CAMPUS SEOM

Área de formación virtual SEOM

Tumores esófago-gástricos

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SEOM
Sociedad Española de Oncología Médica

0.- Introducción

1.- Estrategias de tratamiento en el **Cáncer de Esófago Locorregional**
- Escamoso
- Adenocarcinoma

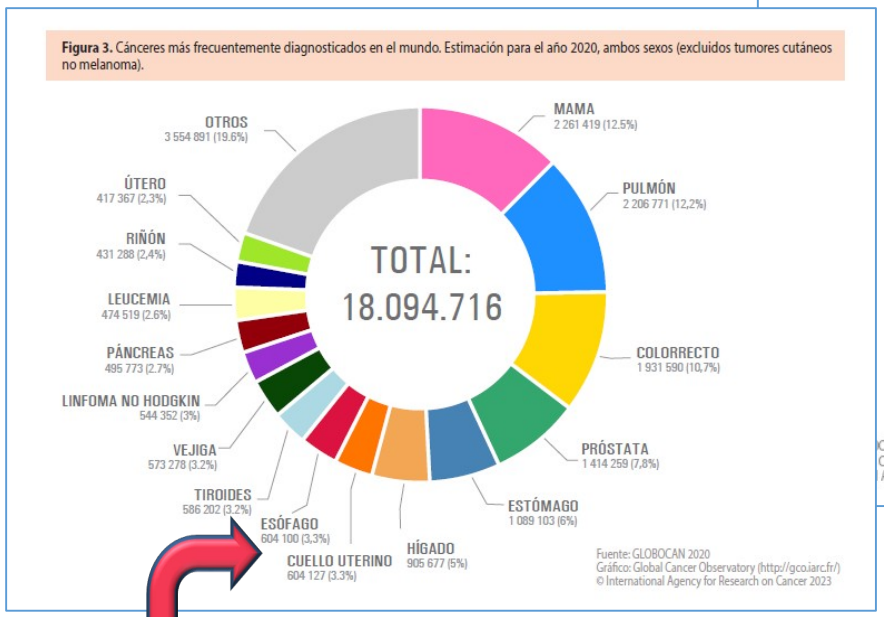
2.- Estrategias de tratamiento en el **Cáncer de Esófago Metastásico**

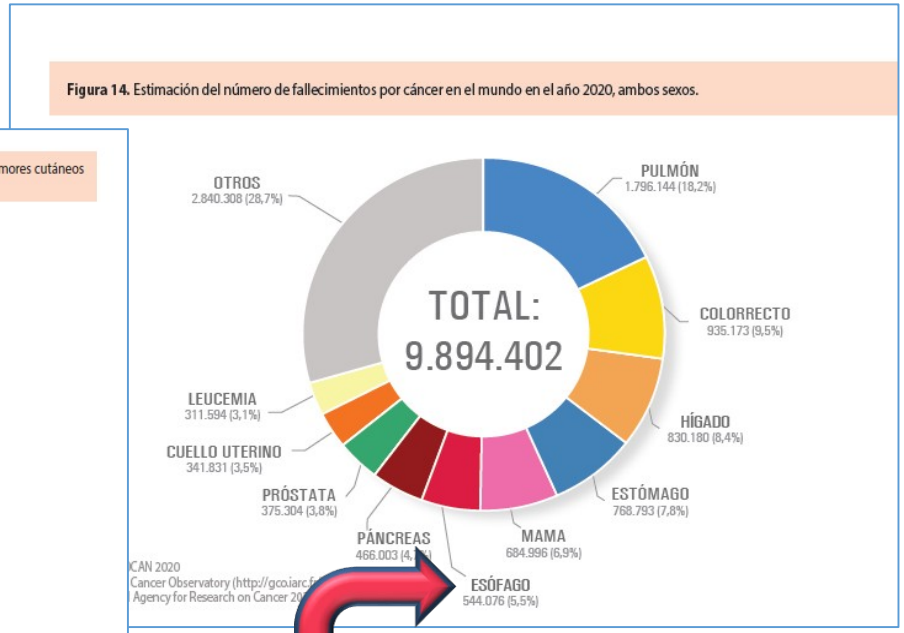
3.- Estrategias de tratamiento en el **Adenocarcinoma Gástrico Locoregional**

4.- Estrategias de tratamiento en el **Adenocarcinoma Gástrico Metastásico**

Cáncer de esófago: epidemiología global

-. 7º cáncer en frecuencia
-. 6º causa de muerte por cáncer
-. S a 5 años 15-25%.
-. Mal px, diagnóstico tardío.





604.100 casos

2020

544.076 muertes

El 50% de los pacientes tienen enfermedad localmente avanzada.

Fuente: GLOBOCAN 2020
Gráfico: Global Cancer Observatory (http://gco.iarc.fr/)
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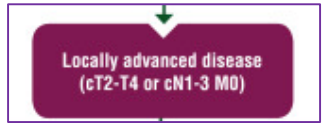
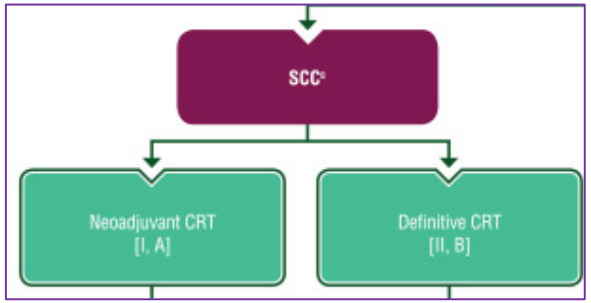
1.1- Estrategias de tratamiento en el **SCC** locorregional

cTNM staging (endoscopy, EUS, MS-CT, FDG-PET)
Functional assessment (symptoms, comorbidity, nutritional status, patient preferences)

1.- Clasificación de la AJCC (8º edición)

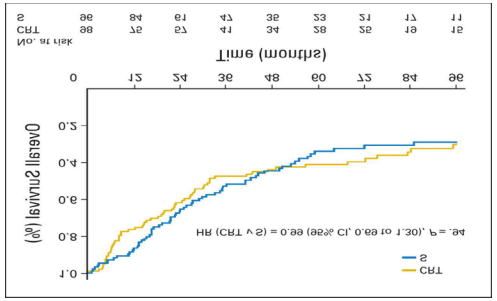




VOLUME 32 · NUMBER 23 · AUGUST 10 2014
JOURNAL OF CLINICAL ONCOLOGY ORIGINAL REPORT

Surgery Alone Versus Chemoradiotherapy Followed by Surgery for Stage I and II Esophageal Cancer: Final Analysis of Randomized Controlled Phase III Trial FFCD 9901

Christophe Mariette, Laetitia Dahan, Françoise Mornex, Emilie Maillard, Pascal-Alexandre Thomas, Bernard Meunier, Valérie Boige, Denis Pezet, William B. Robb, Valérie Le Brun-Ly, Jean-François Bosset, Jean-Yves Mabrut, Jean-Pierre Triboulet, Laurent Bedenne, and Jean-François Seitz



QT-RT no impacta en la supervivencia!!!

❑ Esófago cervical: QT-RT radical

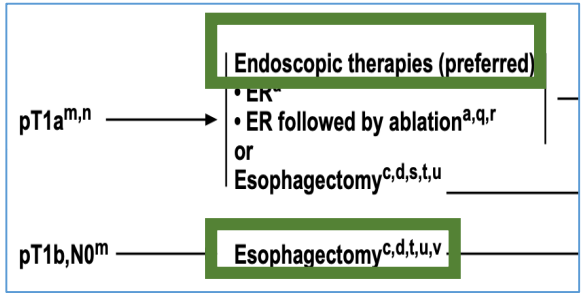
❑ Esófago torácico:

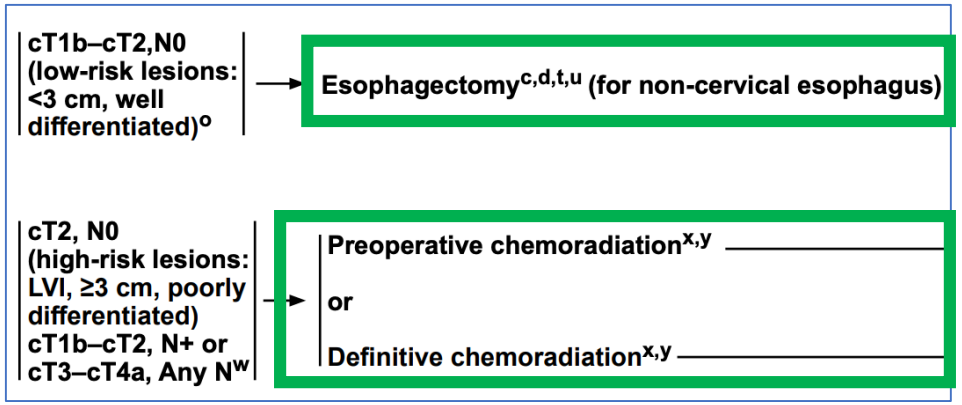
- **T1N0:** Cia vs resección endoscopica
- **T2N0**: **CIA** (FFCD 9901)
  QT_RT>>CIA
  QT-RT definitiva

National Comprehensive Cancer Network®

NCCN Guidelines Version 3.2023
Esophageal and Esophagogastric Junction Cancers

Squamous cell carcinoma



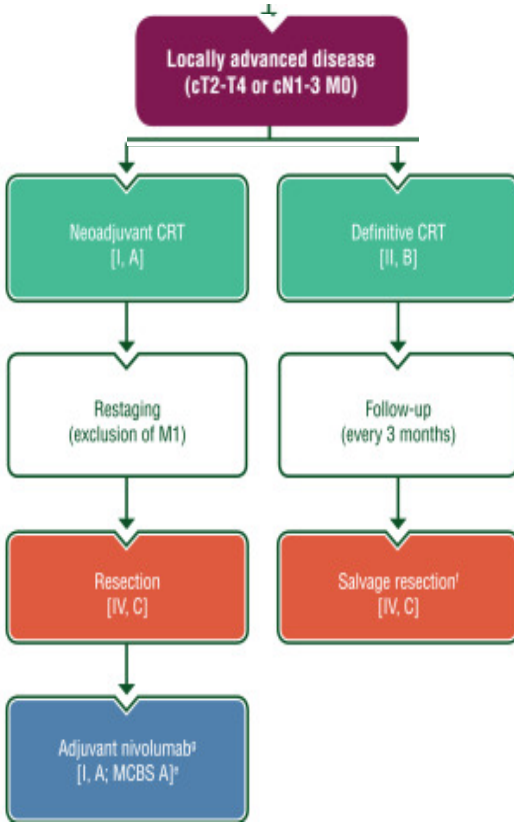


1.- Ann Oncol 2022;33(10):992-1004 2.- J Natl Compr Canc Netw 2023;21(4):393–422 3.JCO 2014 32:23, 2416-2422

Estrategias de tratamiento en el SCC locorregional

- **T3-4 y/o N1-3:**

  QT_RT >>Cia>>+/- IT
  QT-RT radical



25% R1
OS 5 años < 40%

CROSS
Carbo+pac/41 .4Gy

CALGB 9781
CF/50,4 Gy

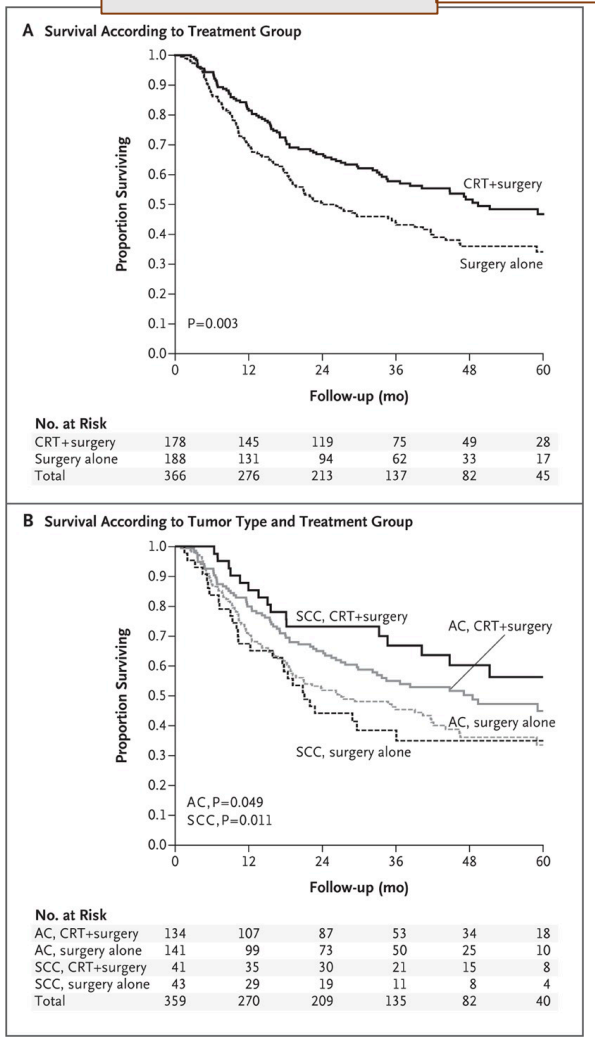
NEOCRETE5010
Sólo CCE
cis + vin/40Gy

SWOG
PROTECT
Fase II
con FOLFOX

CROSS TRIAL: SG a 5 años de >60 %

SG 48 vs 24 m
(HR 0,68 p=0·003).

SCC 81m
AC 43m



1. N Engl J Med 1998 ; 339: 1979 - 1984

2. *Lancet Oncol*. 2015;16(9):1090-1098.

Adyuvancia: Checkmate 577

Estudio global de fase III, aleatorizado,doble ciego y controlado con placebo

Key eligibility criteria

- Stage II/III EC/GEJC
- Adenocarcinoma or squamous cell carcinoma
- Neoadjuvant chemoradiotherapy + surgery (R0, performed within 4-16 weeks before randomization)
- Residual pathologic disease: ≥ypT1 or ≥ypN1
- ECOG PS 0-1

N=794

Stratification factors:
- Histology (squamous vs. adenocarcinoma)
- Pathologic lymph node status (≥ypN1 vs ypN0)
- Tumor cell PD-L1 expression (≥1% vs <1%[b])

R 2:1

n=532 → Nivolumab 240mg Q2W × 16 weeks Then 480mg Q4W

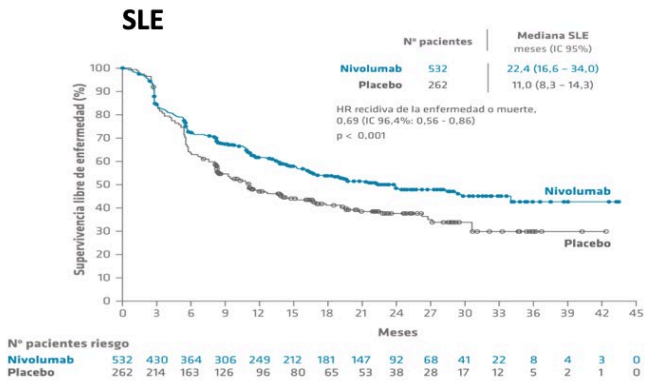
n=262 → Placebo Q2W × 16 weeks Then Q4W

Total treatment duration: 1 year

Primary endpoint:
- DFS

Secondary endpoints:
- OS
- OS rate at 1, 2, and 3 year

Exploratory endpoint:
- safety
- DMFS
- PROs (FACT-E, FACT-E GP5, EQ-5D-3L)
- PFS2



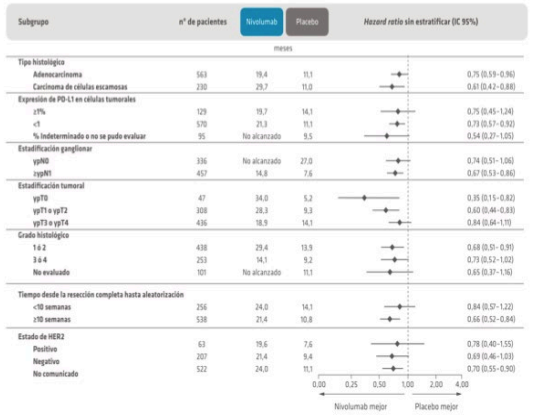
SLE m: 22,4 meses vs 11,0 meses HR 0.67 (p<0,001)

Reducción del 31% del riesgo de recidiva o muerte.

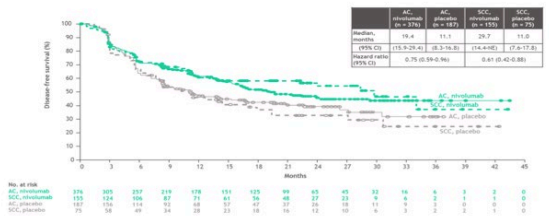
- Median follow-up was 24.4 months (range, 6.2 to 44.9)
- Geographical areas: Europe (38%), Canada and USA (32%), Asia (13%), others (16%)

ADC y ESC de esófago

***Forest plot* de la SLE por subgrupos[1]**



SLE según histología



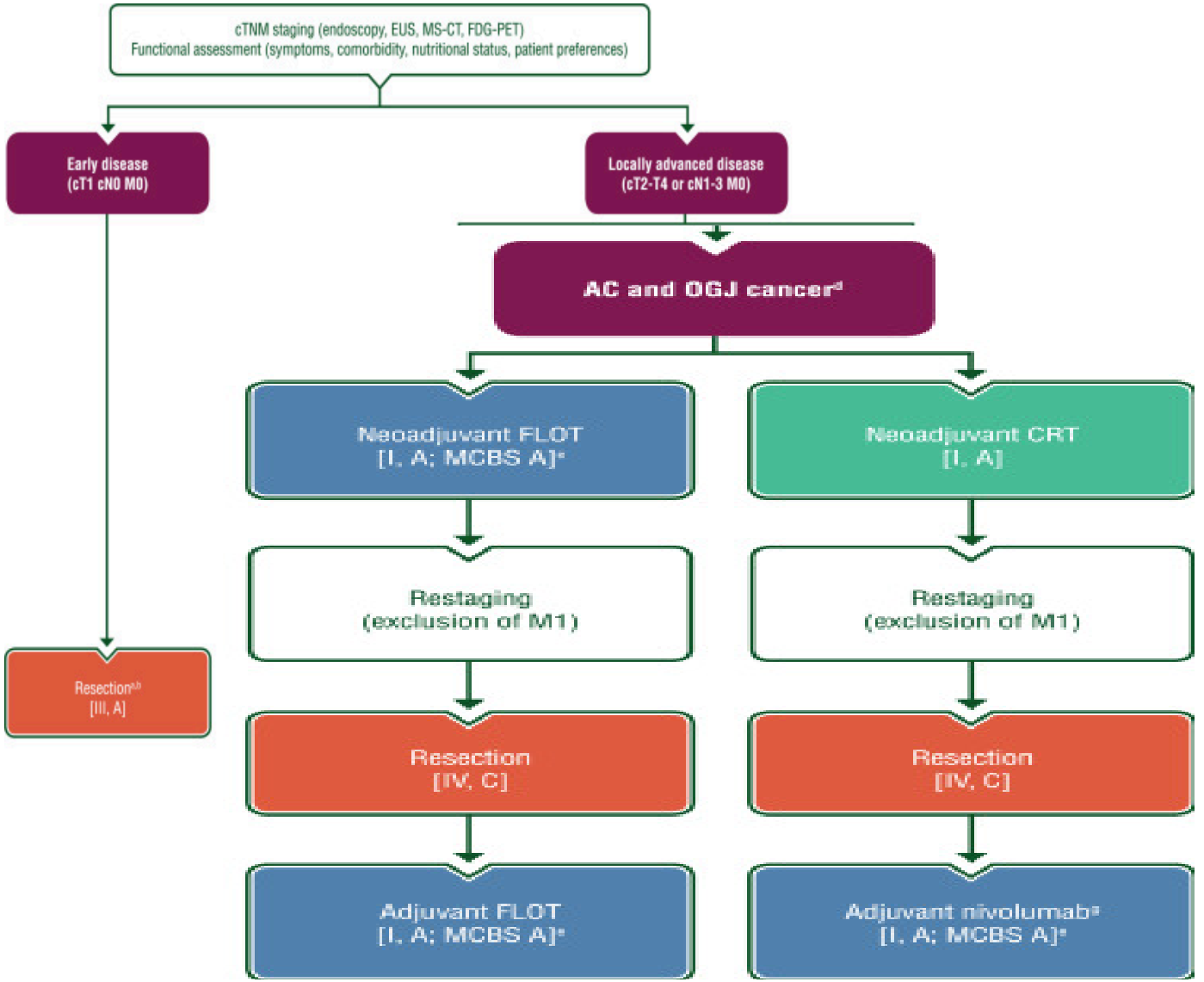
Beneficio independiente de histología, PDL-1, y de localización.

Seguro y no impactó en la calidad de vida vs P

N Engl J Med 2021; 384:1191-1203

1.2.- Estrategias de tratamiento en el **AC esofágico** locorregional

- Adenocarcinoma:
  - **T1N0:** resección endoscópica o Cia
  - **T2-4 y/o N1-3:**
    QT_RT >>Cia>>+/- IT
    QT perioperatoria



QT perioperatoria vs QT_RT neo

OS 5a con Cia +/-QT 20-30%

MAGIC

ECF perioperatoria vs CIA

SG 36 % vs 23 %
HR 0,75;
IC 95 %, 0,60–0,93; *P* = .0009

2006

FNCLCC ACCORD 07-FFCD

5FU-P perioperatoria vs CIA

SG 38% v 24%
HR 0.69;
IC 95% CI, 0.50 to 0.95; P = .02

2011

FLOT4-AIO

FLOT vs ECF/ECX

Mediana OS 50 vs 35 meses
HR 0,77;
95 IC %: 0,63–0,94; *P* = . 012

2017

European Journal of Cardio-Thoracic Surgery 51 (2017) 421–431
doi:10.1093/ejcts/ezw315 Advance Access publication 1 October 2016

REVIEW

Cite this article as: Deng H-Y, Wang W-P, Wang Y-C, Hu W-P, Ni P-Z, Lin Y-D *et al.* Neoadjuvant chemoradiotherapy or chemotherapy? A comprehensive systematic review and meta-analysis of the options for neoadjuvant therapy for treating oesophageal cancer. Eur J Cardiothorac Surg 2017;51:421–31.

Neoadjuvant chemoradiotherapy or chemotherapy? A comprehensive systematic review and meta-analysis of the options for neoadjuvant therapy for treating oesophageal cancer

2019

Han-Yu Deng[a,b], Wen-Ping Wang[a], Yun-Cang Wang[a,b], Wei-Peng Hu[a,b], Peng-Zhi Ni[a,b], Yi-Dan Lin[a] and Long-Qi Chen[a,*]

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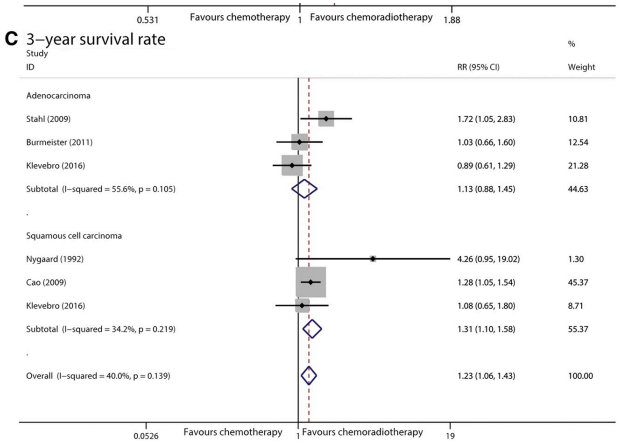


Journal of Clinical Oncology®
An American Society of Clinical Oncology Journal
ASCO
2023

Neo-AEGIS (Neoadjuvant Trial in Adenocarcinoma of the Esophagus and Esophago-Gastric Junction International Study): Final primary outcome analysis.

Endpoint	Neo-AEGIS Regimen (Perioperative Chemotherapy/Surgery)	CROSS Regimen (Chemoradiation/Surgery)	*P* Value
3-Year overall survival rate	55%	57%	HR = 1.03 (95% CI = 0.77–1.38)
Nodal downstaging to ypN0 rate	44%	60%	.004
R0 resection	82%	95%	< .001
Pathologic complete response rate	5%	17%	.001
Major pathologic response rate	12%	42%	< .001

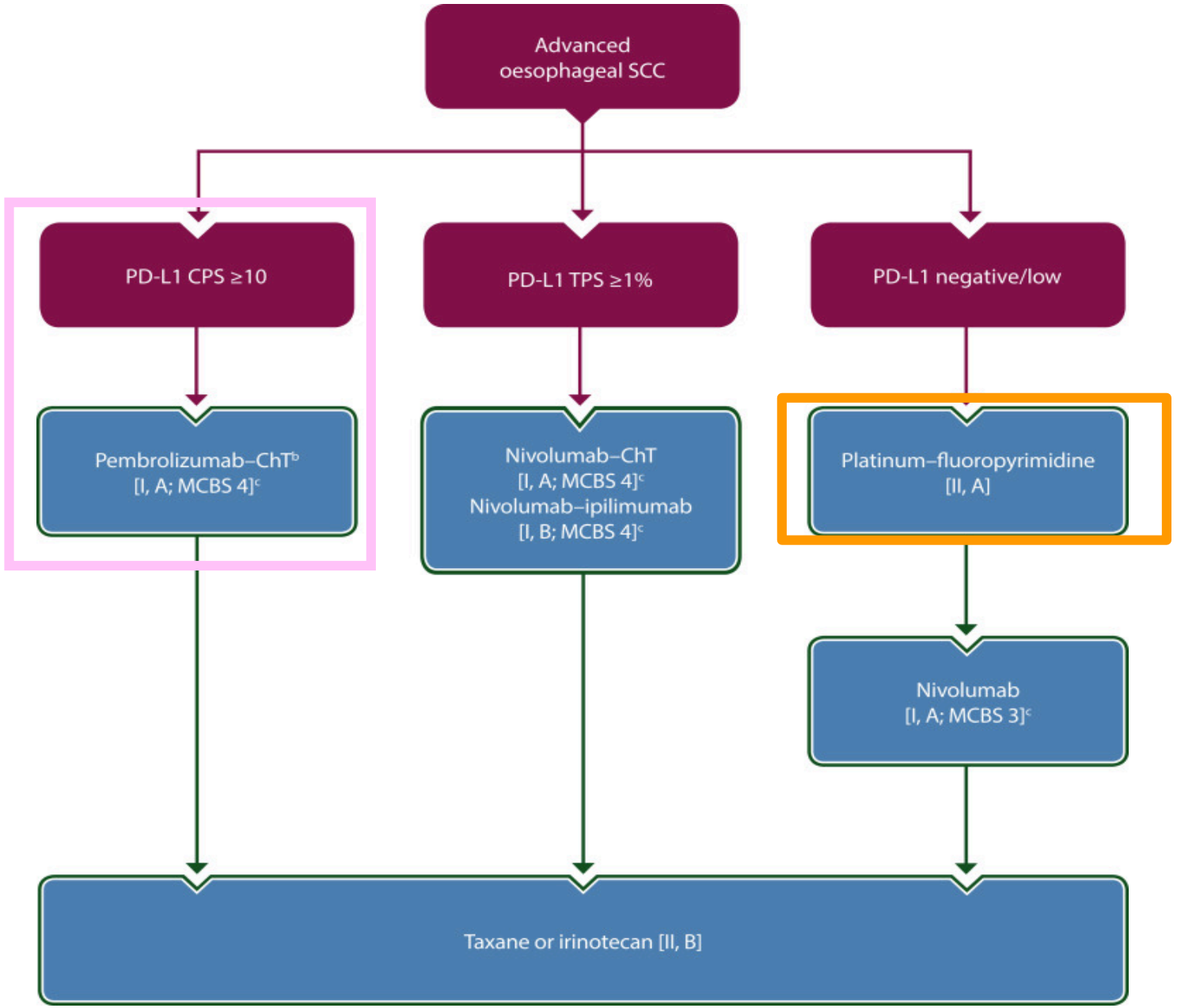
CI = confidence interval; HR = hazard ratio.

1.- N Engl J Med 2006. 2. J Clin Oncol. 2011 3.- Al-Batran S, et al. ASCO Annual Meeting 2017

4.- Lancet. 2019 393:1948-1957 5.- J Clin Oncol 2023 41:4_suppl, 295.

2.- Estrategia de tratamiento en SCC M1

1º línea

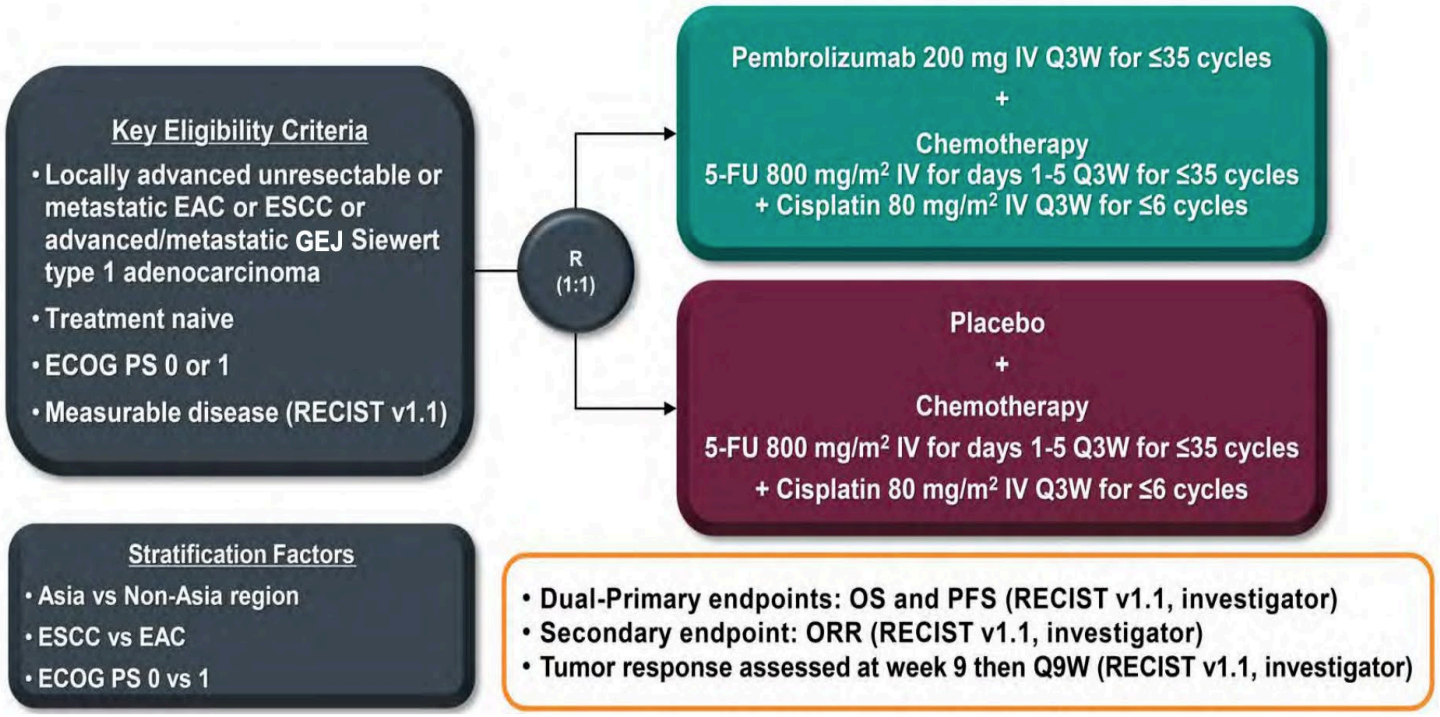


Fase III
ADC y SCC esofágicos gástricos UEG

SLPm 8 m
SGm 7 -13 m
SG 5 años < 20 %.

1.- Ann Oncol 2022;33(10):992-1004

2.2 Pembrolizumab + QT 1º línea de cáncer esófago **PDL 1 CPS ≥ 10**. Fase III Keynote 590



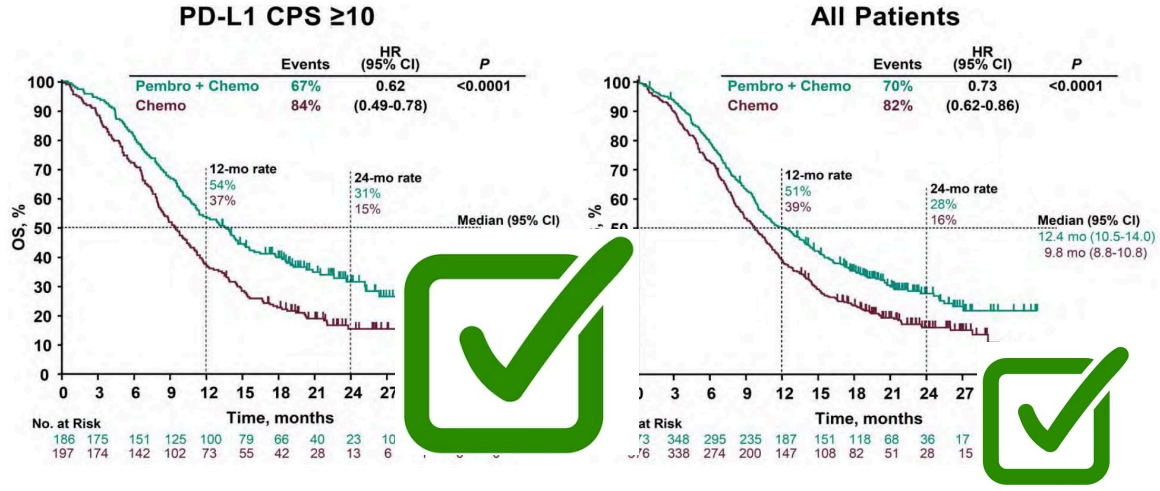
4 subgrupos
- Total
- SCC
- PD-L1 CPS≥10
- SCC PD-L1 CPS≥10

7 hipótesis
- SG en CEE PD-L1 CPS≥10
- SG en CEE
- SG en los todos los pacientes PD-L1 CPS≥10
- SG en todos los pacientes del estudio
- SLP en CEE, según criterios RECIST 1.1
- SLP en PD-L1 CPS≥10 según criterios RECIST 1.1
- SLP en todos los pacientes, según criterios RECIST 1.1

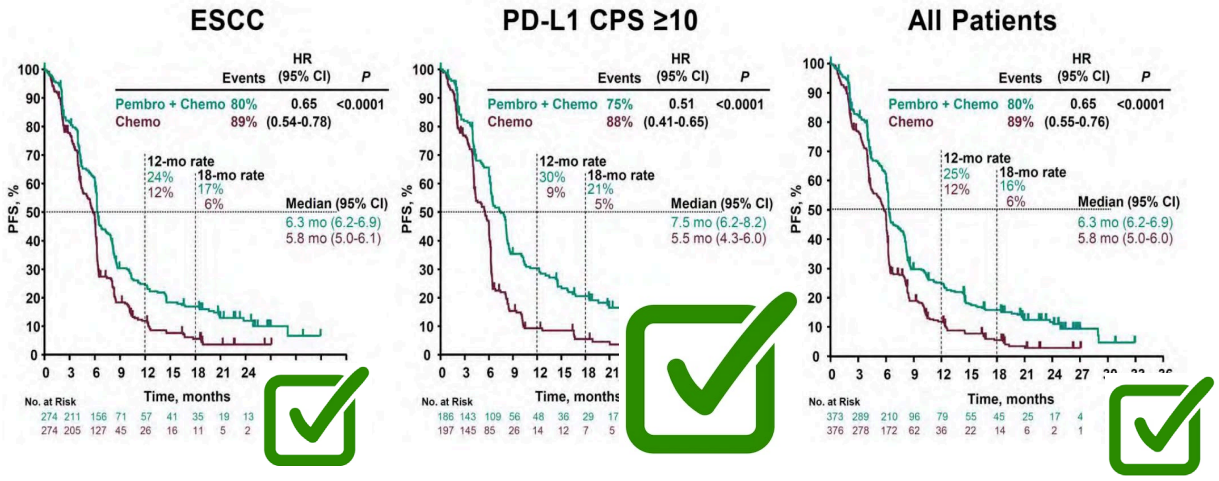
ADC y ESC de esófago y UEG (únicamente Siewert I)

Kato K. ESMO 2020. Abstract LBA8

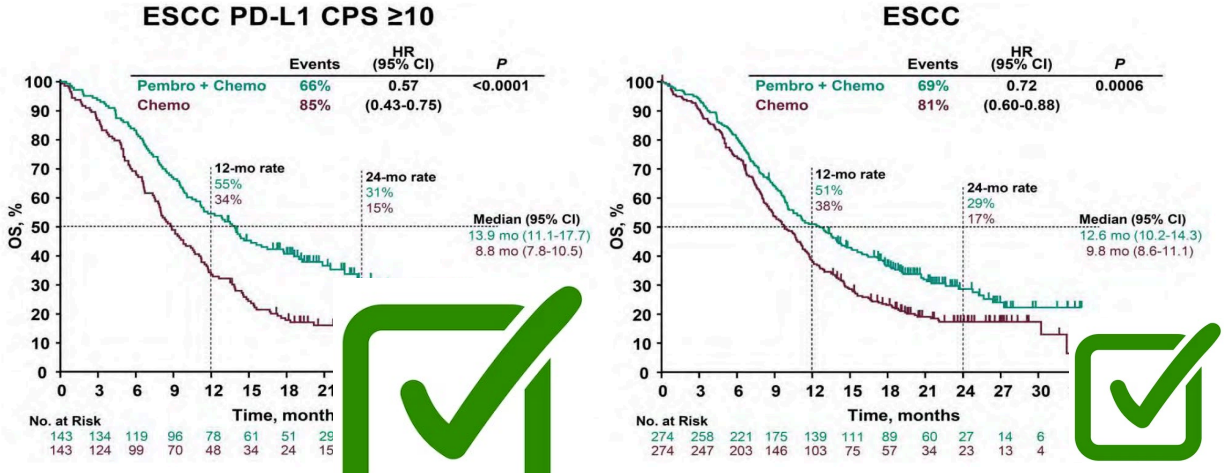
KEYNOTE-590 – Overall Survival in All Patients



KEYNOTE-590 – Progression-Free Survival



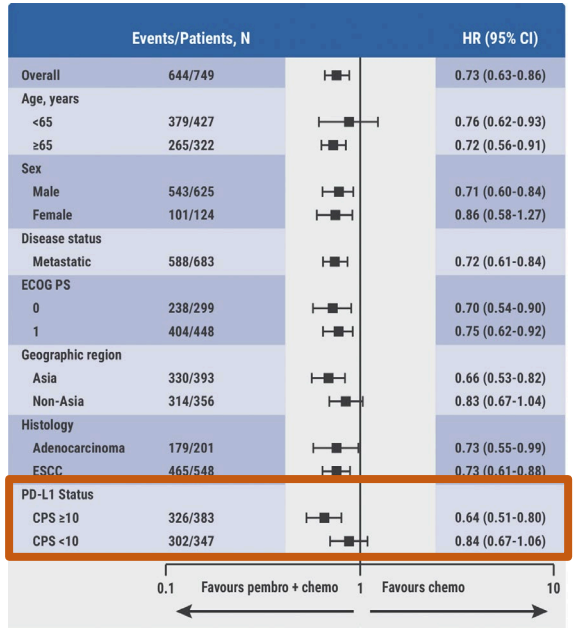
KEYNOTE-590 – Overall Survival in SCC Patients



Kato K. et al. ESMO 2020. Abstract LBA

Courtesy of Zev Wainberg, MD, MS

KEYNOTE-590 – Subgroup Analyses



Estudio post-hoc :
falta de beneficio
en PD-L1 CPS < 10

Todos

CPS ≥ 10

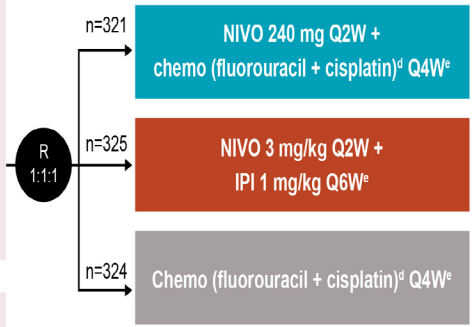
2.3 Nivolumab 1º linea ESC **PDL TPS > 1%.** Checkmate 648

Nivolumab–ChT
[I, A; MCBS 4][c]
Nivolumab–ipilimumab
[I, B; MCBS 4][c]

CheckMate 648 study design

- CheckMate 648 is a global, randomized, open-label phase 3 study[a]

Key eligibility criteria
- Unresectable advanced, recurrent or metastatic ESCC
- ECOG PS 0-1
- No prior systemic treatment for advanced disease
- Measurable disease



Primary endpoints:
- OS and PFS[f] (tumor cell PD-L1 ≥ 1%)

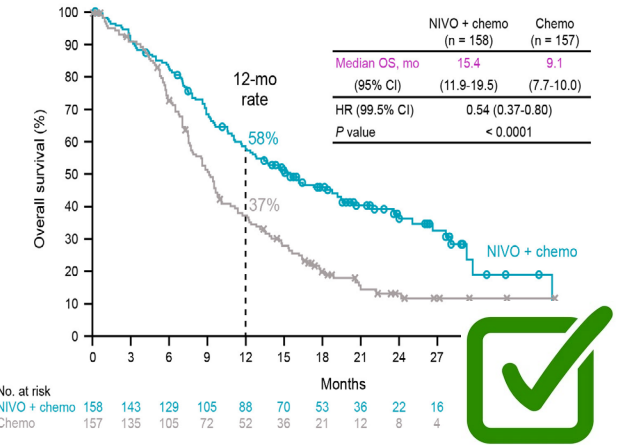
Secondary endpoints:
- OS and PFS[f] (all randomized)
- ORR[f] (tumor cell PD-L1 ≥ 1% and all randomized)

Stratification factors
- Tumor cell PD-L1 expression (≥ 1% vs < 1%[b])
- Region (East Asia[c] vs rest of Asia vs ROW)
- ECOG PS (0 vs 1)
- Number of organs with metastases (≤ 1 vs ≥ 2)

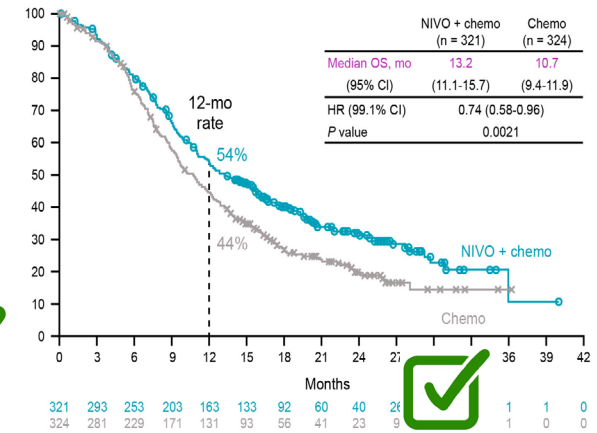
ESC de esófago

Overall survival: NIVO + chemo vs chemo : 1º análisis

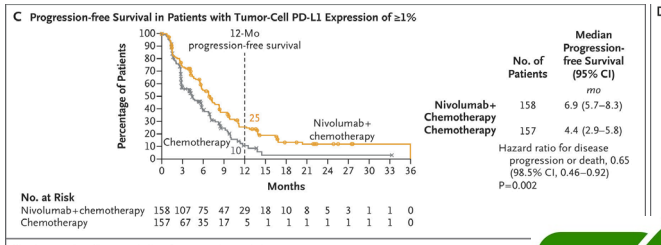
Primary endpoint (tumor cell PD-L1 ≥ 1%)[a]

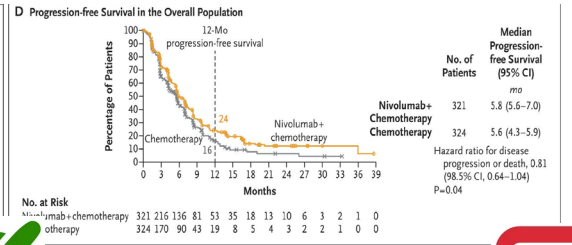


All randomized[a]



PFS Nivo+ Chemo vs Chemo

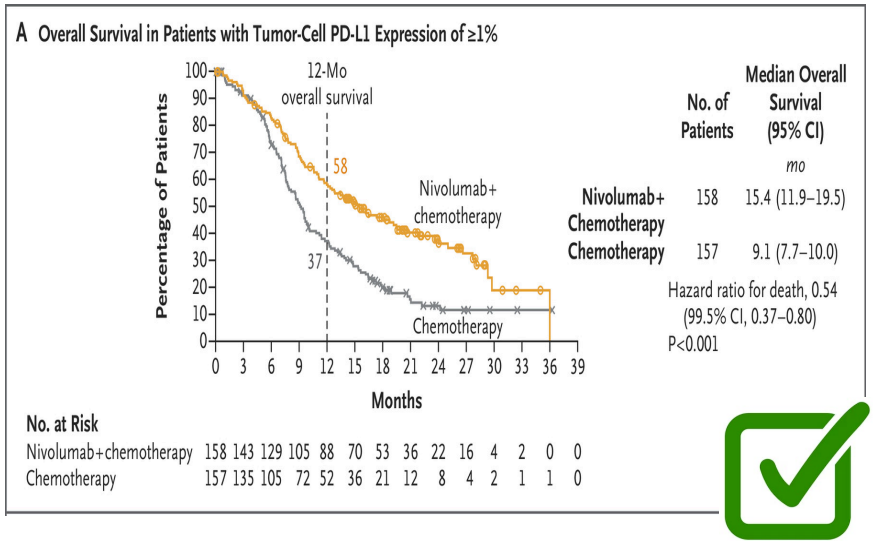


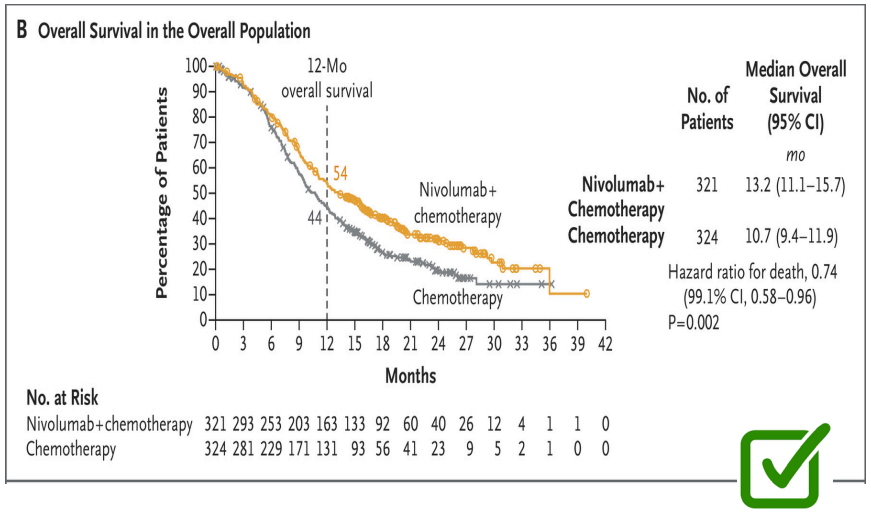


N Engl J Med. 2022;386(5):449-462.

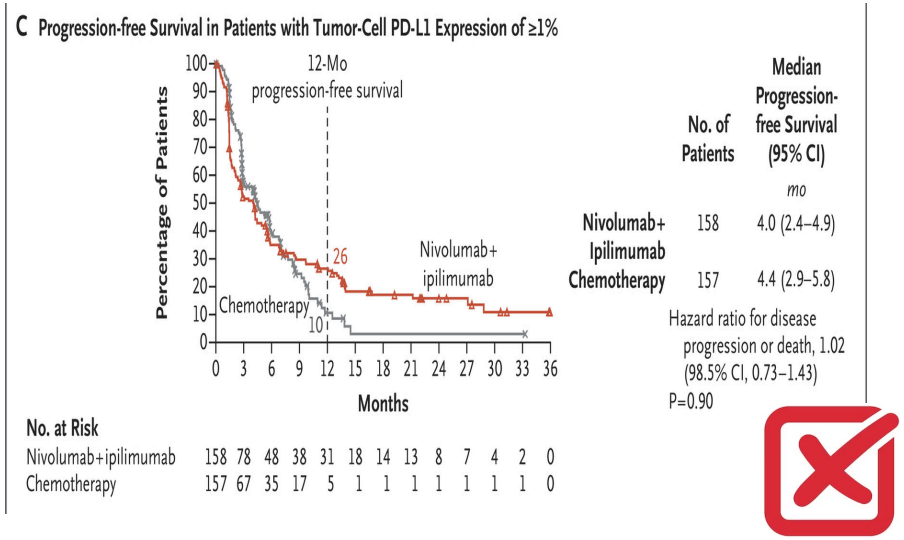
Nivolumab + Ipi 1º linea **PDL TPS ≥ 1%.** Checkmate 648

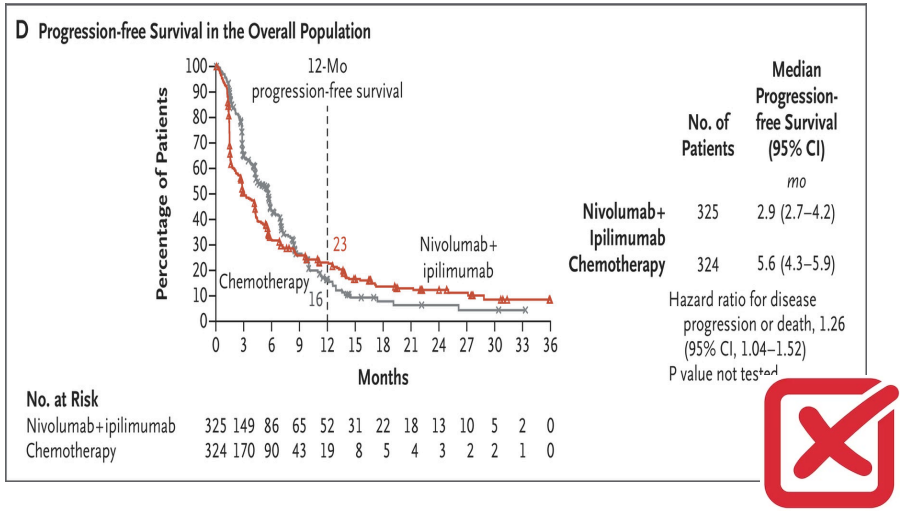
Overall survival: Nivo + Ipi vs Chemo





PFS: Nivo + Ipi vs Chemo





Nivolumab–ChT
[I, A; MCBS 4][c]
Nivolumab–ipilimumab
[I, B; MCBS 4][c]

Todos

ESC
TPS ≥ 1%.

Otros fase III IT en SCC sin aprobación: Mejora SG, SLP, RRO, seguro

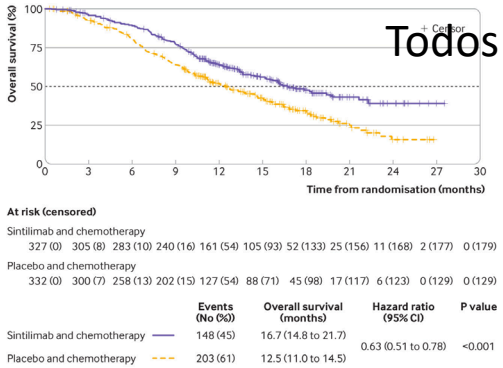
Rational 306: SCC QT+/- Tislelizumab

TABLE 1: Median Overall Survival From the RATIONALE-306 Trial

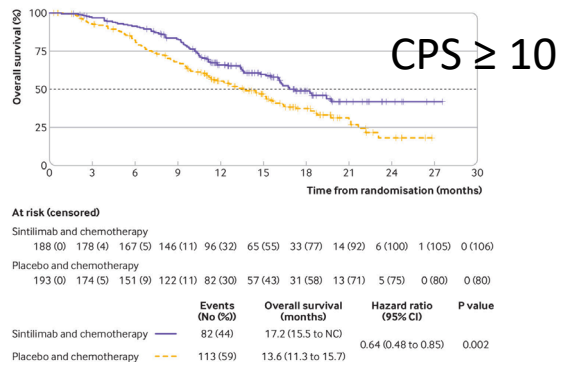
Patient Population	Tislelizumab + Chemotherapy	Placebo + Chemotherapy	Hazard Ratio *P* Value
All randomly assigned patients	17.2 months	10.6 months	0.66 *P* < .0001
PD-L1 ≥ 10%	16.6 months	10.0 months	0.62 *P* = .0020
PD-L1 < 10%	16.7 months	10.4 months	0.72 (95% CI = 0.55–0.94)

CI = confidence interval.

Orient 15: SCC QT+/-Sintilimab



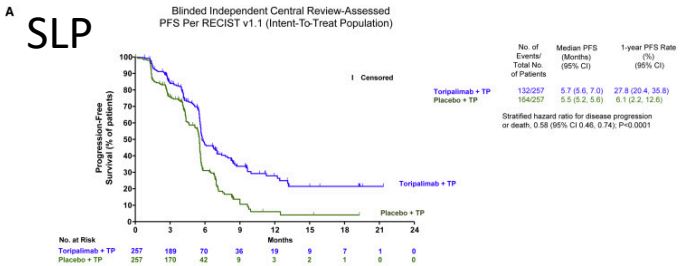
Todos

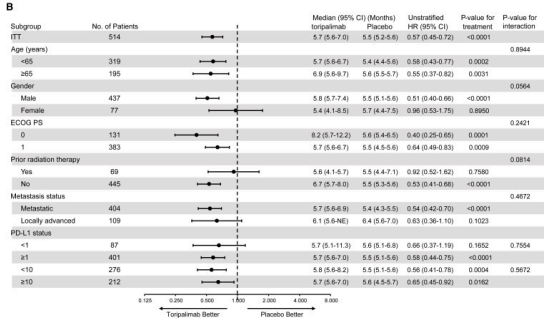


CPS ≥ 10

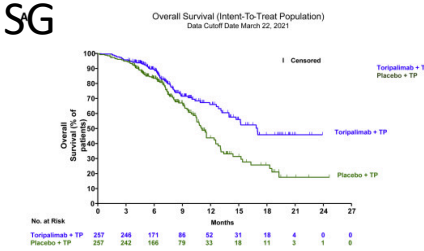
Jupiter 06: SCC QT+/- Toripalimab

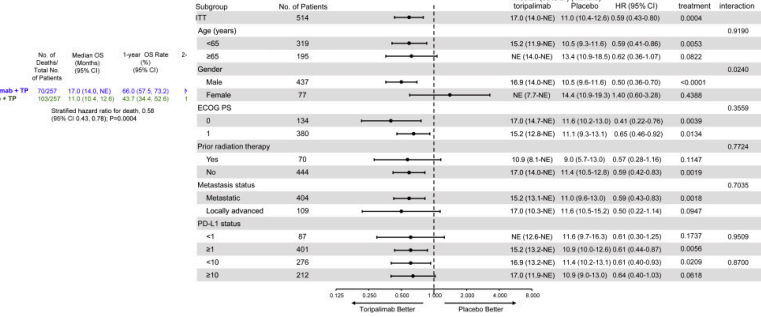
SLP





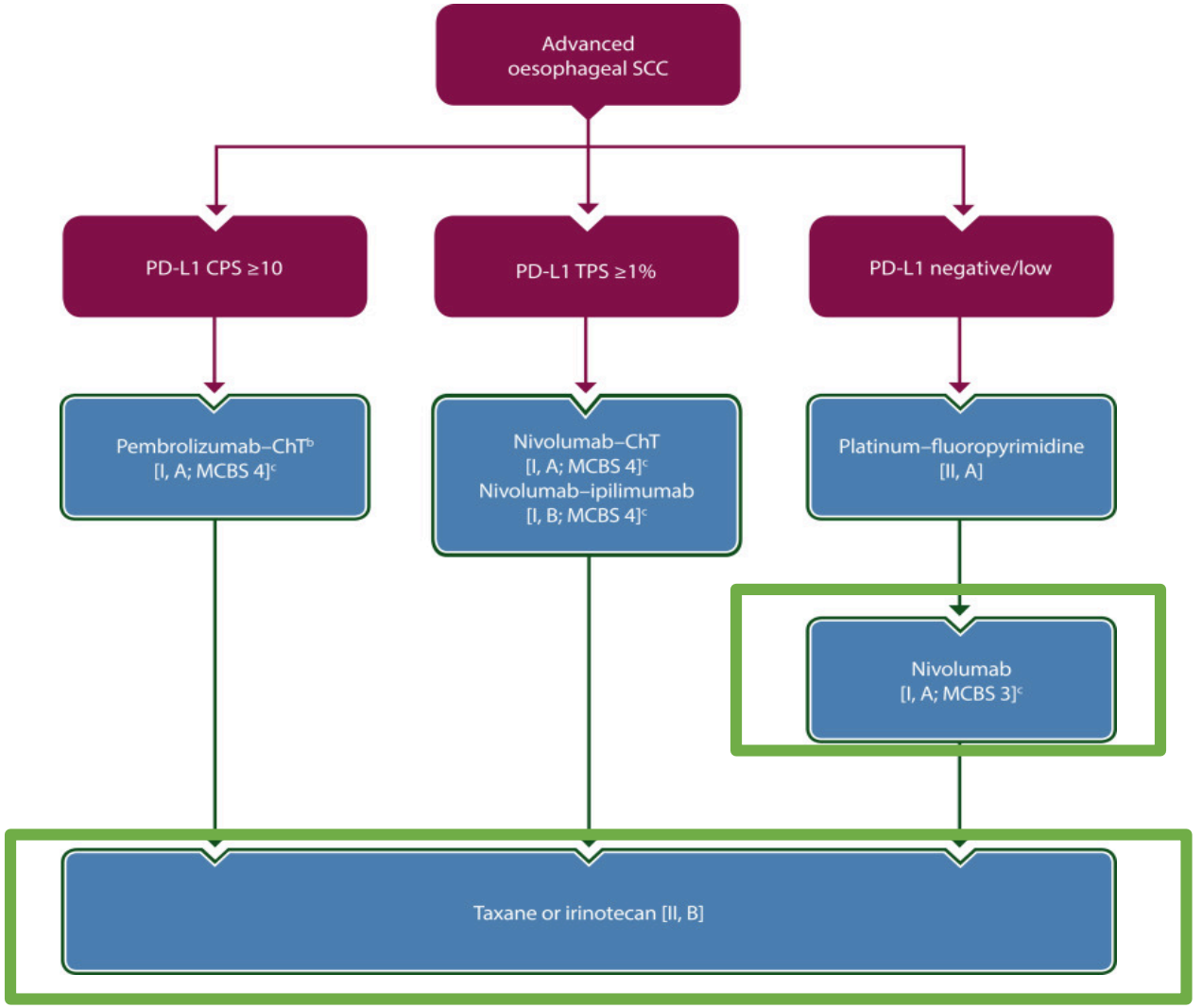
SG





1.- Lancet Oncol. 2023;24(5):483-495. 2.-*BMJ* 2022;377:e068714. 3.- Cancer Cell 40, 277–288

2.3 Estrategia de tratamiento en **SCC M1** 2º línea



1.- Ann Oncol 2022;33(10):992-1004

Nivolumab en 2º línea. ATTRACTION 3.

ATTRACTION-3 Study Design

- ATTRACTION-3 is a randomized, open-label, phase 3 study of nivolumab versus docetaxel or paclitaxel in patients with ESCC

Key eligibility criteria
- Unresectable advanced or recurrent ESCC
- Refractory to or intolerant of 1 prior fluoropyrimidine/ platinum-based therapy
- ECOG performance status 0 or 1

R 1:1

Stratification[b]:
- Region
- No. of organs with metastases
- PD-L1 expression

Nivolumab 240 mg IV Q2W[c]

Docetaxel 75 mg/m² IV Q3W[c] **or paclitaxel** 100 mg/m² IV QW × 6 weeks, then 1 week off[c]

Primary endpoint:
- OS

Other key endpoints:
- PFS, ORR, DCR, TTR, DOR, HRQoL, and safety

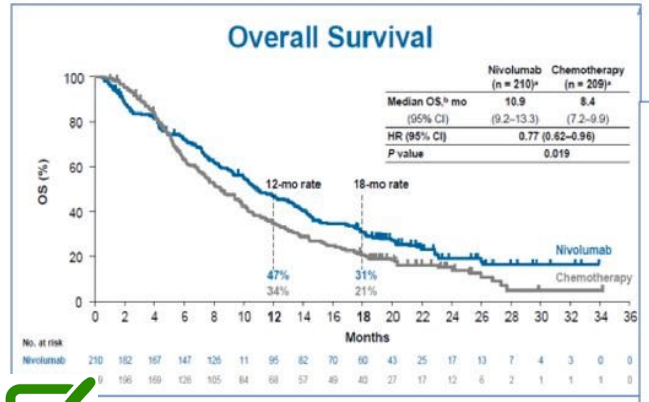
SCC

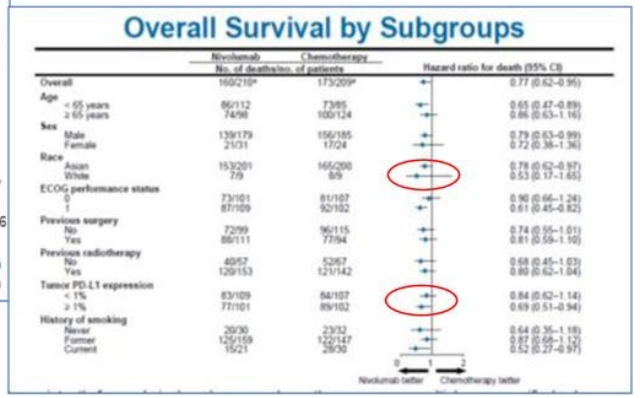
Lancet Oncol. 2019;20(11):1506-1517

Advanced Esophageal Cancer: Nivolumab

P. III ATTRACTION-3 [1]: Nivo vs Chemo in 2nd line SC Esop.Cancer

Kato K, Lancet Oncol 2019
Cho BC et al. ESMO 2019





2.5m HR 0.77

Beneficio en OS independientemente PDL1 y calidad de vida
Sin diferencia en SLP ni en RR.

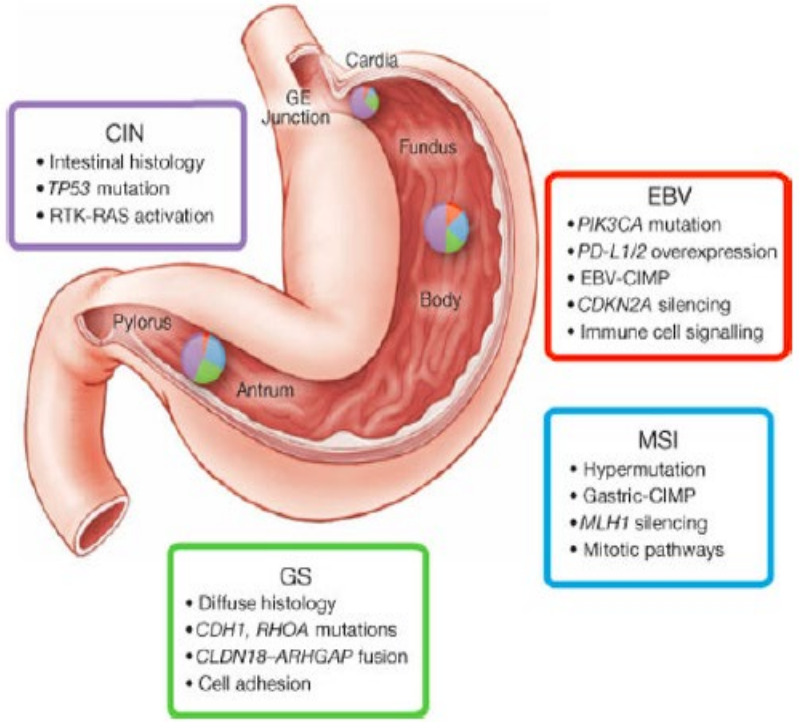
IT 2º Línea Fase III
sin aprobación

Pembrolizumab Nivolumab Tislelizumab Camrelizumab.

	KEYNOTE-181[8]	ATTRACTION-03[9]	RATIONALE-302[10]	ESCORT[11]
N	628	419	512	448
Población	63% escamosos 62% no asiáticos	100% escamosos 4% no asiáticos	100% escamosos 21.3% no asiáticos	100% escamosos 100% Asiáticos
PD-L1	CPS >10/<10	TPS >1%/<1%	TAP >10%/<10%	TPS > 1%/<1%
Objetivo primario	SG CPS >10	SG ITT	SG ITT	SG ITT
SG ITT **SG SCC**	7.1 vs. 7.1 meses HR 0.89 (0.75-1.05) 8.2 vs. 7.1 meses HR 0.78 (0.63-0.96)	10.9 vs. 8.4 meses HR 0.77 (0.62-0.96)	8.6 vs. 6.3 meses HR 0.70 (0.57-0.85)	8.3 vs 6.2 HR 0.71 (0.57-0.87)
SG **PD-L1**	CPS >10 9.3 vs. 6.7 meses HR 0.69 (0.52-0.93) ESC CPS > 10 HR 0.64 (0.46-0.90)	TPS >1% HR 0.69 (0.51-0.94) TPS < 1% HR 0.84 (0.62-1.14)	TAP >10% 10.3 vs. 6.8 meses HR 0.54 (0.36-0.79) TAP <10% HR 0.82 (0.62-1.09)	TPS >1% 9.2 vs 6.3 HR 0.58 (0.42-0.81)
SLP **SLP 12 meses**	CPS >10 2.6 vs. 3 meses HR 0.73 (0.54-0.97) 20.8% vs. 6.7%	ITT 1.7 vs. 3.4 meses HR 1.08 (0.87-1.34) 12% vs. 7%	ITT 1.6 vs. 2.1 meses HR 0.83 (0.67-1.01) 12.7% vs. 1.9%	ITT 1.9 vs 1.9 HR 0.69 (0.56-0.86) 10% vs NA
TR	--- CPS> 10: 21.5 vs. 6.1%	ITT: 19 vs. 22% ---	ITT: 20.3 vs. 9.8% TAP > 10: 28 vs. 11.7%	ITT : 21 vs 7%

1.J Clin Oncol. 2020; 38(35):4138-4148.
2.Lancet Oncol. 2019;20(11):1506-1517.
3.Clin Oncol. 2022; 20:JCO2101926.
4.Lancet Oncol. 2020; 21(6):832-842.

Adenocarcinoma gástrico. Introducción y subtipos moleculares



5º

Neoplasia maligna más común

3º

Causa de mortalidad relacionada con el cáncer en todo el mundo

50%

de los pacientes la QT sigue siendo el estándar

11 a 17 meses

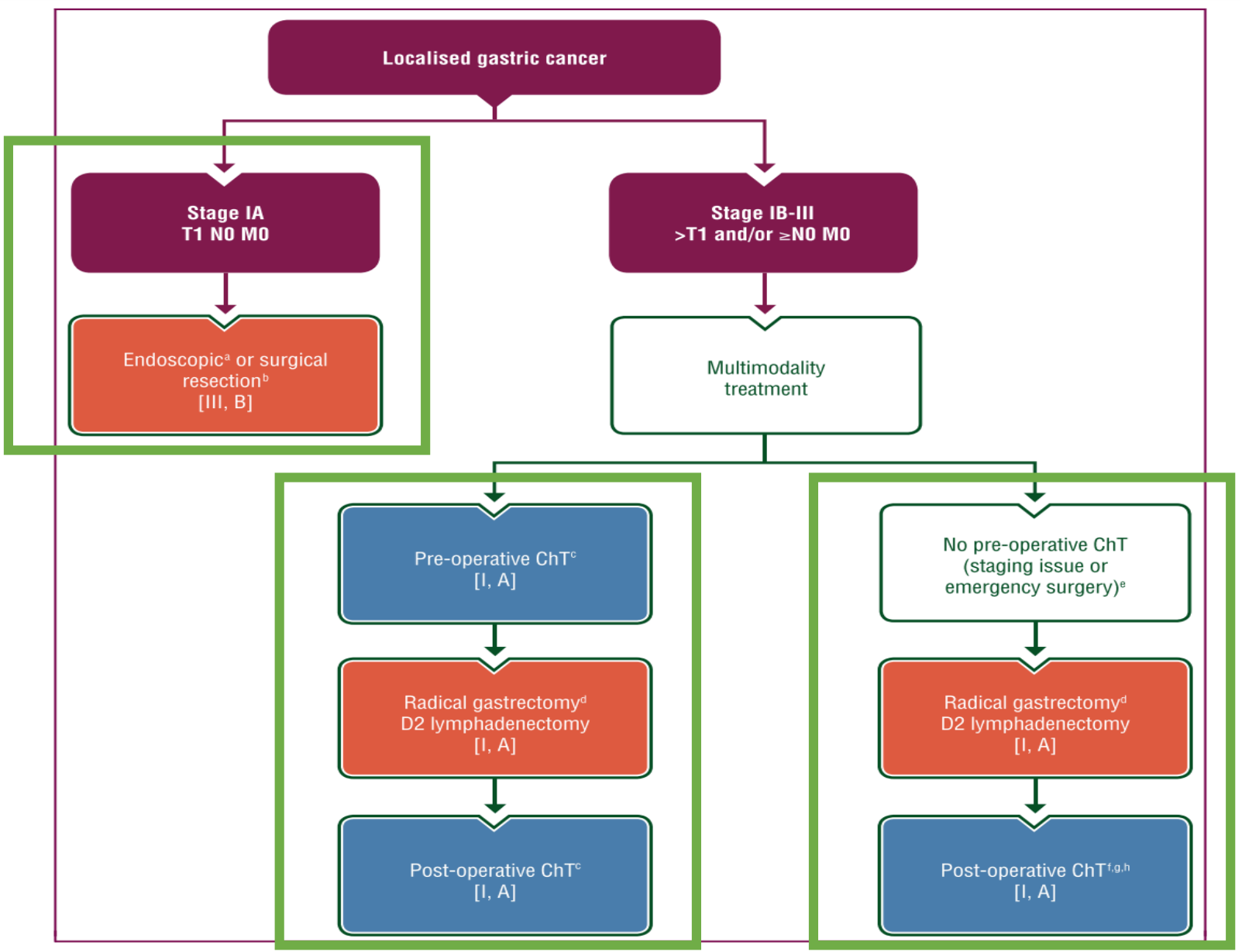
Mediana de SG

1. Nature. 2014; 513(7517): 202–209

2. CA Cancer J Clin 2021;71:209–249

3.- Estrategia en cáncer gástrico localizado : Guias ESMO

R endoscopica:
-. T1a (confinado a mucosa)
-. bien diferencido (G1-2)
-. < 2 cm
-. No ulcerado



Annals of Oncol 2022;33(10):1005-1020.

Evolución de tratamiento adyuvante: Cirugía adecuada??

ACTS-GC
12 months adjuvant S1
vs surgery alone

CLASSIC
6 months capecitabine/oxaliplatin
vs. surgery alone

CRITICS
ARTIST 1
ARTIST 2

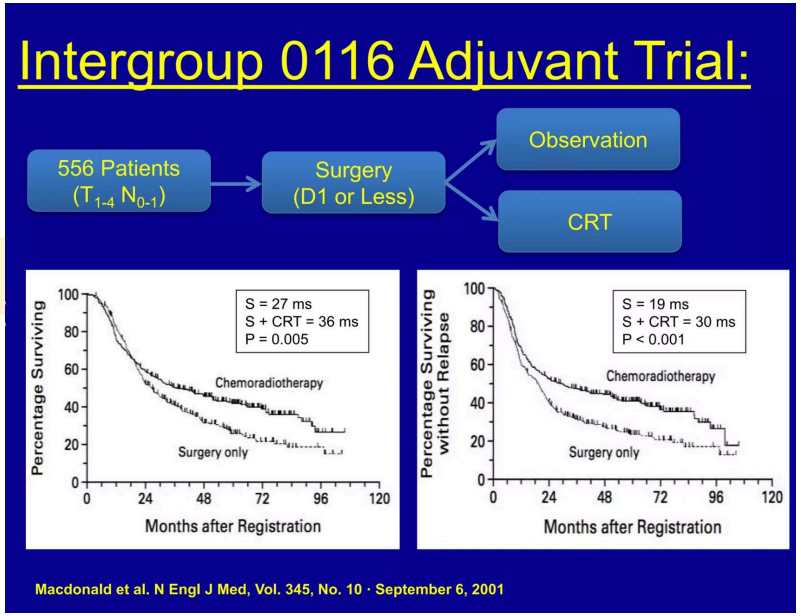
RT
no beneficio
más toxicidad

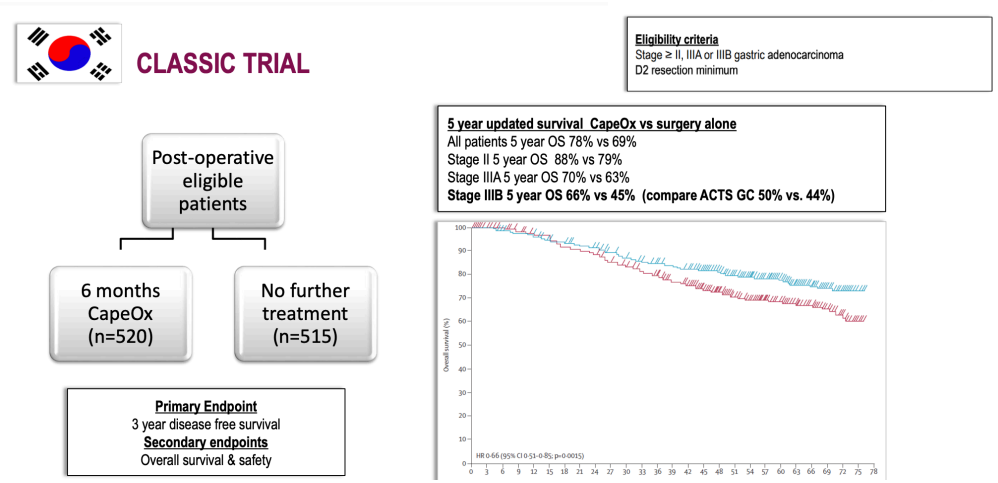
2001 — 2007 — 2010 — 2012 — 2018 — 2020

INT-0116
Adjuvant bolus 5FU/RT
vs surgery alone

GASTRIC Group Meta-analysis (17 estudios)

10% disección D2





Beneficio en OS del 10%

1. Macdonald et al, N Engl J Med. 2001 Sep 6;345(10):725-30.
2. Sakuramoto et al, N Engl J Med. 2007 Nov 1;357(18):1810-20.
3. Bang et al, Lancet. 2012 Jan 28;379(9813):315-21.
4. Pignon et al, JAMA. 2010 May 5;303(17):1729-37.

4.1-Estrategia en AC gástrico irresecable o M1 (IoM). 1º Línea

CLAUDINA positivo

1. Sin BM
2. HER 2 positivo (15 y el 20 %)
3. PDL1 CPS > 5
4. CLAUDINA positivo

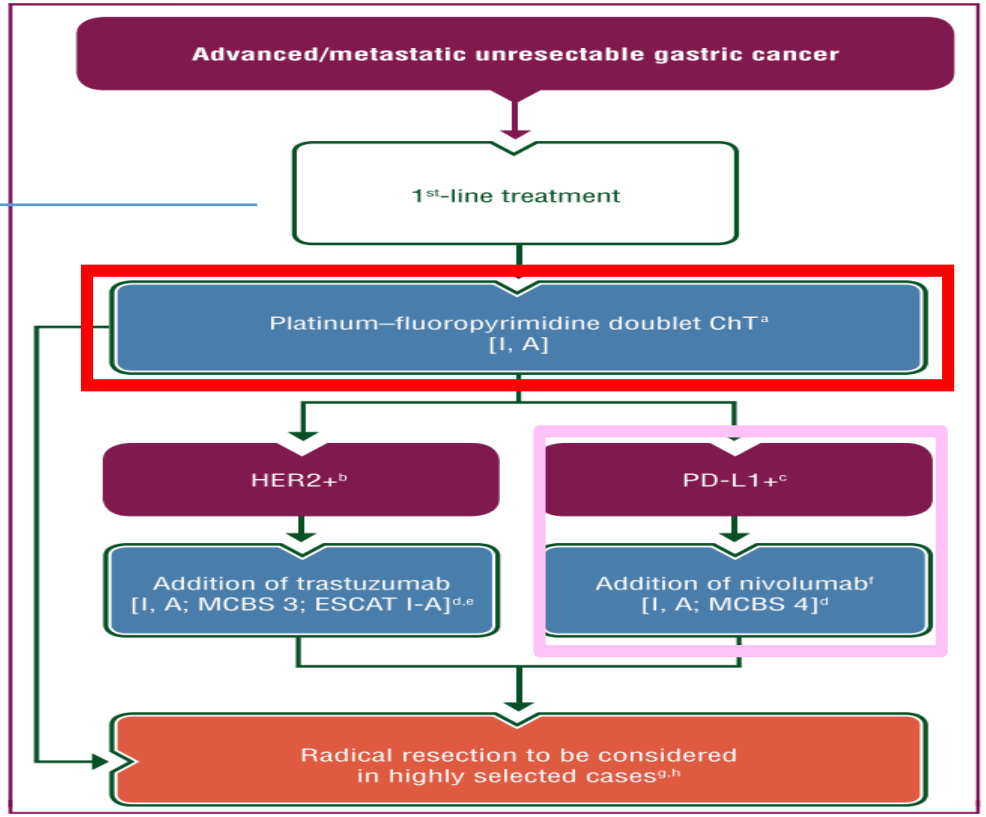
ESMO GOOD SCIENCE BETTER MEDICINE BEST PRACTICE

ANNALS OF ONCOLOGY driving innovation in oncology

SPECIAL ARTICLE

Gastric cancer: ESMO Clinical Practice Guideline for diagnosis, treatment and follow-up☆

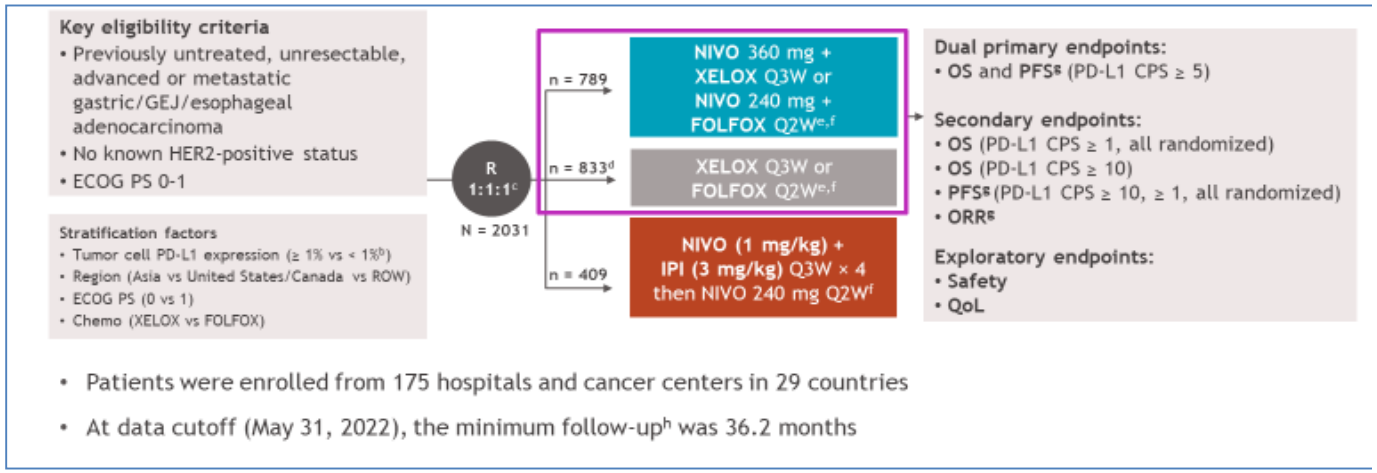
F. Lordick[1], F. Carneiro[2,3,4], S. Cascinu[5], T. Fleitas[6], K. Haustermans[7], G. Piessen[8,9,10,11], A. Vogel[12] & E. C. Smyth[13], on behalf of the ESMO Guidelines Committee*



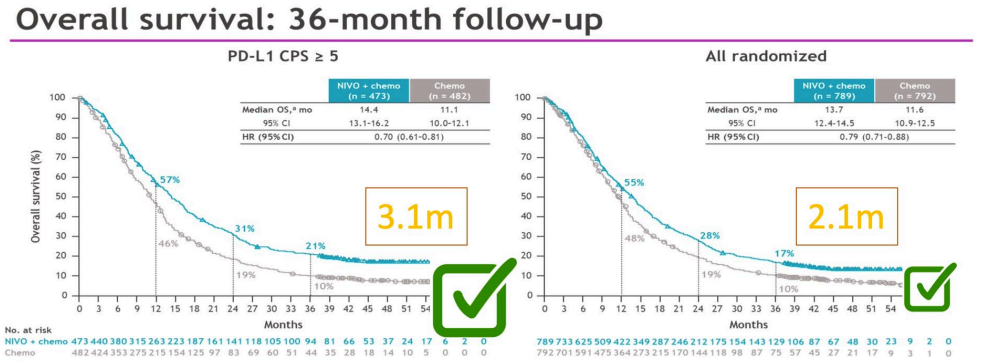
Annals of Oncology 2022;33(10):1005-1020.

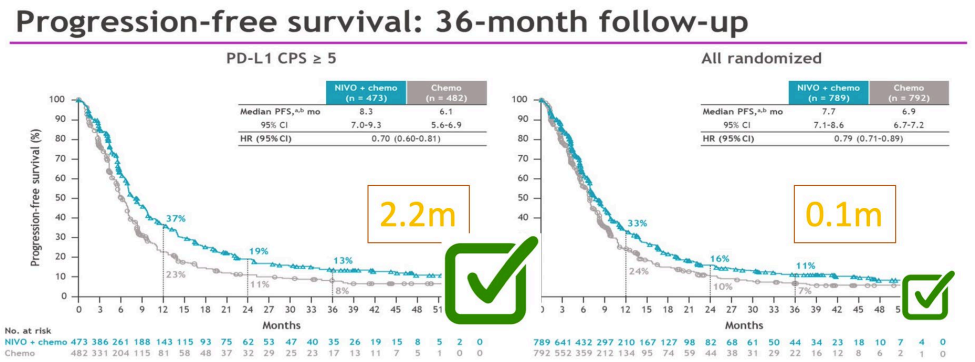
4.2 ACG-UEG Her 2 neg PDL-1 CPS>5 Inmunoterapia 1º línea

CheckMate 649: fase III aleatorizado abierto



- Patients were enrolled from 175 hospitals and cancer centers in 29 countries
- At data cutoff (May 31, 2022), the minimum follow-up[h] was 36.2 months





Características: 76% no asiáticos, 70% CG, 3% MSI-H

AC gástrico, UEG y esófago

1.- Lancet. 2021 Jul 3;398(10294):27-40. 2.- Janjigian YY, ASCO GI 2023;LBA 291

Otros fase III con Inmunoterapia en Her2 neg

KEYNOTE-859 Study Design

Randomized, Double-Blind, Phase 3 Trial

Rha KEYNOTE-859 ESMO Plenary 2023

Key Eligibility Criteria

- Histologically or cytologically confirmed adenocarcinoma of the stomach or GEJ
- Locally advanced unresectable or metastatic disease
- No prior treatment
- Known PD-L1 status (assessed centrally using PD-L1 IHC 22C3)
- HER2-negative status (assessed locally)
- ECOG PS 0 or 1

Estratificó:

- Región geográfica
- PD-L1 CPS (<1 versus ≥1)
- QT(FP versus CAPOX)

N 1579 → Pembrolizumab 200 mg IV Q3W for ≤35 cycles (~2 yr) + Chemotherapy[a] (FP or CAPOX)

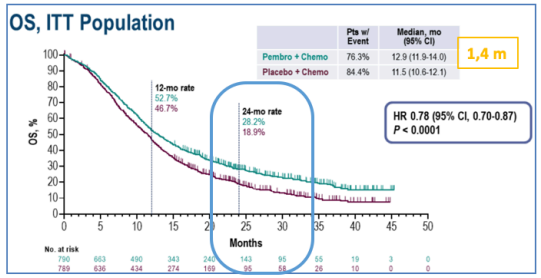
R 1:1

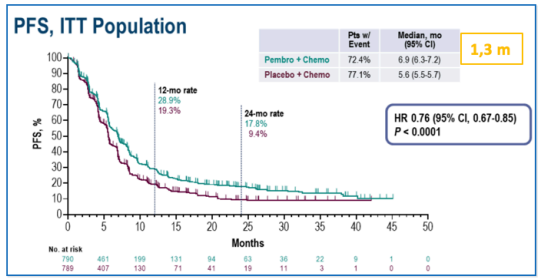
N 790 → Placebo IV Q3W for ≤35 cycles (~2 yr) + Chemotherapy[a] (FP or CAPOX)

N 789

OP: SG ITT, SG PD-L1 CPS ≥ 1, SG PD-L1 CPS ≥ 10

AC gástrico, UEG y esófago

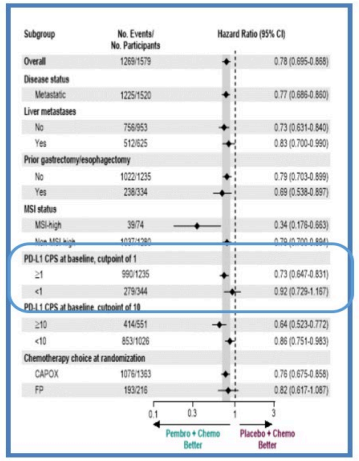




Rha KEYNOTE-859 ESMO Plenary 2023

Beneficio en SG, la SLP y ORR

Análisis subgrupos ITT



PDL1 CPS <1 no se beneficia

PD-L1 with a CPS ≥ 1.

RATIONALE-305: Phase 3 Study of Tislelizumab + Chemotherapy vs Placebo + Chemotherapy as First-line Treatment of Advanced Gastric or Gastroesophageal Junction Adenocarcinoma

N 997

Key eligibility criteria:

- Histologically confirmed GC/GEJC
- Exclude patients with HER2-positive tumors
- No previous therapy for unresectable, locally advanced or metastatic GC/GEJC

R 1:1

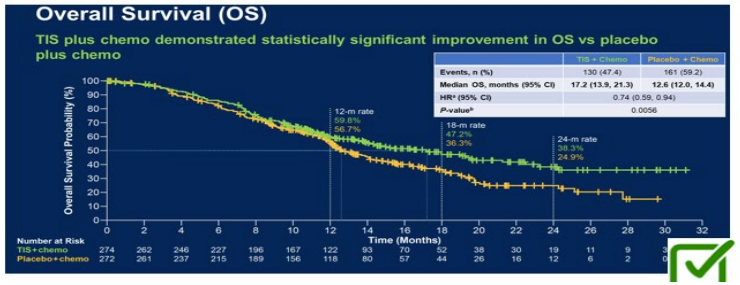
Initial up to 6 treatment cycles[a]

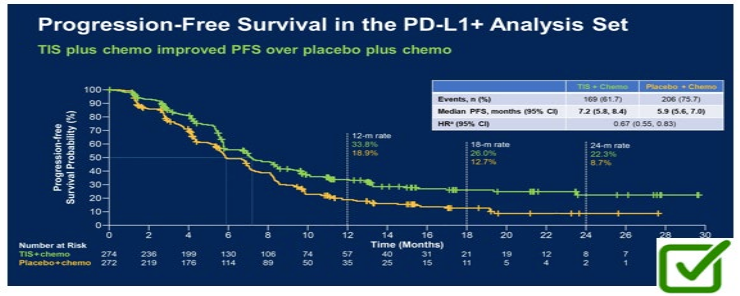
TIS 200 mg IV Q3W + chemo (XELOX or FP[d])

Maintenance treatment until unacceptable toxicity or disease progression

Placebo IV Q3W + chemo (XELOX or FP[d])

OP: OS PDL1 + (PDL1 score >5%)





Interim analysis in the PD-L1+

Moheler M, ASCO GI 2023

4.3 ACG-UEG **Her 2 positiva** PDL1 CPS ≥ 1 **KEYNOTE-811** Fase III abierto aleatorizado

Patients (N≈692)

- Previously untreated, locally advanced, unresectable, or metastatic HER2+ gastric or GEJ AC
- ECOG PS 0 or 1

R 1:1

Pembrolizumab 200 mg IV Q3W + Trastuzumab (8 mg/kg IV loading dose, 6 mg/kg IV maintenance thereafter) Q3W + FP or CAPOX (global cohort) or SOX (Japanese cohort)

Placebo IV Q3W + Trastuzumab (8 mg/kg IV loading dose, 6 mg/kg IV maintenance thereafter) Q3W + FP or CAPOX (global cohort) or SOX (Japanese cohort)

- **Stratification:** PD-L1 CPS (≥1 vs <1), region (Australia/EU/Israel/North America vs Asia vs ROW), chemotherapy (FP vs capecitabine + oxaliplatin)

Continue until: 24 months, disease progression, intolerable toxicity, withdrawal of consent

Primary End Points

OS, PFS (RECIST 1.1) by BICR

Key Secondary End Points

ORR and DOR per mRECIST v1.1 by BICR, safety

MADRID 2023 ESMO congress

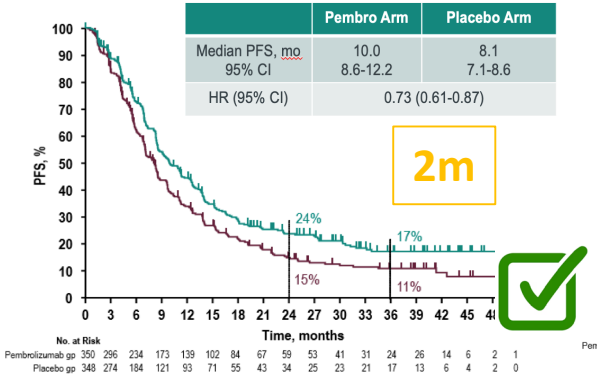
MADRID SPAIN
20-24 OCTOBER 2023

KEYNOTE-811: Progression-Free Survival at IA3[1] (Data cutoff: March 29, 2023)

All Patients

	Pembro Arm	Placebo Arm
Median PFS, mo 95% CI	10.0 8.6-12.2	8.1 7.1-8.6
HR (95% CI)	0.73 (0.61-0.87)	

2m

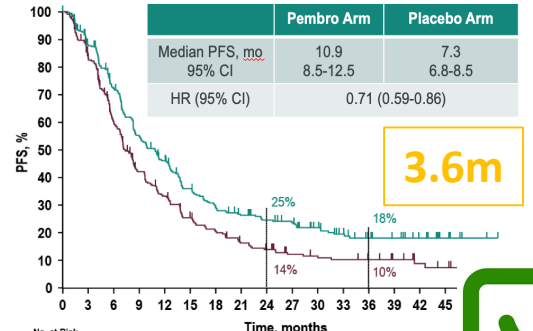


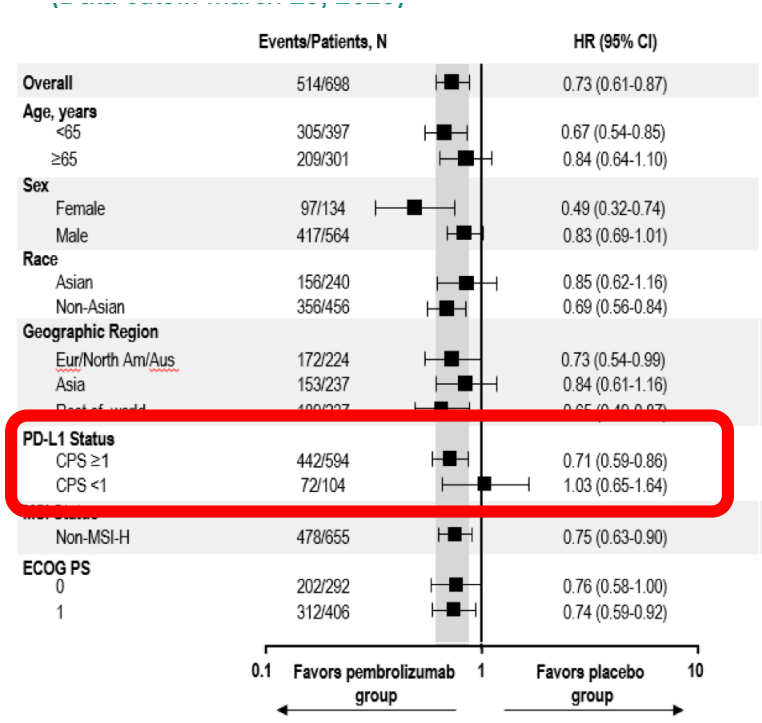
Data cutoff date: March 29, 2023

PD-L1 CPS ≥1

	Pembro Arm	Placebo Arm
Median PFS, mo 95% CI	10.9 8.5-12.5	7.3 6.8-8.5
HR (95% CI)	0.71 (0.59-0.86)	

3.6m

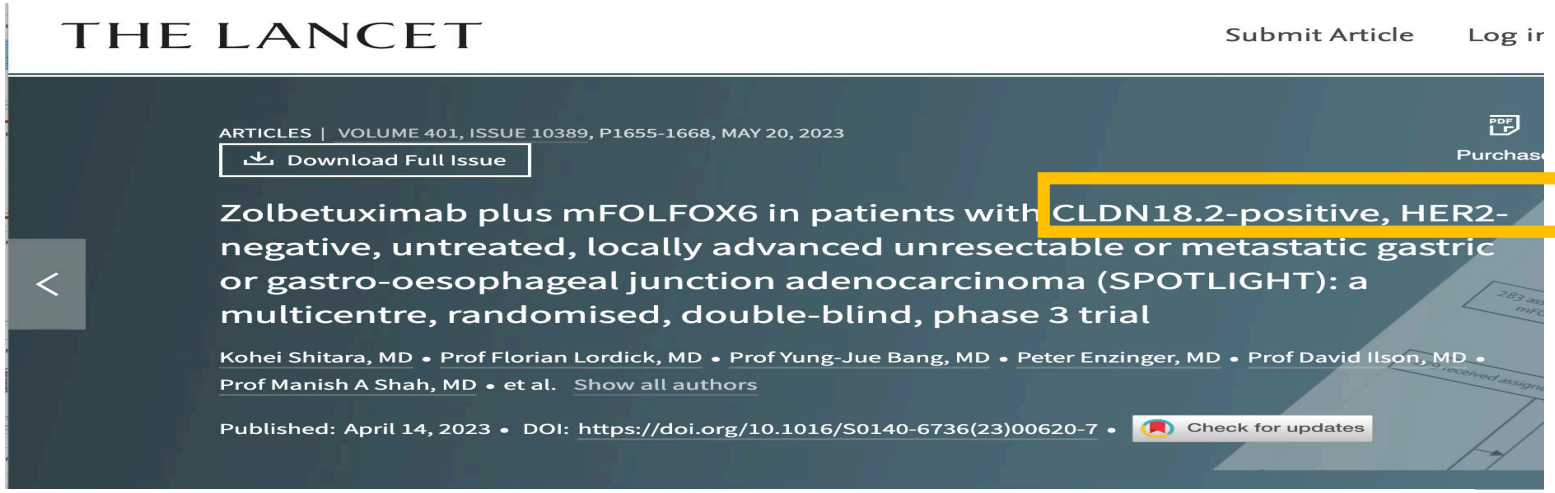


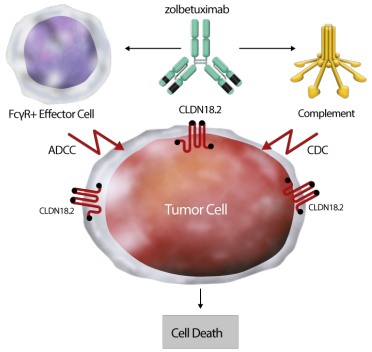


PD-L1 with a CPS ≥ 1.

Lancet. 2023;402 (10418):2197-2208.

4.4 ACG-UEG her2 neg Claudina positivo





38 % CLDN18.2 positivos

Global[a], randomized, double-blinded, placebo-controlled, phase 3 trial

Key Eligibility Criteria

- Previously untreated, locally advanced unresectable or metastatic G/GEJ adenocarcinoma
- CLDN18.2-positive (moderate-to-strong staining in ≥75% of tumor cells)[b]
- HER2-negative[c]
- ECOG PS 0-1

Stratification Factors

- Region (Asia vs non-Asia)
- Number organs with metastases (0–2 vs ≥3)
- Prior gastrectomy (yes vs no)

Planned (N ≈ 550) → R 1:1

(N = 283): Zolbetuximab 800/600[d] mg/m² IV Q3W + mFOLFOX6 IV Q2W (Cycles 1–4 (42 days/cycle)) → Zolbetuximab 600 mg/m² IV Q3W + 5-FU + folinic acid IV Q2W (Cycles 5+)

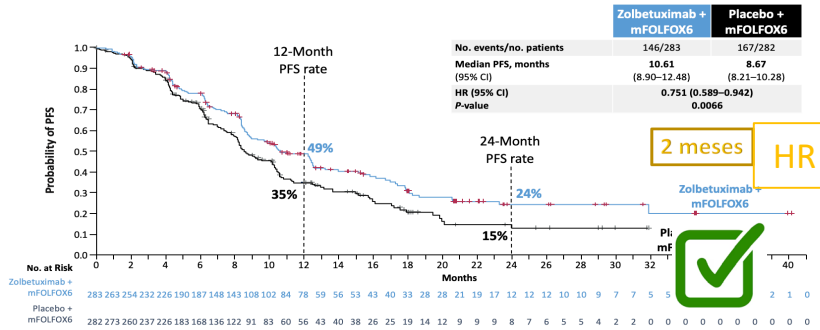
(N = 282): Placebo IV Q3W + mFOLFOX6 IV Q2W (Cycles 1–4 (42 days/cycle)) → Placebo IV Q3W + 5-FU + folinic acid IV Q2W (Cycles 5+)

Primary End Point
- PFS[e]

Key Secondary End Points
- OS
- TTCD in GHS/QoL, PF, and OG25-Pain

Secondary End Points
- ORR[e]
- DOR[e]
- Safety
- PROs

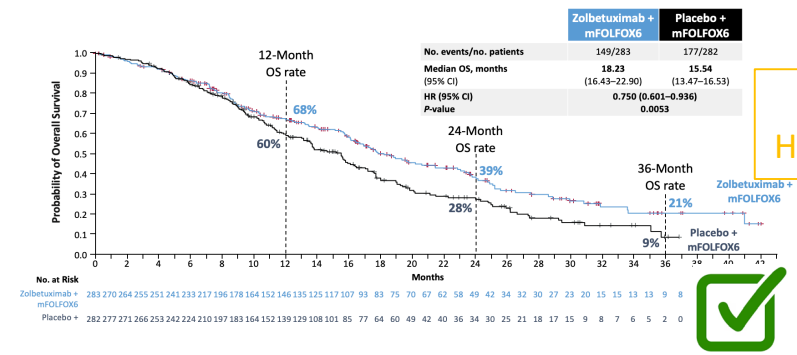
PRIMARY END POINT: PFS BY INDEPENDENT REVIEW COMMITTEE[a]



2 meses

HR 0.75

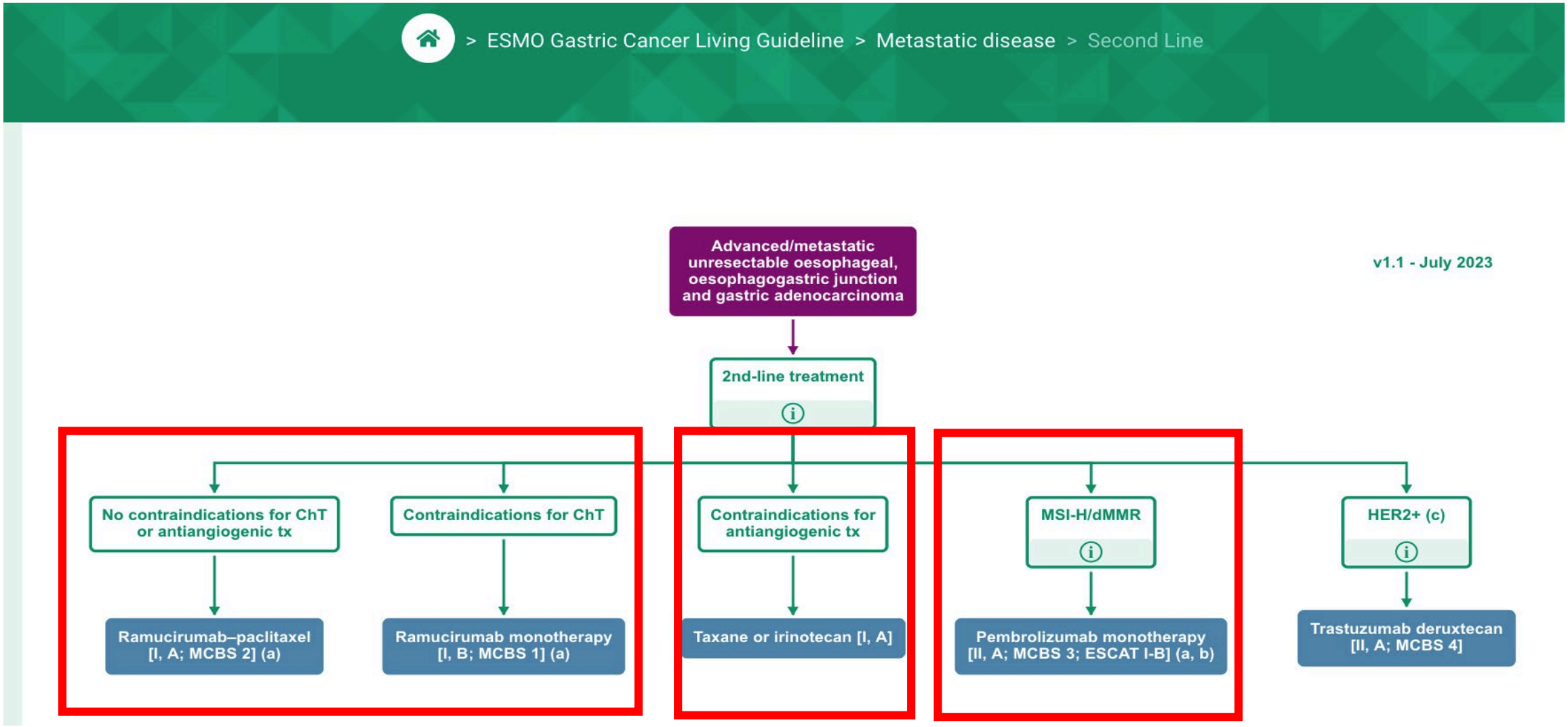
KEY SECONDARY END POINT: OS



3 m
HR 0.75

Lancet 2023;401 (1039) : 1655-1668.

2º Línea en adenocarcinoma gástrico-UEG



Wilke H et al. *Lancet Oncol* 2014;15:1224–1235
Fuchs CS et al. *Lancet* 2014;383:31–39

MSI: pembrolizumab. Keynote 158. Fase II

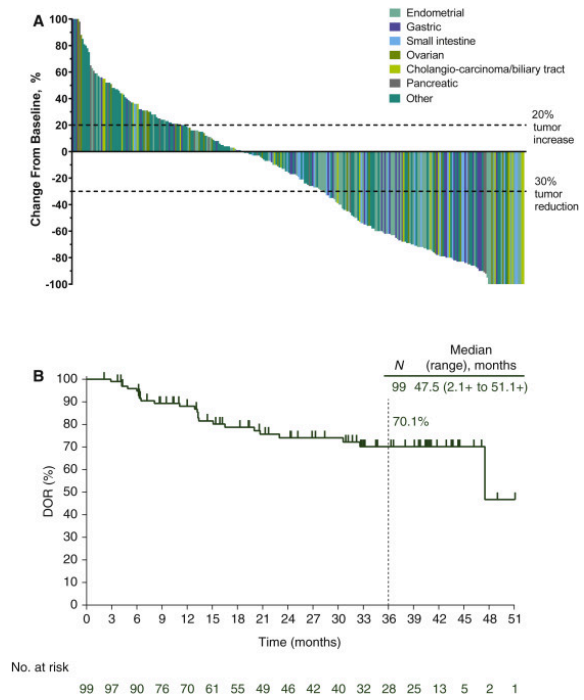
KEYNOTE-158: Study Design

- Ongoing, international, multicohort, open-label, phase 2 study of pembrolizumab in select advanced solid tumors that have progressed on standard-of-care therapy (NCT02628067)
- End points
  - Primary: ORR (RECIST v1.1, independent central review)
  - Secondary: DOR, PFS, OS

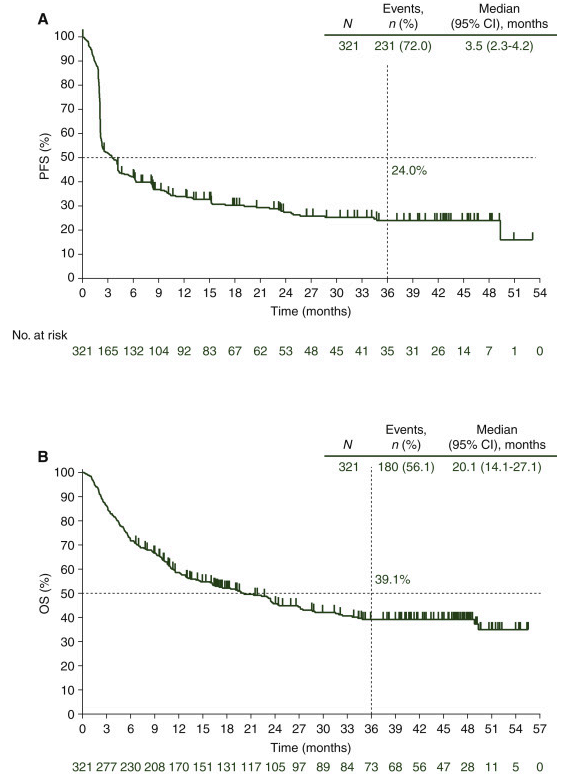
Patients
- Age ≥18 years
- Histologically or cytologically confirmed advanced cervical cancer
- Progression on/intolerance to ≥1 line of standard therapy
- ECOG PS 0 or 1
- Tumor sample for biomarker analysis

→ Pembrolizumab 200 mg Q3W → Treat for 2 years[a] or until progression[b], intolerable toxicity, or study withdrawal → Survival follow-up

Endometrio, gástrico, colangiocarcinoma y páncreas



RR C gástrico: 48%



SGm 20,1 meses
(IC del 95 %: 14,1-27,1 m)
SLPm 3,5 meses
(IC del 95 %: 2,3 a 4,2 m

J Clin Oncol.38(1):1-10

2º Línea en adenocarcinoma gástrico-UEG **HER-2** +.DESTINY-GASTRIC (

DESTINY-GASTRIC02

Trastuzumab deruxtecan in patients in the USA and Europe with HER2-positive advanced gastric or gastroesophageal junction cancer with disease progression on or after a trastuzumab-containing regimen (DESTINY-Gastric02): primary and updated analyses from a single-arm, phase 2 study

Key eligibility criteria

- Pathologically documented, unresectable or metastatic gastric or GEJ cancer
- Centrally confirmed HER2 positive disease (defined as IHC 3+ or IHC 2+/ISH+) on biopsy after progression on first-line trastuzumab-containing regimen
- ECOG PS 0 or 1

→ T-DXd 6.4 mg/kg Q3W N = 79[a] →

Primary endpoint

- Confirmed ORR by ICR

Secondary endpoints[b]

- PFS by ICR
- OS
- DoR
- Safety
- Patient-reported outcomes

EFFICACY

Response assessment by ICR	April 9, 2021 data cutoff[a] patients (N=79)	November 8, 2021 data cutoff[b] patients (N=79)
Confirmed ORR[c], % (n) (95% CI)	38.0 (30) (27.3-49.6)	41.8 (33) (30.8-53.4)
Confirmed best overall response, % (n)		
CR	3.8 (3)	5.1 (4)
PR	34.2 (27)	36.7 (29)
SD	43.0 (34)	39.2 (31)
PD	16.5 (13)	16.5 (13)
Not evaluable	2.5 (2)	2.5 (2)
Confirmed DCR,[d] % (n) (95% CI)	81.0 (64) (70.6-89.0)	81.0 (64) (70.6-89.0)
Median DoR, months, (95% CI)	8.1 (4.1-NE)	8.1 (5.9-NE)[e]
Median TTR, months, (95% CI)	1.4 (1.4-2.6)	1.4 (1.4-2.7)
Median OS, months	–	12.1 (9.4-15.4)
Median PFS, months	–	5.6 (4.2-8.3)

[a]Median follow up was 5.9 months (range 0.7-15.4 months); [b]Median follow up was 10.2 months (range, 0.7-22.1); [c]Primary endpoint; [d]Exploratory endpoint; [e]Secondary endpoint analysis based on responders (n=33); 18 patients were censored

SAFETY

% (n)	Patients (N=79)
Any TEAE	100 (79)
Drug-related	94.9 (75)
TEAE grade ≥3	55.7 (44)
Drug-related	30.4 (24)
Serious TEAE	41.8 (33)
Drug-related	12.7 (10)
TEAE associated with study drug discontinuation	19.0 (15)
Drug-related	12.7 (10)
TEAE associated with dose reduction	21.5 (17)
Drug-related	17.7 (14)
TEAE associated with an outcome of death	13.9 (11)
Drug-related	2.5 (2)
Adjudicated drug-related ILD/pneumonitis	10.1 (8)
Adjudicated drug-related ILD/pneumonitis grade 5	2.5 (2)

- Median treatment duration was 4.3 months (range, 0.7-22.1 months)
- The most common TEAEs were nausea (67.1%), vomiting (44.3%) and fatigue (41.8%)

DICIEMBRE 2022

N Engl J Med 2020; 382:2419-30
Lancet 2023.24(7): 744-756

TAGS: fase III multicéntrico, aleatorizado, doble ciego, controlado con placebo, en 3º línea ACG-UEG

- **Pacientes con CGm/UGE**
- **≥2 líneas previas:**

- Fluoropirimidinas
- Platinos
- Taxanos y/o irinotecán
- iHER2 en enfermedad HER2+ (si disponible)
- Refractarios/intolerantes a la última línea previa de tratamiento

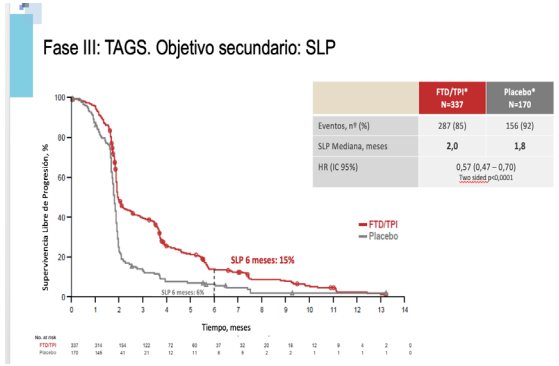
- **ECOG PS 0-1**
- **Edad ≥18años (≥20 en Japón)**

R 2:1

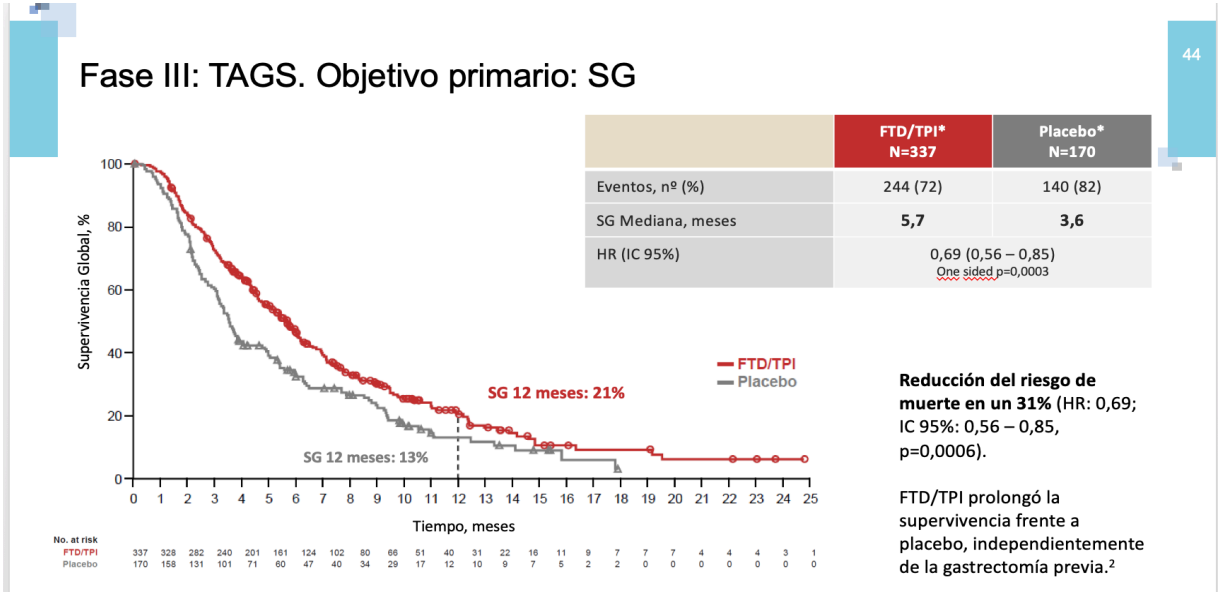
FTD/TPI + MTS
35 mg/m² bid v.o. días 1 – 5 y 8 – 12 ciclos 28 días

Placebo + MTS
Bid v.o. días 1 – 5 y 8 – 12 ciclos 28 días

- **Objetivo primario:**
  - SG
- **Objetivo secundario:**
  - TRG
  - TCE
  - CdV
  - Tiempo hasta ECOG ≥2



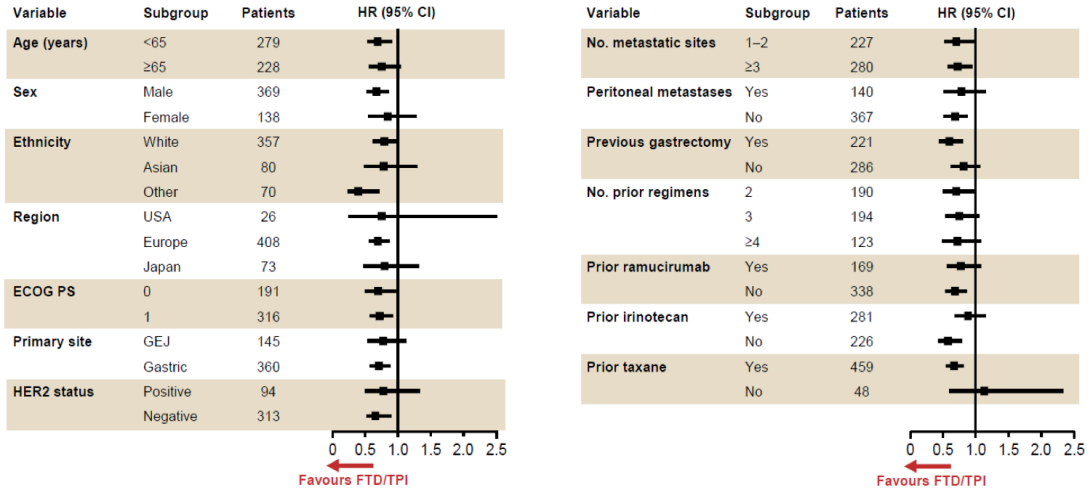
0% RP y 0%RC
Tox G 3-4 80% vs 58%



Reducción del riesgo de muerte en un 31% (HR: 0,69; IC 95%: 0,56 – 0,85, p=0,0006).

FTD/TPI prolongó la supervivencia frente a placebo, independientemente de la gastrectomía previa.[2]

Fase III: TAGS. Objetivo primario: SG. Subgrupos



Lancet Oncol. 2018;19:1437–48

Muchas gracias
por vuestra atención

SEOM
Sociedad Española
de Oncología Médica