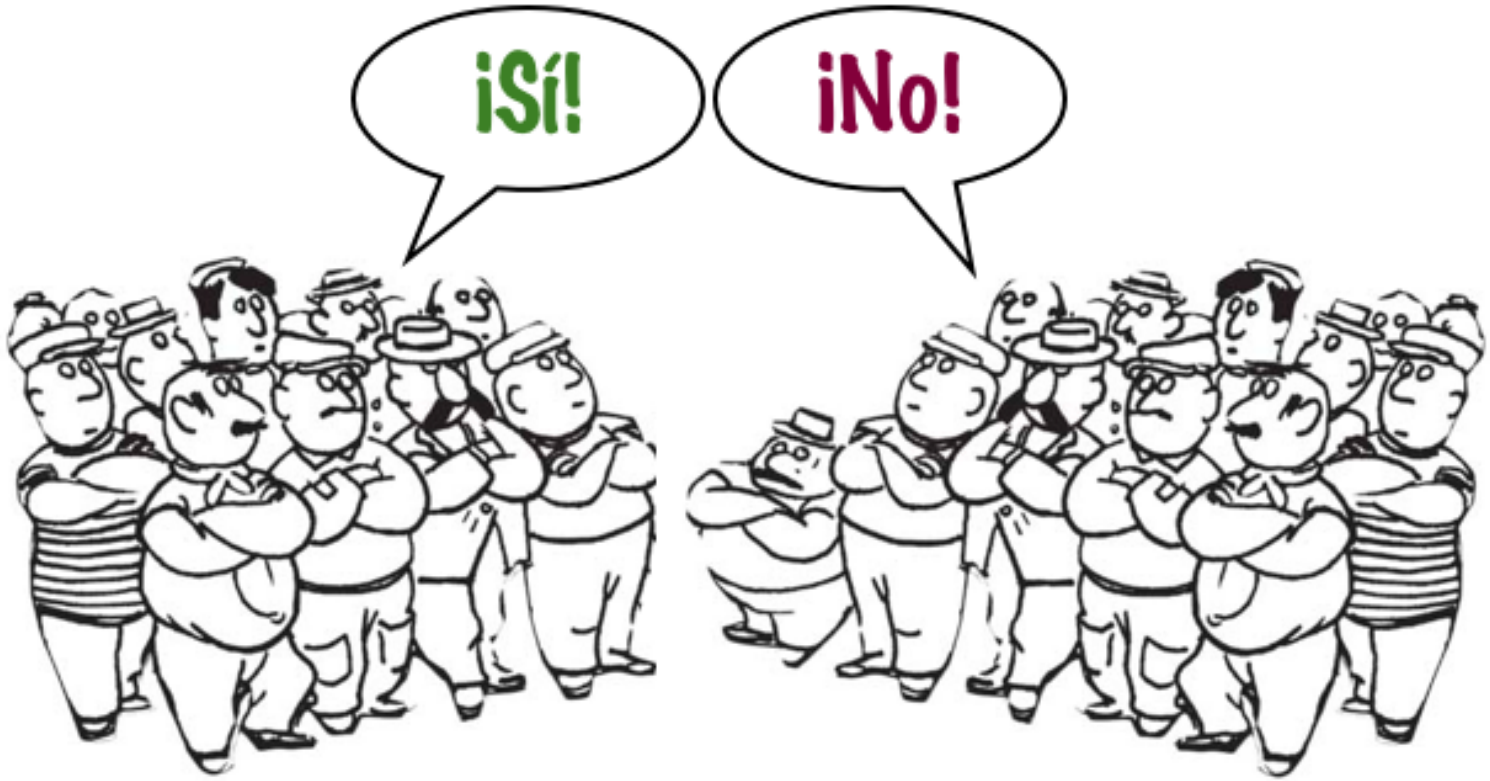
NEUROTOXICIDAD

ESTUDIO SCOT: SHORT COURSE ONCOLOGY TREATMENT



Robles-Zurita, B*ritish Journal of Cancer* 2018

Neurotoxicidad g3 acumulativa: MOSAIC = 12%; NSABP = 8.2%; AVANT = 11%


¡Sí!
¡No!

CONCLUSIONES I

- Cirugía cura 50-60%, la QT añade un 15-20% de beneficio

- ESTADIO II: FACTORES DE RIESGO

- Adyuvancia en estadio III en pacientes de **bajo riesgo T1-3 N1:**

– **CAPOX 3 meses** es no inferior a 6 meses
– ↓ neurotoxidad G2-G4

- Adyuvancia en estadio III en pacientes de **alto riesgo T4 y/o N2**

(y otros factores):

– **CAPOX o FOLFOX 6 meses**

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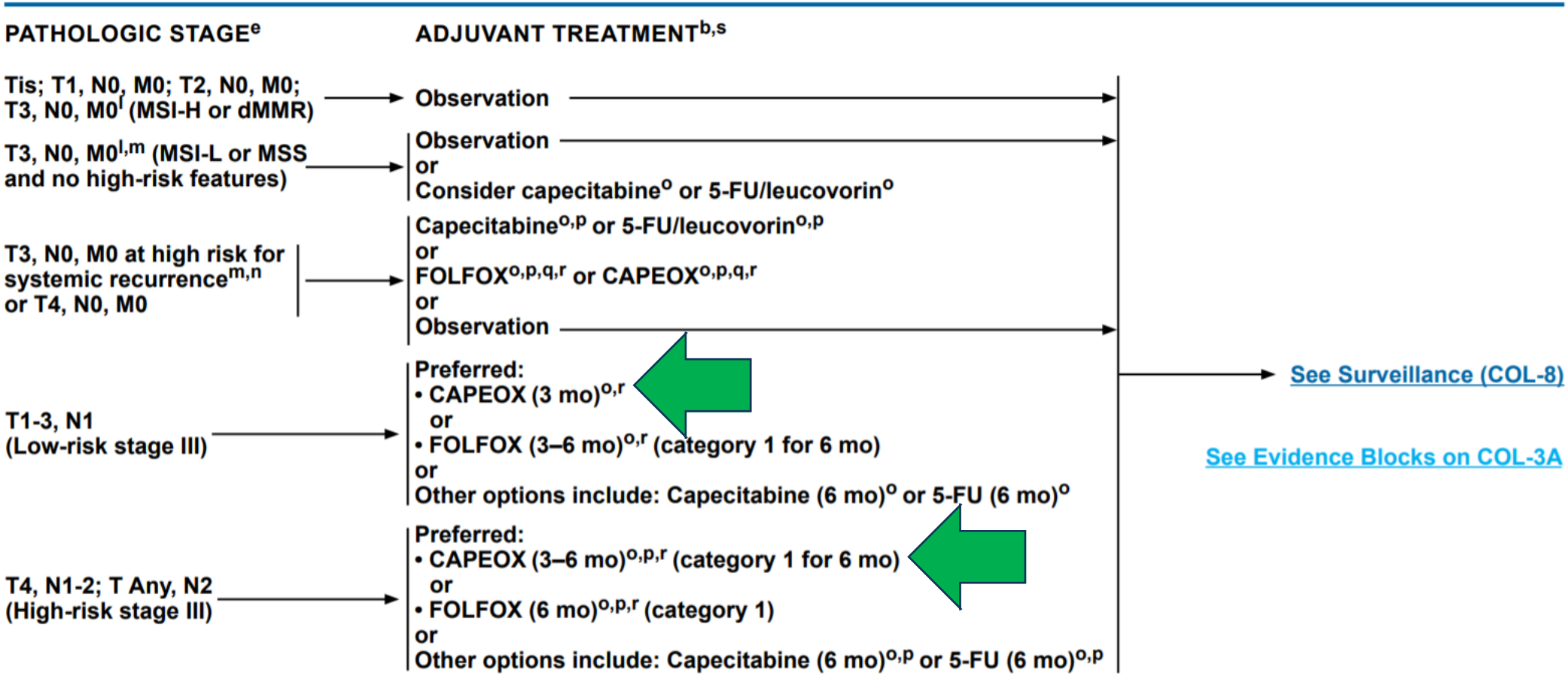

CONCLUSIONES II

IDEA ---- CONTROVERSIAS

1. **DIFERENCIAS INTERNAS**
2. **SLE vs SPG**
3. **DOSIS**
4. **COSTO-EFICACIA. CALIDAD DE VIDA**

Abraham Lincoln *(1808-1865)*

AGRADECIMIENTOS

María Teresa Perez-Hoyos, por las controversias

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