



18^{as} Jornadas HITOS
ONCOLÓGICOS: LO MEJOR DE 2023

Madrid, 22 y 23 de noviembre de 2023

Un nuevo paradigma en el tratamiento de los tumores esofagogástricos

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- Employment: Complexo Hospitalario Universitario de Ourense
- Consultant or Advisory Role: MSD, Merck, Amgen, Eisai, AstraZeneca, Lilly
- Speaking: Servier, Amgen, Lilly, Merck, Eisai, AstraZeneca, Roche, Pierre Fabre, Asofarma, MSD

Objetivo de la Charla

Mensajes claros sobre HITOS en el abordaje de tumores esófago-gástricos “recientes”

¿Qué mensajes podemos dar de “nuevos paradigmas”?

BLOQUE I:

ADENOCARCINOMA GÁSTRICO

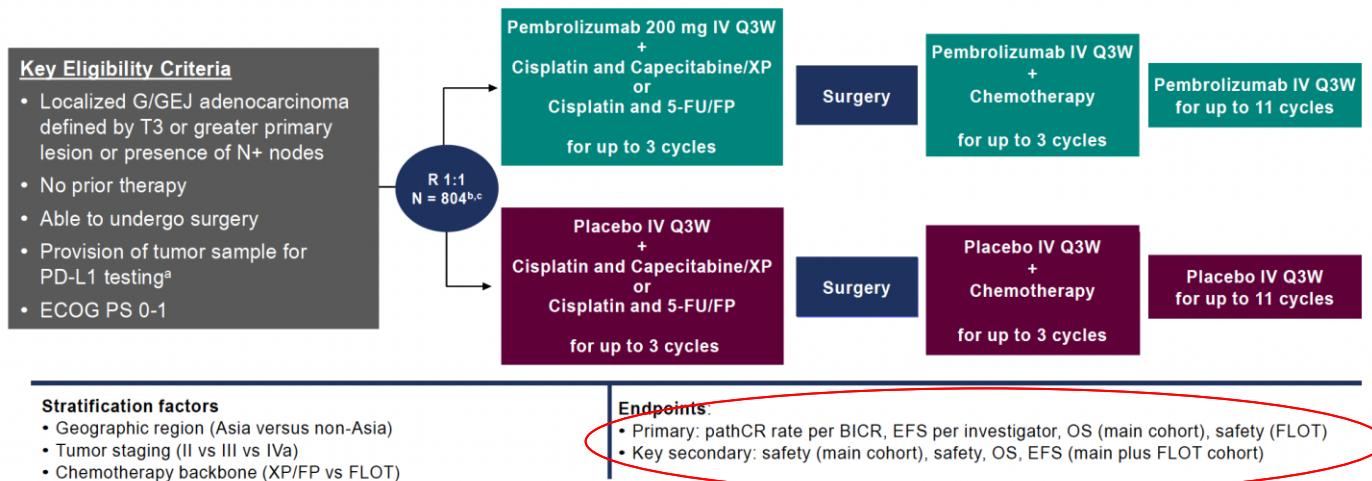
ESCENARIO PERIOPERATORIO

1. ¿Tendremos que incorporar la IO?

Pembrolizumab plus chemotherapy vs chemotherapy as neoadjuvant and adjuvant therapy in locally-advanced gastric and gastroesophageal junction cancer: The Phase 3 KEYNOTE-585 study

KEYNOTE-585 Study Design

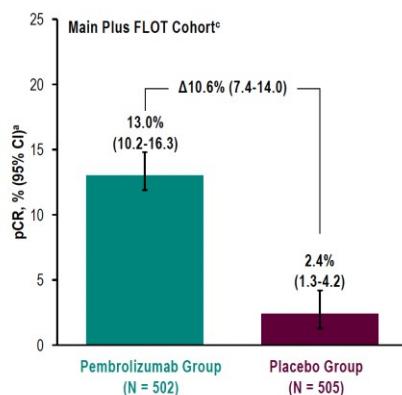
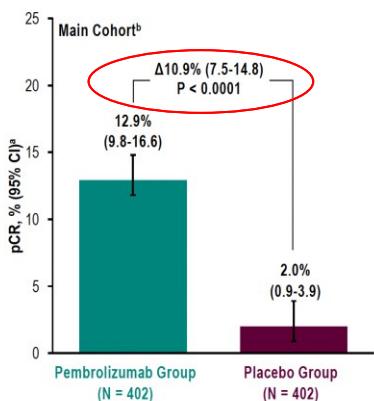
Randomized, Double-Blind, Phase 3 Trial of Neoadjuvant and Adjuvant Pembrolizumab Plus Chemotherapy Versus Placebo Plus Chemotherapy in G/GEJ Adenocarcinoma (Main Cohort)



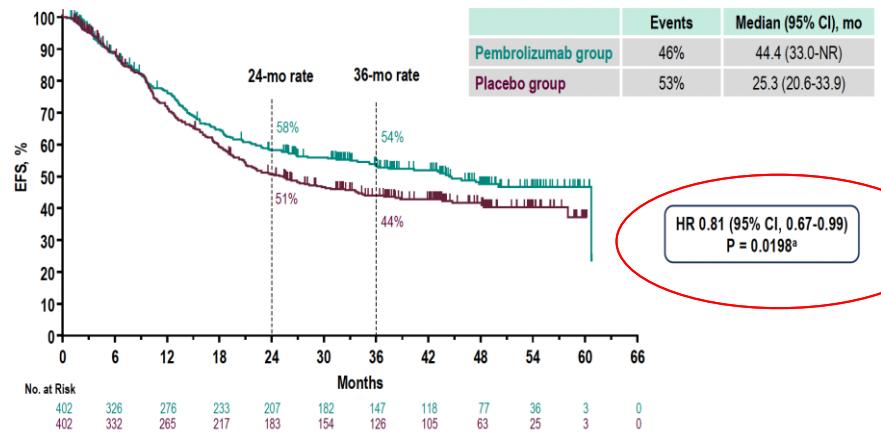
The Phase 3 KEYNOTE-585 study: Primary Objective pRC

Pathological Complete Response^a

Assessed by Blinded, Independent Central Review



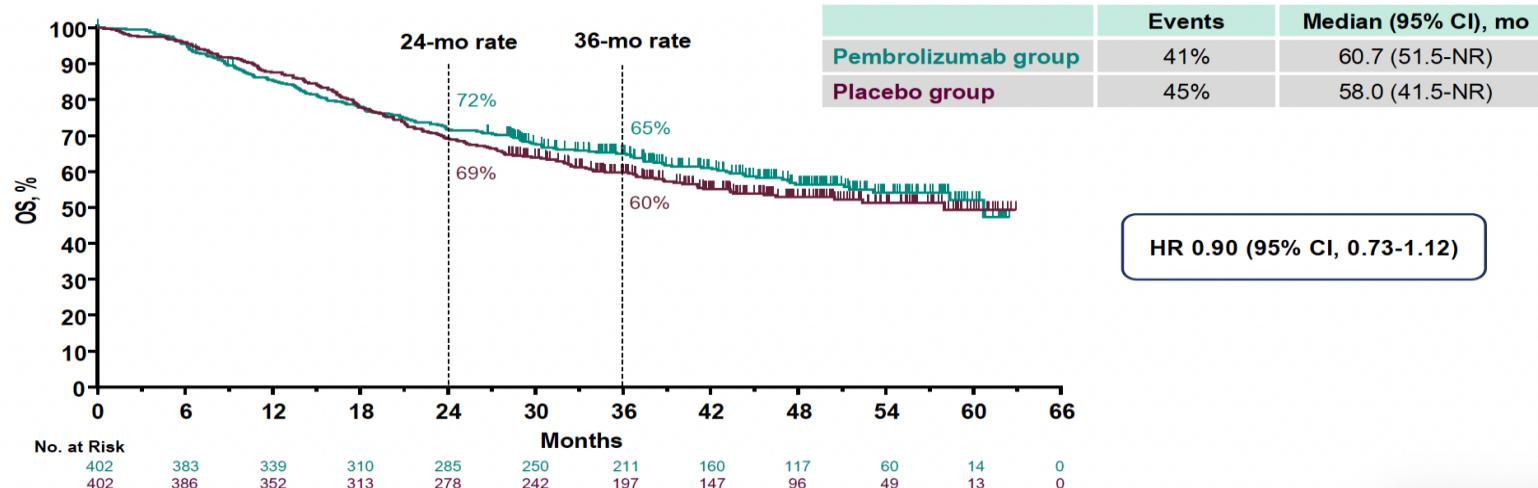
Event-Free Survival: Main Cohort





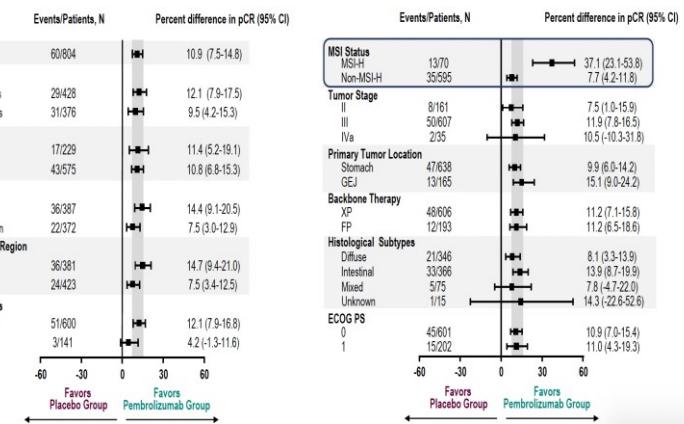
The Phase 3 KEYNOTE-585 study: Primary Objective OS

Overall Survival: Main Cohort

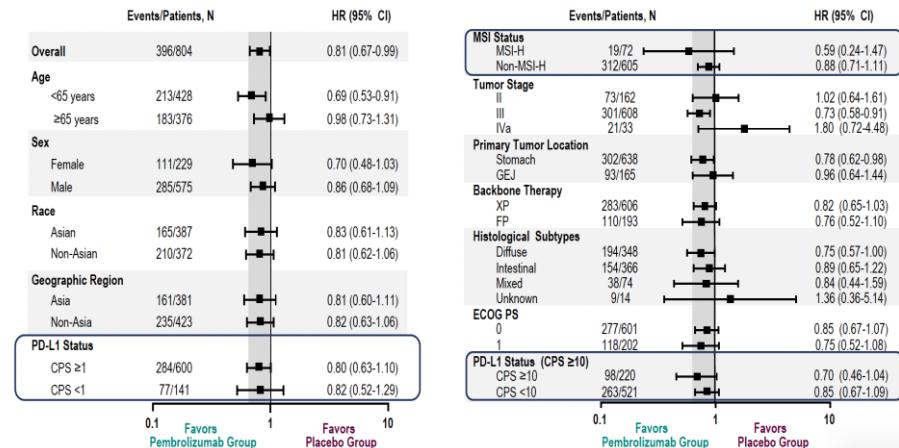


The Phase 3 KEYNOTE-585 study:Subgroup analyses

Pathological Complete Response in Key Subgroups: Main Cohort



Event-Free Survival in Key Subgroups: Main Cohort

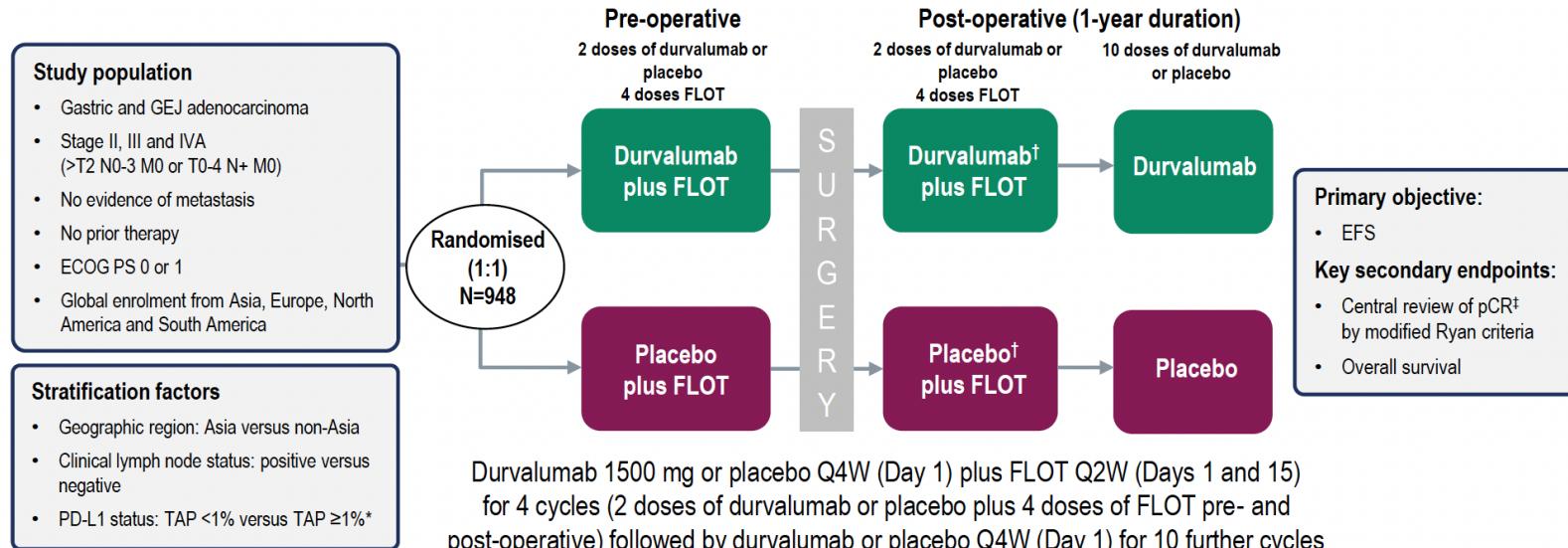


Pembrolizumab aumenta la “pathological complete response rate” pero no “EFS”
SG inmadura pero no significativa



Pathological complete response (pCR) to **durvalumab** plus 5-fluorouracil, leucovorin, oxaliplatin and docetaxel (FLOT) in resectable gastric and gastroesophageal junction cancer (GC/GEJC): interim results of the global, phase 3 MATTERHORN study

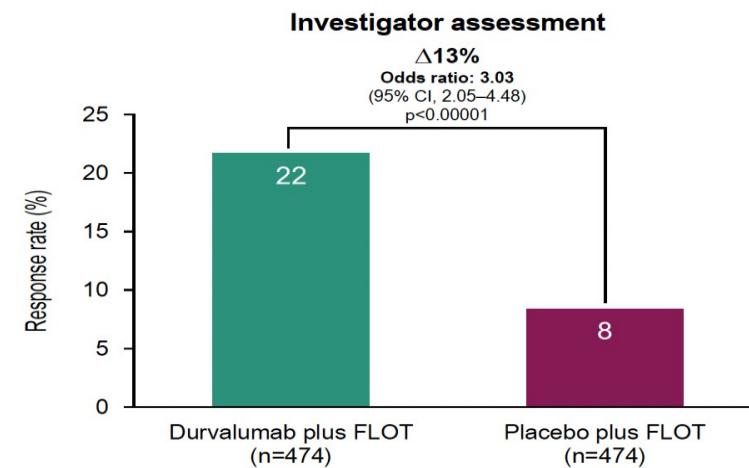
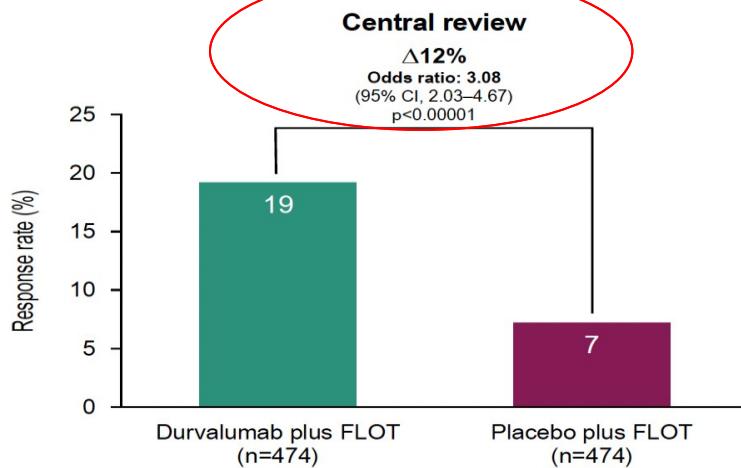
MATTERHORN is a global, Phase 3, randomised, double-blind, placebo-controlled study





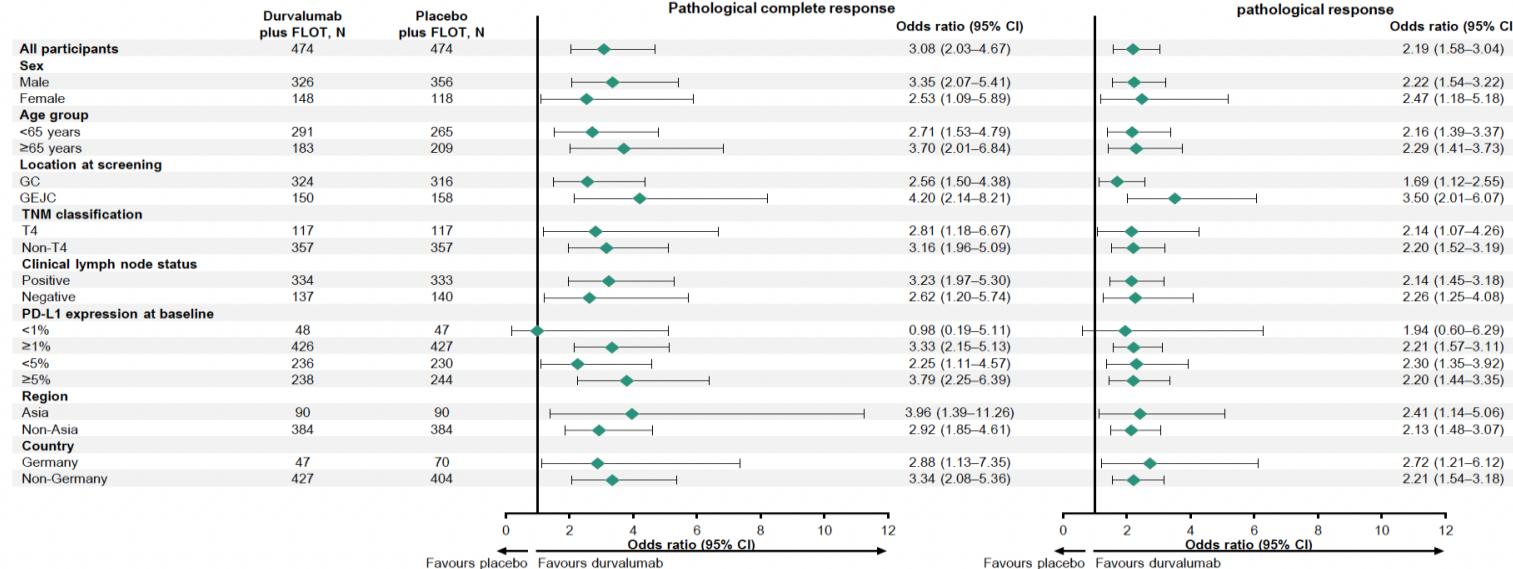
Interim results of the global, phase 3 MATTERHORN study:pRC

Pathological complete response



Pathological complete response (pCR) to **durvalumab** plus 5-fluorouracil, leucovorin, oxaliplatin and docetaxel (FLOT) in resectable gastric and gastroesophageal junction cancer (GC/GEJC): interim results of the global, phase 3 MATTERHORN study

Pathological response subgroup analysis (central review)



1. La IO perioperatoria aumenta las **pRC**, estando pendiente su impacto en SG y EFS

ESCENARIO PERIOPERATORIO

2.¿Qué sabemos de la **IO adyuvante** frente a QT?
¿Qué hemos aprendido del tto postoperatorio?

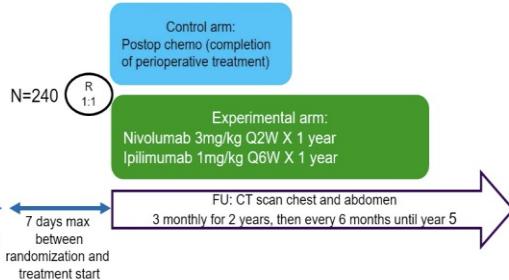
EORTC 1707 VESTIGE: Adjuvant immunotherapy in patients (pts) with resected gastroesophageal adenocarcinoma (GEA) following preoperative chemotherapy with high risk for recurrence (ypN+ and/or R1)—an open-label randomized controlled **phase II study**

Main eligibility criteria & design



- Gastric or EGJ adenocarcinoma stage Ib-IV
- Completed pre-operative chemotherapy with a fluoropyrimidine/platin-containing regimen followed by surgery within 12 weeks prior to randomization
- Recovered from surgery
- ypN1-3 status according to current (8th) version of TNM classification system AND/OR
- R0 or R1 resection according to current (8th) version of TNM

Surgery



Statistical design



- Primary objective: to detect an **increase in DFS rate at 1 year** from 65% to 74% with nivolumab plus ipilimumab ($HR=0.7$) with a one-sided alpha of 10% and 80% power.

-In the MAGIC trial, of 92 node positive patients who had surgery and postoperative chemotherapy, PFS (from surgery) rate at 1 year was 58.3% (95% CI: 47.5 - 67.7).

-In ST03, DFS rate at 1 year for node positive patients was 68% (95% CI: 62%-73%)

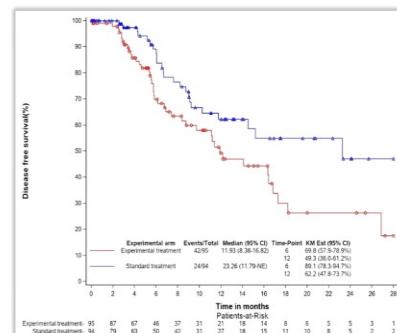
- Using a one-sided log-rank test at a level of significance of 10%, a total of **142 events** are required to reach 80% power.

- ✓ Total sample size : **240 patients randomized**
- ✓ Target accrual: 8 patients/month
- ✓ Accrual duration: 30 months
- ✓ Total study duration: 52 months

Obj.1º: Aumentar DFS (65% al 74% al año)

EORTC 1707 VESTIGE: Adjuvant immunotherapy in patients (pts) with resected gastroesophageal adenocarcinoma (GEA) following preoperative chemotherapy with high risk for recurrence (ypN+ and/or R1)—an open-label randomized controlled phase II study

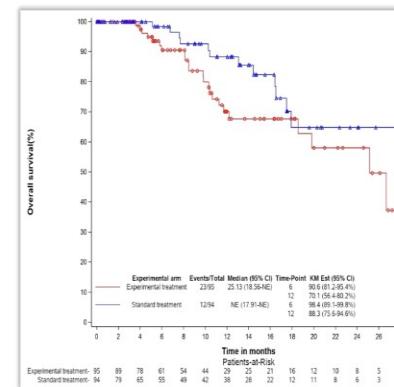
Primary Endpoint Disease free survival - ITT



| | CT arm | Nivo/Ipi arm |
|---------------------------|---------------------|---|
| Median DFS(m) (95% CI) | 23.26 (11.79-NE) | 11.93 (8.36-16.82) |
| 12m DFS % (95% CI) | 62.2 (47.8-73.7) | 49.3 (36.0-61.2) |
| | | |
| | Event/Total | Hazard Ratio (95% CI) ^{Cox} |
| Nivo/Ipi arm | 42/95 | 1.80 (1.09-2.98) |
| CT arm | 24/94 | Reference |
| | | P=0.0195* |

^{Cox} model; *Logrank test

Secondary Endpoint – OS - ITT



| | Event/Total | Hazard Ratio (95% CI) ^{Cox} | P-value |
|-------------------------------------|-----------------------------------|---|---------|
| Nivo/Ipi arm | 23/95 | 1.79 (0.89-3.59) | 0.0994* |
| CT arm | 12/94 | Reference | |
| ^{Cox} model; *Logrank test | | | |
| | CT arm | Nivo/Ipi arm | |
| Median OS(m) (95% CI) | NE (18.56-NE) | 23.13 (18.56-16.NE) | |
| Main cause of death | Treatment arm (ITT population) | | |
| | CT (N=12) | Nivo/Ipi (N=23) | |
| PD | 9 (75.0) | 21 (91.3) | |
| Other | 2 (16.7) | 2 (8.7) | |
| 05:59 p | 1 (8.3) | 0 (0.0) | |

¿Y el biomarcador?

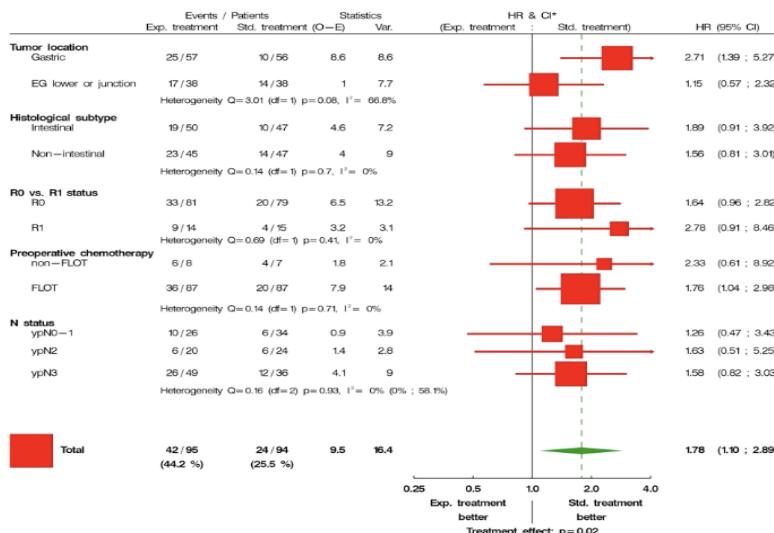


EORTC 1707 VESTIGE: Adjuvant immunotherapy in patients (pts) with resected gastroesophageal adenocarcinoma (GEA) following preoperative chemotherapy with high risk for recurrence (ypN+ and/or R1)—an open-label randomized controlled phase II study

Subgroup analyses DFS -ITT population



The future of cancer therapy



*95% CI everywhere

2. La IO sola frente a QT perioperatoria no aumenta la SLR...
En un escenario perioperatorio la QT postoperatoria aporta

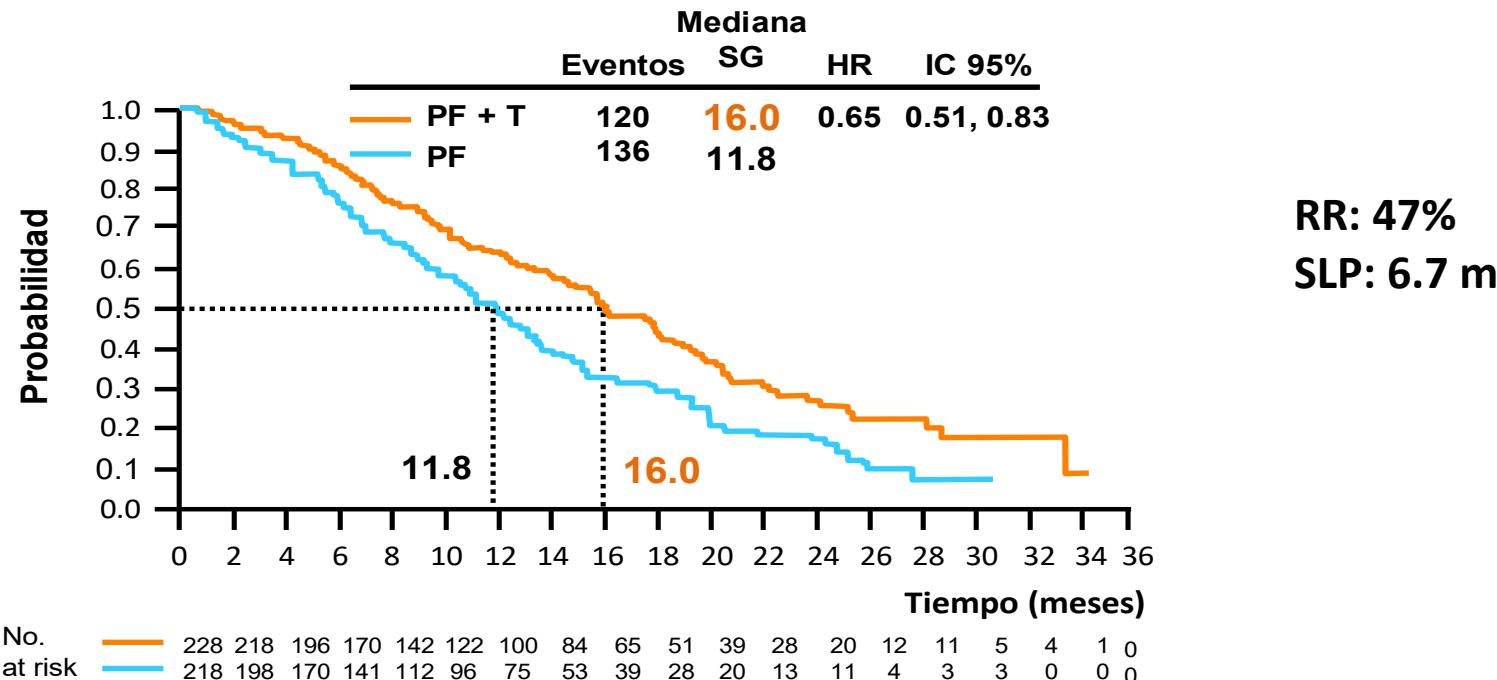
ESCENARIO METASTÁSICO

1. ¿Podemos decir que estamos ante una enfermedad heterogénea a nivel molecular?

1. Para la toma de decisiones en 1L necesitamos saber **diferentes biomarcadores: CPS y Her 2**
-

En HER 2 +:

Trastuzumab con platino/5Fu es superior a platino /5FU (TOGA Trial)



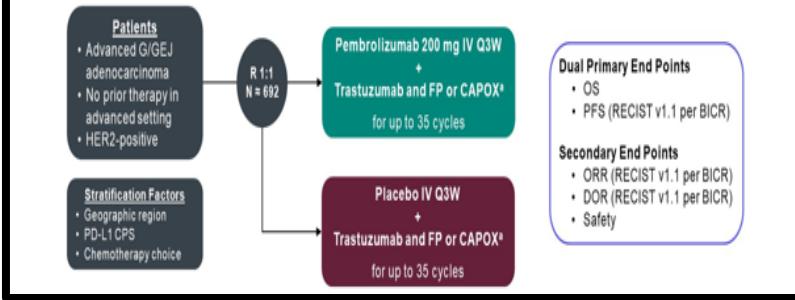


En HER 2 +:

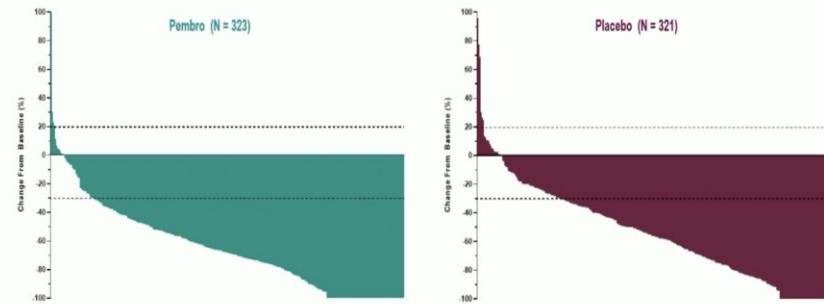
Trastuzumab/pembrolizumab con platino/5Fu es superior a trastuzumab/pembrolizumab en CPS ≥1 (85%) (**KEYNOTE 811**)

KEYNOTE-811 Global Cohort

Double-Blind Phase 3 Study of Pembrolizumab + Trastuzumab and Chemotherapy vs Placebo + Trastuzumab and Chemotherapy as First-Line Therapy For HER2-Positive Unresectable or Metastatic G/GEJ Cancer (NCT03615326)



Antitumor Response at IA3



| Response and Duration | Pembro N = 350 | Placebo N = 348 |
|-------------------------|----------------------|---------------------|
| ORR, % (95% CI) | 73 (68-77) | 60 (55-65) |
| Best response, n (%) | | |
| CR | 58 (17) | 39 (11) |
| PR | 196 (56) | 170 (49) |
| SD | 67 (19) | 95 (27) |
| DCR, % (95% CI) | 92 (88-94) | 87 (83-91) |
| DOR, median (range), mo | 11.3 (1.1+ to 49.7+) | 9.5 (1.4+ to 48.7+) |

Janjigian YY, Nature. 2021 Dec;600(7890):727-730.

Janjigian YY, Lancet. 2023 Oct 19:S0140-6736(23)02033-0.

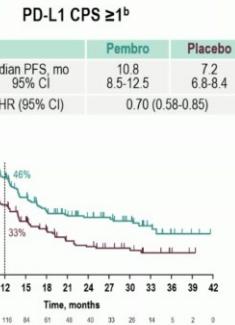
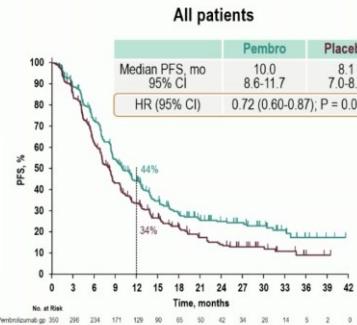


En HER 2 +:

Trastuzumab/pembrolizumab con platino/5Fu es superior a trastuzumab/pembrolizumab en CPS ≥1 (85%) (KEYNOTE 811)

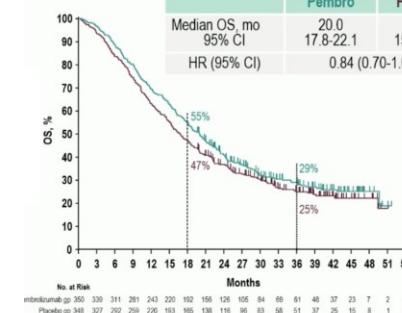
Progression-Free Survival at IA2: 28.4 months follow-up^a

RECIST V1.1, BICR

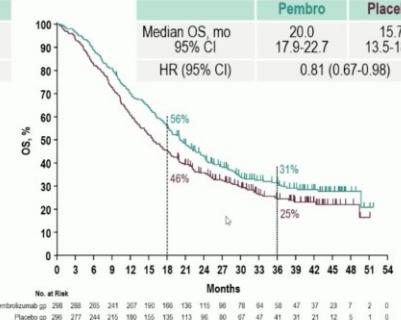


Overall Survival at IA3

All patients



PD-L1 CPS ≥1^a



Janjigian YY, Nature. 2021 Dec;600(7890):727-730.

Janjigian YY, Lancet. 2023 Oct 19:S0140-6736(23)02033-0.

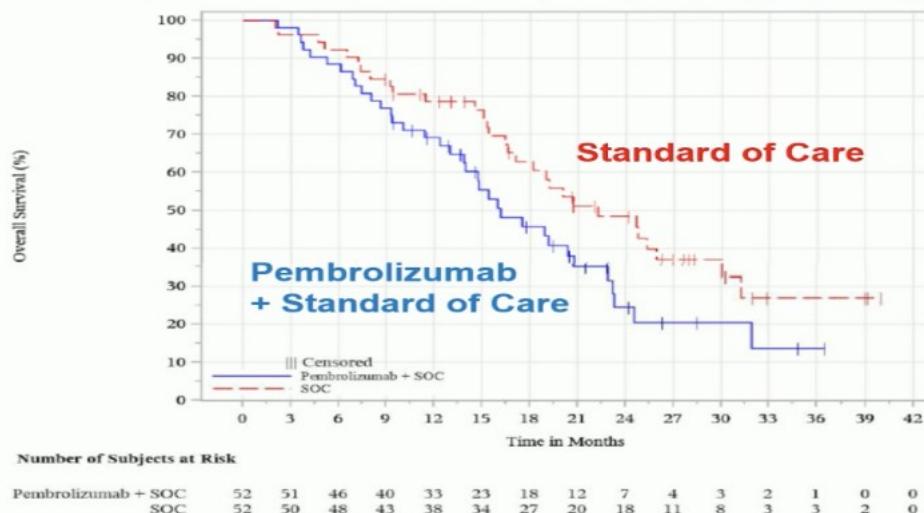


En HER 2 +:

Trastuzumab/pembrolizumab con platino/5Fu es superior a trastuzumab/pembrolizumab en CPS ≥ 1 (85%) (**KEYNOTE 811**)

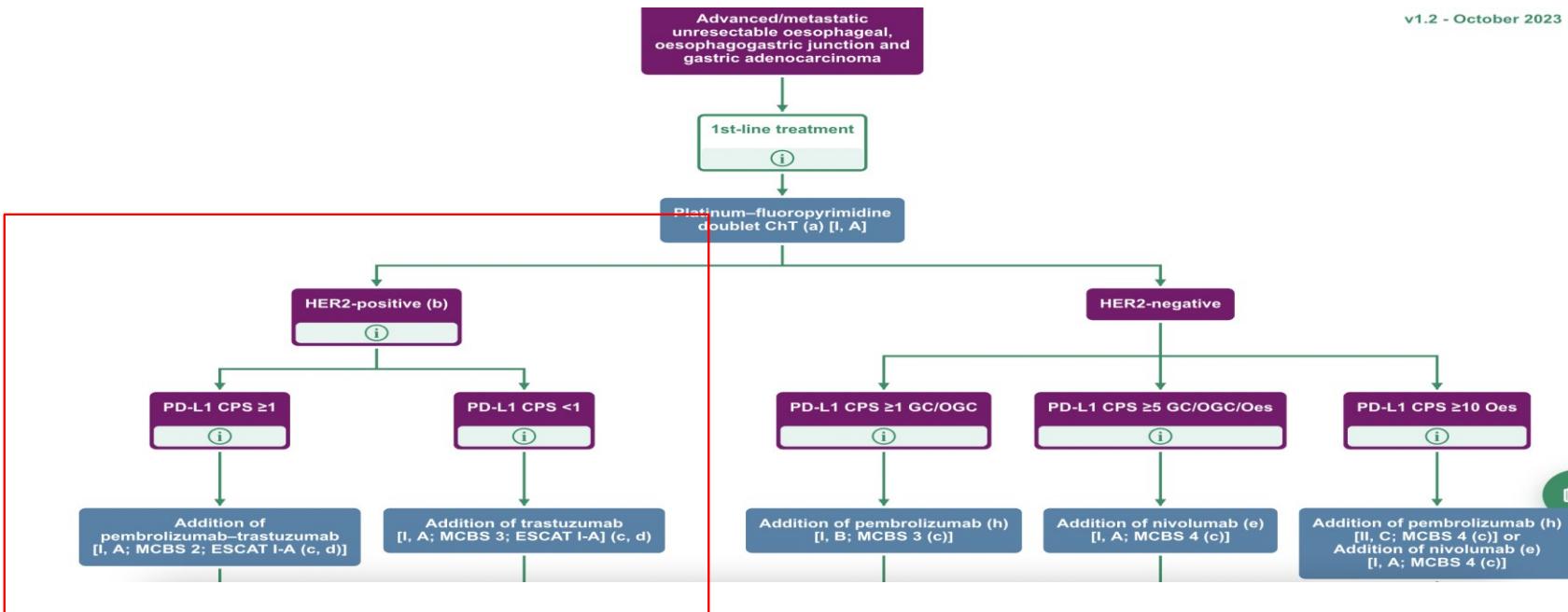
SG para PD-L1 CPS<1

Figure 14.2-22: Kaplan-Meier estimates of overall survival (CPS <1 participants) (global cohort) (ITT population)



GUÍAS CLÍNICAS

v1.2 - October 2023





CPS es un biomarcador predictivo de eficacia a Inmunoterapia (CheckMate 649)

CheckMate 649 study design

- CheckMate 649 is a randomized, open-label, global phase 3 study¹⁻⁴

Key eligibility criteria

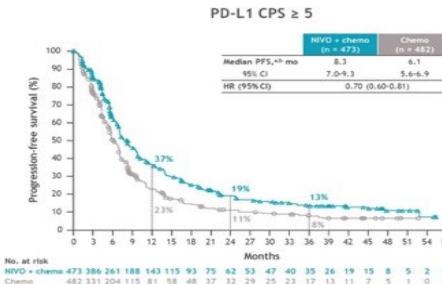
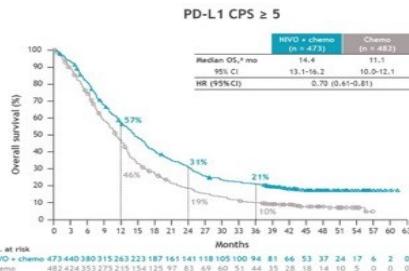
- Previously untreated, resectable, advanced or metastatic gastric/GEJ/esophageal adenocarcinoma
- No known HER2 positive status
- ECOG PS 0-1

Stratification factors

- Tumor cell PD-L1 expression ($\geq 1\%$ vs $< 1\%$)
- Region (Asia vs United States/Canada vs ROW)
- ECOG PS (0 vs 1)
- Chemotherapy (XELOX vs FOLFOX)



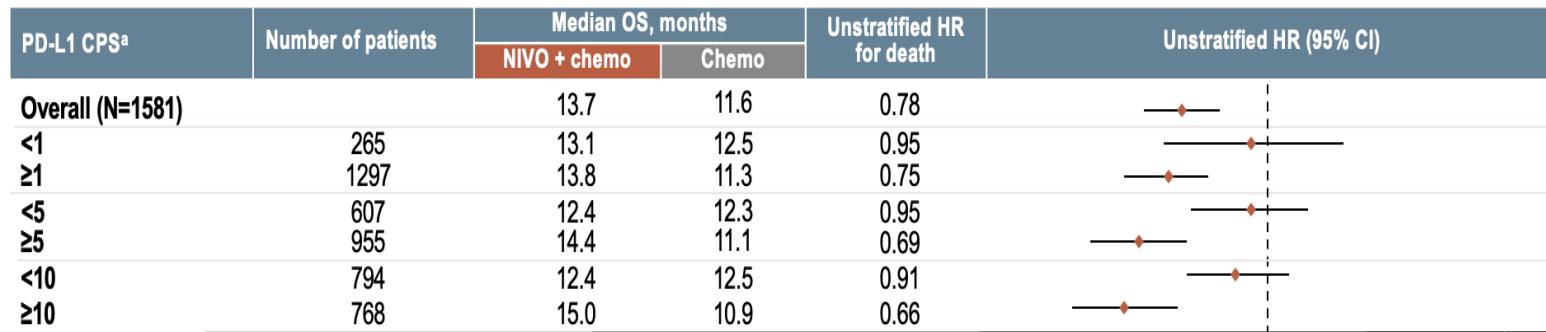
- Patients were enrolled from 175 hospitals and cancer centers in 29 countries
- At data cutoff (May 31, 2022), the minimum follow-up^b was 36.2 months





CPS es una variable cuantitativa continua

Overall survival

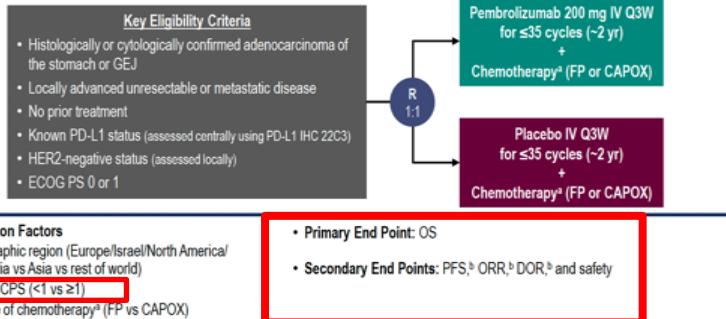




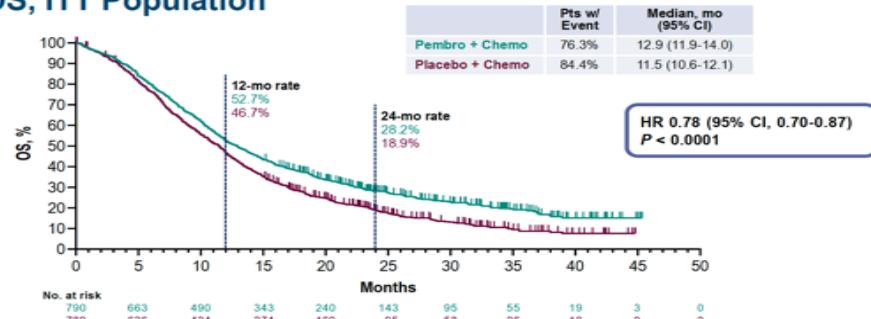
CPS es un biomarcador predictivo de eficacia a Inmunoterapia (KEYNOTE -859)

KEYNOTE-859 Study Design

Randomized, Double-Blind, Phase 3 Trial



OS, ITT Population



SG in ITT, CPS ≥1 and CPS≥ 10

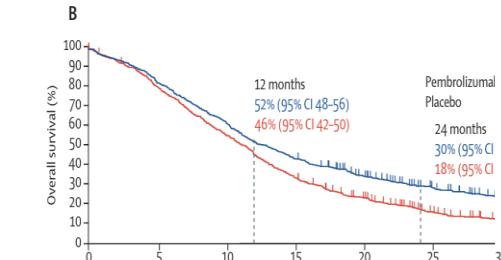
Seguimiento de 31 meses

33% Asia

Rha SY, Oh Lancet Oncol. 2023 Oct 19:S1470-2045(23)00515-6.

CPS es un biomarcador predictivo de eficacia a Inmunoterapia (KEYNOTE -859), subgrupos CPS ≥ 1 y CPS ≥ 10

CPS ≥ 1



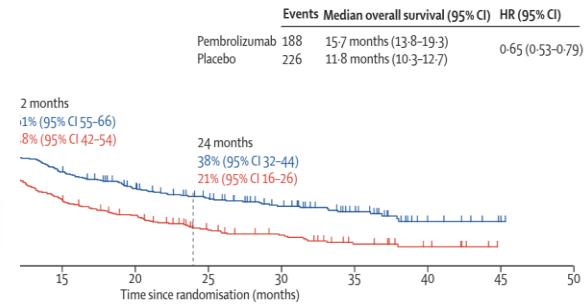
- Long term benefits are meaningful
- At 2 years
 - 9.3% absolute benefit,
 - ~50% relative improvement

- 1/3 patients are alive at 2 years
- How do we identify these patients?

| Number at risk (number censored) | | | | | | | | | |
|----------------------------------|-----|-----|-----|-----|------|------|------|-------|-------|
| Pembrolizumab | 618 | 511 | 383 | 269 | 192 | 121 | 81 | 46 | 17 |
| | (0) | (0) | (0) | (0) | (24) | (66) | (88) | (114) | (137) |
| Placebo | 617 | 493 | 339 | 206 | 126 | 66 | 41 | 20 | 7 |
| | (0) | (5) | (6) | (6) | (27) | (51) | (62) | (74) | (84) |

CPS ≥ 10

C



| | Events | Median overall survival (95% CI) | HR (95% CI) |
|---------------|--------|----------------------------------|------------------|
| Pembrolizumab | 188 | 15.7 months (13.8-19.3) | 0.65 (0.53-0.79) |
| Placebo | 226 | 11.8 months (10.3-12.7) | |

CPS es un biomarcador predictivo de eficacia a Inmunoterapia (KEYNOTE -859), análisis de subgrupos

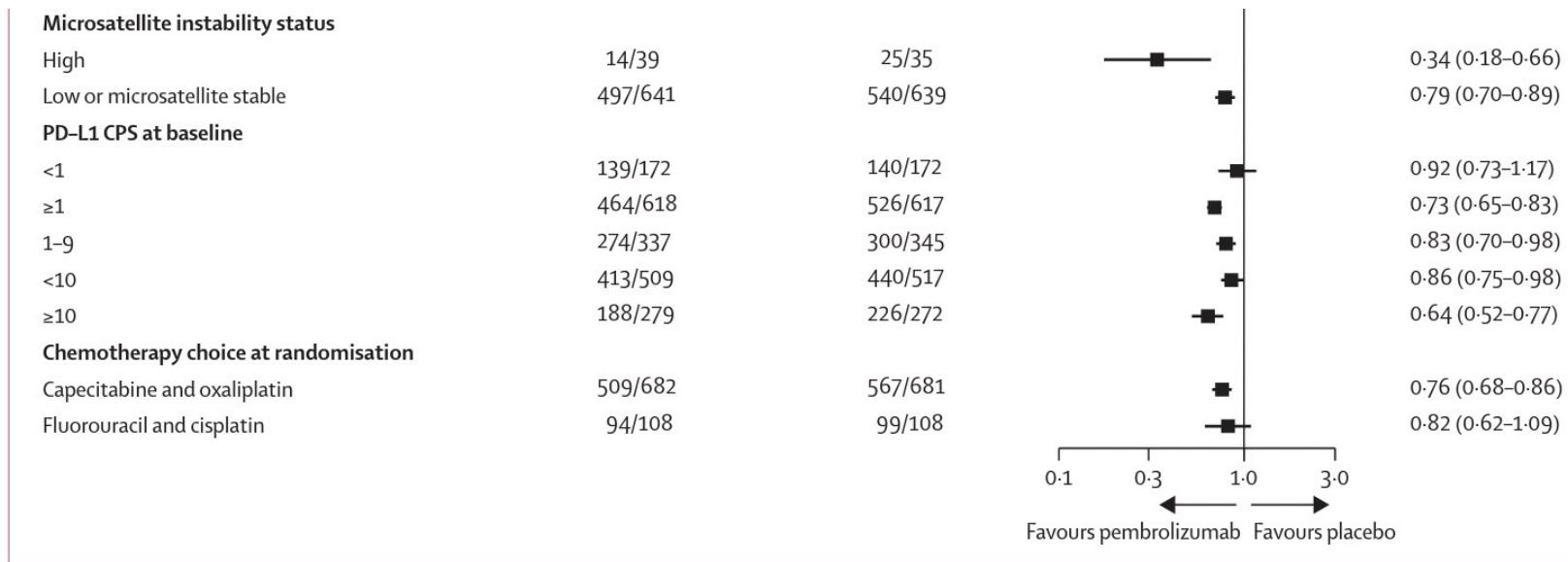
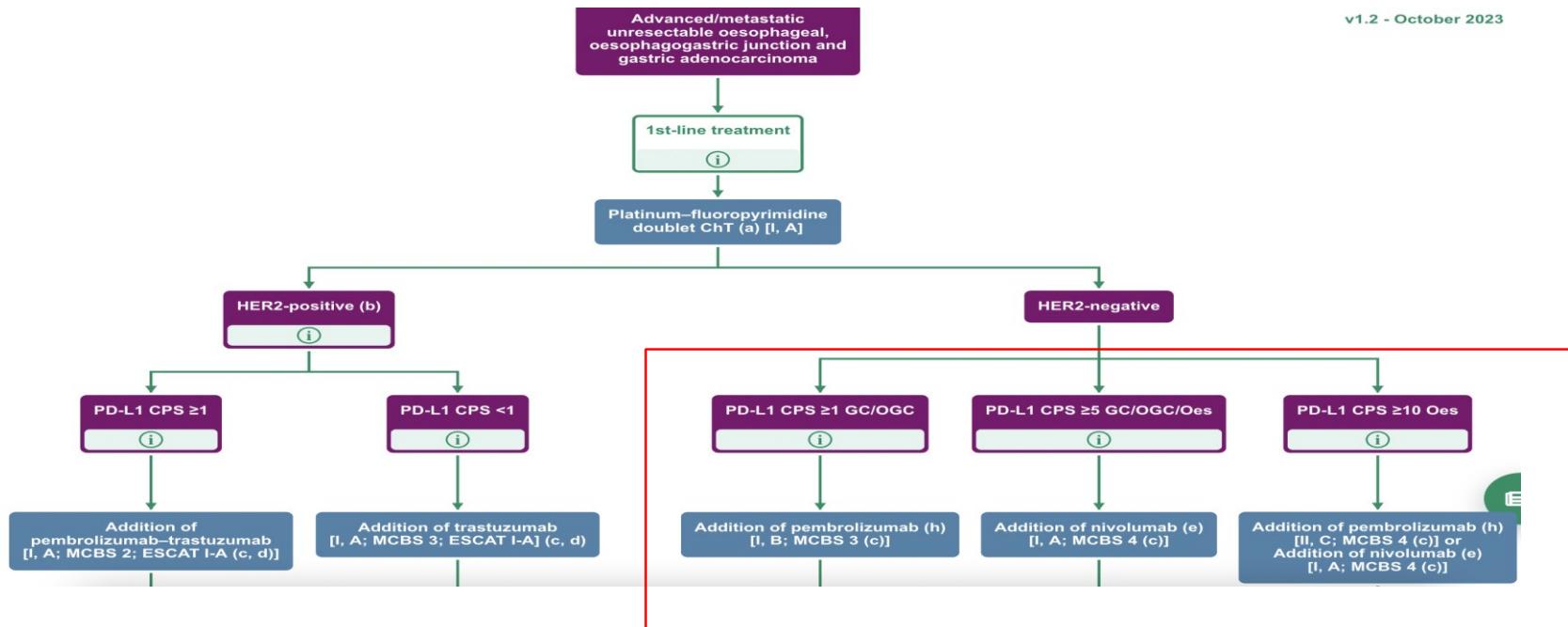


Figure 2: Overall survival



GUÍAS CLÍNICAS: Presente

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Futuro...

2. La sobreexpresión de claudina 18.2 es un biomarcador predictivo de beneficio de zolbetuximab (GLOW y Spotlight)

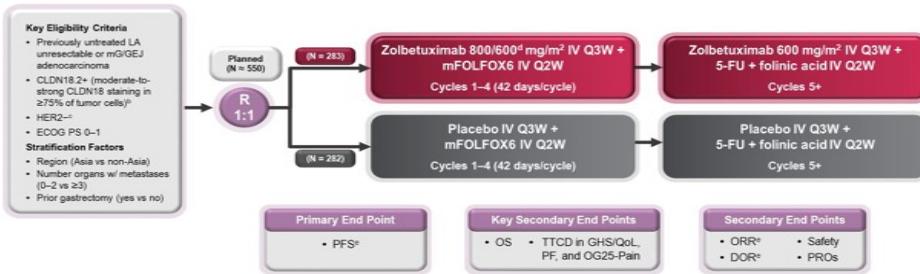
¿tendremos que incorporarlo a la toma de decisiones futuras?



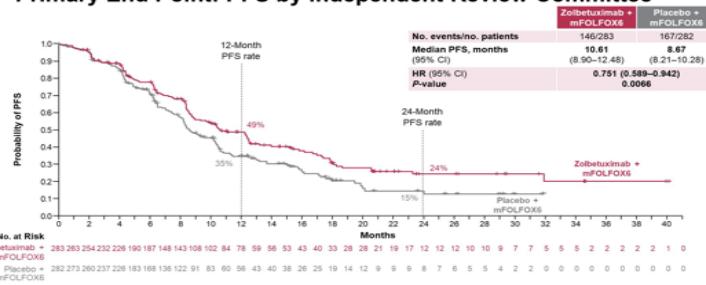
La sobreexpresión de claudina 18.2 es un biomarcador predictivo de beneficio de zolbetuximab (GLOW y Spotlight)

Study Design: SPOTLIGHT

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

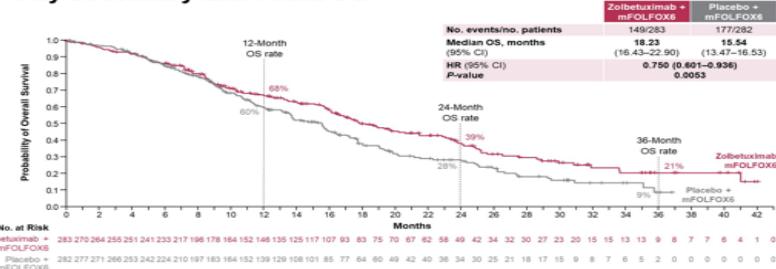


Primary End Point: PFS by Independent Review Committee^a



- PFS was significantly longer in patients treated with zolbetuximab + mFOLFOX6 vs placebo + mFOLFOX6

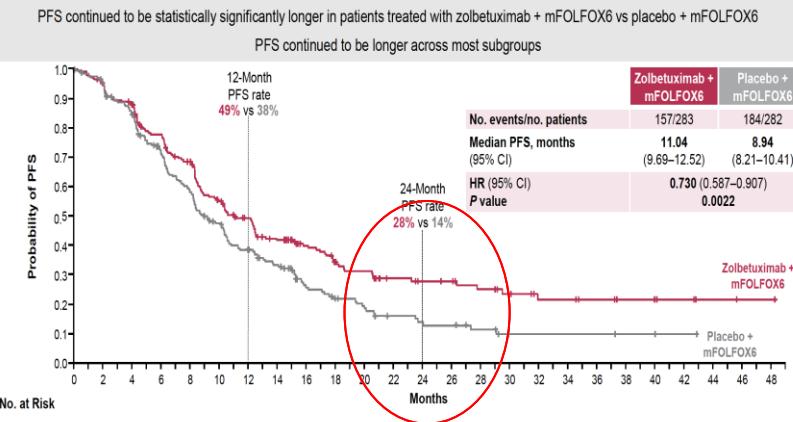
Key Secondary End Point: OS



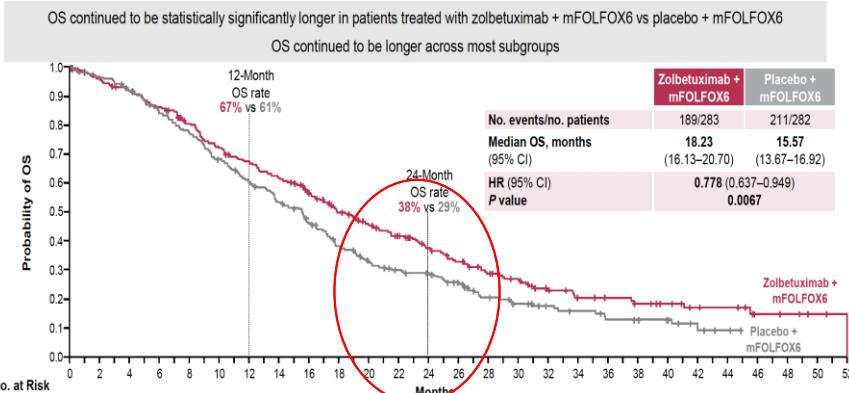


La sobreexpresión de claudina 18.2 es un biomarcador predictivo de beneficio de zolbetuximab (GLOW y Spotlight), con 9.7 meses adicionales de seguimiento

Primary Endpoint: PFS by Independent Review Committee^a Updated Analysis With 9.7 Months Additional Follow-Up



Key Secondary Endpoint: OS Updated Analysis With 9.7 Months Additional Follow-Up



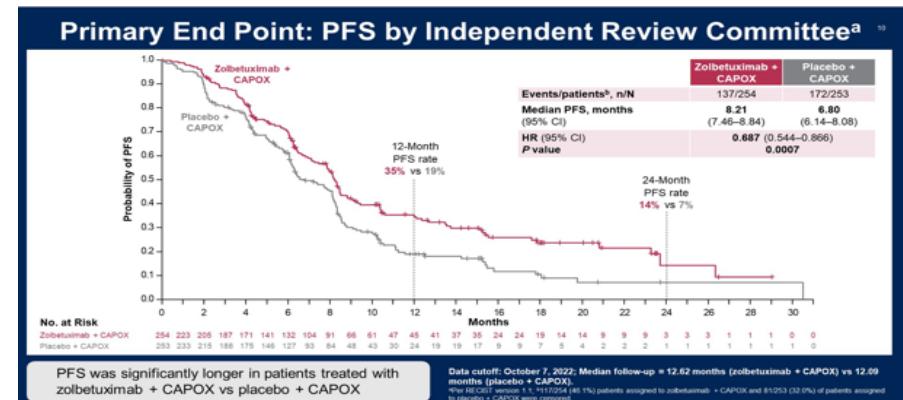
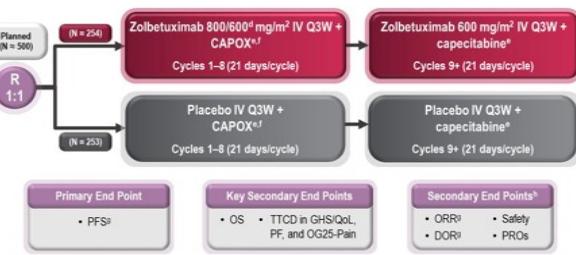


La sobreexpresión de claudina 18.2 es un biomarcador predictivo de beneficio de zolbetuximab (GLOW y Spotlight)

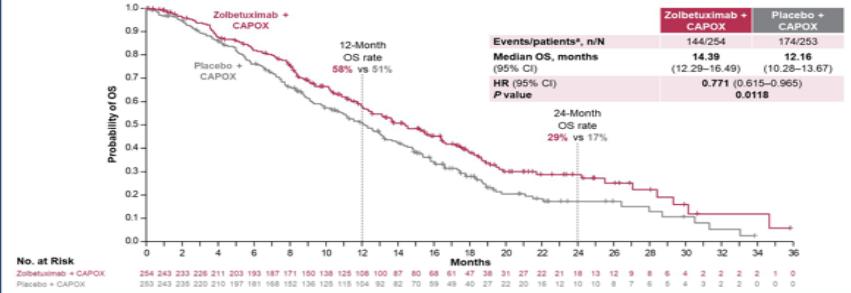
Study Design: GLOW

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

| Key Eligibility Criteria | |
|---|--|
| Previously untreated LA unresectable or mGI/GEJ adenocarcinoma | |
| CLDN18.2+ ($\geq 75\%$ of tumor cells with moderate-to-strong membranous CLDN18 staining) ^b | |
| HER2 ≤ 0 | |
| ECOG PS 0-1 | |
| Stratification Factors | |
| Region (Asia vs non-Asia) | |
| Number of organs w/ metastases (0-2 vs ≥ 3) | |
| Prior gastrectomy (yes vs no) | |



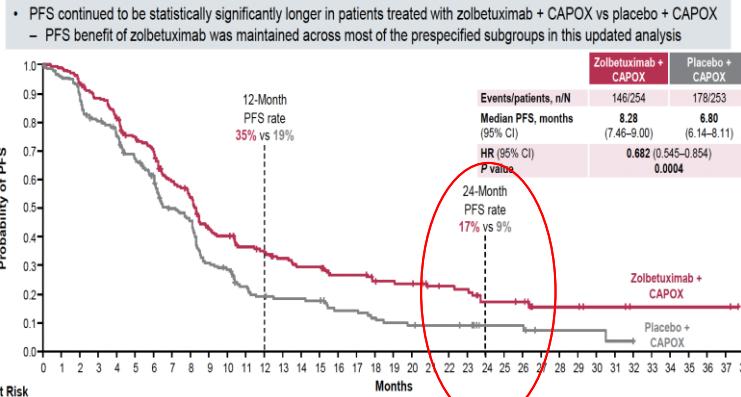
Key Secondary End Point: OS





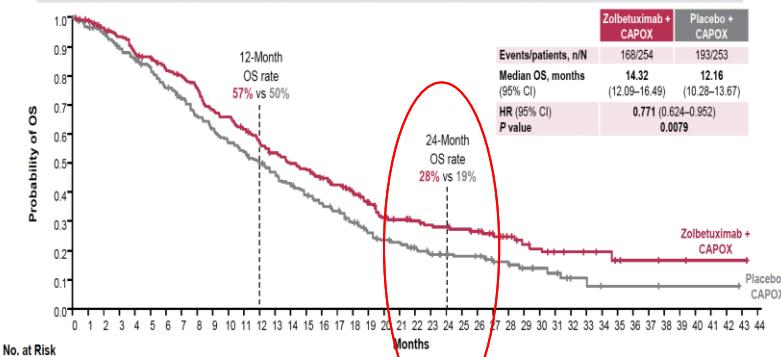
La sobreexpresión de claudina 18.2 es un biomarcador predictivo de beneficio de zolbetuximab (GLOW y Spotlight), 8.7 meses más de seguimiento

Primary Endpoint: PFS as Assessed by Independent Review Committee^a Updated analysis with 8.7 months additional follow-up



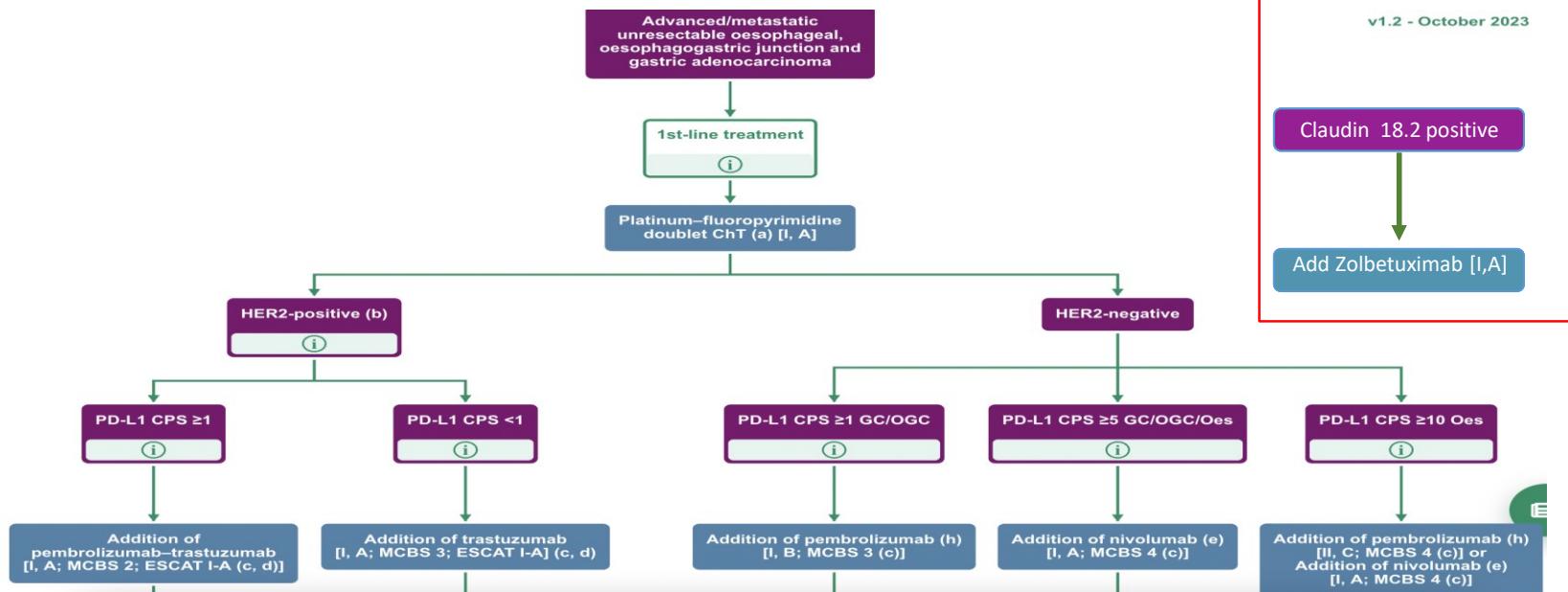
Key Secondary Endpoint: OS Updated analysis with 8.7 months additional follow-up

- OS continued to be statistically significantly longer in patients treated with zolbetuximab + CAPOX vs placebo + CAPOX
 - OS remained longer in the zolbetuximab arm across most of the prespecified subgroups in the updated analysis





GUÍAS CLÍNICAS: Futuro



ESCENARIO METASTÁSICO

1. ¿Podemos decir que estamos ante una enfermedad heterogénea a nivel molecular?

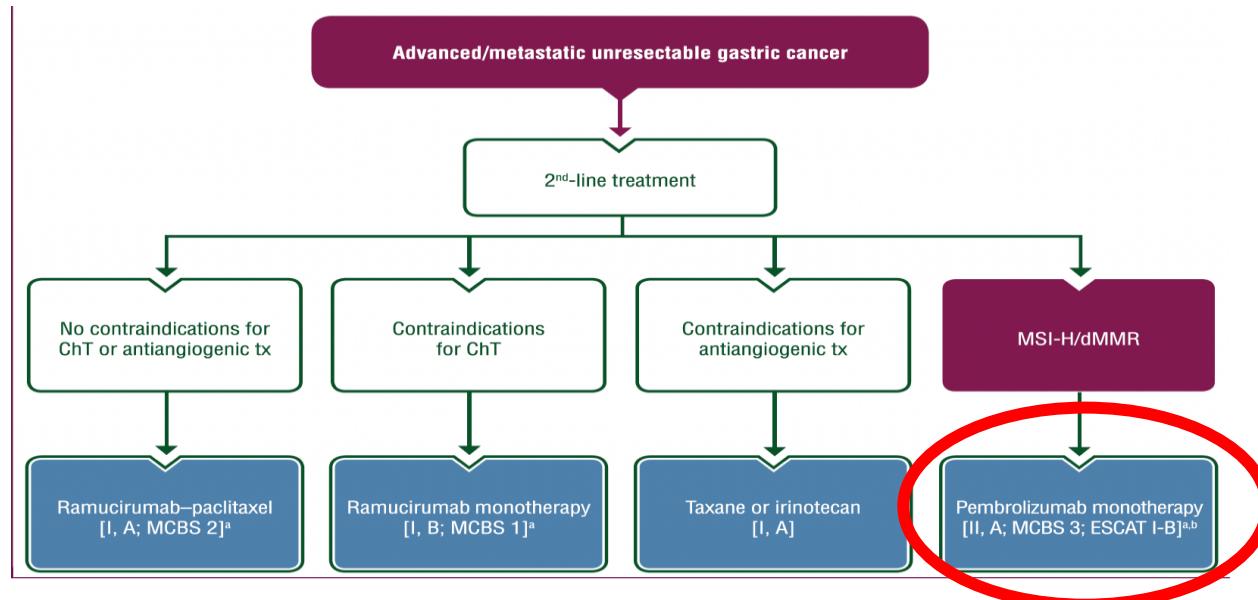
Sí!

ESCENARIO METASTÁSICO

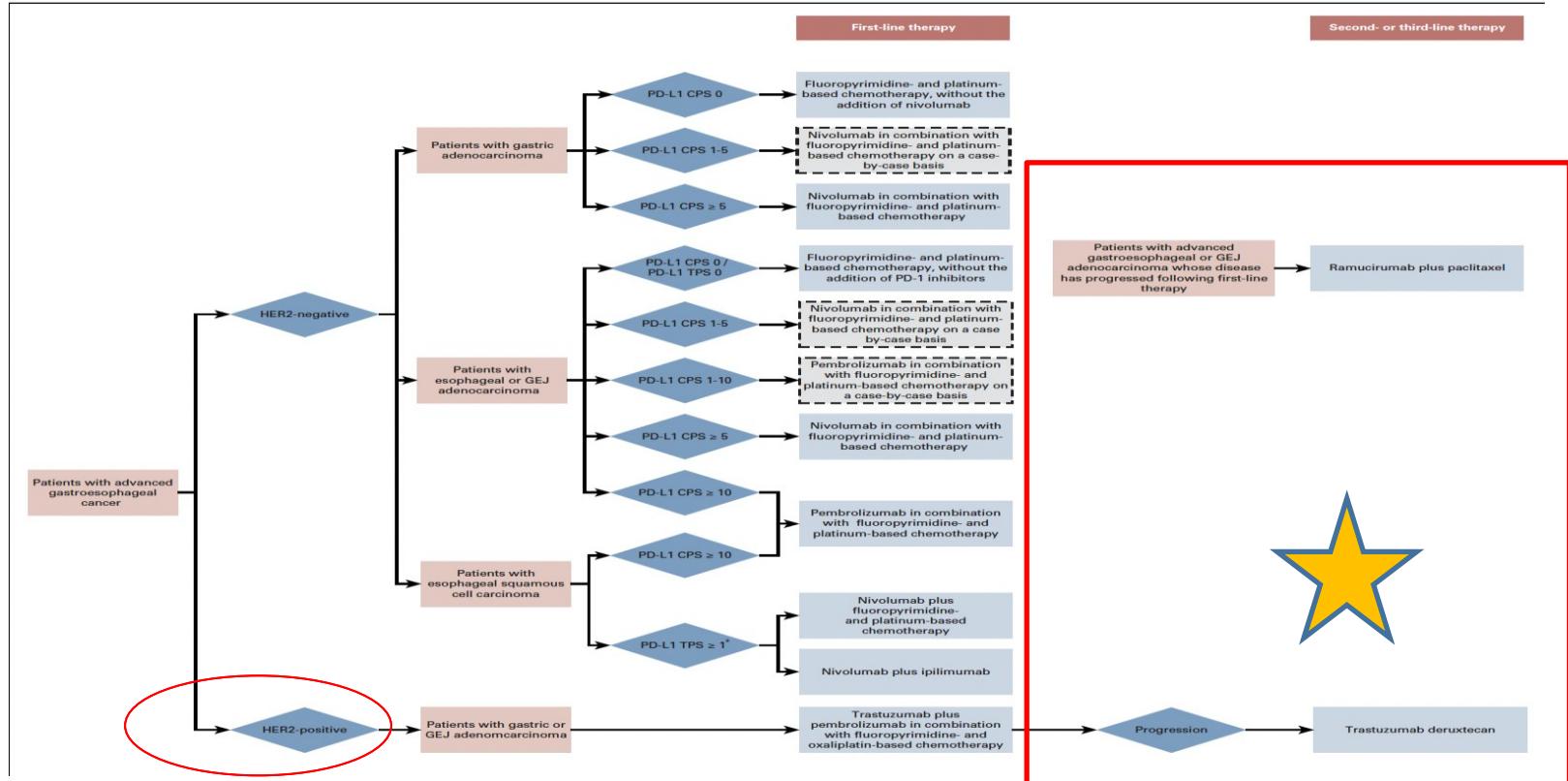
2. ¿Estamos incorporando la heterogeneidad molecular a la segunda línea?

**Dos subgrupos de pacientes son candidatos a terapias dirigidas en 2L:
Her 2 amplificado y MSI-H/dMMR**

Dos subgrupos de pacientes son candidatos a terapias dirigidas en 2L: Her 2 amplificado y MSI-H/dMMR



Immunotherapy and Targeted Therapy for Advanced Gastroesophageal Cancer: ASCO Guideline



Efficacy of Pembrolizumab in Patients With Noncolorectal High Microsatellite Instability/Mismatch Repair-Deficient Cancer: Results From the Phase II

KEYNOTE-158 Study

(n:42)

| Gastric n = 42 | |
|--|-------------------|
| ORR, % (95% CI) | 31.0 (17.6-47.1) |
| Best objective response, n (%) | |
| CR | 4 (9.5) |
| PR | 9 (21.4) |
| SD | 7 (16.7) |
| PD | 15 (35.7) |
| Not evaluable | 1 (2.4) |
| No assessment | 6 (14.3) |
| DOR, median (range), months | NR (6.3 to 51.1+) |
| Median PFS, months (95% CI) | 3.2 (2.1-12.9) |
| PFS rate \geq 3 years ^a , % | 28.5 |
| Median OS, months (95% CI) | 11.0 (5.8-31.5) |
| OS rate \geq 3 years ^a , % | 34.5 |

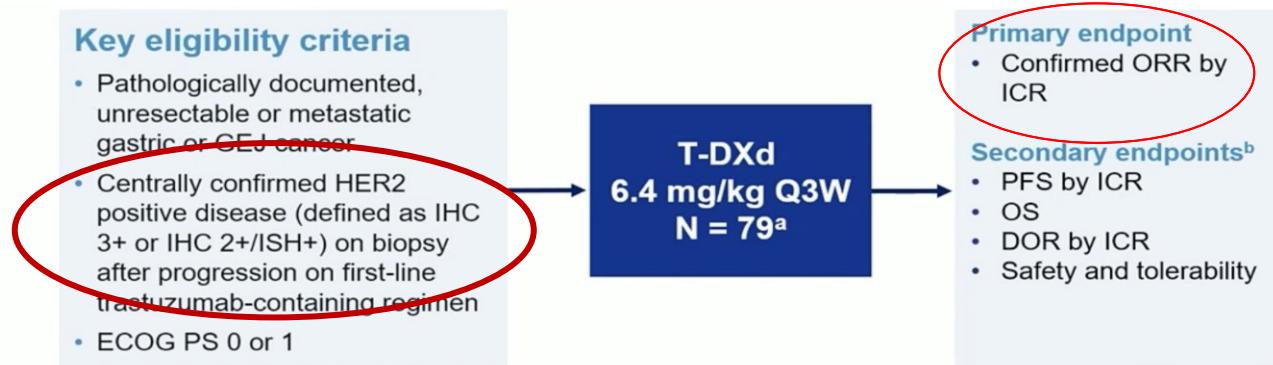
Marabelle A., J Clin Oncol. 2020 Jan 1;38(1):1-10.

Maio M. Ann Oncol. 2022 Sep;33(9):929-938.



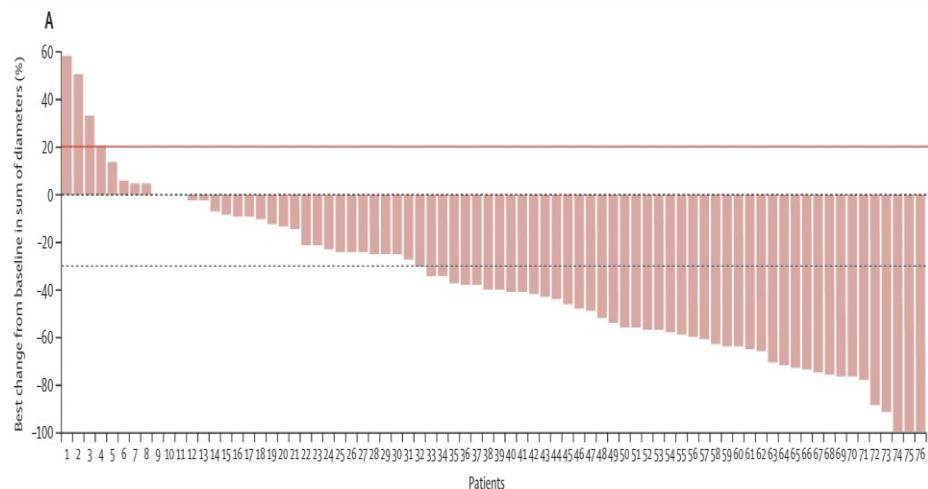
Trastuzumab deruxtecan in patients in the USA and Europe with HER2-positive advanced gastric or gastroesophageal junction cancer with disease progression on or after a trastuzumab-containing regimen (**DESTINY-Gastric02**):
primary and updated analyses from a single-arm, phase 2 study

DESTINY-Gastric02 Study Design



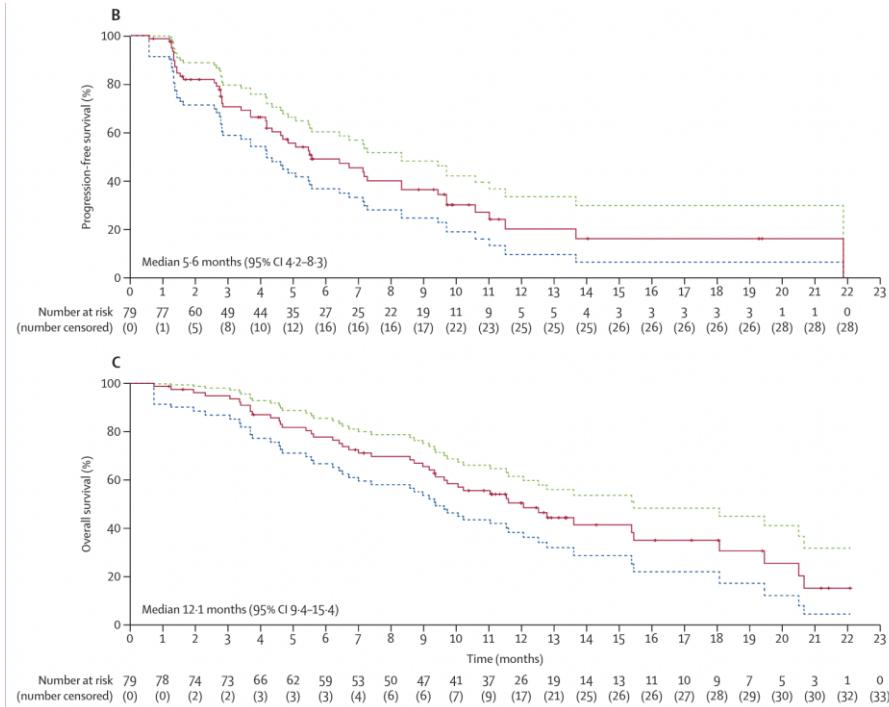
Trastuzumab deruxtecan in patients in the USA and Europe with HER2-positive advanced gastric or gastroesophageal junction cancer with disease progression on or after a trastuzumab-containing regimen (**DESTINY-Gastric02**):
primary and updated analyses from a single-arm, phase 2 study

| | April 9, 2021, data cutoff; patients (N=79) | Nov 8, 2021, data cutoff; patients (N=79) |
|--|--|--|
| Confirmed objective response | 30 (38%; 27.3-49.6) | 33 (42%; 30.8-53.4) |
| Confirmed best overall response | | |
| Complete response | 3 (4%) | 4 (5%) |
| Partial response | 27 (34%) | 29 (37%) |
| Stable disease | 34 (43%) | 31 (39%) |
| Progressive disease | 13 (16%) | 13 (16%) |
| Not evaluable | 2 (3%) | 2 (3%) |
| Median progression-free survival, months | 5.5 (4.2-7.2)* | 5.6 (4.2-8.3)† |
| Patients with events | 44 (56%) | 51 (65%) |
| Progressive disease | 37 (47%) | 44 (56%) |
| Death | 7 (9%) | 7 (9%) |
| Median overall survival, months | 12.1 (8.6-NE)‡ | 12.1 (9.4-15.4)§ |
| Patients with events | 26 (33%) | 46 (58%) |
| Patients without events (censored) | 53 (67%) | 33 (42%) |
| Alive | 46 (58%) | 26 (33%) |
| Lost to follow-up | 7 (9%) | 7 (9%) |
| Confirmed disease control | 64 (81%; 70.6-89.0) | 64 (81%; 70.6-89.0) |
| Median time to response, months | 1.4 (1.4-2.6) | 1.4 (1.4-2.7) |
| Median duration of response, months | 8.1 (4.1-NE) | 8.1 (5.9-NE) |





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



ESCENARIO METASTÁSICO

2. ¿Estamos incorporando la heterogeneidad molecular a la segunda línea?

Sí, claro

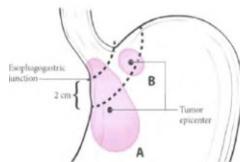
BLOQUE II:

UNIÓN ESÓFAGO-GÁSTRICA

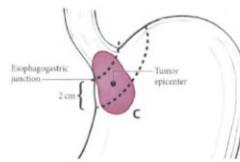
Unión Esófago-Gástrica

1. ¿Qué "hitos" tenemos?

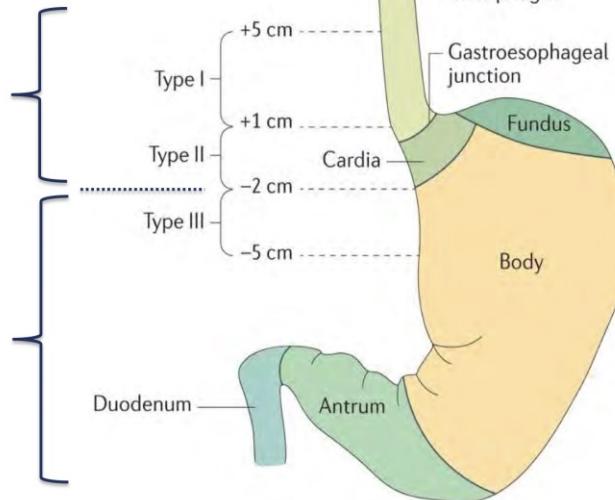
1. Disponemos de múltiples definiciones de la UEG



Adenocarcinomas with epicenters no more than 2 cm into the gastric cardia are staged as esophageal adenocarcinomas (TNM 8th ed)



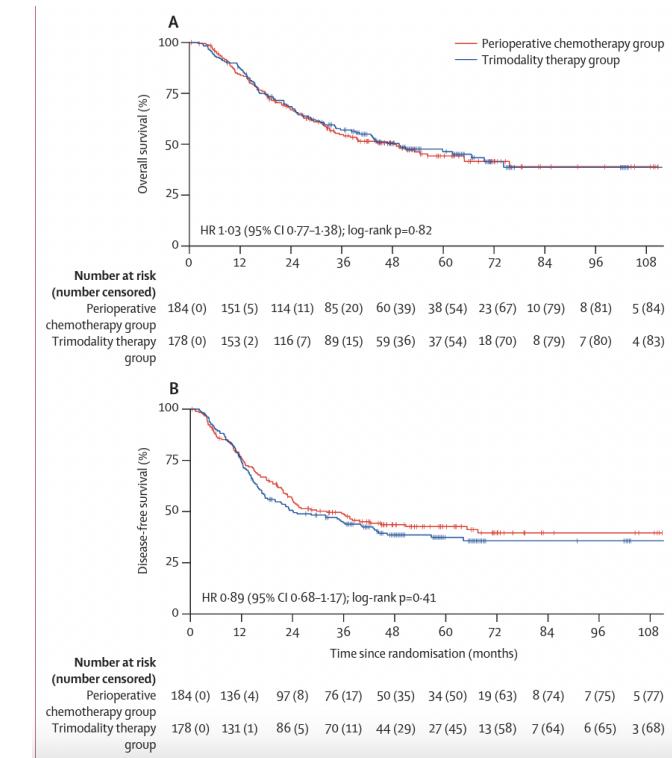
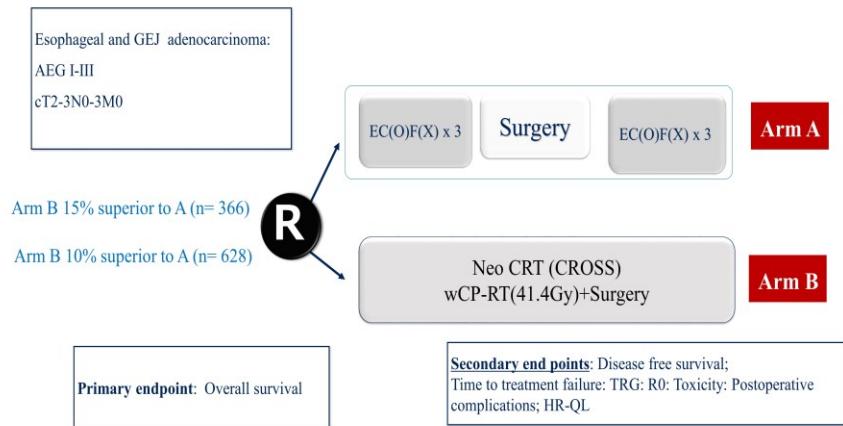
Staging criteria for stomach cancers



TNM:

Tumores que afectan la UEG con epicentro no más allá 2 cms estómago proximal esófagos
Tumores cuyo epicentro >2 cm UEG :estómago

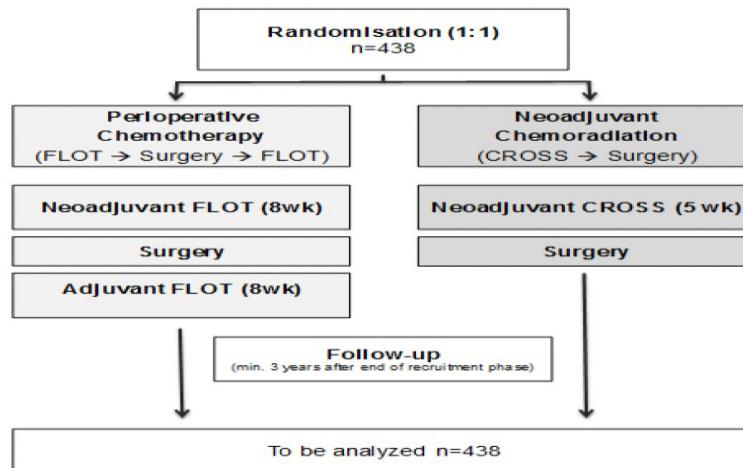
Trimodality therapy versus perioperative chemotherapy in the management of locally advanced adenocarcinoma of the oesophagus and oesophagogastric junction (Neo-AEGIS): an open-label, randomised, phase 3 trial



1. No se puede asumir la no inferioridad, es preciso esperar el resultado de ESOPEC que va a comparar CROSS vs FLOT

Study Design

ESOPEC



Adenocarcinoma of the esophagus / GEJ

Prospective RCT / Phase III

Multicenter (18 sites)

438 randomized patients

Primary endpoint: Overall survival

Secondary endpoints:

- PFS / RFS
- postoperative M&M
- Quality of life

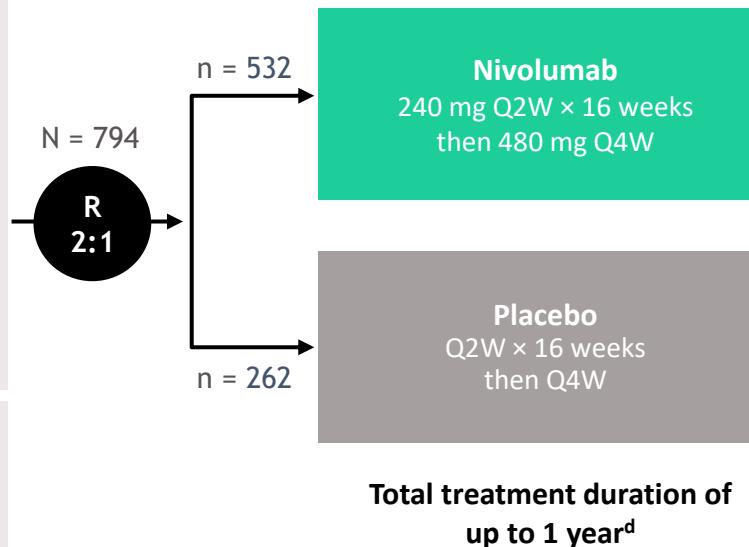
Adjuvant Nivolumab in Resected Esophageal or Gastroesophageal Junction Cancer

Key eligibility criteria

- Stage II/III EC/GEJC
- Adenocarcinoma or squamous cell carcinoma
- Neoadjuvant CRT + surgical resection (R0,^b performed within 4-16 weeks prior to randomization)
- Residual pathologic disease
 - \geq ypT1 or \geq ypN1
- ECOG PS 0-1

Stratification factors

- Histology (squamous vs adenocarcinoma)
- Pathologic lymph node status (\geq ypN1 vs ypN0)
- Tumor cell PD-L1 expression (\geq 1% vs < 1%^c)



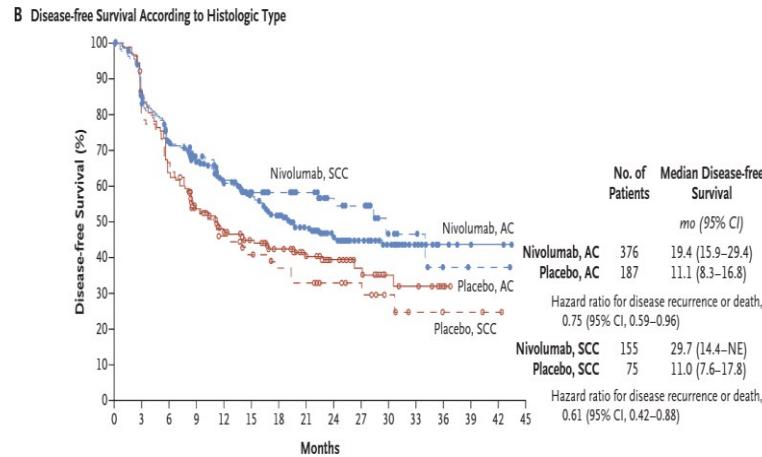
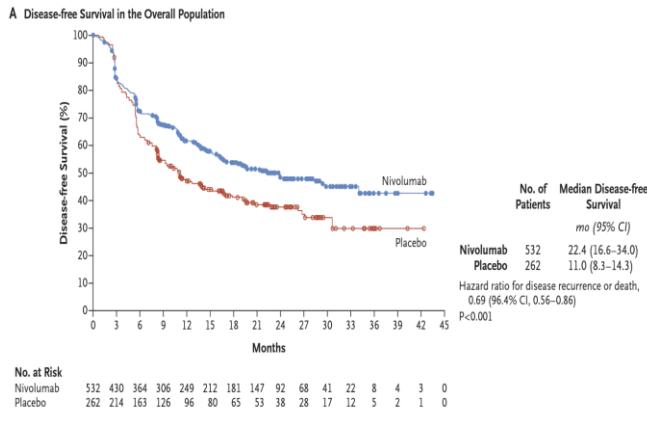
Primary endpoint:

- DFS^e

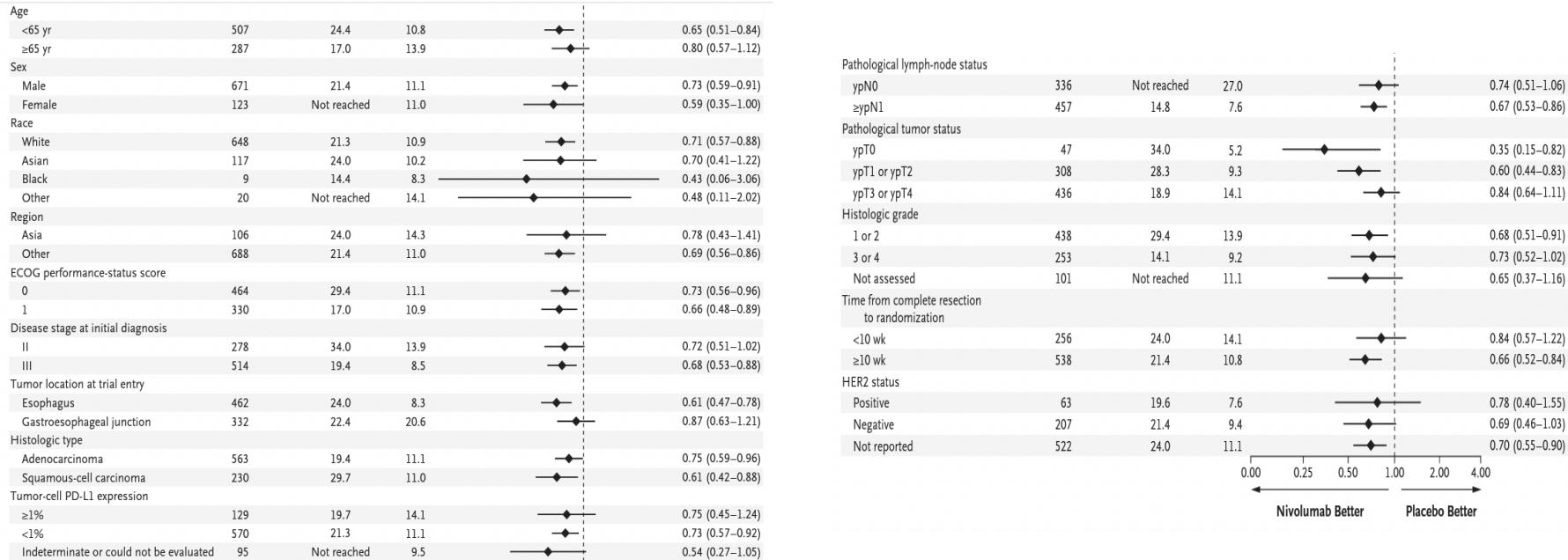
Secondary endpoints:

- OS^f
- OS rate at 1, 2, and 3 years

Adjuvant Nivolumab in Resected Esophageal or Gastroesophageal Junction Cancer



Adjuvant Nivolumab in Resected Esophageal or Gastroesophageal Junction Cancer



2. Si estamos ante ausencia de respuesta patológica hay que considerar Nivolumab adyuvante

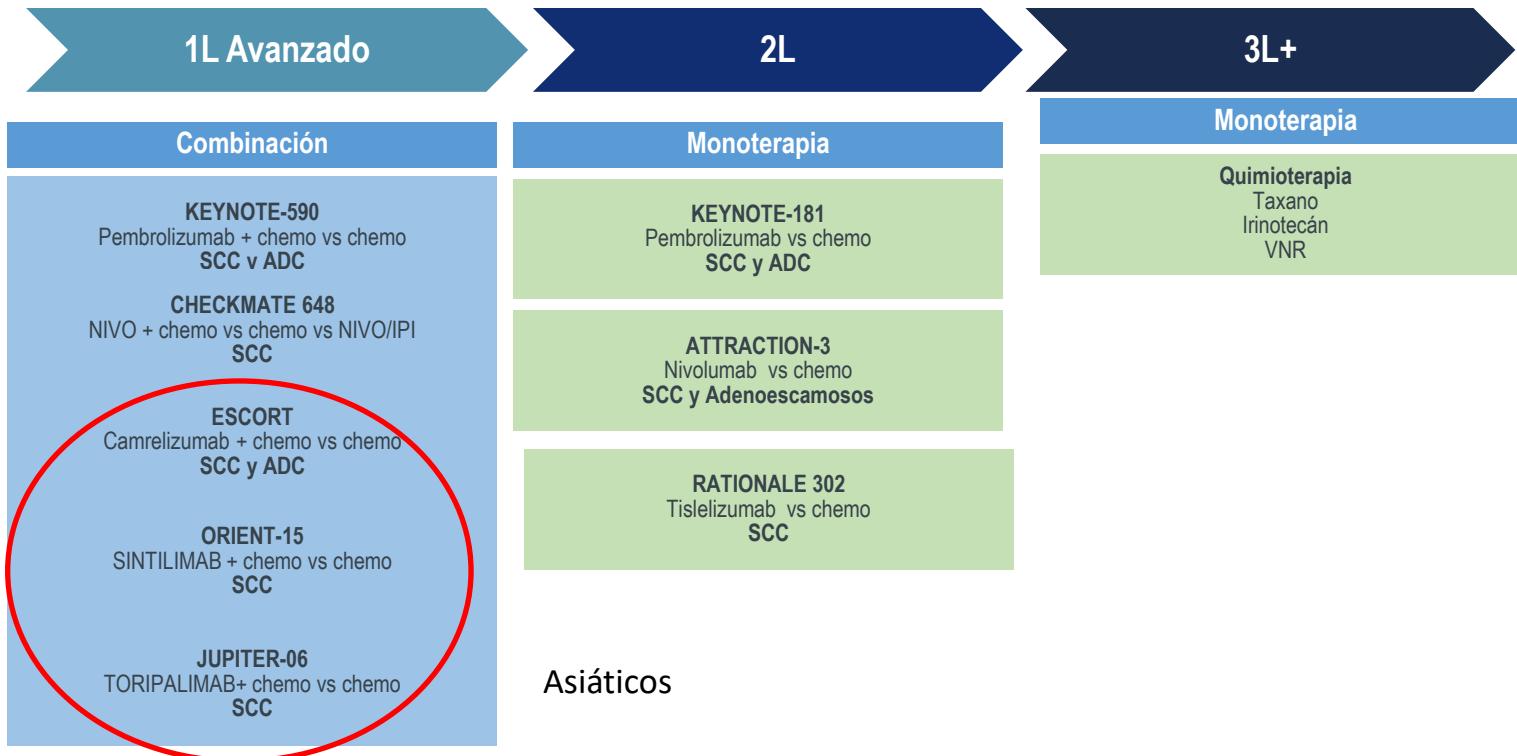
3. NEOAEGIS me genera muchas dudas ¿ESOPEC?

BLOQUE III:

CÁNCER ESCAMOSO ESÓFAGO

ESCENARIO METASTÁSICO

1. ¿Tiene algún papel la IO en 1L?



ESCENARIO METASTÁSICO

1. Varios estudios Fase III han constatado el papel de la IO en 1L (Asia), empleando diferentes biomarcadores

En pacientes asiáticos Camrelizumab, Torpalimab y Sintilimab asociados a quimoterapia son superiores a quimioterapia sola.

| | ESCORT-1 Luo H. JAMA. 2021 14;326(10):916-925 | JUPITER 06 Wang ZX et al. Cancer Cell. 2022 14;40(3):277-288.e3. | ORIENT-15 Lu Z, et al BMJ. 2022 Apr 19;377:e068714 |
|------------|--|--|---|
| Esquema | Camrelizumab /QT vs QT (paclitaxel/cisplatino) | Toripalimab/QTvs QT (cisplatino/paclitaxel) | Sintilimab/QT vsQT (cisplatino/5FU o paclitaxel) |
| N | 596 SCC | 524 SCC | 659 SCC |
| Región | China | China | China |
| ECOG | 76% PS 1 | 74%PS1 | 76% PS 1 |
| Edad Media | 62 | 63 | 63 |
| PD-L1 | PD-L1 IHC 6E8 ab TPS>1% 57% | CPS>1 76% CPS>10 % 45% | PDL1 TPS>10% 36% CPS>10% 57% |
| Obj.1º | SG y SLP | SG y SLP | SG (CPS>10 y toda la población) |
| | SG 15.2 vs 12 ms (HR 0.70;p:0.001) SLP 6.9 vs 5.6 ms (HR:0.56; p<0.001) | SG 17 ms vs 12 ms (HR 0.58;p=0.0004) SLP 5.7 vs 5.5 ms (HR 0.58;p<0.0001) | SG 16.7 vs 12.5 ms (HR 0.63,p<0.001) SG CPS≥ 10 17.2 vs 13.6 ms (HR 0.64; p=0.002) |

2. Dos estudios **KN 590** y **Checkmate 648** han supuesto un cambio de paradigma en población “global” positiva para PD-L1

Pembrolizumab plus chemotherapy versus chemotherapy as first-line therapy in patients with advanced esophageal cancer: The phase 3 KEYNOTE-590 study

HITOS
LO MEJOR
DE
2023

ADC o SCC localmente avanzados

IRRESECATABLE o M1 Sw I

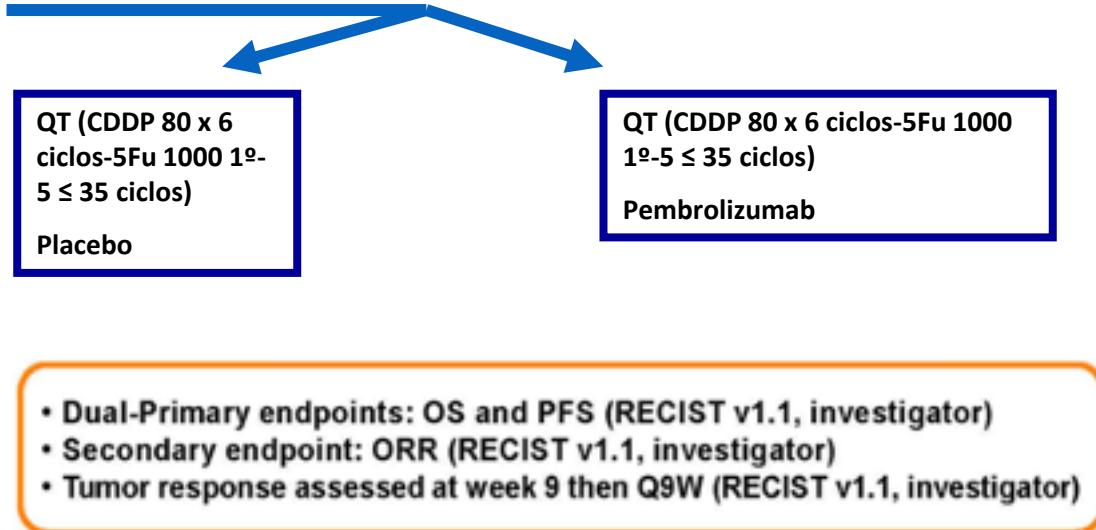
- LA, 7%
- IV, 93%
- ADC , 27%
- SCC, 73%

Naives de tto (52% Asiáticos)

ECOG 0-1

Enfermedad medible

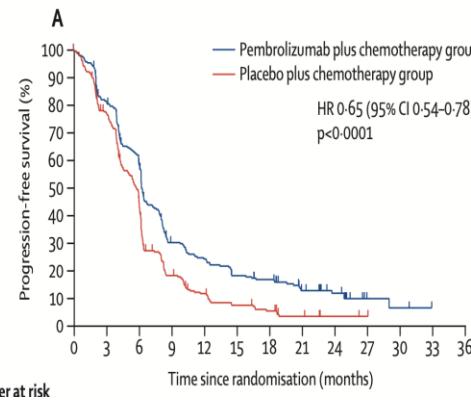
Independencia expresión de PD-L1
(CPS ≥10: 49%)



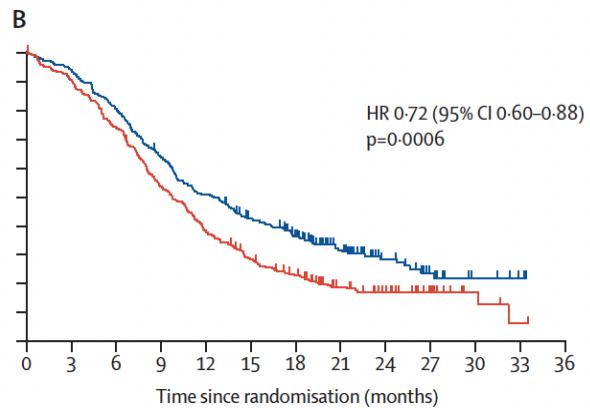
73% SCC y 52% Asiáticos
49% CPS≥10

Hay un mayor beneficio de la combinación Pembrolizumab/QT en Escamosos y CPS ≥10

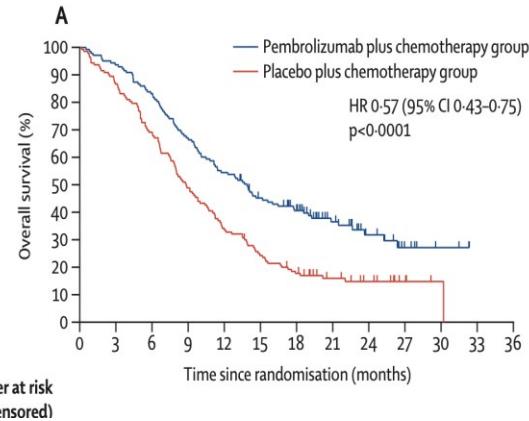
SLP Escamoso
6.3 vs 5.8 ms
(n:548, 73%)



SG Escamoso
12.6 vs 9.8 ms
(n:548, 73%)



SG Escamoso CPS ≥10
13.9 vs 8.8 ms
(n:286, 38%)



Significativo en todos obj.2º, destacando:

TR (todos) 45% vs 29.3% (p<0.001)

SG (todos) 12.4 ms vs 9.8 ms

SG CPS ≥10 (n:383, 51% muestra): 13.5 vs 9.4 ms



Checkmate 648. Nivolumab Combination Therapy in Advanced Esophageal Squamous-Cell Carcinoma

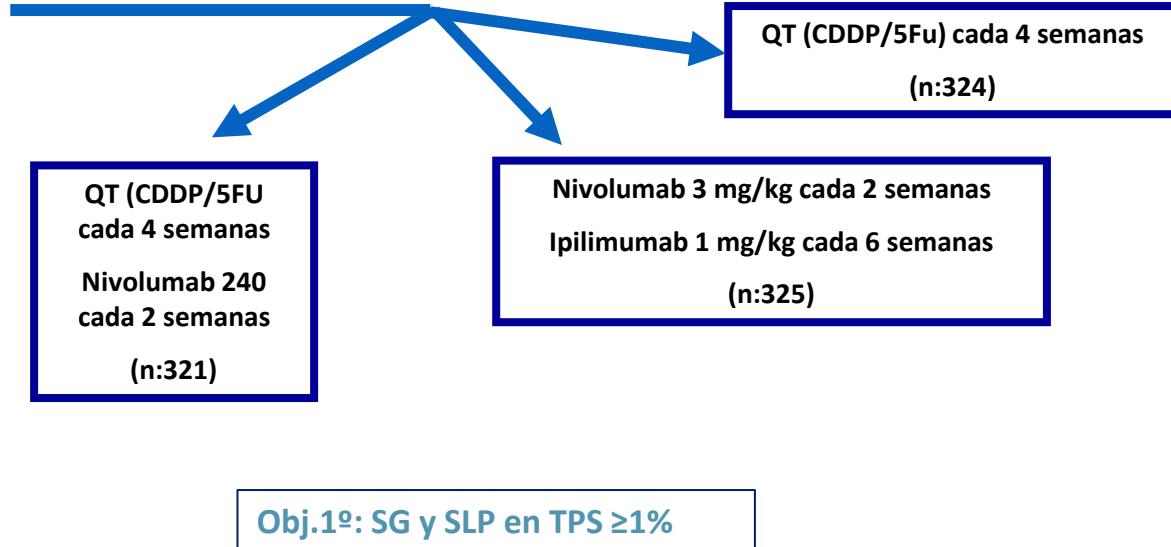
18^{as} Jornadas HITOS
ONCOLÓGICOS: LO MEJOR DE 2023

SCC localmente avanzados
IRRESECABLE o M1 Sw I
- Irresecables, 14%

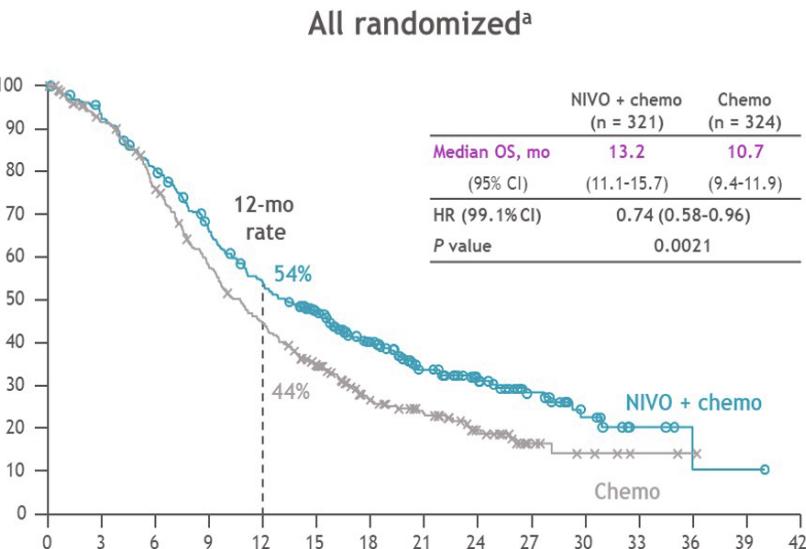
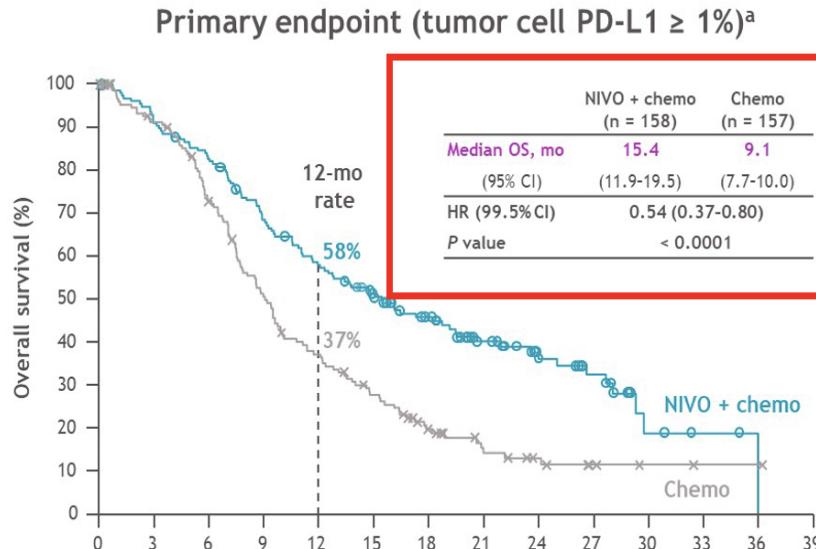
Naives de tto (70% Asiáticos)

ECOG 0-1

Enfermedad medible
Independencia de TPS



1.Brazo de Nivo/QT vs QT positivo en TPS≥1 %y en todos



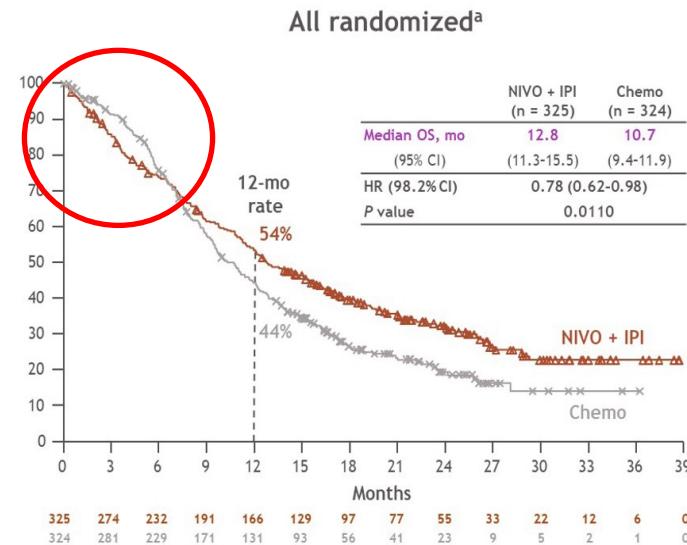
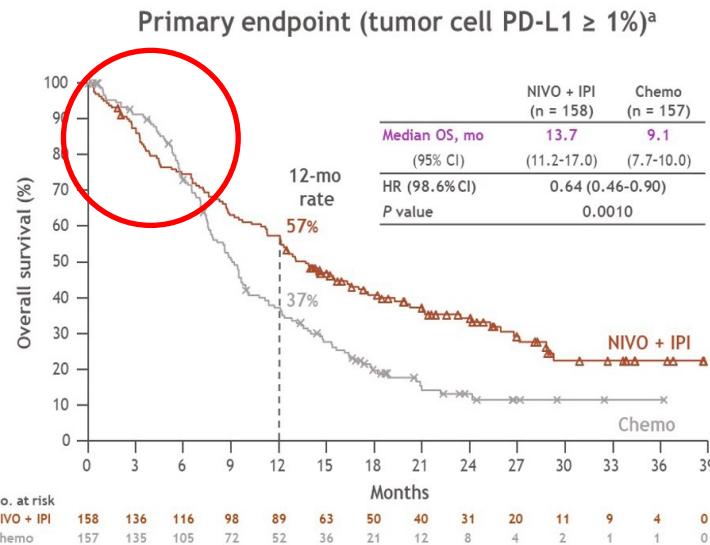
También beneficio en SLP

- TPS≥1% 6.9 vs 4.4 ms (p:0.0023)
- Todos 5.8vs 5.6 ms (p:0.0355)

Más respuesta

- RR 53% vs 20% en TPS≥1%
- RR 47 vs 27% en todos

2. Brazo de Nivo/ipilimumab superior a QT en TPS $\geq 1\%$ y en todos



La SLP no es significativa ni en TPS $\geq 1\%$ ni en toda la población

ESCENARIO METASTÁSICO

2. La IO había demostrado beneficio en
2L

CONCLUSIONES

ADENOCARCINOMA GÁSTRICO

1. ESCENARIO PERIOPERATORIO (**inmunoterapia**)

- La IO asociada a QT aumenta pRC
- La IO adyuvante no aumenta la SLR frente a QT

2. ESCENARIO METASTÁSICO: **Enfermedad Heterogénea a nivel molecular**

Primera Línea

- CPS define subgrupos de pacientes candidatos a IO
- Nuevo estándar en Her 2 , CPS 1:TOGA+Pembrolizumab
- Claudina 18.2 biomarcador predictivo respuesta a zolbetuzimab

Segunda Línea

- Dos subgrupos Her 2 y MSI-H candidatos a ttos dirigidos (trastuzumab deruxtecan y pembrolizumab)

CONCLUSIONES

CÁNCER ESCAMOSO DE ESÓFAGO

1. ESCENARIO METASTÁSICO:

CPS \geq 10 (pembrolizumab) y TPS >1% (nivolumab) definen beneficios en 1L a IO en 1L

Muchas gracias!!!!