VIII SIMPOSIO NACIONAL
de ONCOLOGÍA de PRECISIÓN
Vigo, 19 y 20 de febrero de 2026

Cáncer de origen digestivo no-colorrectal

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Hospital La Paz Institute for Health Research

AGENDA

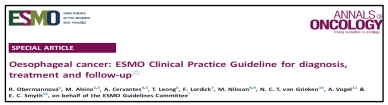
- ✓ Gastroesophageal Cancer
- ✓ Pancreatic Cancer
- ✓ Billiary Tract Carcinoma
- ✓ Hepatocellular Carcinoma

AGENDA

- ✓ **Gastroesophageal Cancer**
- ✓ Pancreatic Cancer
- ✓ Billiary Tract Carcinoma
- ✓ Hepatocellular carcinoma

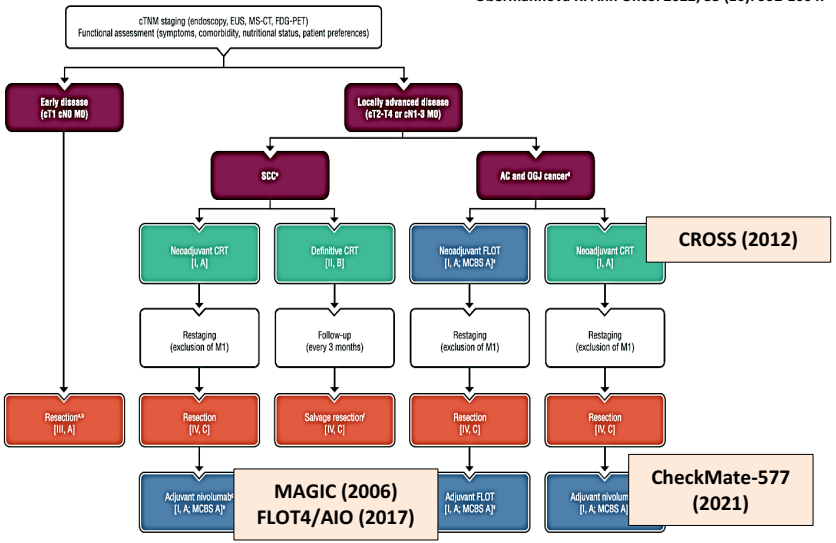
RESECTABLE GASTROESOPHAGEAL ADENOCARCINOMA: NEW STANDARD OF CARE

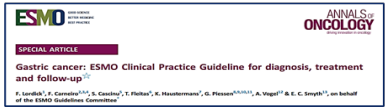
- ## Clinical practice guidelines as of early 2024



- Curative treatment should include surgery.
- Any tumor>T1 requires systemic therapy in addition to surgery:
  1. Perioperative CT [IA].
  2. Neoadjuvant CRT [IA] → Adjuvant nivolumab in non-pCR [IA].

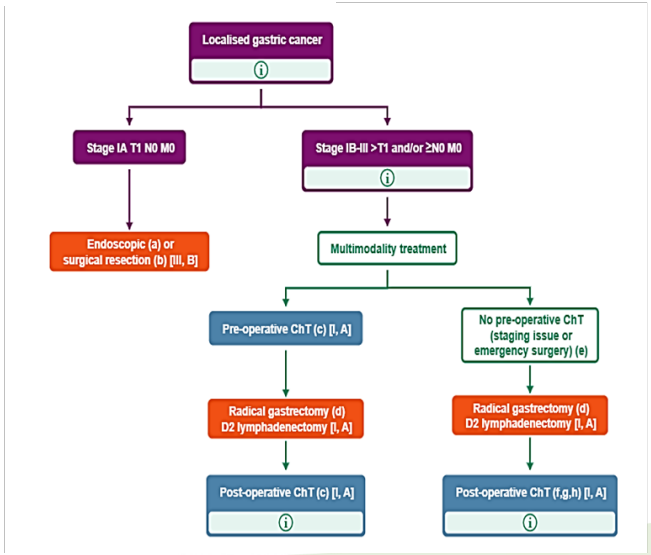
Obermannová R. Ann Oncol 2022; 33 (10): 992-1004.





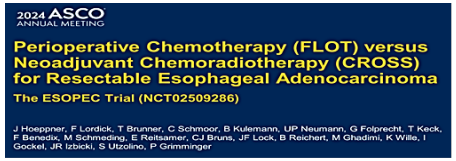
- Any tumor>T1 requires systemic therapy in addition to surgery:
  1. Perioperative CT [IA] (preffered)
  2. Adjuvant CT [IA]

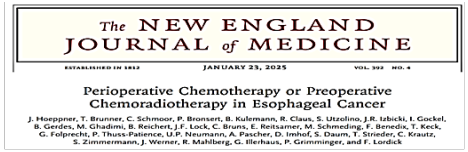
Lordick F. Ann Oncol 2022; 33 (10): 1005-1020..

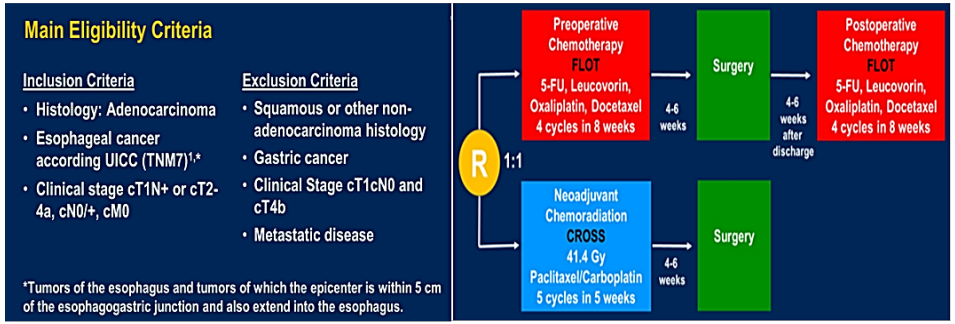


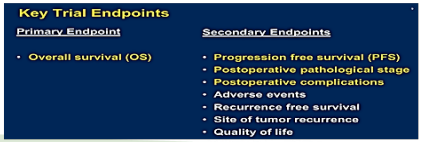
RESECTABLE GASTROESOPHAGEAL ADENOCARCINOMA: NEW STANDARD OF CARE

- **ESOPEC trial: Perioperative FLOT compared with neoadjuvant CRT improves survival among resectable esophageal/GEJ AC patients**









Hoeppner J. NEJM 2025; 392 (4): 23-35.

Baseline characteristics-ITT population

Characteristic	FLOT (N=221)	Preoperative Chemoradiotherapy (N=217)
Median age (range) — yr	63 (37–86)	63 (30–80)
Sex — no. (%)		
Male	197 (89.1)	194 (89.4)
Female	24 (10.9)	23 (10.6)
ECOG performance-status score — no. (%)†		
0	162 (73.3)	156 (71.9)
1	54 (24.3)	59 (27.2)
2	5 (2.3)	2 (0.9)
Clinical tumor stage — no./total no. (%)‡		
cT1	3/220 (1.4)	4/216 (1.9)
cT2	40/220 (18.2)	33/216 (15.3)
cT3	155/220 (70.5)	167/216 (77.3)
cT4	19/220 (8.6)	10/216 (4.6)
cTx	3/220 (1.4)	2/216 (0.9)
Clinical lymph-node stage — no. (%)§		
cN0	49 (22.2)	40 (18.4)
cN+	172 (77.8)	177 (81.6)
Tumor location before therapy — no./total no. (%)¶		
Esophagus, Siewert type I, or both	98/215 (45.6)	97/212 (45.8)
Siewert type II	70/215 (32.6)	62/212 (29.2)
Siewert type III	5/215 (2.3)	5/212 (2.4)
Not classifiable	42/215 (19.5)	48/212 (22.6)

RESECTABLE GASTROESOPHAGEAL ADENOCARCINOMA: NEW STANDARD OF CARE

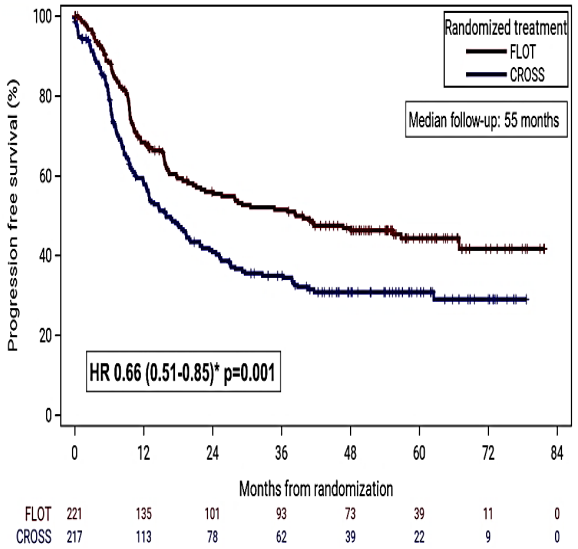
Pathology results-Surgery population

	FLOT Group	CROSS Group
N	191	180
Resection status		
No resection	0.5%	1.1%
R0	94.2%	95.0%
R1	5.2%	3.9%
Postoperative N-Stage		
ypN-	50.8%	54.4%
ypN+	48.7%	44.4%
Pathological complete remission		
ypT0 ypN0	16.8%	10.0%
Tumor regression grade (Becker[1])		
Complete regression	18.3%	13.3%
Near complete regression (<10% vital tumor)	25.1%	39.4%

per local pathology assessment

- **pCR: 16.8% (FLOT) vs. 10.0% (CROSS)**

Progression-free survival



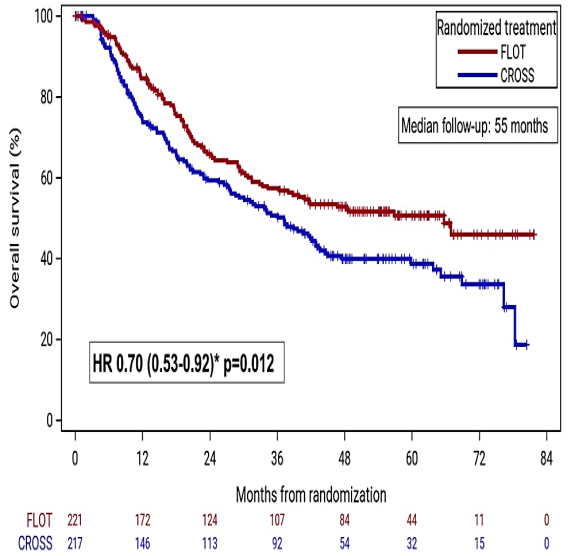
	FLOT	CROSS
Events	107	137
Median PFS time (months)	38 95% CI 21 – n.e.	16 95% CI 12 – 22
3-year PFS rate	51.6%	35.0%
5-year PFS rate	44.4%	30.9%

- **Clear PFS benefit in favor of perioperative CT compared with neoadyuvant CRT**

Hoeppner J. NEJM 2025; 392 (4): 23-35.

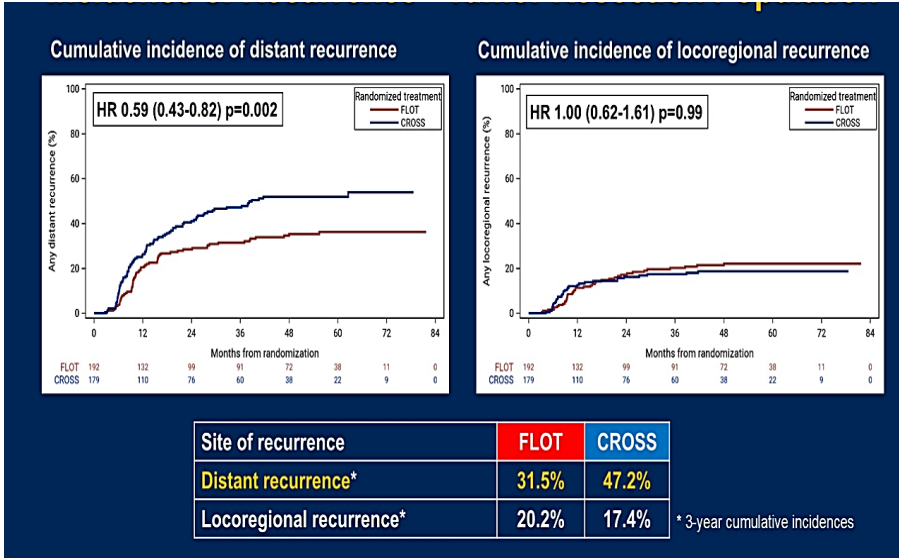
RESECTABLE GASTROESOPHAGEAL ADENOCARCINOMA: NEW STANDARD OF CARE

Overall survival



	FLOT	CROSS
Events	92	110
Median OS time (months)	66 95% CI 38 – n.e	39 95% CI 29 – 45
3-year OS rate	58.1%	52.6%
5-year OS rate	51.8%	40.5%

Incidence of recurrence-Tumor resection population



Site of recurrence	FLOT	CROSS
Distant recurrence*	31.5%	47.2%
Locoregional recurrence*	20.2%	17.4%

* 3-year cumulative incidences

- **Clear OS benefit in favor of perioperative CT compared with neoadyuvant CRT**
- **FLOT improves OS through a significant reduction in distant recurrence compared to CROSS**

Hoeppner J. NEJM 2025; 392 (4): 23-35.

RESECTABLE GASTROESOPHAGEAL ADENOCARCINOMA: NEW STANDARD OF CARE

- **MATTERHORN: DURVALUMAB with FLOT significantly improved EFS and OS vs. FLOT alone in resectable gastric/GEJ adenocarcinoma**

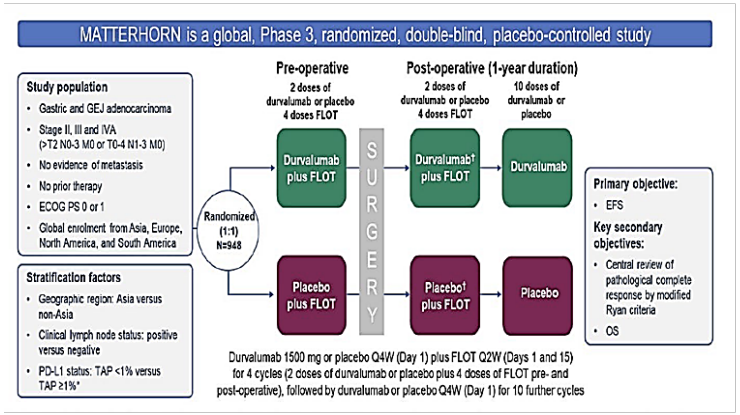
ORIGINAL ARTICLE

Perioperative Durvalumab in Gastric and Gastroesophageal Junction Cancer

Y.Y. Janjigian,[1] S.-E. Al-Batran,[2] Z.A. Wainberg,[3] K. Muro,[4] D. Molena,[5] E. Van Cutsem,[6] W.J. Hyung,[7] L. Wyrwicz,[8] D.-Y. Oh,[9] T. Omori,[10] M. Moehler,[11] M. Garrido,[12] S.C.S. Oliveira,[13] M. Liberman,[14] V.C. Oliden,[15] E.C. Smyth,[16] A. Stein,[17] M. Bilici,[18] M.L. Alvarenga,[19] V. Kozlov,[20] F. Rivera,[21] A. Kawazoe,[22] O. Serrano,[23] E. Heilbron,[24] A. Negro,[24] J.F. Kurland,[24] and J. Tabernero,[25] for the MATTERHORN Investigators*

BREAKING NEWS

2025 ASCO ANNUAL MEETING



Janjigian YY. N Engl J Med 2025; 393 (3): 217-230.

Baseline Characteristics

Balanced in both arms

		Durvalumab + FLOT (n=474)*	Placebo + FLOT (n=474)*
Age, years	Median (range)	62 (26–84)	63 (28–83)
Sex, %	Male	69	75
Geographic region, %	Non-Asia	81	81
	Asia	**19**	**19**
ECOG PS, %	0 (normal activity)	71	77
	1 (restricted activity)	29	23
Site of tumor, %	Gastric	68	67
	GEJ	**32**	**33**
Primary tumor stage, %	**T4**	**25**	**25**
	Non-T4	75	75
Clinical lymph node status, %†	**N+**	**69**	**70**
PD-L1 expression by TAP, %‡	<1%	10	10
	≥1%	90	90
Histology type (investigator assessed), %	Intestinal	52	50
	Diffuse	27	25
	Unspecified adenocarcinoma or mixed / other	21	25
MSI status, %§	**MSI-high**	**5**	**5**
	Not-MSI-high	64	65
	Not evaluable / missing	31	30

Treatment Delivery

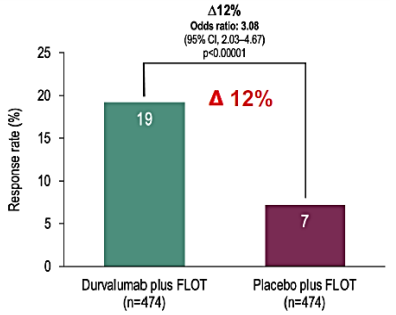
Similar in both arms; durvalumab did not affect FLOT administration

	Durvalumab + FLOT (n=475)*		Placebo + FLOT (n=469)*	
	Durvalumab	FLOT	Placebo	FLOT
Median number of neoadjuvant cycles	2.0	2.0	2.0	2.0
Median number of adjuvant cycles†	12.0	2.0	12.0	2.0
Number of neoadjuvant cycles of durvalumab or placebo + FLOT (Days 1 and 15), %				
≥1	100	100	100	100
=2	97	97	96	96
Number of adjuvant cycles of durvalumab or placebo ± FLOT (Days 1 and 15 for first 2 cycles), %				
≥1	76	75	74	74
≥2 (2 cycles for FLOT)	73	67	72	68
≥3‡	72	-	71	-
=12	52	-	51	-

RESECTABLE GASTROESOPHAGEAL ADENOCARCINOMA: NEW STANDARD OF CARE

Pathological response

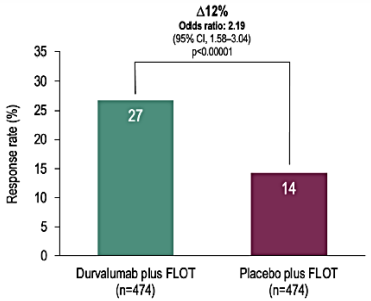
Pathological complete response



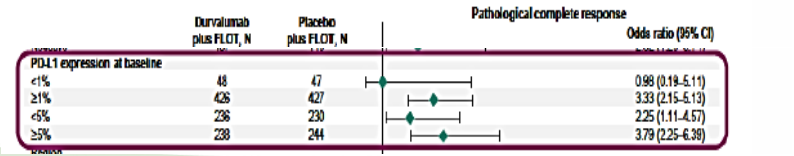
Control arm

Lower pCR than in pivotal studies (15% in FLOT-4)

Combined complete and near-complete pathological response

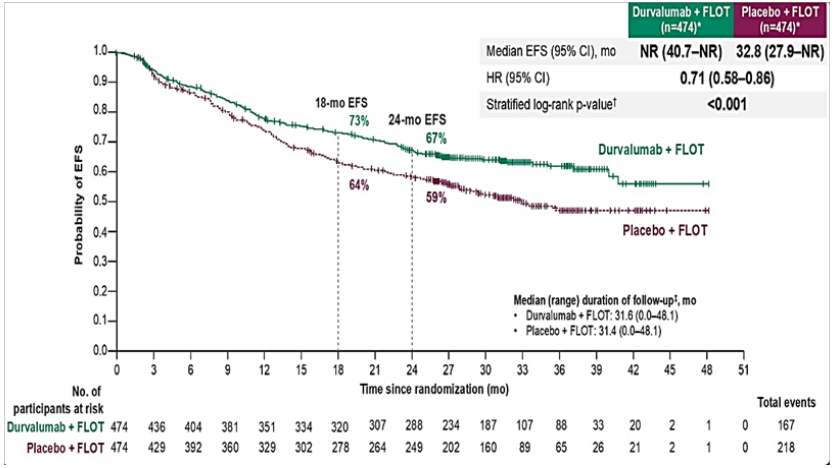


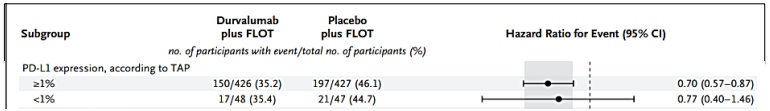
**Near-complete pathological response = single cells or rare small groups of cancer cells at the time of resection.



Primary endpoint: Event free survival (EFS)

A statistically significant improvement in EFS was observed with durvalumab with FLOT vs. placebo with FLOT



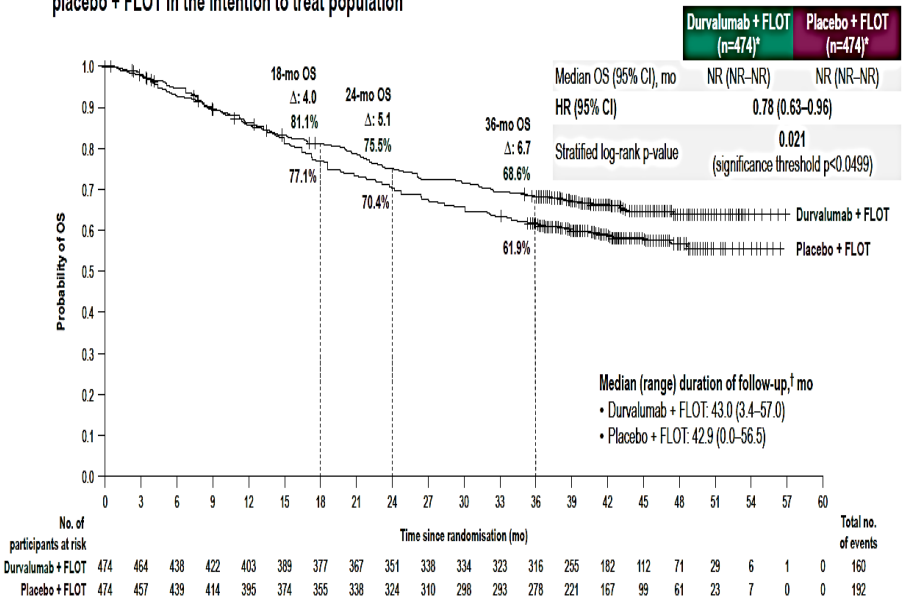


Janjigian YY. N Engl J Med 2025; 393 (3): 217-230.

RESECTABLE GASTROESOPHAGEAL ADENOCARCINOMA: NEW STANDARD OF CARE

Final overall survival

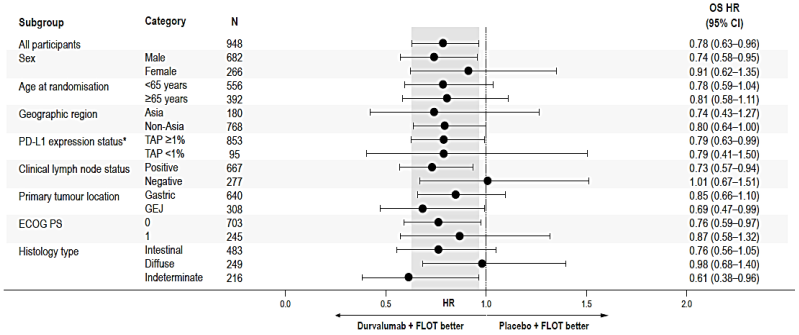
Durvalumab + FLOT demonstrated a statistically significant and clinically meaningful improvement in OS versus placebo + FLOT in the intention to treat population



Janjigian YY. N Engl J Med 2025; 393 (3): 217-230. Tabernero J. ESMO 2025.

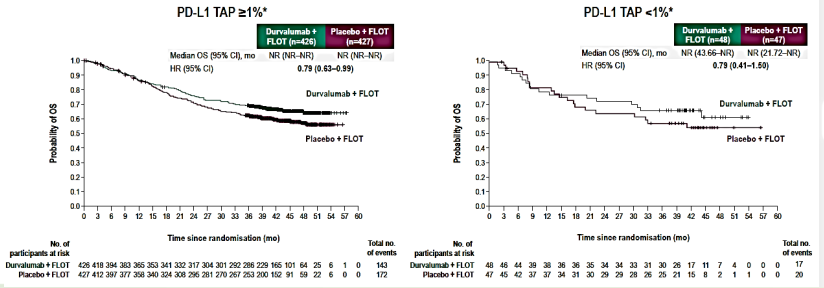
OS in key subgroups

A consistent benefit in OS was observed with durvalumab + FLOT versus placebo + FLOT in most key subgroups



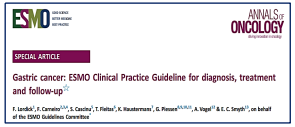
OS by PD-L1 status

OS was improved with durvalumab + FLOT versus placebo + FLOT regardless of PD-L1 status

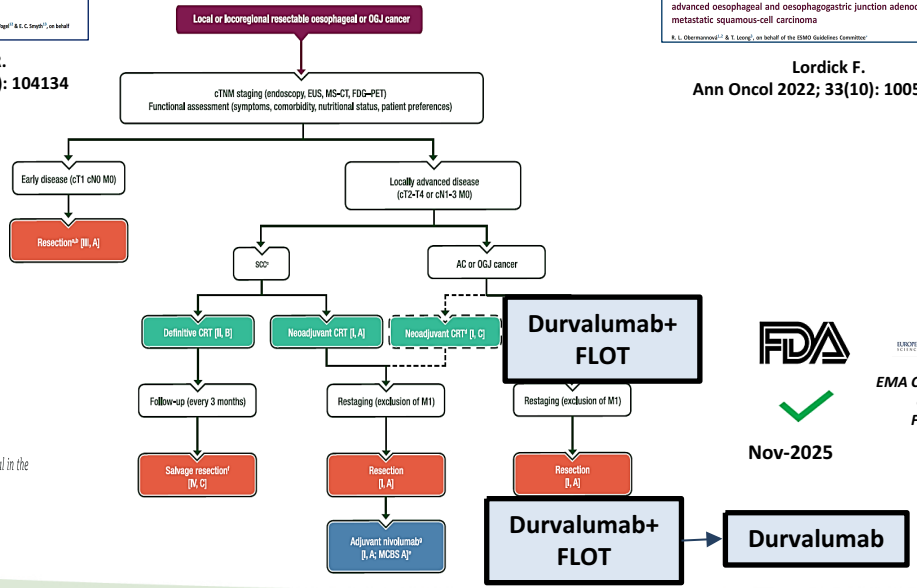


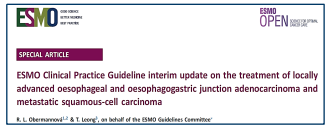
RESECTABLE GASTROESOPHAGEAL ADENOCARCINOMA: NEW STANDARD OF CARE

MATTERHORN supports global adoption of perioperative durvalumab with FLOT as a new standard for patients with localized gastric and gastroesophageal adenocarcinoma

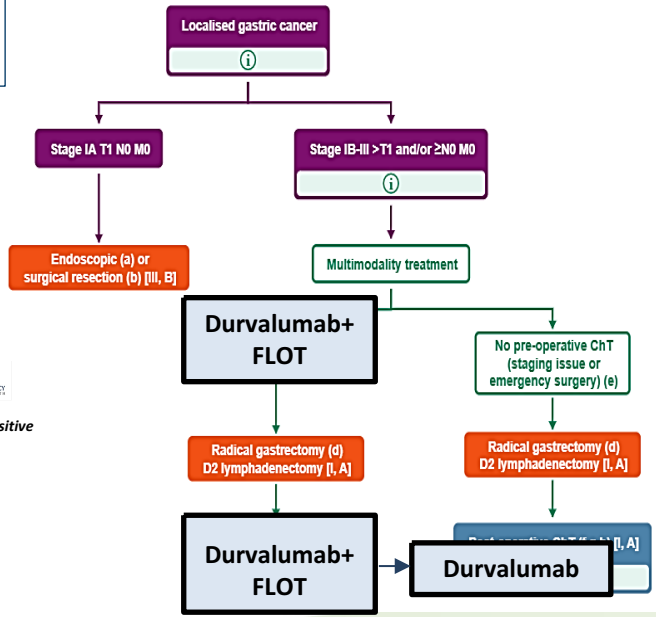


Obermannová R.
ESMO Open 2025; 10 (2): 104134





Lordick F.
Ann Oncol 2022; 33(10): 1005-1020



FDA

Nov-2025

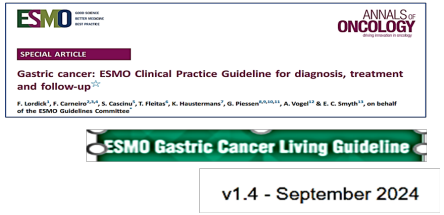
EUROPEAN MEDICINES AGENCY

EMA CHMP positive opinion Feb-2026

Imfinzi perioperative regimen recommended for approval in the EU by CHMP for patients with early gastric and gastroesophageal cancers

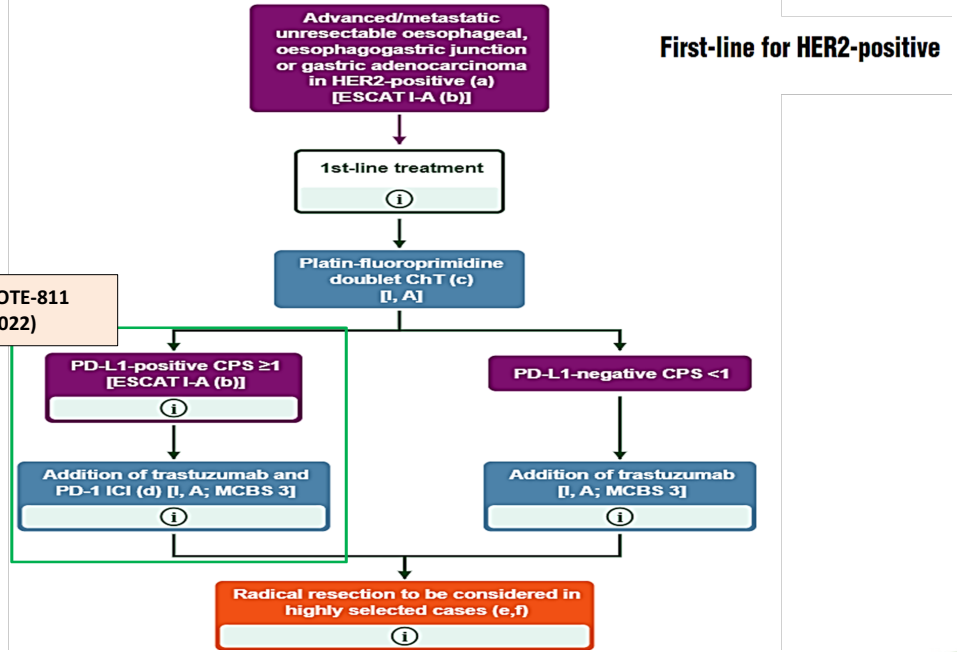
TREATMENT STRATEGIES IN HER2-POSITIVE ADVANCED GASTROESOPHAGEAL ADENOCARCINOMA

- **Clinical practice guidelines: FIRST-LINE therapy in HER2+ disease**



KEYTRUDA, en combinación con trastuzumab, y quimioterapia basada en fluoropirimidina y platino, está indicado para el tratamiento de primera línea del adenocarcinoma gástrico o de la unión gastroesofágica HER-2 positivo localmente avanzado irresecable o metastásico en adultos cuyos tumores expresen PD-L1 con una CPS mayor o igual a 1.	Resuelto	No incluida

KEYNOTE-811 (2022)



Lordick F. Ann Oncol 2022; 33 (10): 1005-1020.

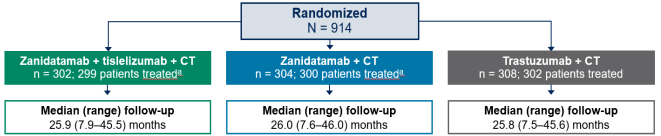
TREATMENT STRATEGIES IN HER2-POSITIVE ADVANCED GASTROESOPHAGEAL ADENOCARCINOMA

- **HERIZON-GEA-01: FIRST-LINE ZANIDATAMAB+/- TISLELIZUMAB +CT significantly improved PFS and OS in advanced gastric/GEJ adenocarcinoma.**

Zanidatamab + chemotherapy ± tislelizumab for first-line HER2-positive locally advanced, unresectable, or metastatic gastroesophageal adenocarcinoma: Primary analysis from HERIZON-GEA-01

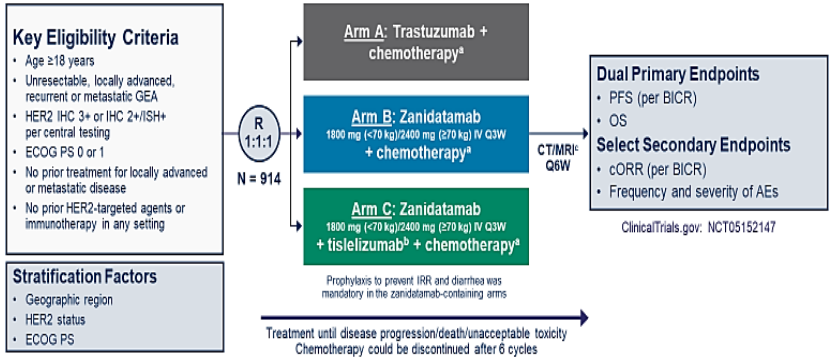
Patient Disposition

A total of 914 patients were randomized, and median follow-up was >2 years



HERIZON-GEA-01 Study Design

Global phase 3 trial of zanidatamab + chemotherapy ± tislelizumab vs trastuzumab + chemotherapy in previously untreated patients with HER2+ mGEA



Baseline Demographics and Disease Characteristics

Demographics and clinical characteristics were balanced across all 3 treatment arms

	Zanidatamab + tislelizumab + CT (n = 302)	Zanidatamab + CT (n = 304)	Trastuzumab + CT (n = 308)
Age, median (range), years	63.0 (22–81)	62.5 (25–87)	64.0 (21–84)
Male sex	244 (80.8)	244 (80.3)	238 (77.3)
Geographic region			
Asia	159 (52.6)	163 (53.6)	165 (53.6)
EU/North America	95 (31.5)	91 (29.9)	93 (30.2)
Rest of the world	48 (15.9)	50 (16.4)	50 (16.2)
ECOG PS[a]			
0	121 (40.1)	134 (44.1)	120 (39.0)
1	180 (59.6)	170 (55.9)	188 (61.0)
Disease status			
Metastatic	284 (94.0)	295 (97.0)	299 (97.1)
Unresectable locally advanced	18 (6.0)	9 (3.0)	9 (2.9)

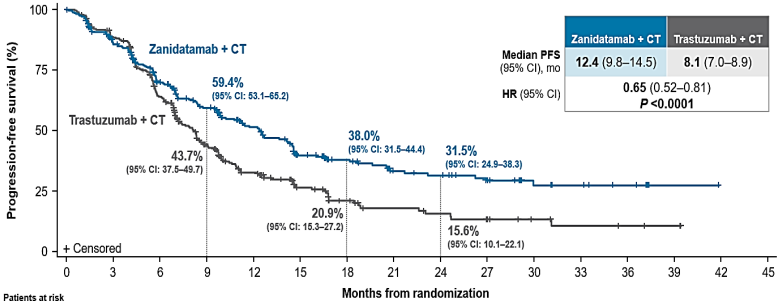
	Zanidatamab + tislelizumab + CT (n = 302)	Zanidatamab + CT (n = 304)	Trastuzumab + CT (n = 308)
Anatomical subtype			
Gastric	208 (68.9)	204 (67.1)	226 (73.4)
GEJ	74 (24.5)	61 (20.1)	60 (19.5)
Esophageal	20 (6.6)	39 (12.8)	22 (7.1)
HER2 IHC 3+	251 (83.1)	251 (82.6)	255 (82.8)
PD-L1 status[b]			
TAP score <1%	90 (29.8)	108 (35.5)	98 (31.8)
TAP score ≥1%	187 (61.9)	178 (58.6)	188 (61.0)
Choice of chemotherapy backbone			
CAPOX	273 (90.4)	276 (90.8)	282 (91.6)
FP	29 (9.6)	28 (9.2)	26 (8.4)

Elimova E. J Clin Oncol 44, 2026 (suppl 2; abstr LBA285)

TREATMENT STRATEGIES IN HER2-POSITIVE ADVANCED GASTROESOPHAGEAL ADENOCARCINOMA

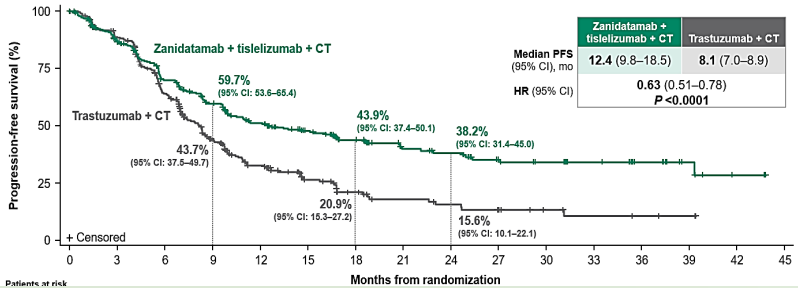
Primary Endpoint: PFS per BICR

Statistically significant and clinically meaningful improvement in PFS with zanidatamab + CT vs trastuzumab + CT (>4-month prolongation in median PFS)



	Zanidatamab + CT	Trastuzumab + CT
Median PFS (95% CI), mo	12.4 (9.8–14.5)	8.1 (7.0–8.9)
HR (95% CI)	0.65 (0.52–0.81)	
	P <0.0001	

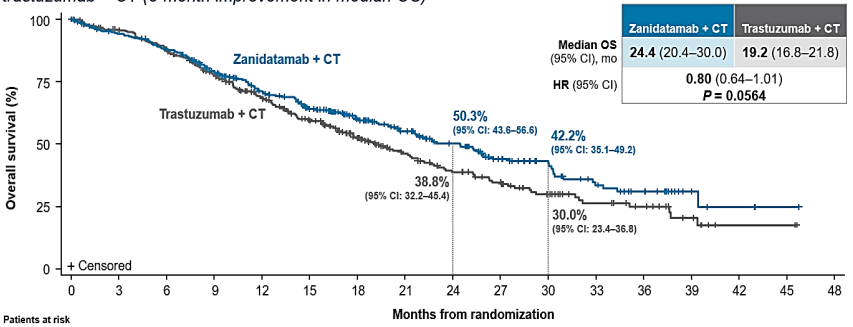
Statistically significant and clinically meaningful improvement in PFS with zanidatamab + tislelizumab + CT vs trastuzumab + CT (>4-month prolongation in median PFS)



	Zanidatamab + tislelizumab + CT	Trastuzumab + CT
Median PFS (95% CI), mo	12.4 (9.8–18.5)	8.1 (7.0–8.9)
HR (95% CI)	0.63 (0.51–0.78)	
	P <0.0001	

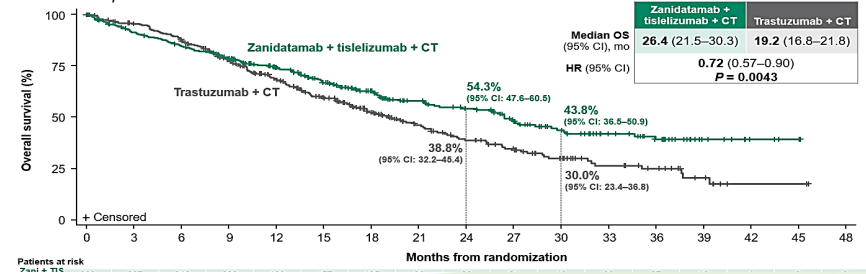
Primary Endpoint: Overall survival

At this interim analysis, there was a strong trend toward significance for OS favoring zanidatamab + CT vs trastuzumab + CT (5-month improvement in median OS)



	Zanidatamab + CT	Trastuzumab + CT
Median OS (95% CI), mo	24.4 (20.4–30.0)	19.2 (16.8–21.8)
HR (95% CI)	0.80 (0.64–1.01)	
	P = 0.0564	

Zanidatamab + tislelizumab + CT demonstrated a statistically significant and clinically meaningful OS benefit with a >7-month improvement in median OS vs trastuzumab + CT



	Zanidatamab + tislelizumab + CT	Trastuzumab + CT
Median OS (95% CI), mo	26.4 (21.5–30.3)	19.2 (16.8–21.8)
HR (95% CI)	0.72 (0.57–0.90)	
	P = 0.0043	

Elimova E. J Clin Oncol 44, 2026 (suppl 2; abstr LBA285)

TREATMENT STRATEGIES IN HER2-POSITIVE ADVANCED GASTROESOPHAGEAL ADENOCARCINOMA

- **DESTINY-Gastric04: TRASTUZUMAB DERUXTECAN significantly improved OS in SECOND-LINE treatment of HER2+ advanced gastric/GEJ adenocarcinoma.**

ORIGINAL ARTICLE

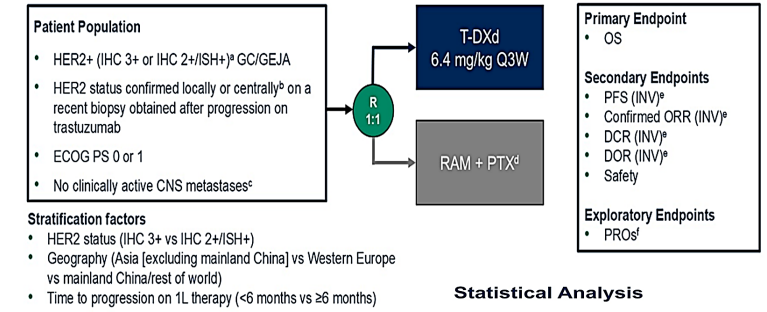
Trastuzumab Deruxtecan or Ramucirumab plus Paclitaxel in Gastric Cancer

K. Shitara,[1] E. Van Cutsem,[2,3] M. Gümüş,[4,5] S. Lonardi,[6] C. de la Fouchardière,[7] C. Coutzac,[7] J. Dekervel,[2,3] D. Hochhauser,[8] L. Shen,[9,10] W. Mansoor,[11] B. Liu,[12] L. Fornaro,[13] M.-H. Ryu,[14,15] J. Lee,[16] C. Faustino,[17] J.-P. Metges,[18] J. Tabernero,[19,20] F. Franke,[21] Y.Y. Janjigian,[22] F. Souza,[23] L. Jukofsky,[23] Y. Zhao,[23] T. Kamio,[23] A. Zaanan,[24,25] and F. Pietrantonio,[26] for the DESTINY-Gastric04 Trial Investigators*

BREAKING NEWS

2025 ASCO ANNUAL MEETING

DESTINY-Gastric04: A Global, Multicenter, Randomized, Phase 3 Trial (NCT04704934)



Statistical Analysis

Planned sample size: 490

- 339 OS events were needed to ensure 90% power to detect an OS hazard ratio of 0.70 (overall 2-sided α error of 5%*)

Interim OS analysis (planned after enrollment completion and 237 OS events [~70%*])

Shitara K, et al.
N Engl J Med 2025; 393 (4): 336-348.

Demographics and baseline characteristics

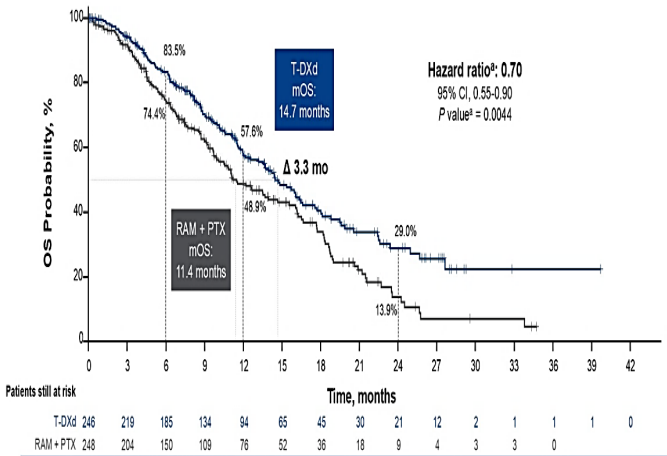
	T-DXd n = 246	RAM + PTX n = 248
Age, median (range), years	63.2 (21.1-84.1)	64.3 (31.9-87.0)
Male, n (%)	187 (76.0)	205 (82.7)
Geography,[a] n (%)		
Asia (excluding mainland China)	57 (23.2)	60 (24.2)
Western Europe	140 (56.9)	139 (56.0)
Mainland China/ROW	49 (19.9)	49 (19.8)
Race, n (%)		
White	116 (47.2)	130 (52.4)
Black/African American	0	2 (0.8)
Asian	101 (41.1)	97 (39.1)
Other	28 (11.4)	19 (7.7)
ECOG PS, n (%)		
0 | 1	97 (39.4) | 148 (60.2)	88 (35.5) | 158 (63.7)
2 | missing	1 (0.4) | 0	1 (0.4) | 1 (0.4)
Primary tumor location, n (%)		
Gastric	153 (62.2)	149 (60.1)
GEJ	93 (37.8)	99 (39.9)

	T-DXd n = 246	RAM + PTX n = 248
HER2 status,[a,b] n (%)		
IHC 2+/ISH+	39 (15.9)	40 (16.1)
IHC 3+	207 (84.1)	208 (83.9)
Time to progression on 1L therapy,[a] n (%)		
<6 months	61 (24.8)	61 (24.6)
≥6 months	185 (75.2)	187 (75.4)
Prior treatment with ICI, n (%)		
Yes	39 (15.9)	38 (15.3)
No	207 (84.1)	210 (84.7)
Metastatic sites, n (%)		
<2	73 (29.7)	75 (30.2)
≥2	173 (70.3)	173 (69.8)
Presence of liver metastases, n (%)	147 (59.8)	158 (63.7)
Presence of brain metastases, n (%)	16 (6.5)	18 (7.3)

1L, first-line; ECOG PS, Eastern Cooperative Oncology Group performance status; GEJ, gastroesophageal junction; HER2, human epidermal growth factor receptor 2; ICI, immune checkpoint inhibitor; IHC, immunohistochemistry; ISH, in si hybridization; PTX, paclitaxel; RAM, ramucirumab; ROW, rest of world; T-DXd, trastuzumab deruxtecan.
[a]Stratification factor by interactive response technology. [b]Local or central HER2 status.

TREATMENT STRATEGIES IN HER2-POSITIVE ADVANCED GASTROESOPHAGEAL ADENOCARCINOMA

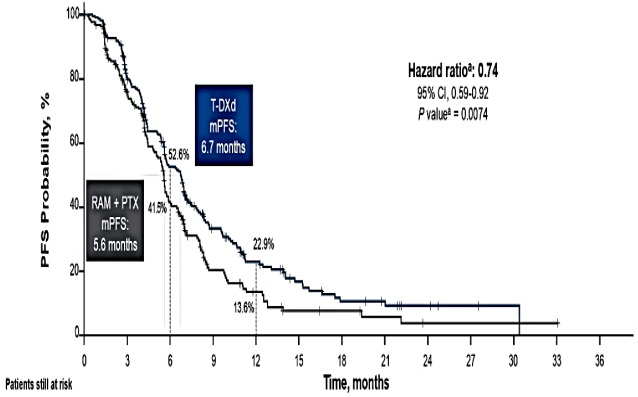
Primary endpoint: Overall Survival



T-DXd demonstrated a statistically significant and clinically meaningful improvement in OS compared with RAM + PTX in HER2+ GC/GEJA, showing a 30% reduction in risk of death

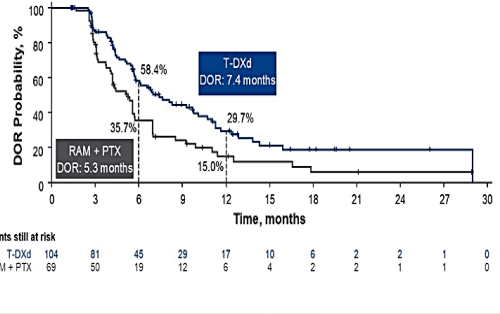
Shitara K, et al.
N Engl J Med 2025; 393 (4): 336-348.

PFS by investigator



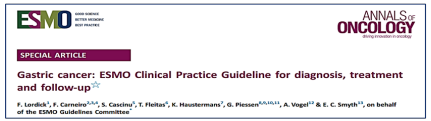
Confirmed ORR and duration of response

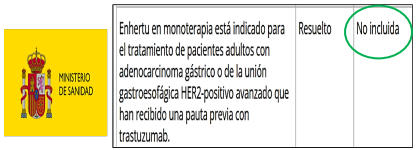
	T-DXd n = 246	RAM + PTX n = 248
Confirmed ORR (95% CI),[c] %	44.3 (37.8-50.9)	29.1 (23.4-35.3)
P value[d]	0.0006	
Difference (95% CI),[e] %	15.1 (6.1-24.2)	
DOR, median (95% CI), mo	7.4 (5.7-10.1)	5.3 (4.1-5.7)
DCR (95% CI), %	91.9 (87.7-95.1)	75.9 (70.0-81.2)
Confirmed BOR, n (%)		
CR[f]	7 (3.0)	3 (1.3)
PR	97 (41.3)	66 (27.8)
SD[g]	112 (47.7)	111 (46.8)
PD	13 (5.5)	22 (9.3)
NE	6 (2.6)	35 (14.8)



TREATMENT STRATEGIES IN HER2-POSITIVE ADVANCED GASTROESOPHAGEAL ADENOCARCINOMA

- ## Clinical practice guidelines: SECOND-LINE therapy in HER2+ disease





Lordick F. Ann Oncol 2022; 33 (10): 1005-1020.

AGENDA

- ✓ Gastroesophageal Cancer
- ✓ **Pancreatic Cancer**
- ✓ Billiary Tract Carcinoma
- ✓ Hepatocellular carcinoma

RESECTABLE/BORDERLINE RESECTABLE STAGE I-III PDAC

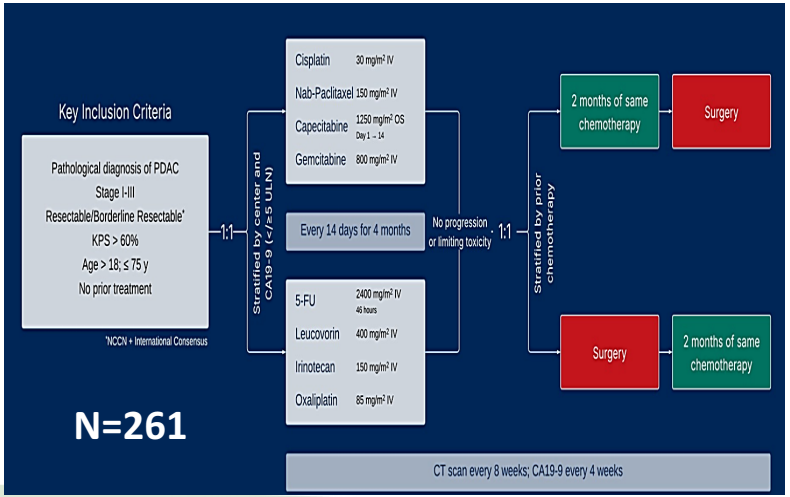
- **PACT-21 CASSANDRA: Neoadjuvant PAXG significantly prolongs EFS compared to mFOLFIRINOX in resectable and borderline resectable stage I-III PDAC.**

2025 ASCO ANNUAL MEETING

Results of a randomized phase 3 trial of pre-operative chemotherapy with mFOLFIRINOX or PAXG regimen for stage I-III pancreatic ductal adenocarcinoma CASSANDRA - PACT-21 trial

Reni M, Macchini M, Orsi G, Procaccio L, Mafese G, Balzano G, Rapposelli IG, Bercardino K, Scartozzi M, Carconi C, Tamburrino D, Merelli B, Sperti E, Belfiori G, Liscia N, Bozzarelli S, Di Marco M, Palumbo D, Torri V, Falconi M

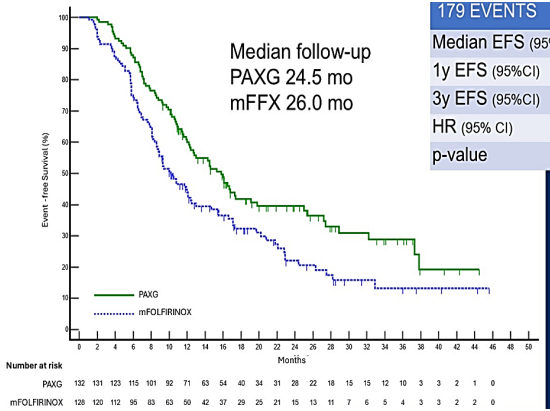
Preoperative mFOLFIRINOX versus PAXG for stage I–III resectable and borderline resectable pancreatic ductal adenocarcinoma (PACT-21 CASSANDRA): results of the first randomisation analysis of a randomised, open-label, 2 × 2 factorial phase 3 trial



Primary endpoint: Event-free Survival

PRIMARY ENDPOINT

EFS EVENT = RECIST 1.1 progression; recurrence; unresectability; intraop M+; CA19-9 failure (=2 consecutive increases ≥20%, separated by ≥4 w); death



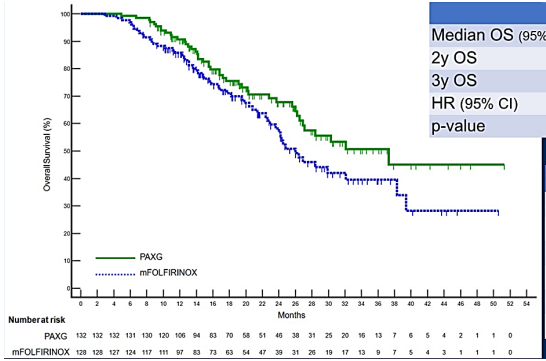
179 EVENTS	PAXG	mFFX
Median EFS (95%CI)	**16.0** (12.4-19.8)	**10.2** (8.7-13.0)
1y EFS (95%CI)	**61%** (56-65%)	**45%** (41-49%)
3y EFS (95%CI)	**31%** (25-36%)	**13%** (9-17%)
HR (95% CI)	**0.64** (0.48-0.86)	
p-value	**0.003**	

Type of event	PAXG	mFFX
Event-free	*38%*	*25%*
Progression	16%	20%
Unresectable	4%	2%
Recurrence	27%	31%
Intraop M+	3%	5%
CA19-9	9%	16%
Death	3%	2%

Reni M. Lancet 2026; 406(10522): 2945-2956.

RESECTABLE/BORDERLINE RESECTABLE STAGE I-III PDAC

Overall survival (immature data)



	PAXG	mFFX
Median OS (95%CI)	**37.3** (26.9-NR)	**26.0** (23.6-39.4)
2y OS	**68%** (63-73%)	**58%** (53-63%)
3y OS	**51%** (45-57%)	**40%** (34-46%)
HR (95% CI)	**0.70** (0.47-1.04)	
p-value	**0.07**	

Subsequent therapy	PAXG	mFFX
Any therapy (%)	*71 (87)*	*79 (81)*
Single agent	10 (12)	8 (8)
Nab-Gem based	32 (39)	57 (59)
(nal)iri-FU	20 (24)	5 (5)
Others	9 (11)	9 (10)
None	11 (13)	18 (19)

Secondary endpoints

	PAXG N= 132	mFFX N= 128	RRi	95% CI	p-value
RECIST best response PR / SD / PD %	46 / 52 / 2	39 / 52 / 9			
Disease Control Rate (PR + SD)	98%	91%	1.08	1.02-1.14	**0.01**
CA19-9 response ≥ 50%	88%	64%	1.38	1.15-1.65	**<0.001**
Resection rate	75%	67%	1.12	0.96-1.30	0.16
Pathological Complete Response	4 (3%)	0			**0.047**
No nodal involvement (N0)	36%	23%	1.57	1.06-2.33	**0.02**
R0	67 (51%)	66 (52%)	1.06	0·83-1.35	0.63
Intra or postoperative metastases	6 (5%)	15 (12%)	1.07	1.01-1.14	**0.03**

Selected Adverse Events (AEs)

	PAXG (N= 132)		mFOLFIRINOX (N= 128)	
	Any Grade (%)	Grade 3-4 (%)	Any grade	Grade 3-4
Neutropenia	93 (70)	56 (42) *	71 (56)	37 (29) *
Thrombocytopenia	31 (24)	1 (1)	29 (23)	1 (1)
Anemia	45 (34)	3 (2)	30 (23)	0
Diarrhea	52 (39)	3 (2)	83 (65)	7 (6)
AST or ALT increased	11 (8)	4 (3)	31 (24)	10 (8)
Infusion related reaction	8 (6)	1 (1)	9 (7)	5 (4)
Hand-Foot Syndrome	52 (36)	5 (4)	2 (2)	0
Vomit	33 (25)	3 (2)	43 (34)	5 (4)
Fatigue	97 (73)	11 (8)	91 (71)	10 (8)
Nausea	82 (62)	6 (5)	98 (77)	8 (6)
Peripheral neuropathy	61 (46)	7 (5)	86 (68)	4 (3)
Paresthesia	33 (25)	3 (2)	48 (38)	1 (1)
Infection + sepsis	22 (15)	9 (7)	17 (13)	10 (8)°

- **Quality-of-life: No significant difference between groups at baseline and month 4.**

PAXG appears to be the most suitable option for neoadjuvant treatment of patients with R and BR stage I-III PDAC

Reni M. Lancet 2026; 406(10522): 2945-2956.

LOCALLY ADVANCED PDAC: TUMOR TREATMENT FIELDS (TTFIELDS)

- **PANOVA-3: TTFields with gemcitabine and nab-paclitaxel significantly improved OS in locally advanced pancreatic adenocarcinoma**

2025 ASCO ANNUAL MEETING

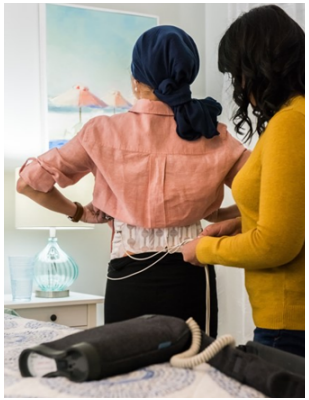
PANOVA-3: Phase 3 study of Tumor Treating Fields (TTFields) with gemcitabine and nab-paclitaxel (GnP) for locally advanced pancreatic adenocarcinoma (LA-PAC)

Vincent Picozzi, Hani Babiker, Sreenivasa Chandana, Bohuslav Melichar, Anup Kasi, Jin Gang, Javier Gallego, Andrea Bullock, Hao Chunyi, Lucjan Wyrwicz, Arsen Osipov, Christelle de la Fouchardiere, Tomislav Dragovich, Woojin Lee, Kynan Feeney, Philip A. Philip, Makoto Ueno, Eric Van Cutsem, Thomas Seufferlein, Teresa Macarulla on behalf of the PANOVA-3 study investigators

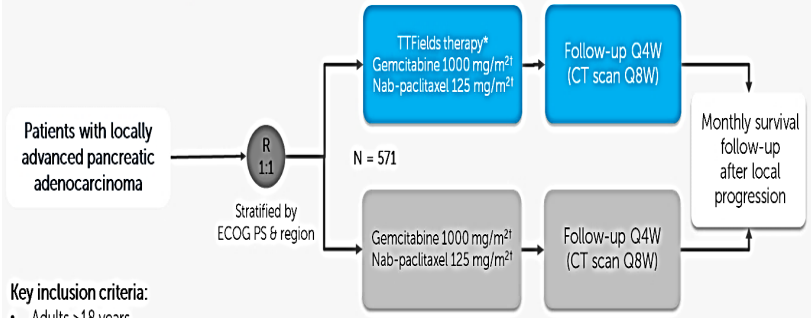
Tumor Treating Fields With Gemcitabine and Nab-Paclitaxel for Locally Advanced Pancreatic Adenocarcinoma: Randomized, Open-Label, Pivotal Phase III PANOVA-3 Study

Hani M. Babiker, MD[1]; Vincent Picozzi, MD[2]; Sreenivasa R. Chandana, MD, PhD[3]; Bohuslav Melichar, MD, PhD[4]; Anup Kasi, MD[5]; Jin Gang, MD[6]; Javier Gallego, MD[7]; Andrea Bullock, MD[8]; Hao Chunyi, MD[9]; Lucjan Wyrwicz, MD, PhD[10]; Erika Hitre, PhD[11]; Arsen Osipov, MD[12]; Christelle de la Fouchardiere, MD[13]; Inmaculada Ales, MD[14]; Tomislav Dragovich, MD, PhD[15]; Woojin Lee, MD, PhD[16]; Kynan Feeney, MD[17]; Philip Philip, MD, PhD[18]; Makoto Ueno, MD[19]; Eric Van Cutsem, MD, PhD[20]; Thomas Seufferlein, MD[21]; and Teresa Macarulla, MD, PhD[22]; on behalf of the PANOVA-3 Study Investigators

- TTFields are a locoregional therapy that use a portable device to administer alternating electric fields through 4 transducer arrays adhered to the skin.
- The goal is electric field delivery for 18 hours per day with array changes 2-3 times per week
- The mechanisms of action of TTFields appear to be diverse, with potential effects on cancer cell division, DNA damage response, and stimulation of anti-tumor immunity.



PANOVA-3 (NCT03377491) trial design



Key inclusion criteria:
- Adults ≥18 years
- Previously untreated, biopsy confirmed disease
- Life expectancy ≥3 months
- ECOG PS 0-2

Key exclusion criteria:
- Prior palliative treatment to the tumor
- Implanted electronic medical device in torso
- Known allergies to medical adhesives, hydrogel or chemotherapies

Study sites: 198 across 20 countries (North and South America, Europe, Asia)‡
Enrollment: March 2018 – March 2023
Data cut-off: October 16, 2024

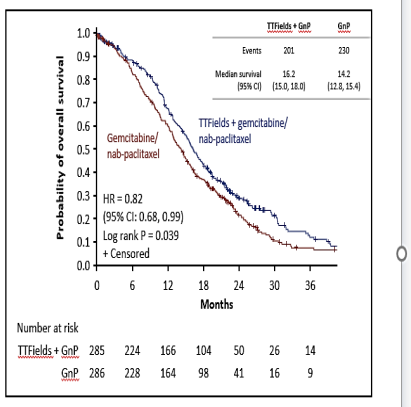
Primary Endpoint: OS
Secondary Endpoints: PFS, local PFS, ORR, 1y OS, QoL, pain-free survival§, puncture-free survival, resectability rate, adverse events

Babiker HM. J Clin Oncol 2025; 43 (21): 2350-2360.

LOCALLY ADVANCED PDAC: TUMOR TREATMENT FIELDS (TTFIELDS)

Primary endpoint: Overall Survival

Overall Survival ITT

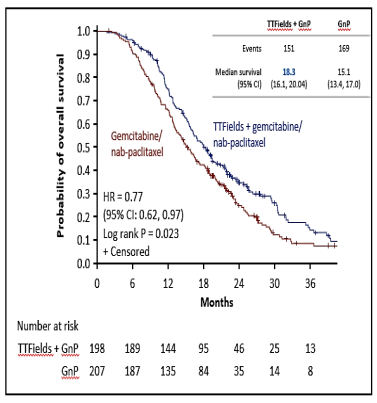


Overall Survival	TTFields + GnP	GnP	HR (95% CI)	P-Value
Median, months (95% CI)	16.20 (15.01–17.97)	14.16 (12.81–15.44)	0.819 (0.676–0.991)	0.039

OS Rate, % (95% CI)	TTFields + GnP	GnP	P-Value
12 Months	68.1 (62.0–73.5)	60.2 (54.2–65.7)	0.029
24 Months	29.2 (23.4–35.2)	21.9 (16.9–27.3)	0.035

Overall Survival mITT

(At least 28 days and 1 GnP cycle for the treatment arm and 1 GnP cycle for the control)

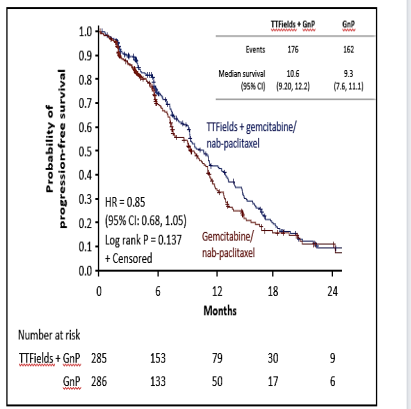


Overall Survival	TTFields + GnP	GnP	HR (95% CI)	P-Value
Median, months (95% CI)	18.3 (16.1, 20.04)	15.08 (13.40–17.02)	0.73 (0.623–0.972)	0.022

OS Rate, % (95% CI)	TTFields + GnP	GnP	P-Value
12 Months	75.2 (68.5–80.7)	65.9 (59.0–72.0)	0.023
24 Months	34.3 (27.4–41.3)	24.8 (18.8, –31.3)	0.024

Secondary endpoint: Progression-free survival

PFS ITT

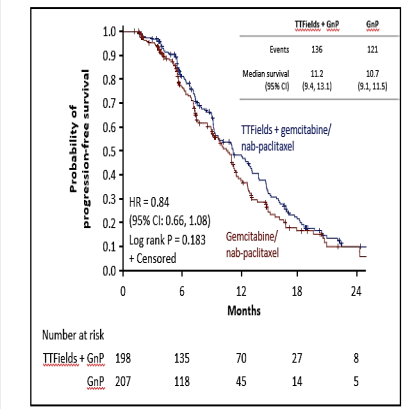


Progression-free Survival	TTFields + GnP	GnP	HR (95% CI)	P-Value*
Median, months (95% CI)	10.61 (9.199–12.19)	9.33 (7.589–11.07)	0.849 (0.683–1.054)	0.137

PFS Rate, % (95% CI)	TTFields + GnP	GnP	% Improv.	P-Value*
12 Months	43.9 (36.9–50.6)	34.1 (27.1–41.2)	28.8	0.026

PFS mITT

(At least 28 days and 1 GnP cycle for the treatment arm and 1 GnP cycle for the control)



Progression-free Survival	TTFields + GnP	GnP	HR (95% CI)	P-Value*
Median, months (95% CI)	11.24 (9.396–13.11)	10.71 (9.133–11.47)	0.844 (0.657–1.084)	0.183

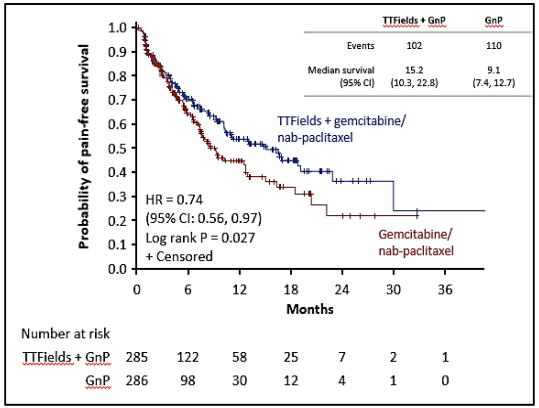
PFS Rate, % (95% CI)	TTFields + GnP	GnP	% Improv.	P-Value*
12 Months	48.5 (40.5–56.0)	38.7 (30.5–46.8)	25.4	0.044

Babiker HM. J Clin Oncol 2025; 43 (21): 2350-2360.

LOCALLY ADVANCED PDAC: TUMOR TREATMENT FIELDS (TTFIELDS)

Secondary endpoint: Pain-free survival

Pain-Free Survival ITT



Pain-Free Survival	TTFields + GnP	GnP	HR (95% CI)	P-Value
Median, months (95% CI)	15.18 (10.28–22.77)	9.133 (7.425–12.68)	0.735 (0.559–0.967)	0.027

Pain-Free Survival Rate, % (95% CI)	TTFields + GnP	GnP	P-Value
12 Months	54.1 (46.2–61.3)	45.1 (36.8–53.0)	0.056

Safety Summary

AEs occurring in ≥20% of patients overall, n (%)	TTFields + GnP (N=274)		GnP (N=273)	
	All grades	Grade ≥3	All grades	Grade ≥3
Any AE	268 (97.8)	243 (88.7)	270 (89.9)	230 (84.2)
Neutropenia	172 (62.8)	131 (47.8)	180 (65.9)	130 (47.6)
Fatigue	165 (60.2)	29 (10.6)	148 (54.2)	21 (7.7)
Anemia	161 (58.8)	60 (21.9)	158 (57.9)	61 (22.3)
Thrombocytopenia	122 (44.5)	39 (14.2)	133 (48.7)	32 (11.7)
Diarrhea	119 (43.4)	11 (4.0)	125 (45.8)	15 (5.5)
Neuropathy peripheral	112 (40.9)	20 (7.3)	81 (29.7)	18 (6.6)
Nausea	107 (39.1)	11 (4.0)	121 (44.3)	7 (2.6)
Edema peripheral	107 (39.1)	5 (1.8)	99 (36.3)	2 (0.7)
Leukopenia	85 (31.0)	47 (17.2)	98 (35.9)	42 (15.4)
Dermatitis	**82 (29.9)**	**8 (2.9)**	**8 (2.9)**	**0**
Vomiting	82 (29.9)	7 (2.6)	79 (28.9)	15 (5.5)
Hepatic enzyme increased	75 (27.4)	35 (12.8)	72 (26.4)	24 (8.8)
Pyrexia	74 (27.0)	6 (2.2)	64 (23.4)	2 (0.7)
Abdominal pain	73 (26.6)	11 (4.0)	83 (30.4)	12 (4.4)
Rash	**71 (25.9)**	**5 (1.8)**	**23 (8.4)**	**1 (0.4)**
Alopecia	71 (25.9)	0	86 (31.5)	2 (0.7)
Musculoskeletal pain	70 (25.5)	3 (1.3)	79 (28.9)	5 (1.8)
Constipation	65 (23.7)	1 (0.4)	57 (20.9)	0
Hypokalemia	63 (23.0)	12 (4.4)	70 (25.6)	20 (7.3)
Pruritus	**61 (22.3)**	**0**	**23 (8.4)**	**0**

Device-related AEs, n (%)	TTFields + GnP (N=274)	
	All grades	Grade ≥3
Any AE	222 (81.0)	26 (9.5)
Any serious AE	1 (0.4)	0
Any AE leading to TTFields discontinuation	23 (8.4)	7 (2.6)
Any AE leading to death	0	0
AEs occurring in ≥2% of patients		
Dermatitis	76 (27.7)	8 (2.9)
Rash	48 (17.5)	4 (1.5)
Pruritus	41 (15.0)	0
Rash maculo-papular	33 (12.0)	3 (1.1)
Erythema	29 (10.6)	0
Skin irritation	25 (9.1)	2 (0.7)
Skin reaction	17 (6.2)	1 (0.4)
Skin ulcer	14 (5.1)	1 (0.4)
Blister	10 (3.6)	0
Fatigue	12 (4.4)	2 (0.7)
Abdominal pain	9 (3.3)	0
Diarrhea	7 (2.6)	0
Skin injury	8 (2.9)	0
Thermal burn	6 (2.2)	0

- **PANOVA-3 establishes TTFields with GnP as a potential new standard paradigm for unresectable LA-PAC**

Babiker HM. J Clin Oncol 2025; 43 (21): 2350-2360.

KRAS INHIBITORS IN KRAS MUTANT ADVANCED PDAC

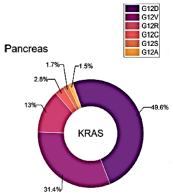
BERLIN 2025 ESMO congress

Efficacy and Safety of GFH375 Monotherapy in Previously Treated Advanced *KRAS G12D* Mutant Pancreatic Ductal Adenocarcinoma (PDAC)

Aiping Zhou[1], Zhihua Li[2], Yuping Sun[3], Zuoxing Niu[4], Heshui Wu[5], Lingjun Zhu[6], Hong Zong[7], Ying Yuan[8], Zhengbo Song[9], Ziming Li[10], Lin Wu[11], Xiujuan Qu[12], Jingdong Zhang[13], Yu Wang[14], Haige Shen[14], Huaqiang Zhu[14], Sharley Zheng[14], Shuang Wang[14], Zhao Cui[14]

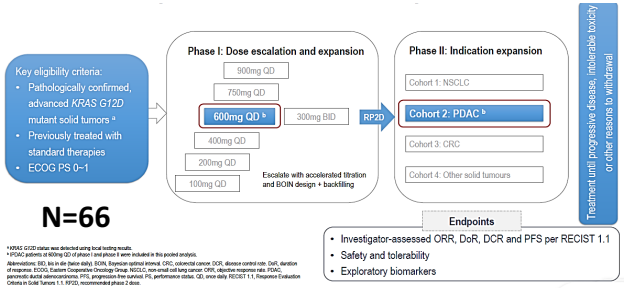
KRAS-G12D mutation:

- The *KRAS-G12D* mutation is present in nearly half patients with PDAC;[2,3]
- *KRAS-G12D* inhibitors, by blocking MEK/ERK phosphorylation, may further improve GA's efficacy in *KRAS-G12D* mutant PDAC.



Phase I/II Study of GFH375 Monotherapy (NCT06500676)

- GFH375 is an oral, potent, highly selective inhibitor of *KRAS G12D* in both GDP-bound (off) and GTP-bound (on) status.

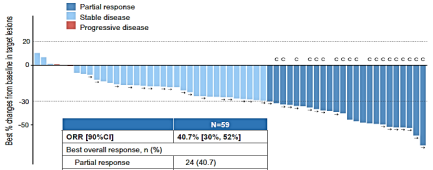


[a] KRAS G12D status was detected using local testing results.
[b] PDAC patients at 600mg QD of phase I and phase II were included in this pooled analysis.

Abbreviations: BID, bis in die (twice daily); BOIN, Bayesian optimal interval; CRC, colorectal cancer; DCR, disease control rate; DoR, duration of response; ECOG, Eastern Cooperative Oncology Group; NSCLC, non-small cell lung cancer; ORR, objective response rate; PDAC, pancreatic ductal adenocarcinoma; PFS, progression free survival; PS, performance status; QD, once daily; RECIST 1.1, Response Evaluation Criteria in Solid Tumors 1.1; RP2D, recommended phase 2 dose.

Best Overall Response

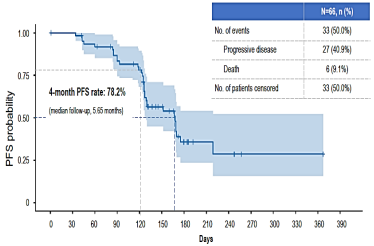
- ORR was **40.7%** (24/59), 90%CI was [30%, 52%] in the 59 evaluated patients.
- DCR was **96.7%** (57/59), 90%CI was [90%, 99%]; Majority (91.5%) had reduction in target lesions.



	N=59
ORR [90%CI]	40.7% [30%, 52%]
Best overall response, n (%)	
Partial response	24 (40.7)
Stable disease	33 (55.9)
Progressive disease	2 (3.4)
DCR [90%CI]	96.7% [90%, 99%]

Progression-Free Survival

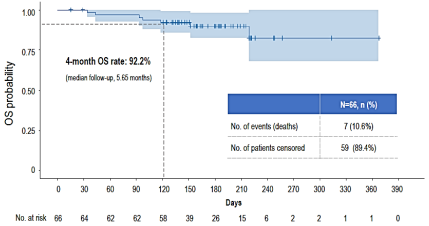
- Median PFS was **5.52 months** (90%CI: 4.27, 7.20), with a median follow-up time 5.65 months (90%CI: 4.96, 6.08).
- 4-month PFS rate was **78.2%** (90%CI: 69.8%, 87.5%).



	N=66, n (%)
No. of events	33 (50.0%)
Progressive disease	27 (40.9%)
Death	6 (9.1%)
No. of patients censored	33 (50.0%)

Overall Survival

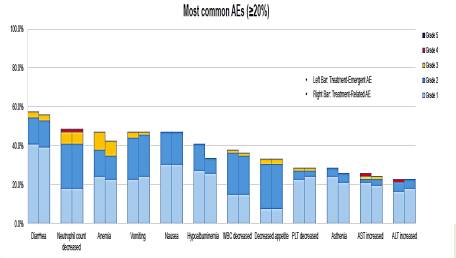
- Median OS was not reached with a median follow-up time 5.65 months (90%CI: 5.22, 6.14).
- 4-month OS rate was **92.2%** (90%CI: 86.8%, 97.9%).



	N=66, n (%)
No. of events (deaths)	7 (10.6%)
No. of patients censored	59 (89.4%)

Common Adverse Events

- The safety profile of GFH375 in *KRAS G12D* mutant PDAC patients is consistent with previous report.[12]
  - Common TRAEs were gastrointestinal and hematological AEs; most were grade 1 or 2 and manageable with supportive treatment.



Zhou A. ESMO 2025. LBA-84

KRAS INHIBITORS IN KRAS MUTANT ADVANCED PDAC

BERLIN 2025 ESMO congress

HRS-4642 Combined with Gemcitabine and Nab-paclitaxel in *KRAS*-G12D Mutant Advanced Pancreatic Cancer: A Phase 1b/2 Study

Prof. Liwei Wang

Department of Oncology, Renji Hospital, Shanghai Jiao Tong University School of Medicine, Shanghai, China

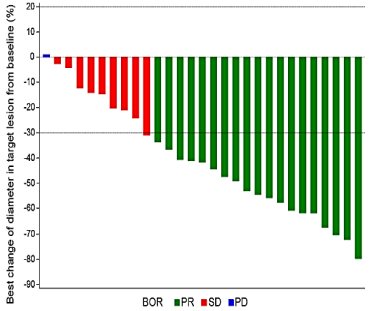
HRS-4642:

- A high-affinity, selective, long-acting, and non-covalent KRAS G12D inhibitor;
- Demonstrated anti-tumor effects for patients with *KRAS-G12D* mutant cancers.[4, 5]

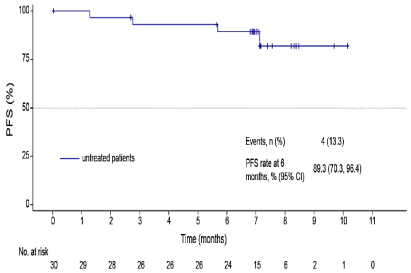
Tumor response in previously untreated patients

	HRS-4642 + GA Previously untreated patients (n = 30)
ORR*, % (95% CI)	63.3 (43.9, 80.1)
DCR, % (95% CI)	93.3 (77.9, 99.2)
BOR, n (%)	
PR*	19 (63.3)
SD	9 (30.0)
PD	1 (3.3)
No post-baseline assessment	1 (3.3)

*Confirmed

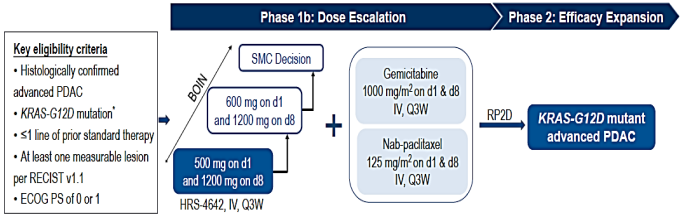


PFS in previously untreated patients



Study design

- A phase 1b/2 study to assess HRS-4642 combined with GA in patients with *KRAS-G12D* mutant advanced PDAC (NCT05533463).



Data cutoff: Jul 8, 2025

- 4 patients enrolled during dose escalation (HRS-4642 500 mg on d1 and 1200 mg on d8, IV, Q3W).
- No DLTs occurred.
- The median follow-up duration was 7.5 months (IQR: 7.2, 8.2).

N=31

ECOG, Eastern Cooperative Oncology Group; RECIST, Response Evaluation Criteria in Solid Tumors; BOIN, Bayesian optimal interval; SMC, Safety Monitoring committee; RP2D, recommended phase 2 dose; DLT, dose-limiting toxicity; ORR, objective response rate; DCR, disease control rate; DoR, duration of response; PFS, progression-free survival; OS, overall survival.

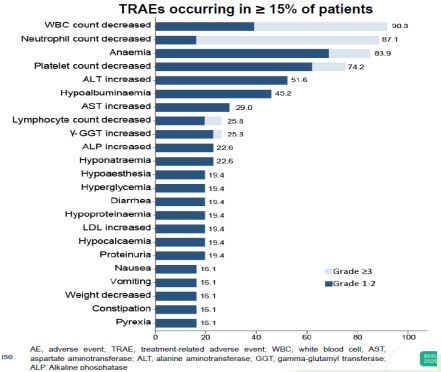
Pro. Liwei Wang

Safety

Safety profile was manageable:

- Most grade ≥ 3 TRAEs were hematologic toxicities;
- No TRAEs led to dose discontinuation or death.

	All patients (N=31)
Any AE, n (%)	31 (100)
Grade ≥ 3	27 (87.1)
Any TRAE, n (%)	31 (100)
Grade ≥ 3	27 (87.1)
Leading to dose reduction	15 (48.4)
Leading to treatment interruption	19 (61.3)
Leading to treatment discontinuation	0
Leading to death	0
Serious	5 (16.1)



AE, adverse event; TRAE, treatment-related adverse event; WBC, white blood cell; AST, aspartate aminotransferase; ALT, alanine aminotransferase; GGT, gamma-glutamyl transferase; ALP Alkaline phosphatase

Wang L. ESMO 2025. Abst 22150.

PANCREATIC CANCER CLINICAL PRACTICE GUIDELINES

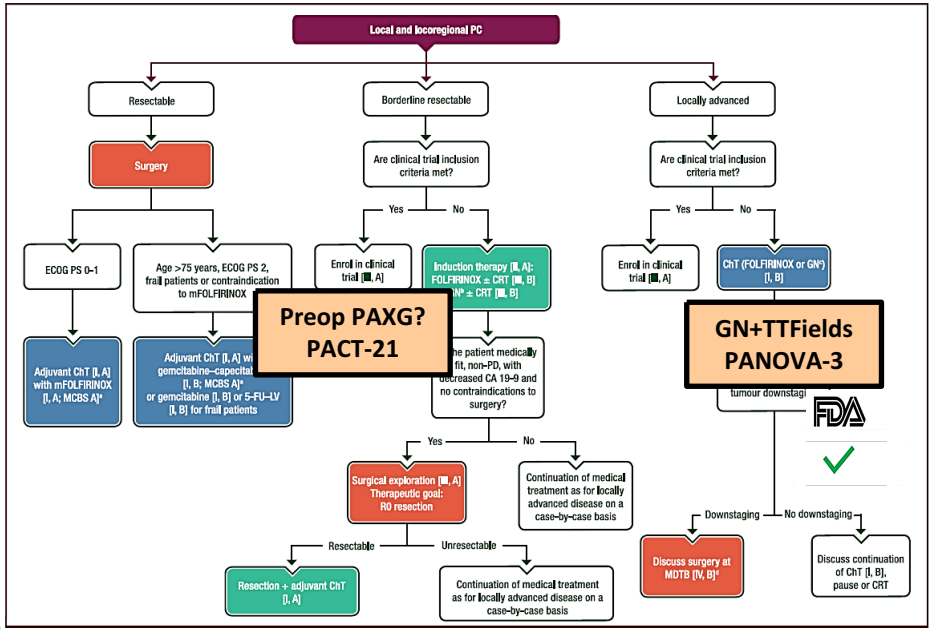
ESMO GOOD SCIENCE BETTER MEDICINE BEST PRACTICE

ANNALS OF ONCOLOGY driving innovation in oncology

SPECIAL ARTICLE

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

T. Conroy[1,2], P. Pfeiffer[3], V. Vilgrain[4,5], A. Lamarca[6], T. Seufferlein[7], E. M. O'Reilly[8], T. Hackert[9], T. Golan[10], G. Prager[11], K. Haustermans[12], A. Vogel[13] & M. Ducreux[14], on behalf of the ESMO Guidelines Committee*



Conroy T. Ann Oncol 2023; 34 (11): 987-1002.

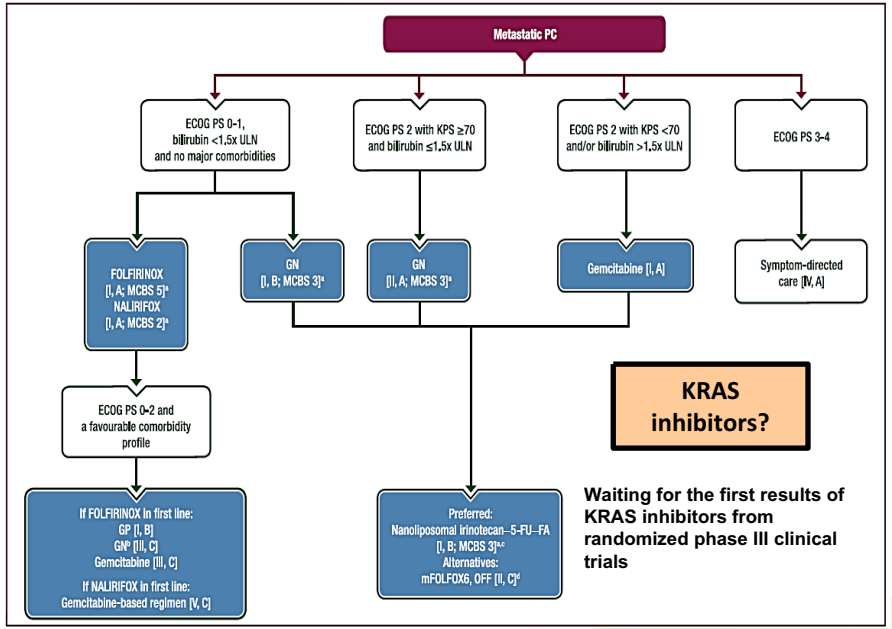
ESMO GOOD SCIENCE BETTER MEDICINE BEST PRACTICE

ESMO OPEN SCIENCE FOR OPTIMAL CANCER CARE

SPECIAL ARTICLE

ESMO Clinical Practice Guideline Express Update on the management of metastatic pancreatic cancer

T. Conroy[1,2] & M. Ducreux[3,4], on behalf of the ESMO Guidelines Committee*



Waiting for the first results of KRAS inhibitors from randomized phase III clinical trials

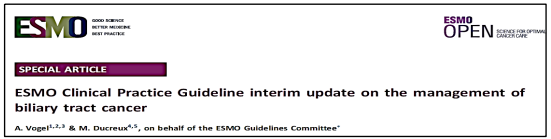
Conroy T. ESMO Open 2025; 10 (4): 104528.

AGENDA

- ✓ Gastroesophageal Cancer
- ✓ Pancreatic Cancer
- ✓ **Billiary Tract Carcinoma**
- ✓ Hepatocellular Carcinoma

LOCAL AND LOCOREGIONAL DISEASE

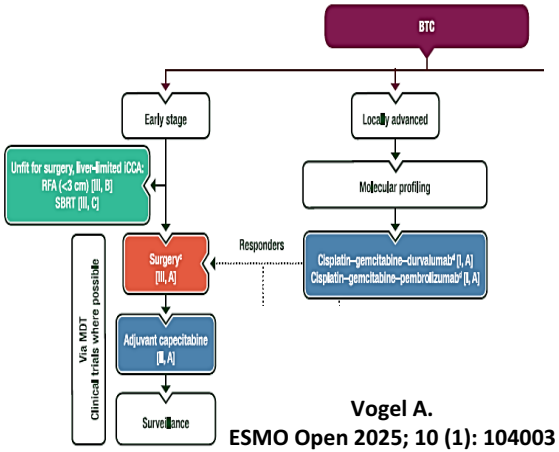
- **NEOADJUVANT/PERIOPERATIVE CT has showed signals of improved survival compared to pure adjuvant approach in patients with LA resectable BTC.**


ESMO OPEN

SPECIAL ARTICLE

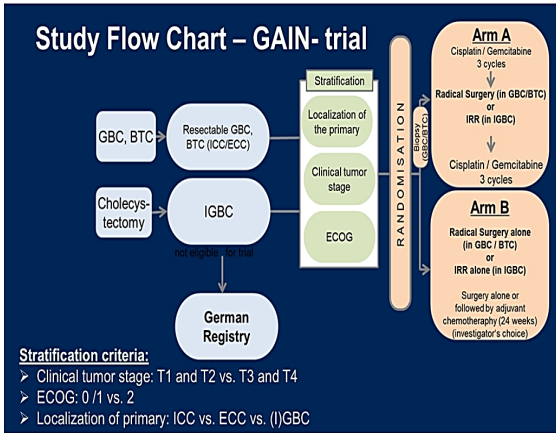
ESMO Clinical Practice Guideline interim update on the management of biliary tract cancer

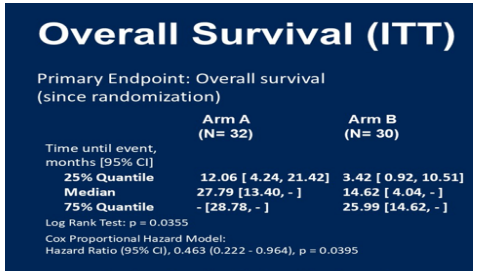
A. Vogel[1,2,3] & M. Ducreux[4,5], on behalf of the ESMO Guidelines Committee*

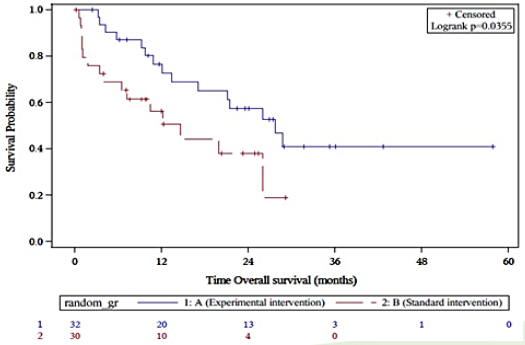


Vogel A.
ESMO Open 2025; 10 (1): 104003

IKF S662 GAIN trial







- **Based on the limited patient court due to premature closure of trial, data are only signal generating and must be interpreted with caution.**

Götze TO. ASCO 2025.

LOCAL AND LOCOREGIONAL DISEASE

- **NEOADJUVANT/PERIOPERATIVE CT has showed signals of improved survival compared to pure adjuvant approach in patients with LA resectable BTC.**

BERLIN 2025 ESMO congress

ZSAB-neoGOLP study

#5317—Neoadjuvant Toripalimab Plus Lenvatinib and GEMOX in Resectable, High-Risk Intrahepatic Cholangiocarcinoma: A Randomized, Multicenter, Open-Label Phase II-III Clinical Trial

Guoming Shi,[1] Jia Fan,[2] Jian Zhou,[1] Xiaoyong Huang,[1] Fei Liang,[3] Xiao Liang,[4] Rui Dong,[5] Qinghai Ye,[1] Qiang Gao,[1] Zhenping Yu,[6] Wenlong Zhai,[7] Jiacheng Lu,[1] Yuan Ji,[8] Xiaowu Li,[9] Fubao Liu,[10] Kui Wang,[11] Wei Yang,[12] Jialin Zhang,[13] Shuangjian Qiu,[1] Jianjun Zou[14]

- The ZSAB-neoGOLP study (NCT04669496) was an investigator-initiated, multicenter, open-label, seamless phase 2-3 controlled trial across 11 hospitals in China.

PI: Prof. Jia Fan

Key eligibility criteria:

- Aged 18-70 years
- Pathologically confirmed resectable iCCA with high-risk factors for recurrence, including at least one of the following: tumor diameter greater than 5 cm, radiographic evidence of vascular invasion, multiple intrahepatic tumors, hepatic portal lymph node metastasis, or an elevated CA19-9 level
- ECOG PS 0
- Child-Pugh class A
- No previous resection or systemic therapies

N=178

R 1:1

GOLP neoadjuvant therapy (Toripalimab 240mg iv q3w for 3 cycles + Lenvatinib 8mg po qd for 9 weeks + GEMOX chemotherapy*) → Surgical resection → Capecitabine adjuvant therapy (capecitabine 2500mg/m2 per day, po, two divided doses on days 1-14 of a 3-week cycle, for 8 cycles)

Surgical resection

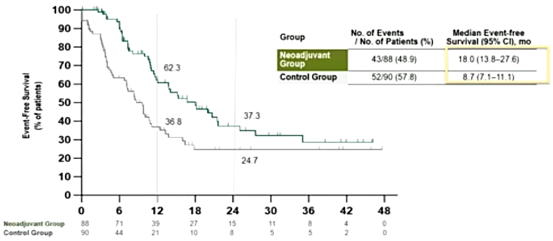
- **Primary endpoint:** investigator-assessed EFS
- **Secondary endpoints:** ORR (RECIST v1.1); MPR(viable tumor cells ≤10%) rate; pCR rate; R0 resection rate; RFS; OS and safety.

*Oxaliplatin at 85 mg/m² intravenously on day 1, and gemcitabine at 1 g/m² intravenously on days 1 and 8 of each 3-week cycle for three cycles
iCCA: Intrahepatic cholangiocarcinoma; EFS: event-free survival; ORR: objective response rate; RECIST v1.1: Response Evaluation Criteria in Solid Tumors, version 1.1; MPR: major pathological response; pCR: pathological complete response; RFS: recurrence-free survival; OS: overall survival

Presented by: Prof. Dr. Guoming Shi

Primary Endpoint: EFS

- Interim analysis, data cutoff on Apr 30, 2025
- With a median follow-up of 16.9 months, EFS was significantly improved with neoadjuvant therapy



Summary of Pathological Responses *

Variable	Neoadjuvant group (N = 88)	Control group (N = 90)
ORR, n (%)	**48 (54.4)**	/
95%CI	44.7-66.5	/
Surgery rate, n (%)	**85 (96.6)**	**89 (98.9)**
R0 Resection rate, n (%)	**84 (95.5)**	**84 (93.3)**
MPR, n (%)	**17 (19.3)**	**0 (0)**
95%CI	11.7-29.1	0.0-4.0
pCR	**4 (4.5)**	**0 (0)**
95%CI	1.3-11.2	0.0-4.0

Shi G. ESMO 2025.

ADVANCED DISEASE: FIRST LINE TREATMENT

- **TOURMALINE STUDY: Activity and safety profile of durvalumab+investigator´s choice of gemcitabine-based CT is comparable to that of the durvalumab+CisGem arm in the TOPAZ-1 study.**

ESMO GOOD SCIENCE BETTER MEDICINE BEST PRACTICE

ESMO OPEN SCIENCE FOR OPTIMAL CANCER CARE

SPECIAL ARTICLE

ESMO Clinical Practice Guideline interim update on the management of biliary tract cancer

A. Vogel[1,2,3] & M. Ducreux[4,5], on behalf of the ESMO Guidelines Committee*

Vogel A. ESMO Open 2025; 10 (1): 104003

Early safety and efficacy from the Phase 3b TOURMALINE study of durvalumab in combination with gemcitabine-based chemotherapy in advanced biliary tract cancer

Do-Youn Oh,[1] Masafumi Ikeda,[2] Teresa Macarulla,[3] Aiwu Ruth He,[4] Joon Oh Park,[5] Masayuki Kitano,[6] Angela Lamarca,[7] David Tai,[8] Farshid Dayyani,[9] Tiziana Pressiani,[10] Graham Wotherill,[11] Alessia Stoll,[12] Peng Sun,[13] Boris Baur,[13] Arndt Vogel[14]

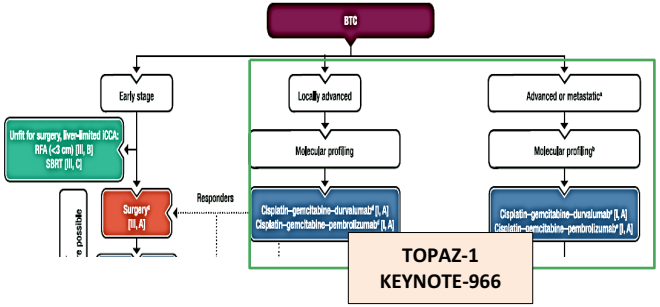


Figure 1. TOURMALINE study design

Participant population
- ≥18 years
- Histologically confirmed locally advanced or metastatic BTC including iCCA, eCCA, GBC and AoV
- ECOG PS 0–2*
- Prior curative treatment permitted, with no minimum time to recurrence, including participants with residual disease

Screening: Day -28 to -1

N=140

Durvalumab + investigator's choice of gemcitabine-based chemotherapy

Durvalumab 1500 mg Q3W + gemcitabine-based chemotherapy Q3W (up to 8 cycles), including:
- Gemcitabine monotherapy
- Gemcitabine + cisplatin (WHO / ECOG PS 2 only)
- Gemcitabine + oxaliplatin
- Gemcitabine + carboplatin
- Gemcitabine + S-1
- Gemcitabine + cisplatin + albumin-bound paclitaxel

OR

Durvalumab 1500 mg Q4W (up to 4 cycles) + gemcitabine + cisplatin + S-1 Q2W

Oh DY. ESMO GI 2025.

ADVANCED DISEASE: FIRST LINE TREATMENT

Figure 2. Overall participant demographics and clinical characteristics (N=121)

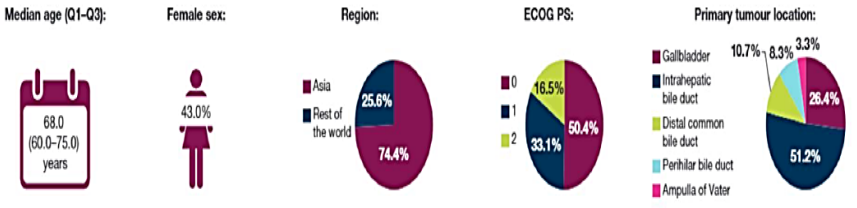
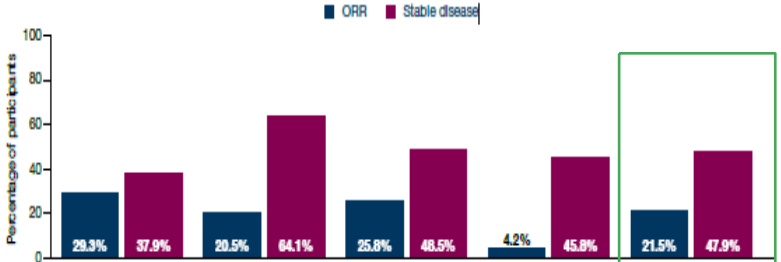


Figure 3. Objective response rate in the safety analysis set



	Platinum double	Platinum triple	Platinum total	Non-platinum	Total
N	58	39	97	24	121
ORR,* % (95% CI)	29.3 (18.1–42.7)	20.5 (9.3–36.5)	25.8 (17.4–35.7)	4.2 (0.1–21.1)	21.5 (14.5–29.9)
Complete, n (%)	1 (1.7)	0	1 (1.0)	0	1 (0.8)
Partial, n (%)	16 (27.6)	8 (20.5)	24 (24.7)	1 (4.2)	25 (20.7)
Stable disease, n (%)	22 (37.9)	25 (64.1)	47 (48.5)	11 (45.8)	58 (47.9)
Not evaluable, n (%)	11 (19.0)	4 (10.3)	15 (15.5)	8 (33.3)	23 (19.0)

Safety and ORR for the D + Gem + Cis subgroup (ECOG PS 2) in the global ITT population

	D + Gem + Cis (n=18)
Any Grade 3 / 4 PRAE within 6 months of treatment initiation, n (%)	9 (50.0)
Any AE, n (%)	17 (94.4)
Any AE possibly related to study treatment*	16 (88.9)
Any Grade 3 / 4 AE	13 (72.2)
Any AE with an outcome of death	1 (5.6)
Any AE leading to discontinuation of any treatment	2 (11.1)
Any SAE, n (%)	6 (33.3)
Any SAE possibly related to any study treatment*	0
Any Grade 3 / 4 SAE	3 (16.7)
SAE leading to discontinuation of any treatment	2 (11.1)
Any immune-mediated AE†, n (%)	4 (22.2)
Any infusion related AE, n (%)	1 (5.6)
Hypersensitivity / anaphylactic reactions AE, n (%)	0

	D + Gem + Cis (n=18)
ORR‡, % (95% CI)§	44.4 (21.53, 69.24)
Complete response	0
Partial response	8 (44.4)
Stable disease	8 (44.4)

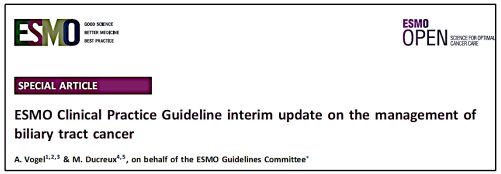
Table 2. Adverse events in the safety analysis set

	Platinum double	Platinum triple	Platinum total	Non-platinum	Total*
N	58	39	97	24	121
Any Grade 3 / 4 PRAE within 6 months of treatment initiation,†‡ n (%)	29 (50.0)	16 (41.0)	45 (46.4)	10 (41.7)	55 (45.5)
Any AE, n (%)	52 (89.7)	38 (97.4)	90 (92.8)	22 (91.7)	112 (92.6)
Any PRAE†	47 (81.0)	38 (97.4)	85 (87.6)	21 (87.5)	106 (87.6)
Any AE leading to discontinuation of any study treatment	8 (13.8)	5 (12.8)	13 (13.4)	2 (8.3)	15 (12.4)
Any AE leading to discontinuation of durvalumab	4 (6.9)	1 (2.6)	5 (5.2)	1 (4.2)	6 (5.0)
Any AE with an outcome of death§	3 (5.2)	0	3 (3.1)	0	3 (2.5)
Any SAE, n (%)	18 (31.0)	12 (30.8)	30 (30.9)	10 (41.7)	40 (33.1)
Any PRSAE†	4 (6.9)	3 (7.7)	7 (7.2)	5 (20.8)	12 (9.9)
Any infusion-related AE,‖ n (%)	2 (3.4)	5 (12.8)	7 (7.2)	0	7 (5.8)
Any infusion-related AE possibly related to durvalumab	1 (1.7)	4 (10.3)	5 (5.2)	0	5 (4.1)
Any immune-mediated AEs,¶ n (%)	7 (12.1)	4 (10.3)	11 (11.3)	2 (8.3)	13 (10.7)
Requiring systemic corticosteroids	6 (10.3)	2 (5.1)	8 (8.2)	2 (8.3)	10 (8.3)
Requiring ≥40 mg prednisone equivalent steroids	2 (3.4)	0	2 (2.1)	2 (8.3)	4 (3.3)

Oh DY. ESMO GI 2025.

ADVANCED DISEASE: SECOND- AND LATER-LINE TREATMENT

- **ProvIDHe STUDY corroborates the efficacy of IVOSIDENIB observed in the ClarIDHy trial in patients with mIDH1 CCA in a real-world setting.**

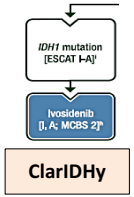

ESMO OPEN

SPECIAL ARTICLE

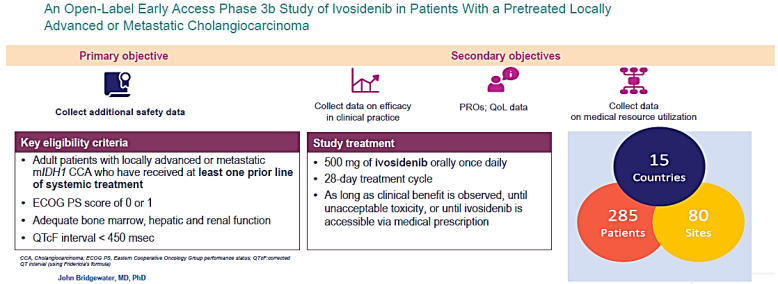
ESMO Clinical Practice Guideline interim update on the management of biliary tract cancer

A. Vogel[1,2,3] & M. Ducreux[4,5], on behalf of the ESMO Guidelines Committee*

Vogel A. ESMO Open 2025; 10 (1): 104003



ProvIDHe study design

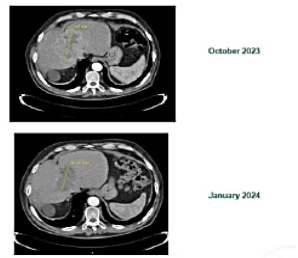


Best Overall Response per Investigator

	N = 262
Best Overall Response, n (%)[1]	
Complete Response (CR)	0
Partial Response (PR)	15 (5.7)
Stable Disease (SD)	120 (45.8)
Progressive Disease (PD)	62 (23.7)
Objective Response Rate (CR or PR), n (%)	**15 (5.7)**
95% CI of Response Rate [2]	(3.2, 9.3)
Duration of Response (months) [3]	**N= 15**
Median (95% CI)	10.1 (3.0, NE)
Disease Control Rate (CR+PR+SD), n (%)	
	135 (51.5)

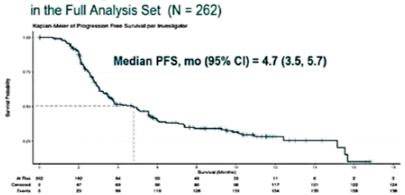
Percentages are based on N.
[1] Patients who did not achieve CR, PR, SD, PD are excluded from Best Overall Response summary as they are considered to not have achieved a best response.
[2] CI: confidence interval. CI of percentage is calculated with the Clopper and Pearson (exact Binomial) method
[3] Duration of Response = (Earliest Date of PD or Death – Date of First CR or PR + 1) / 30.4375.

John Bridgewater, MD, PhD



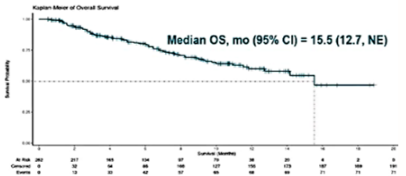
Efficacy results

in the Full Analysis Set (N = 262)



	N = 262
Progression-Free Survival (months) [1]	
Median (95% CI) [2]	4.7 (3.5, 5.7)
Kaplan-Meier PFS Rate (%) [3]	
3 months	64.2
6 months	40.1
12 months	20.2

Percentages are based on N
[1] Progression free survival (PFS) = (Earliest Date of PD or Death – Enrollment Date + 1) / 30.4375
[2] Median estimates from product-limit (Kaplan-Meier) method. Confidence intervals from Brookmeyer and Crowley method with log-log transformation
[3] Based on Survival Distribution Function estimates from product limit method



	N = 262
Overall Survival (months) [1]	
Median (95% CI) [2]	15.5 (12.7, NE)
Kaplan-Meier Survival Rate (%) [3]	
3 months	88.3
6 months	80.3
12 months	60.0

Percentages are based on N
[1] Overall survival (OS) = (Death – Enrollment Date + 1) / 30.4375
[2] Median estimates from product-limit (Kaplan-Meier) method. Confidence intervals from Brookmeyer and Crowley method with log-log transformation
[3] Based on Survival Distribution Function estimates from product limit method

Bridgewater J. ESMO GI 2025.

ADVANCED DISEASE: SECOND- AND LATER-LINE TREATMENT

- **ReFocus STUDY: LIRAFUGRATINIB demonstrated clinically meaningful antitumor activity in patients with previously treated, advanced CCA harboring FGFR2-f/r.**

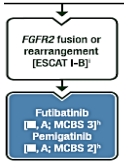
ESMO OPEN

SPECIAL ARTICLE

ESMO Clinical Practice Guideline interim update on the management of [redacted]cer

[redacted]x[4,5], on behalf of the ESMO Guidelines Committee*

[redacted]A. ESMO Open 2025; 10 (1): 104003

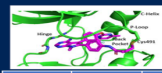


ASCO Gastrointestinal Cancers Symposium

Efficacy and safety of lirafugratinib in patients with FGFRi-naïve cholangiocarcinoma harboring *FGFR2* fusions/rearrangements

Antoine Hollebecque[1], Mitesh Borad[2], Peter Lu[3], Xianzhang Meng[3], Kristin Ryan[3], Laura Alexander[3], Jia Liu[4], Do-Youn Oh[5], and Richard Kim[6]

In contrast to pan-FGFRi, lirafugratinib is a potent and selective FGFR2 inhibitor



Lirafugratinib selectively inhibits FGFR2 based on unique conformational dynamics[1]

Inhibitor	Mechanism of Action	Biochemical IC50 (nM)[2,3]			
		FGFR1	FGFR2	FGFR3	FGFR4
Lirafugratinib	Irreversible FGFR2 selective	864.3	3.1	274.1	17,633
Infigratinib	Reversible Pan-FGFRi	1.1	1	2	61
Pemigatinib	Reversible Pan-FGFRi	0.39	0.46	1.2	30
Futibatinib	Irreversible Pan-FGFRi	1.8	1.4	1.6	3.7

[redacted]

[redacted]en Label Study (NCT04526106)

Part 2
[redacted]mpleted): Cholangiocarcinoma (CCA)

Part 3
Extension(s) (Completed)

[redacted]QDC): *FGFR2*-f/r + CCA with [redacted]herapy + prior FGFRi (N=53)

[redacted]QDC): *FGFR2*-f/r + CCA with [redacted]emotherapy with no prior FGFRi (N=26)

Group 2A Extension (QDC): *FGFR2*-f/r + CCA with prior chemotherapy with no prior FGFRi (N=86)

[redacted]roup 6 (QDC): *FGFR2*-f/r + CCA naive to prior chemotherapy and FGFRi (N=11)

Group 7 (QDC): *FGFR2*-mutant or amplified CCA with no prior FGFRi (N=42)[b]

Pivotal Cohort (N=116)[c]
Part 1 Cohort 2 + Part 2 Group 2A + Part 3 Group 2A Extension

Non-CCA

Group 3 (QDC): *FGFR2*-f/r naive to prior FGFRi (N=46)[b]
Group 4 (QDC): *FGFR2*-amplified naive to prior FGFRi (N=46)[b]
Group 5 (QDC): *FGFR2*-mutant naive to prior FGFRi (N=37)[b]

Key Eligibil[redacted]
- 18 years or ol[redacted]
- Histologically or cytologically confirmed diagnosis of unresectable or metastatic CCA or other solid tumors per RECIST v1.1 that were refractory to or inadequately responded to standard therapy, or for which no standard therapy exists or was declined
- ECOG PS of 0–1
- Documented *FGFR2* genomic alteration (fusion, mutation, or amplification) per local assessment of blood and/or tumor tissue

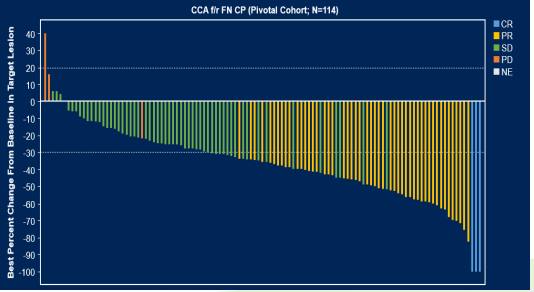
Primary Endpoint:
- Confirmed ORR per RECIST v1.1 by IRC

Key Secondary Endpoints:
- Duration of response
- Disease control rate
- Progression-free survival
- Overall survival
- Safety
- Quality of life per EORTC QLC-C30

Summary of Efficacy by IRC (Primary Efficacy Analysis Set)

	CCA f/r FN CP (Pivotal Cohort; N=114)
Confirmed BOR, n (%)	
Complete response	3 (2.6)
Partial response	50 (43.9)
Stable disease	57 (50.0)
Progressive disease	3 (2.6)
Not evaluable[a]	1 (0.9)
ORR[b], n (%) [95% CI]	53 (46.5) [37.1, 56.1]
DCR[c], n (%) [95% CI]	110 (96.5) [91.3, 99.0]
Median DOR, months [95% CI]	11.8 [7.5, 13.0]
Median PFS, months [95% CI]	11.3 [9.2, 14.8]
Median OS[d], months [95% CI]	22.8 [18.1, 27.2]

Waterfall Plot for BOR From Baseline by IRC (Primary Efficacy Analysis Set)

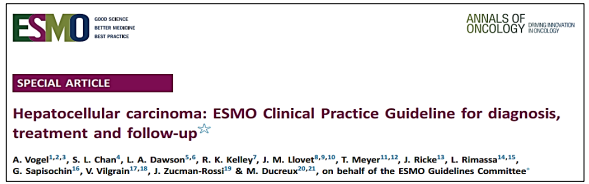


Hollebecque A. ASCO GI 2026.

AGENDA

- ✓ Gastroesophageal Cancer
- ✓ Pancreatic Cancer
- ✓ [redacted]y Tract Carcinoma
- [redacted]ellular Carcinoma

SYSTEMIC THERAPIES FOR ADVANCED DISEASE: FIRST LINE TREATMENT

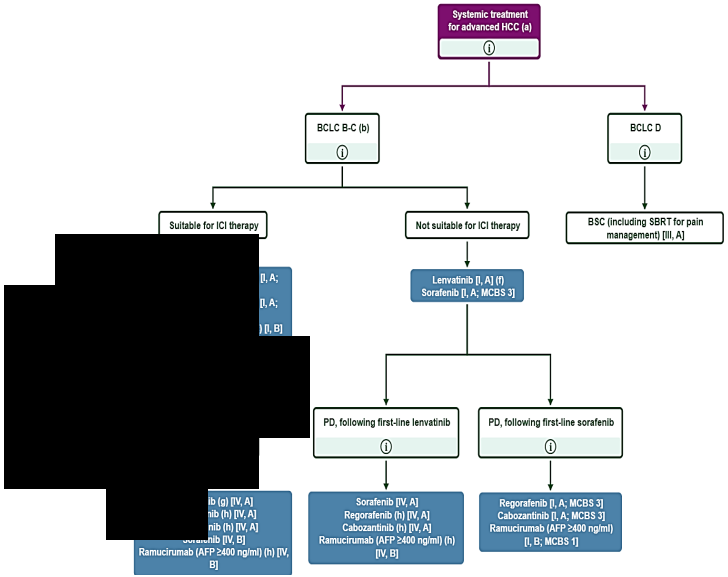

ESMO GOOD SCIENCE BETTER MEDICINE BEST PRACTICE

ANNALS OF ONCOLOGY DRIVING INNOVATION IN ONCOLOGY

SPECIAL ARTICLE

Hepatocellular carcinoma: ESMO Clinical Practice Guideline for diagnosis, treatment and follow-up☆

A. Vogel[1,2,3], S. L. Chan[4], L. A. Dawson[5,6], R. K. Kelley[7], J. M. Llovet[8,9,10], T. Meyer[11,12], J. Ricke[13], L. Rimassa[14,15], G. Sapisochin[16], V. Vilgrain[17,18], J. Zucman-Rossi[19] & M. Ducreux[20,21], on behalf of the ESMO Guidelines Committee*



- **ADVANCED HCC: FIRST-LINE TREATMENT OPTIONS**

Anti PD-1/PD-L1+Antiangiogenic therapy			
Study	N	Control arm	Experimental arm
IMBrave 150	501	Sorafenib	Atezolizumab+ Bevacizumab
ORIENT-32	571	Sorefenib	Sintilimab+ Bevacizumab
SHR 1210	510	Sorafenib	Camrelizumab+ Apatinib
COSMIC-312	640	Sorafenib	Atezolizumab+ Cabozantinib
LEAP-002	750	Lenvatinib	Pembrolizumab+ Lenvatinib

Anti PD-1/PD-L1+Anti CTLA4			
Study	N	Control arm	Experimental arm
HIMALAYA	1200	Sorafenib	Durvalumab or Durvalumab+ Tremelimumab
CHECKMATE 9DW	1084	Sorafenib or Lenvatinib	Nivolumab+ Ipilimumab

Vogel A. Ann Oncol 2025; 36 (5): 491-506

SYSTEMIC THERAPIES FOR ADVANCED DISEASE: FIRST-LINE TREATMENT

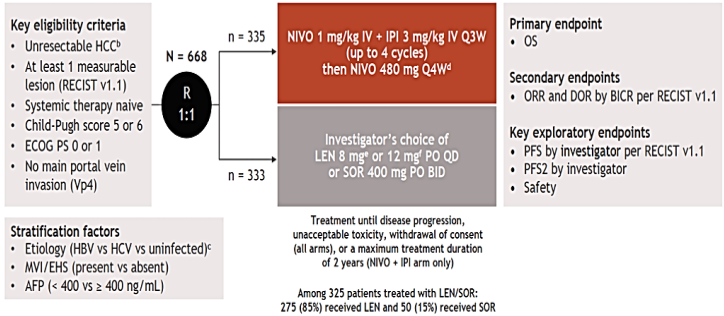
Nivolumab plus ipilimumab versus lenvatinib or sorafenib as first-line treatment for unresectable hepatocellular carcinoma (CheckMate 9DW): an open-label, randomised, phase 3 trial

Thomas Yau, Peter R Galle*, Thomas Decaens, Bruno Sangro, Shukui Qin, Leonardo G da Fonseca, Hatim Karachiwala, Jean-Frederic Blanc, Joong-Won Park, Edward Gane, Matthias Pinter, Ana Matilla Peña, Masafumi Ikeda, David Tai, Armando Santoro, Gonzalo Pizarro, Chang-Fang Chiu, Michael Schenker, Aiwu He, Hong Jae Chon, Joanna Wojcik-Tomaszewska, Gontran Verset, Qi Qi Wang, Caitlyn Stromka, Jadyn Neely, Priyanka Singh, Maria Jesus Jimenez Exposito, Masatoshi Kudo, on behalf of the CheckMate 9DW investigators*

Nivolumab plus ipilimumab vs lenvatinib or sorafenib as first-line treatment for unresectable hepatocellular carcinoma: 4-year follow-up of CheckMate 9DW

Peter R. Galle,[1] Bruno Sangro,[2] Thomas Decaens,[3] Masatoshi Kudo,[4] Shukui Qin,[5] Leonardo Da Fonseca,[6] Hatim Karachiwala,[7] Joong-Won Park,[8] Edward Gane,[9] Matthias Pinter,[10] David Tai,[11] Armando Santoro,[12] Gonzalo Pizarro,[13] Michael Schenker,[14] Qi Wang,[15] Maria Jesus Jimenez Exposito,[15] Thomas Yau[16]

- CheckMate 9DW is a global, phase 3, randomized, open-label study of NIVO in combination with IPI compared with LEN or SOR as 1L treatment in patients with unresectable HCC[a]

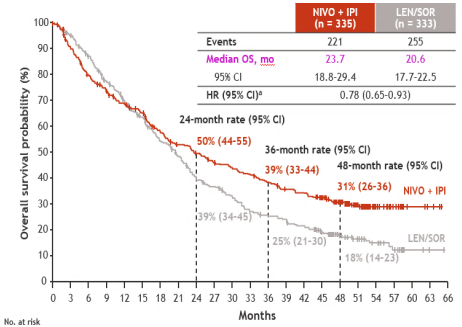


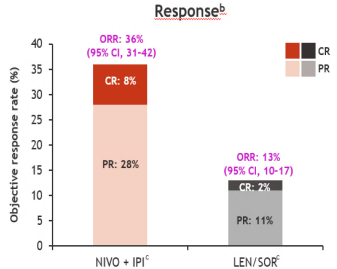
- At data cutoff (January 31, 2024), the median follow-up[g] was 35.2 months (range, 26.8-48.9)

[a]ClinicalTrials.gov: NCT04039607. [b]Disease not eligible for, or progressive disease after, curative surgical and/or locoregional therapies. [c]Based on central lab serology results for stratification purpose. [d]Minimum of 1 dose of NIVO + IPI is required before proceeding to NIVO monotherapy. [e]If body weight < 60 kg. [f]If body weight ≥ 60 kg. [g]Time between randomization date and cutoff date.

CheckMate 9DW

Overall survival, response, and duration of response





	NIVO + IPI (n = 335)	LEN/SOR (n = 333)
Median TTR (range),[d] mo	2.2 (1.1-41.7)	3.7 (0.6-8.0)
Median DOR (95% CI),[d] mo	34.3 (22.6-47.7)	12.9 (10.2-33.9)
Patients with DOR ≥ 48 mo,[d] % (95% CI)	37 (24-50)	12 (1-38)

- Sustained OS benefit with NIVO + IPI vs LEN/SOR with longer follow-up, and higher 48-month OS rates
- Continued ORR benefit with NIVO + IPI vs LEN/SOR, with a higher CR rate and durable responses

Median (range) follow-up, 52.5 (44.0-66.1) months. [a]HR and 95% CI from stratified Cox proportional hazard model. Symbols represent censored observations. [b]Assessed by BICR based on RECIST v1.1. [c]Percentage with BOR of SD (includes non-CR/non-PD, which refers to patients with persistence of 1 or more non-target lesion[s]): NIVO + IPI, 32%; LEN/SOR, 62%. Percentage with BOR of PD: NIVO + IPI, 20%; LEN/SOR, 14%. [d]In confirmed responders (NIVO + IPI: n = 122; LEN/SOR: n = 44).

You T. Lancet Oncol 2025; 405 (10492): 1851-1864.
Galle PR. ASCO GI 2026.

SYSTEMIC THERAPIES FOR ADVANCED DISEASE: FIRST LINE TREATMENT

- The ADDITION OF A THIRD AGENT to atezolizumab+bevacizumab do not show an added benefit in patients with untreated advanced HCC.

IMbrave152/SKYSCRAPER-14: a phase 3, double-blind, placebo-controlled, randomised, global study

- 669 patients randomised to treatment between 14 September 2023 and 23 September 2024

Key eligibility criteria
- Aged ≥18 years
- Unresectable locally advanced or metastatic HCC
- ECOG PS 0 or 1
- Child-Pugh A
- No prior systemic therapy for advanced disease
- Systemic adjuvant treatment permitted (recurrence ≥6 months from treatment completion)[1]

R 1:1

Tira 600 mg + **atezo** 1200 mg + **bev** 15 mg/kg, IV Q3W n=331

Imaging every 6 ± 1 weeks†

Pbo + **atezo** 1200 mg + **bev** 15 mg/kg, IV Q3W n=338

Treat until loss of clinical benefit or unacceptable toxicity

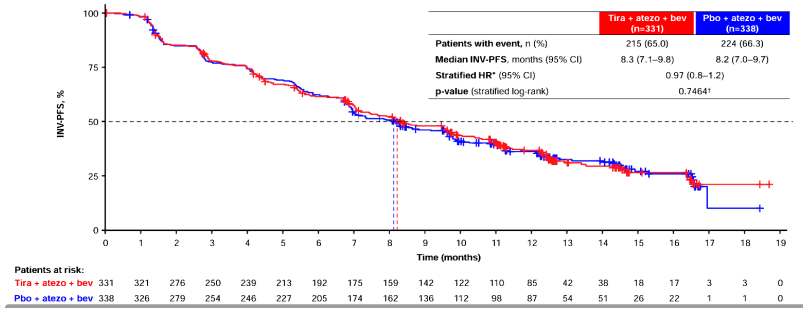
No crossover permitted

Stratification factors
- **Geographic region** (Asia and Africa, excluding Japan, vs rest of world, including Japan)
- **MVI and/or EHS** (presence vs absence)
- **Baseline AFP** (<400 vs ≥400 ng/mL)
- **HCC aetiology** (viral vs non-viral)

Primary endpoints
- **INV-PFS** per RECIST v1.1
- **OS**

Other key secondary endpoints
- **ORR**
- **DOR**
- **PFS/OS rate** at selected time points
- **Safety**
- **PROs**

Primary endpoint: INV-PFS per RECIST v1.1



	Tira + atezo + bev (n=331)	Pbo + atezo + bev (n=338)
Patients with event, n (%)	215 (65.0)	224 (66.3)
Median INV-PFS, months (95% CI)	8.3 (7.1–9.8)	8.2 (7.0–9.7)
Stratified HR* (95% CI)	0.97 (0.8–1.2)	
p-value (stratified log-rank)	0.7464†	

Finn RS. ESMO GI 2025.

BERLIN 2025 ESMO congress

Adding Ipilimumab to Atezolizumab plus Bevacizumab in patients with unresectable hepatocellular carcinoma in first-line systemic therapy

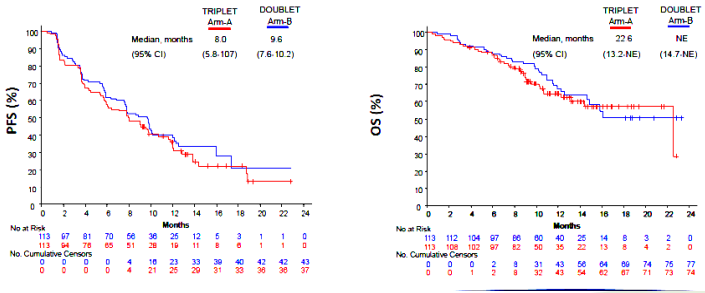
PRODIGE 81/FFCD 2101 - TRIPLET HCC

MERLE Philippe, BLANC Jean-Frédéric, EDELINE Julien, Karine LE MALICOT, PERON Jean-Marie, BOURGEOIS Vincent, BOUATTOUR Mohamed, TOUCHEFEU Yann, VITELLIUS Carole, KHEMISSA AKOUZ Faiza, HEURGUE Alexandra, GIROT Paul, ASSENAT Eric, NGUYEN KHAC Eric, BRONOWICKI Jean-Pierre, VIAUD Juliette, BEN ABDELGHANI Meher, NAULT Jean-Charles, MANFREDI Sylvain, PHELIP Jean-Marc

Objective response Recist 1.1	Objective response	Disease control	Progressive disease	Non evaluable
Arm-A TRIPLET n=113	34 (30.1%)	84 (74.3%)	12 (10.6%)	17 (15.0%)
Arm-B DOUBLET n=113	31 (27.4%)	96 (85.0%)	11 (9.7%)	6 (5.3%)

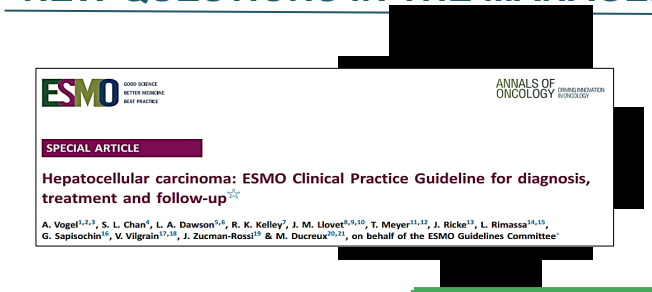
RESULTS (2) – Secondary endpoints of efficacy

median (95% CI) follow-up of 12.0 mo (10.6-13.1) for arm-A vs 12.5 (11.2-13.4) for arm-B



Philippe M. ESMO GI 2025.

NEW QUESTIONS IN THE MANAGEMENT OF INTERMEDIATE-STAGE HCC



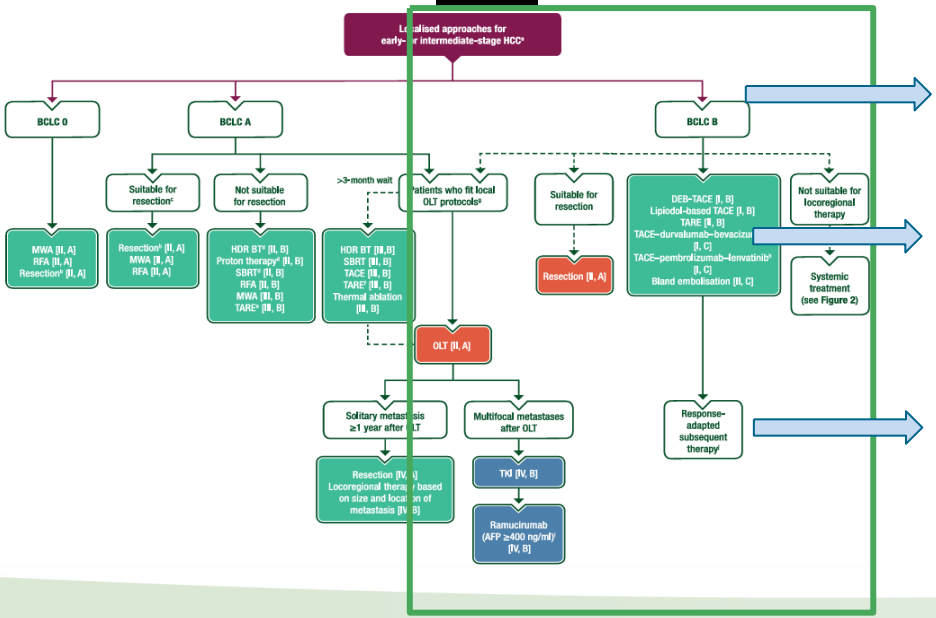
ESMO GOOD SCIENCE BETTER MEDICINE BEST PRACTICE

ANNALS OF ONCOLOGY DRIVING INNOVATION IN ONCOLOGY

SPECIAL ARTICLE

Hepatocellular carcinoma: ESMO Clinical Practice Guideline for diagnosis, treatment and follow-up☆

A. Vogel[1,2,3], S. L. Chan[4], L. A. Dawson[5,6], R. K. Kelley[7], J. M. Llovet[8,9,10], T. Meyer[11,12], J. Ricke[13], L. Rimassa[14,15], G. Sapisochin[16], V. Vilgrain[17,18], J. Zucman-Rossi[19] & M. Ducreux[20,21], on behalf of the ESMO Guidelines Committee*



Selection of patients for salvage therapies
(importance of R0)

Combination of TACE+systemic therapies
(When? How?)

Can TACE be omitted?
(In which patients?)

Vogel A. Ann Oncol 2025; 36 (5): 491-506

INTERMEDIATE-STAGE HCC: COMBINATION OF TACE+SYSTEMIC THERAPIES

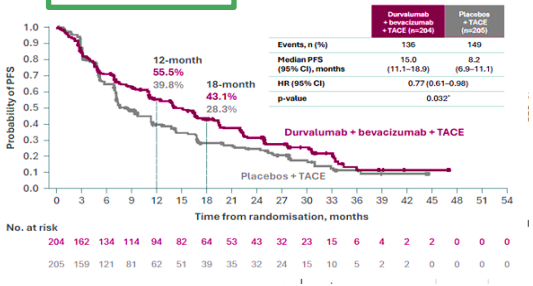
Phase-3 studies evaluating the combination of TACE with immunotherapy in HCC:

	Phase	Investigational arm(s)	Patient enrolment, N	Primary endpoint(s)	Outcomes (primary endpoint)
EMERALD-1[1] NCT03778957	3	Arm A: TACE + durvalumab Arm B: TACE + durvalumab + bevacizumab	724 (actual)	**PFS** (Arm B vs Arm C; BICR)	Showed a statistically significant improvement in PFS
EMERALD-3[2] NCT05301842	3	Arm A: TACE + STRIDE + lenvatinib Arm B: TACE + STRIDE	725 (estimated)	**PFS** (Arm A vs Arm C; RECIST 1.1 by BICR)	Results not yet reported
LEAP-012[3] NCT04246177	3	TACE + pembrolizumab + lenvatinib	450 (estimated)	**PFS** (RECIST 1.1 by BICR) OS	Showed a statistically significant improvement in PFS
TACE-3[4] NCT04268888	2 / 3	TACE / TAE + nivolumab	522 (estimated)	**OS**	Results not yet reported
TALENTACE[5,6] NCT04712643	3	TACE + atezolizumab + bevacizumab	342 (actual)	**TACE PFS** (investigator-assessed) OS	Showed a statistically significant improvement in TACE-PFS
CARES-005[7] NCT04559607	2	TACE + camrelizumab + apatinib	188 (actual)	**PFS** (investigator-assessed)	Showed a statistically significant improvement in PFS

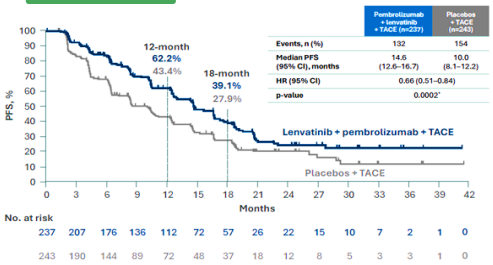
INTERMEDIATE-STAGE HCC: COMBINATION OF TACE+SYSTEMIC THERAPIES

- **Combination immunotherapy improves PFS in embolization eligible HCC...**

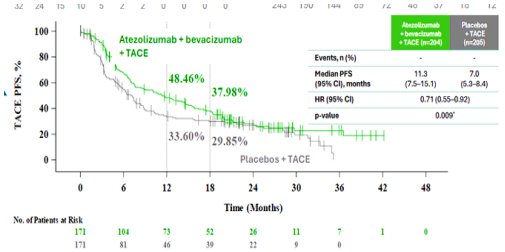
EMERALD-01



LEAP-012

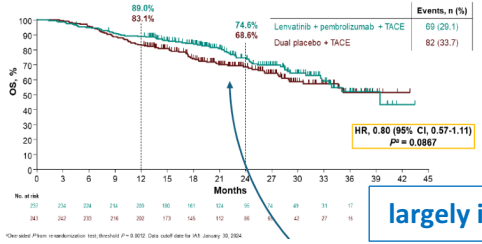


TALENTACE

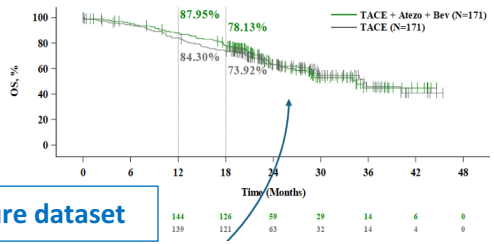


... but without evidence for OS benefit.

LEAP-012



TALENTACE



largely immature dataset

Sangro B. Lancet 2025; 405:216-232.
Kudo M. Lancet 2025; 405: 203-2015
Dong J. ESMO GI 2025, LBA 2.

INTERMEDIATE-STAGE HCC: SYSTEMIC THERAPY COMPARED WITH TACE

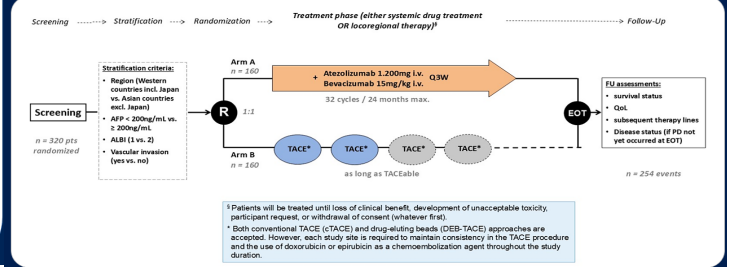
- **ABC-HCC trial: Atezolizumab/bevacizumab seems to be superior compare to TACE in regard to TTFS in intermediate-stage HCC.**

Main Inclusion Criteria

- Intermediate stage HCC - not amenable to curative surgery, liver transplantation or curative ablation BUT disease amenable to TACE (minimal vascular invasion Vp1/Vp2 allowed)
- No massive multinodular pattern preventing adequate TACE
- No extrahepatic disease
- Child-Pugh-Score A or B7
- Performance Status ECOG 0-1
- No presence of untreated or incompletely treated varices with bleeding or high-risk for bleeding
- Absence of other severe comorbidities

IKF-035/ABC-HCC Study Design

an international, randomized, multicenter, open-label, investigator-initiated phase 3b trial



Primary endpoint

allowing a fair comparison between two modalities (systemic Tx vs. locoregional Tx)

Time to failure of treatment strategy (TTFS)

Failure of strategy =	Arm A (Atezo/Bev)	Arm B (TACE)
1st condition →	radiologic progression	radiologic progression or stable disease
2nd condition →	AND any of the following:	

- the loss of clinical benefit OR
  - Progression at critical anatomical sites
  - Development of symptoms and signs (including laboratory values) unequivocal progression of disease
  - Decline in ECOG performance status attributed to disease progression
  - No evidence of clinical benefit as assessed by the investigator
- unacceptable toxicity OR
- liver function deterioration OR
- therapy not further applicable for other reasons

Interim Analyses

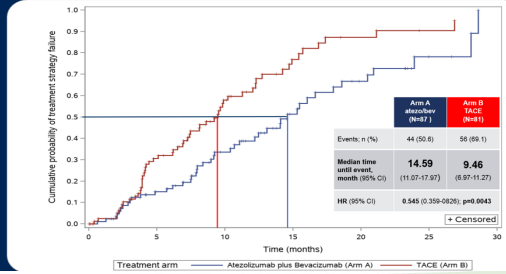
Interim Analysis: at two timepoints for efficacy/futility of TTFS

- 1st IA at 33% of information time (n=85 events)
  - **Reached**
  - Data cut-off: 13-Jun-2025 (100 events considered)
- 2nd IA at 66% of information time (planned at n=169 events)
  - Expected Q3 2026

Disclaimer:
Data at interim analyses is still premature and based on site specific reporting.
Data cleaning is still in progress. Slight changes at final analysis are possible!

Current recruitment: 231/320 patients (Dec-2025)

Time to Failure of Treatment Strategy (TTFS)



Galle PR. ASCO GI 2026.

CONCLUSIONS

GASTROESOPHAGEAL ADENOCARCINOMA

- Durvalumab+FLOT is the new SOC for locally advanced gastric/GEJ adenocarcinoma, showing an impact on EFS and OS.
- HERIZON-GEA-01 supports zanidatamab as new SOC, potentially replacing trastuzumab, as well as the use of tislelizumab in 1L HER2+ advanced GEA.
- Trastuzumab deruxtecan is recommended for HER2+ advanced GEA previously treated with a trastuzumab-based regimen.

PANCREATIC CANCER

- Neoadjuvant PAXG significantly prolongs EFS compared to mFOLFIRINOX in resectable/borderline resectable PDAC. More follow us is needed, but it could potentially change the SOC.
- GnP+TTFields could be considered as a new SOC in locally advanced PDAC.
- Promising early results of KRAS inhibitors. Waiting for results from randomized phase III clinical trials.

CONCLUSIONS

BILLIARY TRACT CARCINOMA

- Perioperative CT seems to improve survival compared to adjuvant CT in LA resectable BTC, but it´s not considered an SOC yet.
- Two phase IIIB clinical trials corroborate the efficacy of first-line durvalumab+gemcitabine-based regimens and ivosidenib in mIDH1 CCA in a real-world setting.
- Lirafrugatinib is a highly selective FGFR2 inhibitor with clinically meaningful antitumor activity in previously treated advanced CCA harboring FGFR2-f/r.

HEPATOCELLULAR CARCINOMA

- Systemic therapy with anti–PD-1/PD-L1 plus an antiangiogenic agent or dual immunotherapy with anti–PD-1/anti–CTLA-4 is the treatment of choice in patients with advanced HCC, patients with diffuse-pattern stage B disease, and after failure of local therapy.
- Dual immune checkpoint blockade combined with an antiangiogenic agent has not demonstrated improved outcomes.
- In patients with stage B HCC who are candidates for TACE, the combination of immunotherapy ± antiangiogenic agents increases PFS but without impact in OS.
- Preliminary results from a phase III study open the possibility of upfront systemic therapy without TACE in stage B disease.