XX JORNADA DE ACTUALIZACIÓN

ASCO GI 2026

24 de febrero de 2026

¿Qué hay de nuevo en los tumores hepato-bilio-pancreáticos?

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DISCLOSURES

Consultant or Advisory Role

- Amgen, Servier, Incyte, Sanofi, AstraZeneca, Taiho, Celgene, Eisai

Institutional financial interests (financial support to research projects):

- Celgene, AstraZeneca, BeiGene, Incyte

Non-financial interests:

- AstraZeneca, Incyte, Servier, Roche, Eisai, MSD

Tumores pancreáticos

Oral presentation

Preliminary phase 1 results of INCB161734, a novel oral KRAS G12D inhibitor, as monotherapy or in combination with chemotherapy for advanced/metastatic PDAC.

Rapid oral abstract presentation

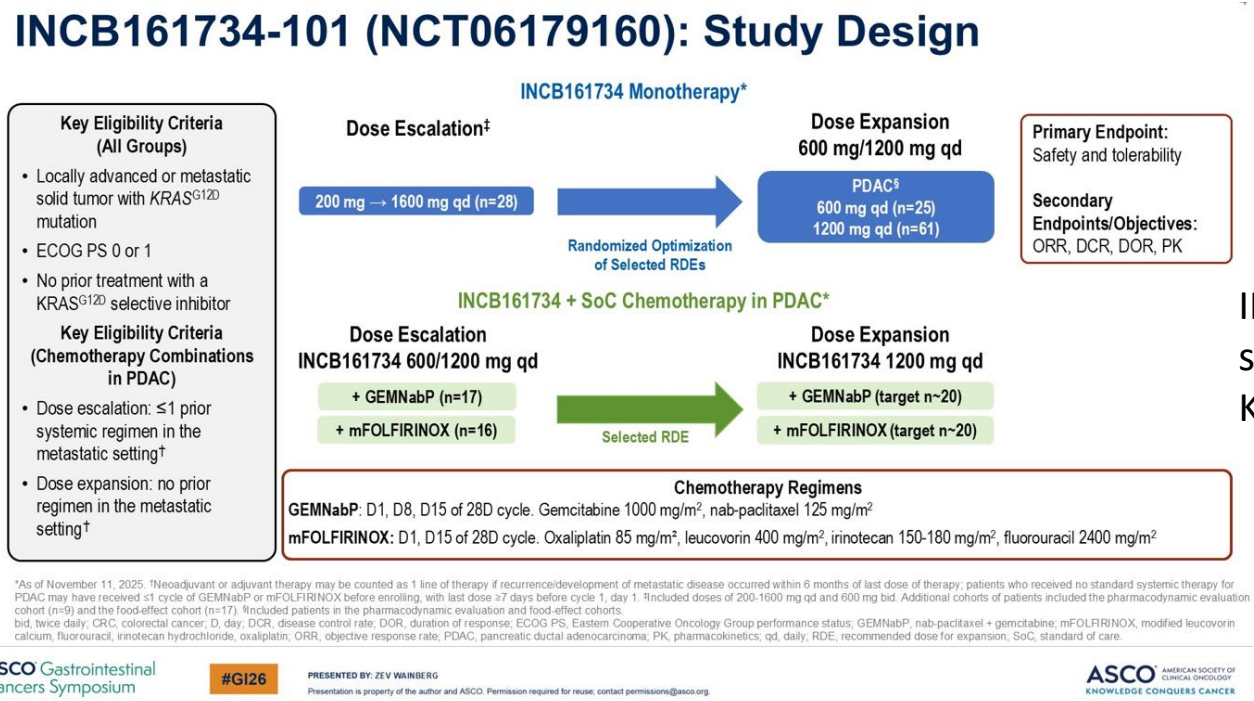
-Results from the randomized phase 2 study of elraglusib plus gem/nab versus gem/nab in previously treated mPDAC.

-Integrated penpulimab (a PD-1 inhib), anlotinib (antiangiogenic), nab and gemas 1L regiment for mPDAC. Multi-centered, randomized controlled trial

-Phase II study of durvalumab plus olaparib in patients with mPDAC and DNA damage repair alterations

-ALTOPANC: Local ablative therapies in oligometastatic PDAC-A binational french-Belgian retrospective study.

Preliminary phase 1 results of INCB161734, a novel oral KRAS G12D inhibitor, as monotherapy or in combination with chemotherapy for advanced/metastatic PDAC.

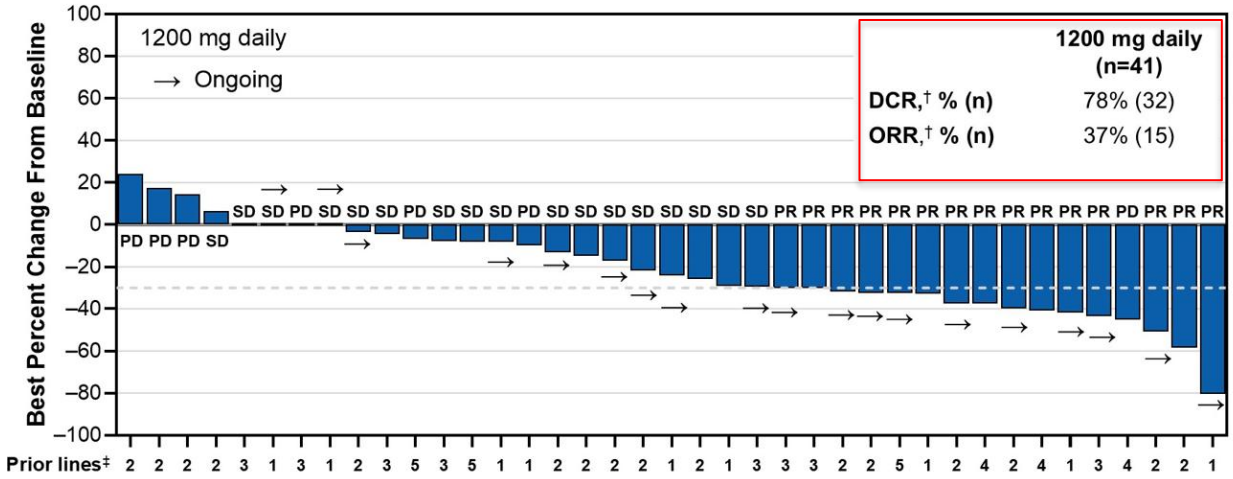


INCB161734 is a novel, selective ON/OFF oral KRAS G12D inhibitor

Preliminary phase 1 results of INCB161734, a novel oral KRAS G12D inhibitor, as monotherapy or in combination with chemotherapy for advanced/metastatic PDAC.

INCB161734 Monotherapy Showed Encouraging Antitumor Activity in Heavily Pretreated Patients With PDAC

- High ORR and DCR for patients with PDAC (mainly 3L+) who received INCB161734 1200 mg daily*



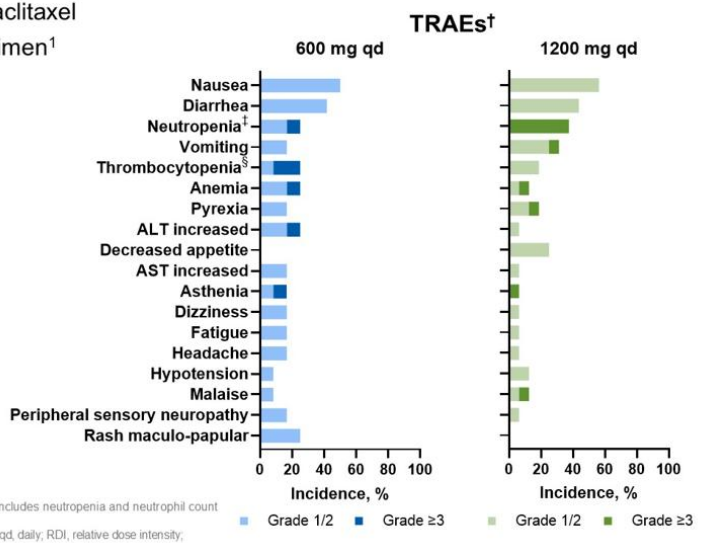
*INCB161734 600 mg bid or 1200 mg qd. †Investigator-assessed per RECIST v1.1 in patients with a baseline scan who either completed ≥2 postbaseline scans or discontinued due to clinical progression or death. Missing data: death before first scan (n=1) and no target lesion measurement recorded (n=1). ‡In the advanced/metastatic setting.
3L, third-line; bid, twice daily; DCR, disease control rate; ORR, objective response rate; PD, progressive disease; PDAC, pancreatic ductal adenocarcinoma; qd, daily; RECIST, Response Evaluation Criteria in Solid Tumors; SD, stable disease.

Preliminary phase 1 results of INCB161734, a novel oral KRAS G12D inhibitor, as monotherapy or in combination with chemotherapy for advanced/metastatic PDAC.

INCB161734 in Combination With GEMNabP Was Well Tolerated Without Compromising Chemotherapy Dose Intensity

- 46% of patients were 2L and had received prior systemic chemotherapy
- Median RDI was 74% for both gemcitabine and nab-paclitaxel
  - Comparable to previous reports for GEMNabP regimen[1]

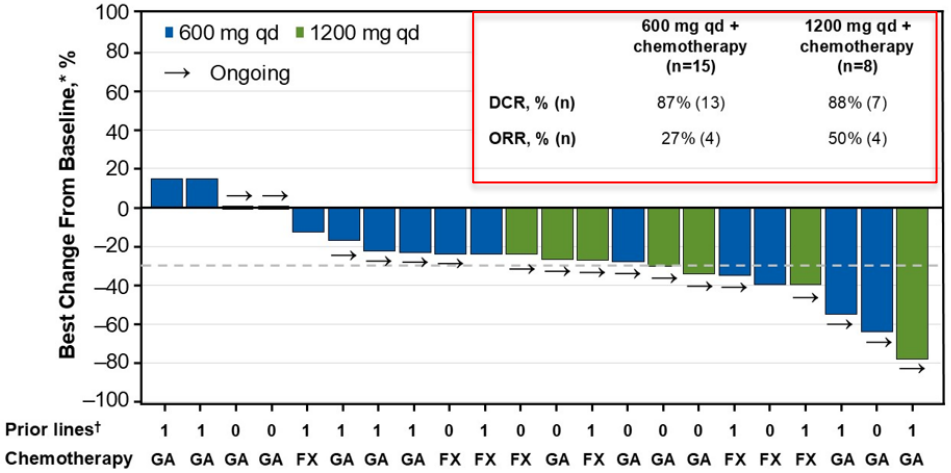
	GEMNabP	
	600 mg qd (n=12)	1200 mg qd (n=16)
TRAE,* n (%)	All Grades	All Grades
Any TRAE	12 (100)	14 (87.5)
TRAE leading to INCB161734		
Interruption	7 (58.3)	7 (43.8)
Reduction	0 (0)	1 (6.3)
Discontinuation	0 (0)	0 (0)
TRAE leading to chemotherapy		
Interruption	8 (66.7)	6 (37.5)
Reduction	3 (25.0)	7 (43.8)
Discontinuation	1 (8.3)	0 (0)



1. Von Hoff DD, et al. *N Engl J Med*. 2013;369(18):1691-1703.
*Assessed in patients who received ≥1 dose of study drug. †Including only TRAEs that occurred in ≥10% of patients. ‡Includes neutropenia and neutrophil count decreased. §Includes thrombocytopenia and platelet count decreased.
2L, second-line; ALT, alanine aminotransferase; AST, aspartate aminotransferase; GEMNabP, nab-paclitaxel + gemcitabine; qd, daily; RDI, relative dose intensity; TRAE, treatment-related adverse event.

Preliminary phase 1 results of INCB161734, a novel oral KRAS G12D inhibitor, as monotherapy or in combination with chemotherapy for advanced/metastatic PDAC.

INCB161734 With SoC Chemotherapy Showed Encouraging Antitumor Activity in Patients With 1L or 2L Metastatic PDAC

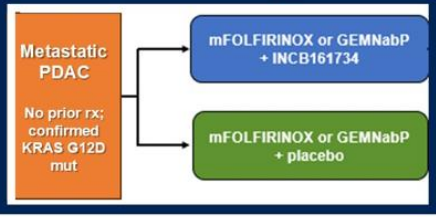


*Investigator-assessed per RECIST v1.1 in patients with ≥1 postbaseline scan or who discontinued due to clinical progression or death. Missing data: death before first scan (n=1). †In the advanced/metastatic setting.
1L, first-line; 2L, second-line; DCR, disease control rate; FX, modified leucovorin calcium, fluorouracil, irinotecan hydrochloride, oxaliplatin; GA, nab-paclitaxel + gemcitabine; ORR, objective response rate; PDAC, pancreatic ductal adenocarcinoma; qd, daily; RECIST, Response Evaluation Criteria in Solid Tumors; SoC, standard of care.

Discussion, Dr. Ko

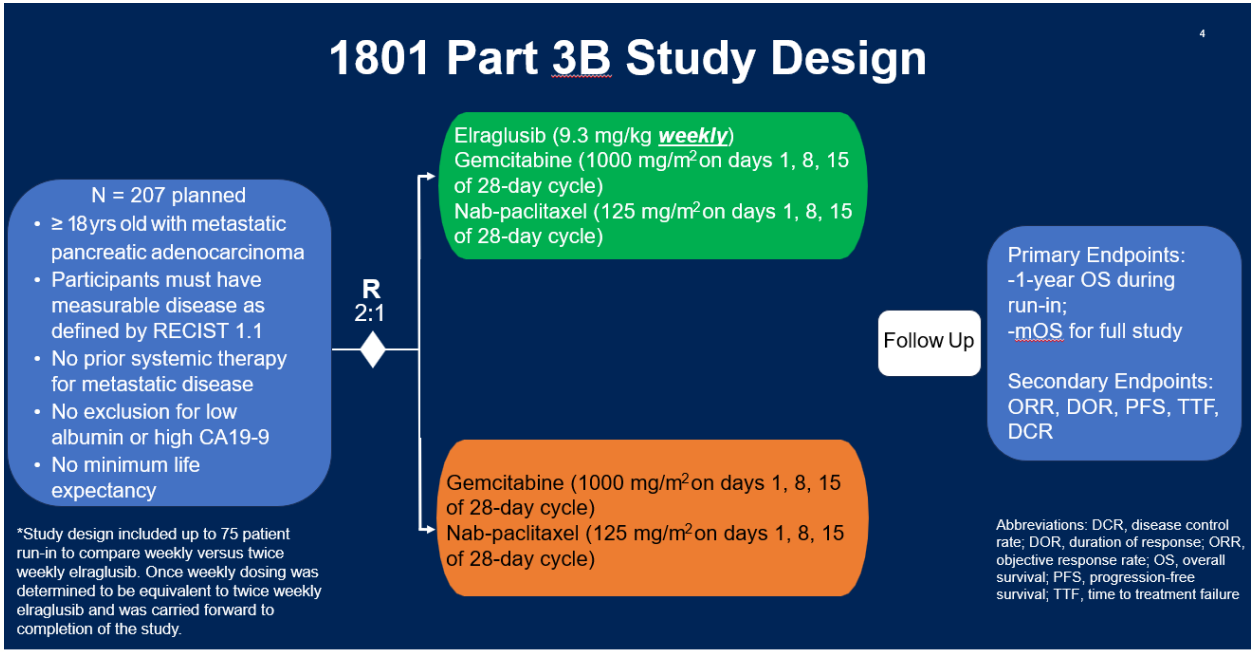
Where we are going in the future with RAS inhibitors: The sky is the limit?

1. Chemotherapy-refractory advanced/ metastatic disease
2. Front-line advanced/ metastatic disease in combination with chemorx …or as monotherapy?
3. Adjuvant (or neoadjuvant) setting – in combo with, after, or in lieu of chemorx
4. ‘Maintenance’ treatment (all disease settings)
5. Novel combinations (e.g. with other targeted rxs or IO)



PRESENTED BY: Andrew H. Ko, MD, FASCO (University of California San Francisco)

Results from the randomized phase 2 study of elraglusib plus gem/nab versus gem/nab in previously treated mPDAC.



Results from the randomized phase 2 study of elraglusib plus gem/nab versus gem/nab in previously treated mPDAC.

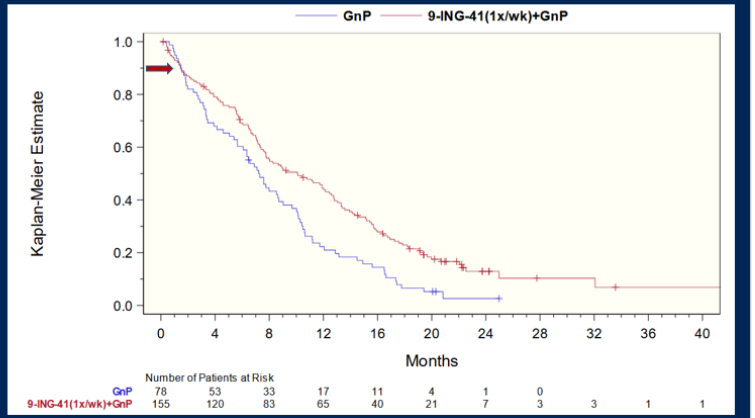
Met Primary Efficacy Endpoint of Improved Survival

38% reduction in risk of death in safety population/mITT

17% of patients still alive in elraglusib/GnP arm as of 22 November 2025 data cutoff

	Elraglusib/GnP (N = 155)	GnP (N = 78)
Primary Endpoint: mOS (months)[95%CI] HR=0.62; log-rank p=0.02*	10.1 [7.7, 12.6]	7.2 [5.7, 9.0]
12-month OS (%)	44.4	22.3
Events (% event)	128 (82.6)	74 (94.9)
18-month OS (%)	22.9	6.6
24-month OS (%)	12.9	2.6

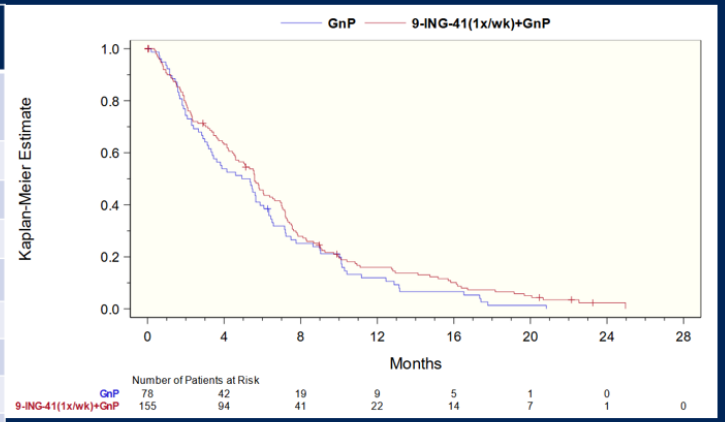
*statistically significant
Abbreviations: GnP, gemcitabine plus nab-paclitaxel; HR, hazard ratio; mOS, median overall survival; OS, overall survival



Results from the randomized phase 2 study of elraglusib plus gem/nab versus gem/nab in previously treated mPDAC.

Progression-Free Survival (PFS) and ORR-mITT

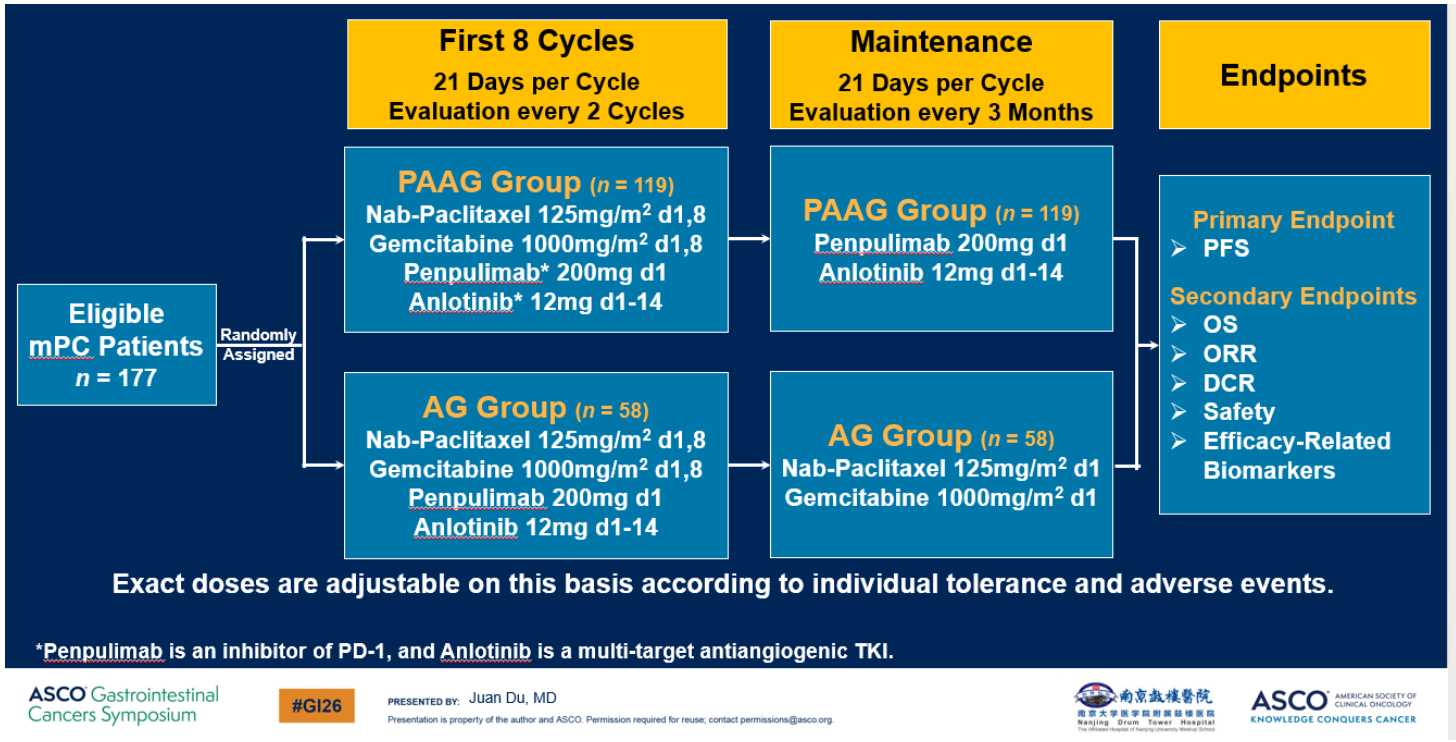
Safety Population	Elraglusib/GnP (N = 155)	GnP (N = 78)
mPFS (months) HR=0.83; log-rank p=NS	5.6	5.1
Events (% events)	143 (92.3)	77 (98.7)
TTF (months) HR=0.78; p=NS	5.0	3.4
ORR, %	28.4	21.8
Best response, n (%)		
Complete Response	1 (0.6)	0
Partial Response	43 (27.8)	17 (21.8)
Stable Disease	51 (32.9)	27 (34.6)
Progressive Disease	21 (13.5)	15 (19.2)
Not Evaluable/Unknown	39 (25.2)	19 (24.4)
DCR[b], %	40.6	33.3
Median DOR (months)[a]	5.5	4.1



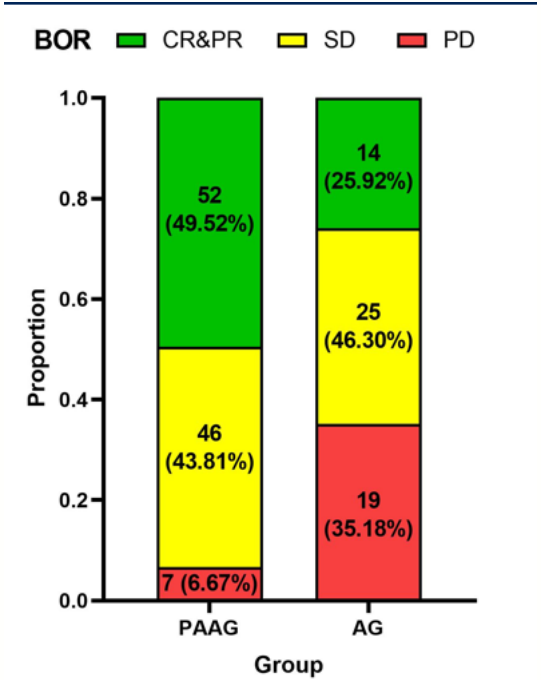
Abbreviations: GnP, gemcitabine plus nab-paclitaxel; HR, hazard ratio; mPFS, median progression-free survival; NS, not significant; TTF, time to treatment failure

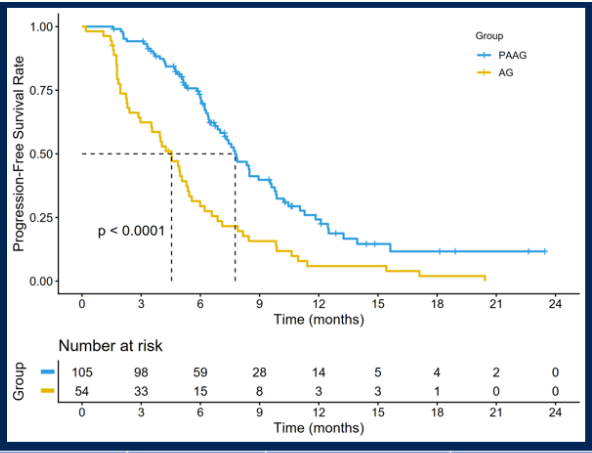
Data cutoff 22 November 2025

Integrated penpulimab (a PD-1 inhib), anlotinib (antiangiogenic), nab and gemas 1L regiment for mPDAC. Multi-centered, randomized controlled trial

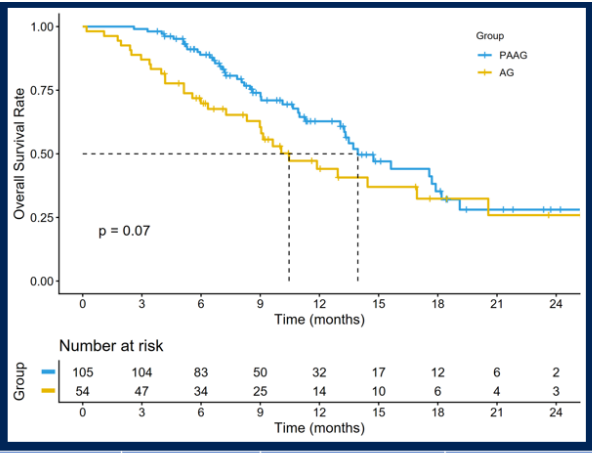


Integrated penpulimab (a PD-1 inhib), anlotinib (antiangiogenic), nab and gemas 1L regiment for mPDAC. Multi-centered, randomized controlled trial





Group	mPFS	95%CI	*P*-Value
PAAG	7.8 mo	7.0 ~ 8.8 mo	< 0.001**
AG	4.5 mo	3.6 ~ 5.5 mo	



Group	mOS	95%CI	*P*-Value
PAAG	13.9 mo	11.6 ~ 16.3 mo	0.070
AG	10.5 mo	6.9 ~ 14.0 mo	

Phase II study of durvalumab plus olaparib in patients with metastatic pancreatic cancer and DNA damage repair genes alterations

Background and study design

Metastatic pancreatic cancer (mPC) with DNA damage repair (DDR) alterations such as *BRCA1*, *BRCA2 and PALB2* is associated with sensitivity to platinum-based chemotherapy (CT) and PARP inhibition.

Evidence suggests PARP inhibition with immune checkpoint blockade may enhance antitumor activity.

This study evaluates the combination of durvalumab and olaparib in DDR-mutated mPC patients with no progression to platinum-based CT.

- Open label
- Single arm
- Multicenter

→

Olaparib:
300 mg PO BID
Durvalumab:
1500 mg IV q4w

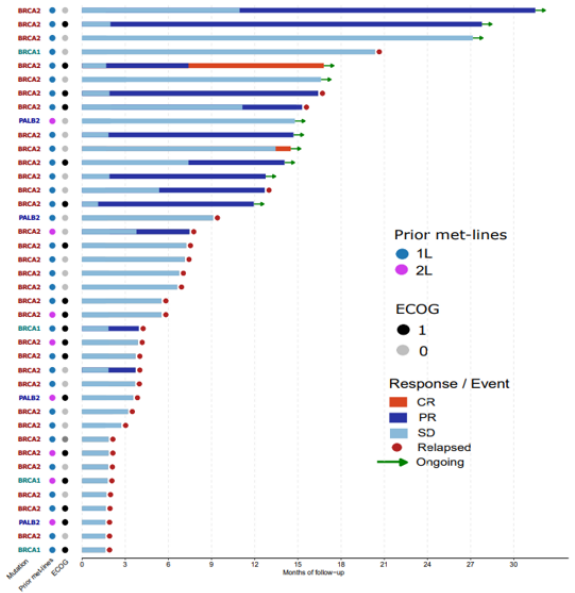
→

Endpoint:
- Primary: ORR
- Secondary: DCR, PFS, OS, Safety

Phase II study of durvalumab plus olaparib in patients with metastatic pancreatic cancer and DNA damage repair genes alterations

Results (ORR, DCR, DoR)

Swimmer plot



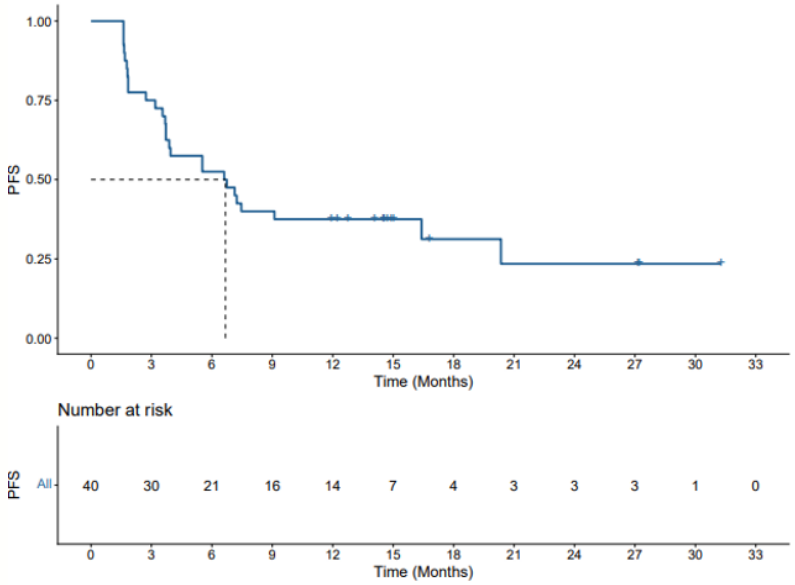
Objective response rate (ORR) and disease control rate (DCR)

Characteristic	N = 40 (%)
Median follow up months (95% CI)	15.0 (14.5, 24.9)
Objective response	
Complete Response (CR)	2 (5.0%)
Partial Response (PR)	12 (30.0%)
Stable Disease (SD)	17 (42.5%)
Progressive Disease (PD)	9 (22.5%)
ORR (CR + PR)	14 (35.0%)
DCR (CR + PR + SD)	31 (77.5%)
DCR 6 months	23 (57.5%)
Median DoR months (95% CI)	14.5 (14.5, -)
Ongoing response	13 (32.5%)

Phase II study of durvalumab plus olaparib in patients with metastatic pancreatic cancer and DNA damage repair genes alterations

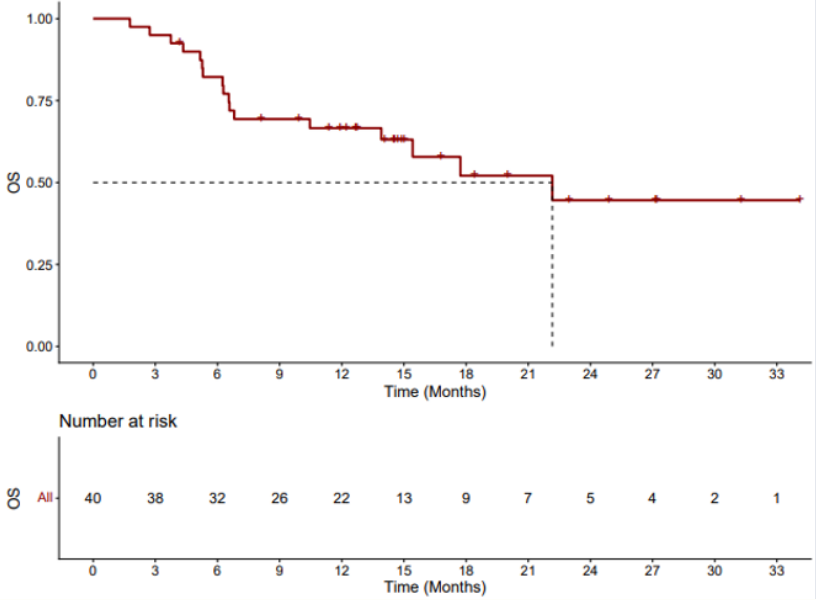
PFS (all patients)

Characteristic	6 months	12 months	24 months	Median (95% CI)
PFS rates (95% CI)	53% (39, 70)	38% (25, 56)	23% (11, 51)	6.7m (3.7, -)

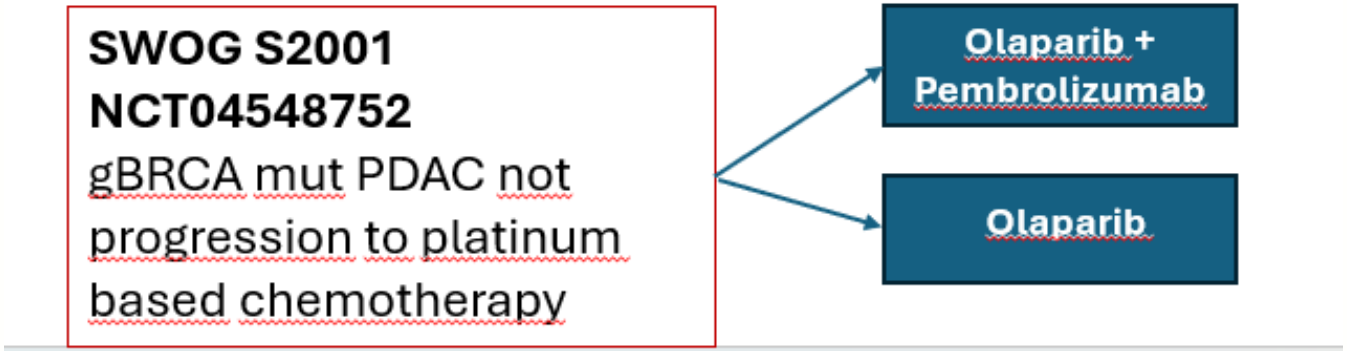


OS (all patients)

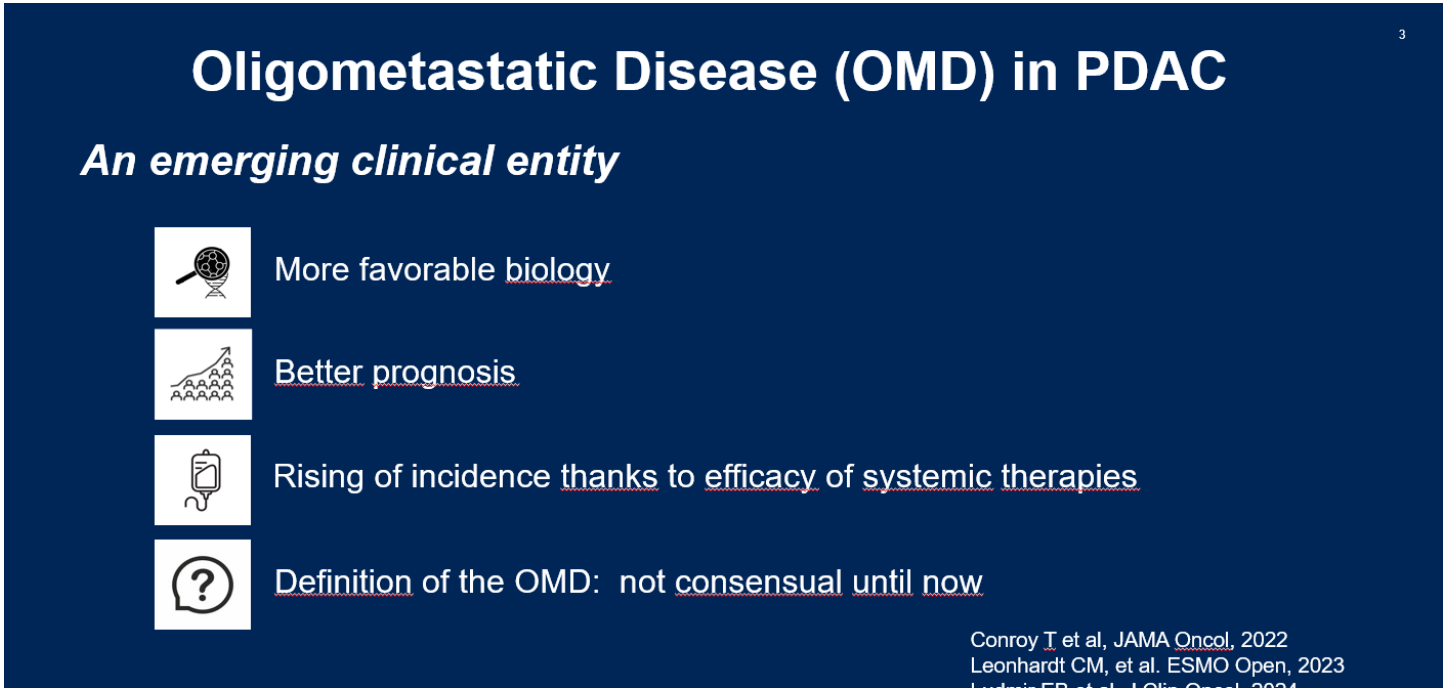
Characteristic	6 months	12 months	24 months	Median (95% CI)
OS rates (95% CI)	82% (71, 95)	67% (53, 83)	45% (28, 72)	22.2m (13.9, -)



Phase II study of durvalumab plus olaparib in patients with metastatic pancreatic cancer and DNA damage repair genes alterations



ALTOPANC: Local ablative therapies in oligometastatic PDAC-A binational french-Belgian retrospective study.



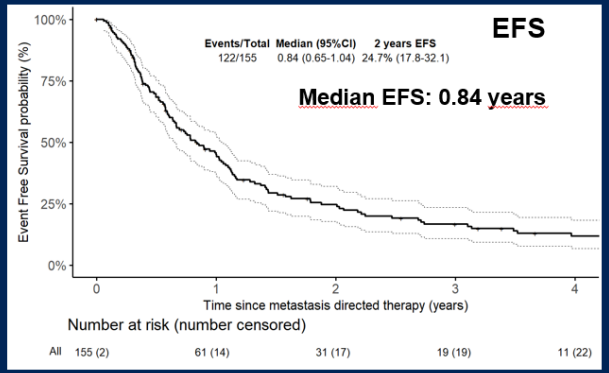
ALTOPANC: Local ablative therapies in oligometastatic PDAC-A binational french-Belgian retrospective study.

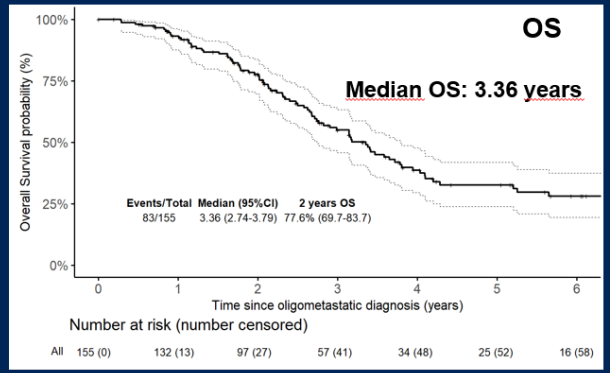
	Surgery n(%)	Radiotherapy n(%)	Radiofrequency n(%)	p-value
Number of metastases				
1	51(77)	31 (63)	25 (71)	p = 0.38
>1	15 (23)	17 (37)	10 (29)	
CA19.9 at metastatic diagnosis(median)	31,5 (15-200)	64 (17-190)	33,7 (17-191)	p = 0.72
Performance Status for metachronous				
0	17(40)	26(55)	11(39)	p = 0.31
1	24(56)	19(41)	14(50)	
>1	2(4)	2(4)	3(11)	
Median size (mm) (Q1-Q3)	15 (5-350)	11 (5-35)	10 (4-120)	p = 0.11
Metastatic sites				
Liver	34(49)	22(44)	15(42)	p = 0.72
Lung	23(33)	16(32)	22(61)	p = 0.0095

PRESENTED BY: Anthony Turpin, MD, PhD

ALTOPANC: Local ablative therapies in oligometastatic PDAC-A binational french-Belgian retrospective study.

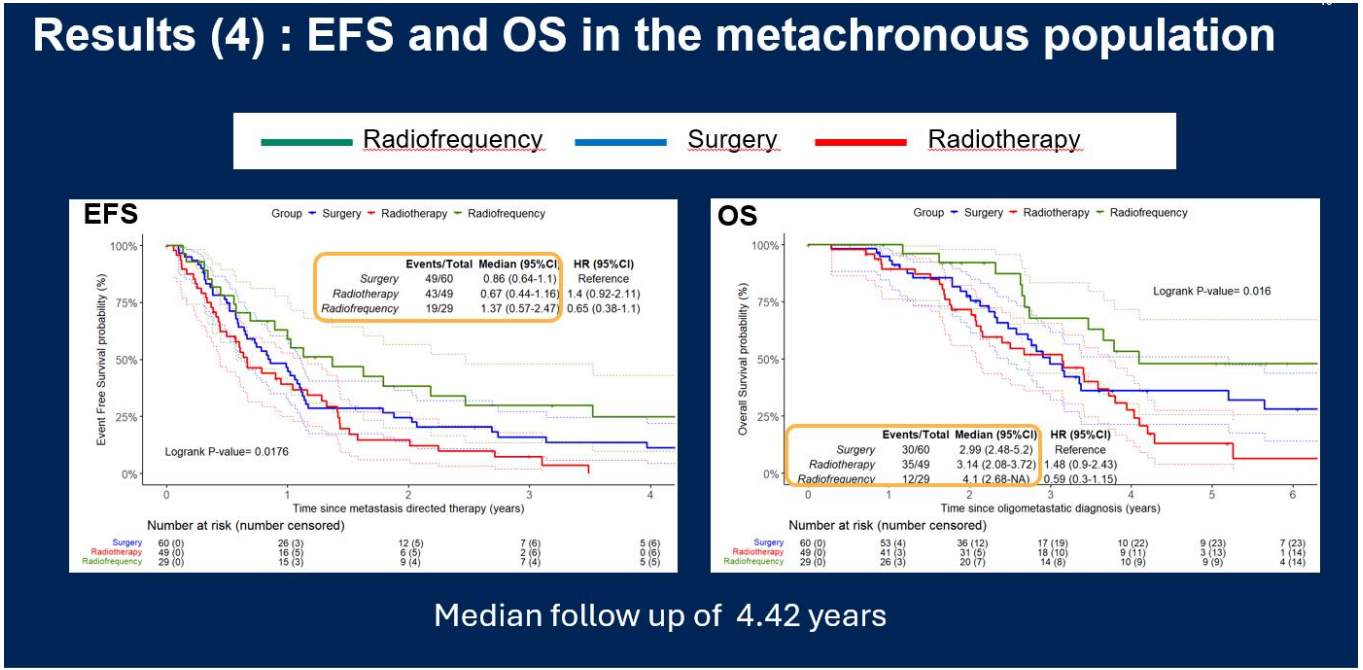
Results (3) : EFS and OS in the whole cohort





Median follow up of 4.42 years

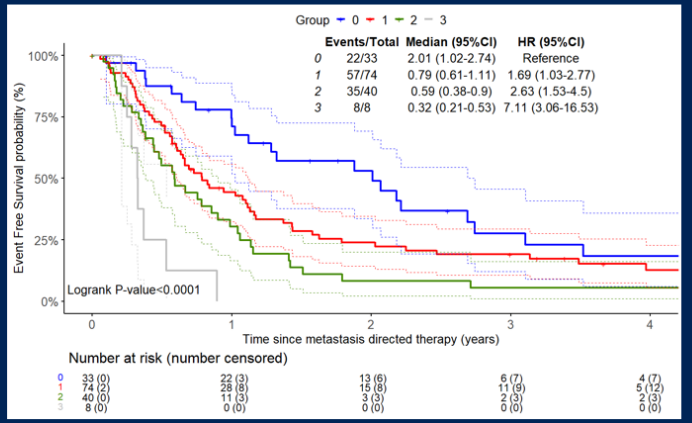
ALTOPANC: Local ablative therapies in oligometastatic PDAC-A binational french-Belgian retrospective study.



ALTOPANC: Local ablative therapies in oligometastatic PDAC-A binational french-Belgian retrospective study.

Results (5) : Prognostic score (« ALTOPANC »)

- Prognostic score for EFS using prognostic factors identified in the multivariate analysis and literature
- 1 point attributed for each variable:
  - CA 19.9 serum level > 90 U/mL,
  - >1 metastases,
  - non-pulmonary site

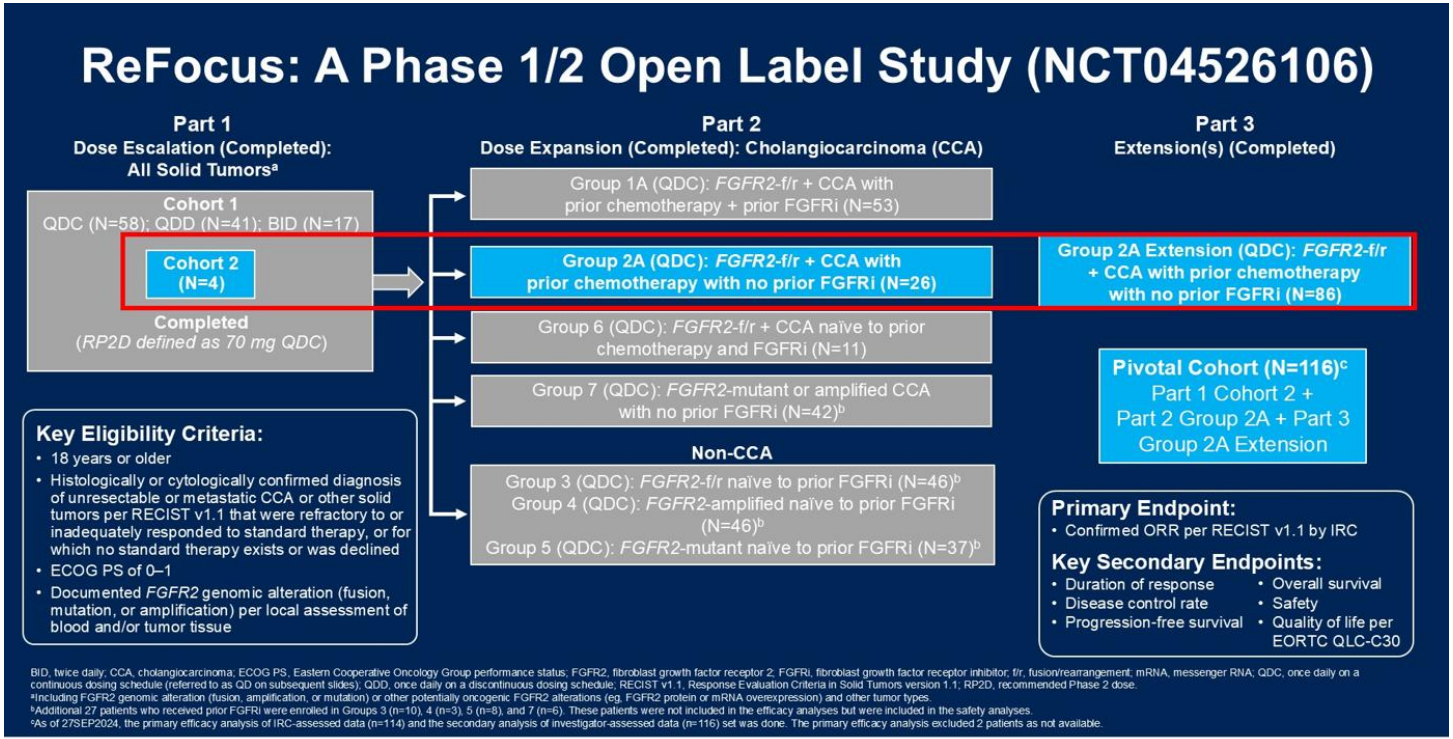


Tumores biliares

Oral presentation

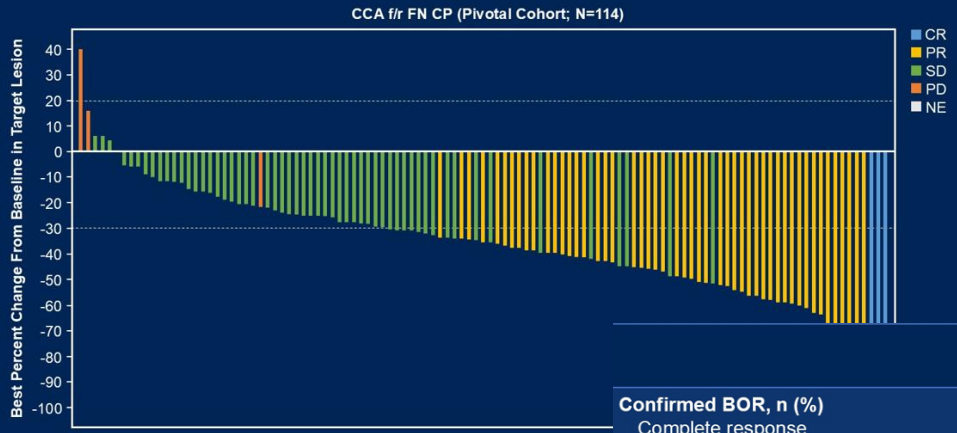
Eficacia and safety of lirafugratinib in FGFRi-naive CCA harboring FGFR2 fusions/rearrangements

Eficacia and safety of lirafugratinib in FGFRi-naive CCA harboring FGFR2 fusions/rearrangements



RLY4008: selective, irreversible FGFR2 inhibitor

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



BOR, best overall response; CCA, cholangiocarcinoma; CP, chemotherapy pretreated; CR, complete response; FN, fibroblast growth factor receptor inhibito
evaluable; PD, progressive disease; PR, partial response; SD, stable disease.

	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]

PRESENTED BY: Antoine Hollebecque, MD

Summary of On-Target TEAEs (Safety Analysis Set)

	All Solid Tumors (70 mg QD Safety Population; N=385)		CCA f/r FN CP (Pivotal Safety Population; N=116)	
	Any Grade	Grade ≥3	Any Grade	Grade ≥3
Stomatitis[a], n (%)	263 (68.3)	47 (12.2)	91 (78.4)	14 (12.1)
Palmar-plantar erythrodysesthesia syndrome, n (%)	255 (66.2)	77 (20.0)	95 (81.9)	38 (32.8)
Nail toxicities[b], n (%)	282 (73.2)	31 (8.1)	102 (87.9)	14 (12.1)
Retinal pigment epithelial detachment[c], n (%)	113 (29.4)	7 (1.8)	43 (37.1)	2 (1.7)

Multicenter real-world study: a comprehensive **characterization of biliary tract cancer** epidemiology in Spain

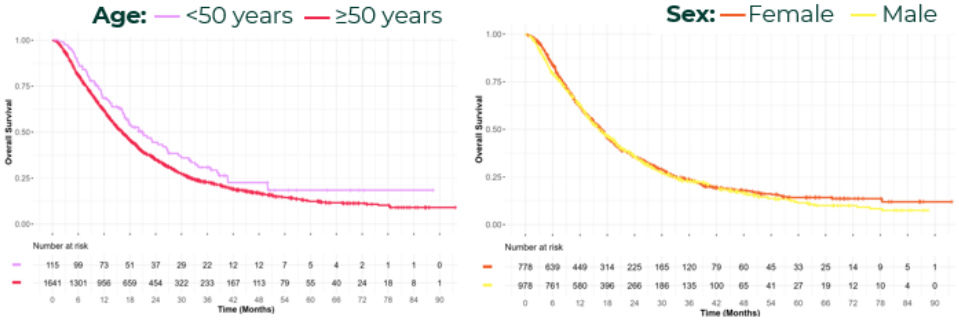
1756 patients **40** hospitals

Variable	N = 1,756'
Age at primary tumor diagnosis [median (Q1, Q3)]	68.6 (61.2, 74.9)
Sex (female)	978 (55.7%)
Location of primary tumor	
Intrahepatic	931 (53.0%)
Gallbladder carcinoma	272 (15.5%)
Extrahepatic distal	253 (14.4%)
Extrahepatic hiliar	226 (12.9%)
Ampulla of vater	47 (2.7%)
Other	27 (1.5%)
Chemotherapy	1586 (90.3%)
Immunotherapy	188 (10.7%)
Targeted therapy	111 (6.3%)
Clinical trial	136 (7.7%)

Biomarker information: Frequent ESCAT-I alterations

ESCAT-I	Biomarker determination (N)	Alteration [N (%)]
IDH1 mutation	447	75 (16.8%)
FGFR2 fusion	401	32 (8.0%)
MSI	491	30 (6.1%)
HER2 ampl./overexpression	449	25 (5.7%)

Overall Survival by Subgroups



Ampl., amplification; **ESCAT**, ESMO Scale for Clinical Actionabilityy of Molecular Targets; **MSI**, microsatellite instability; **RETUD**, Registro Español de Tumores Digestivos

1. Macarulla et al.. *J Clin Oncol.* 2026; 44(2_suppl): DOI: 10.1200/JCO.2026.44.2_suppl.503

Tumores HCC

Oral presentation

-Adjuvant pembrolizumab for patients with HCC and complete radiological response after surgical resection or local ablation. Phase 3 Keynote 937 study

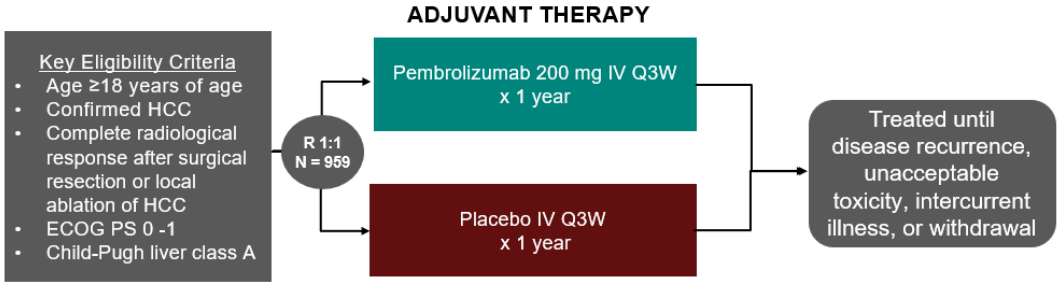
-INKF/ABC-HCC: A pase IIIb, randomized, multicenter, open-label trial of atezolizumab plus bevacizumab versus TACE in intermediate-stage HCC

Rapid oral abstract presentation

Nivolumab plus ipilimumab vs lenvatinib or sorafenib as a first line treatment for unresectable HCC: 4 years follow-up of CheckMate 9DW.

Adjuvant pembrolizumab for patients with HCC and complete radiological response after surgical resection or local ablation. Phase 3 Keynote 937 study

Phase 3 KEYNOTE-937 Study Design



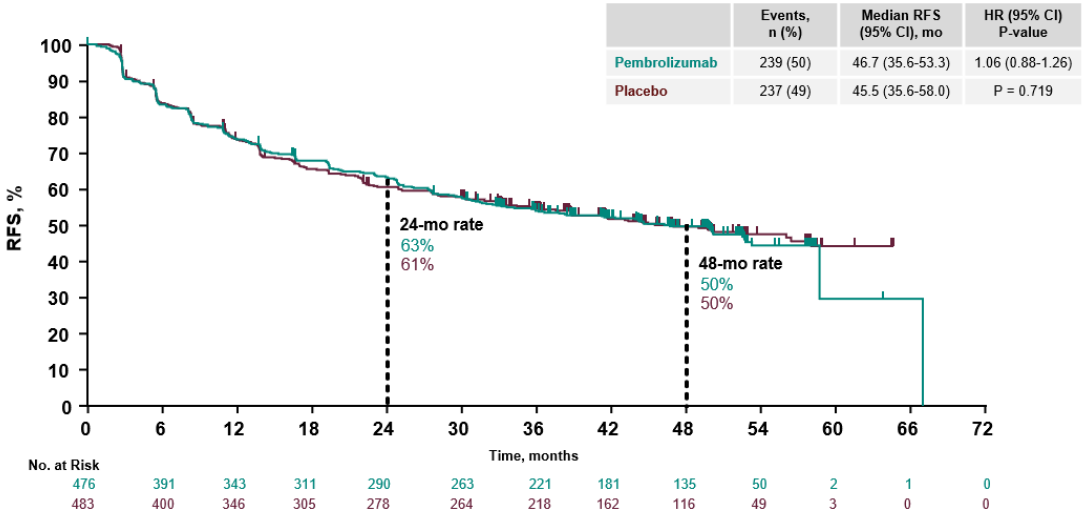
Stratification factors
- Region (Asia [not including Japan] vs non-Asia)
- Prior local therapy (resection vs ablation)
- Risk of recurrence (intermediate vs high vs very high risk)
- AFP at initial diagnosis before resection or ablation (<200 ng/mL vs ≥200 ng/mL)

Endpoints
- Primary: RFS by BICR or pathology; OS
- Key secondary: DMFS by BICR or pathology, safety

Chan et al.

Adjuvant pembrolizumab for patients with HCC and complete radiological response after surgical resection or local ablation. Phase 3 Keynote 937 study

Recurrence-Free Survival



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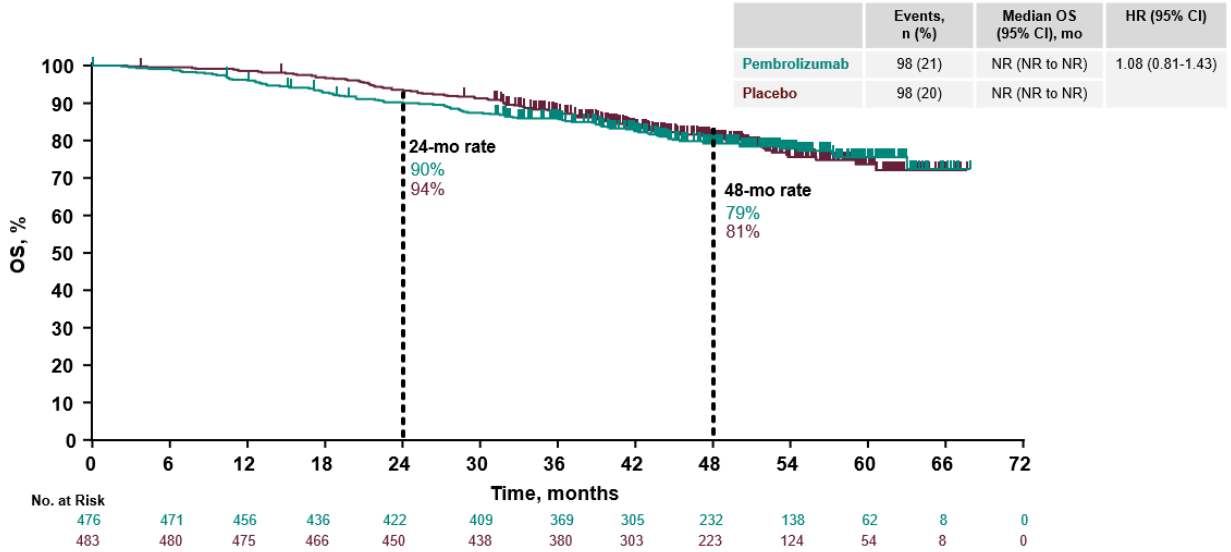
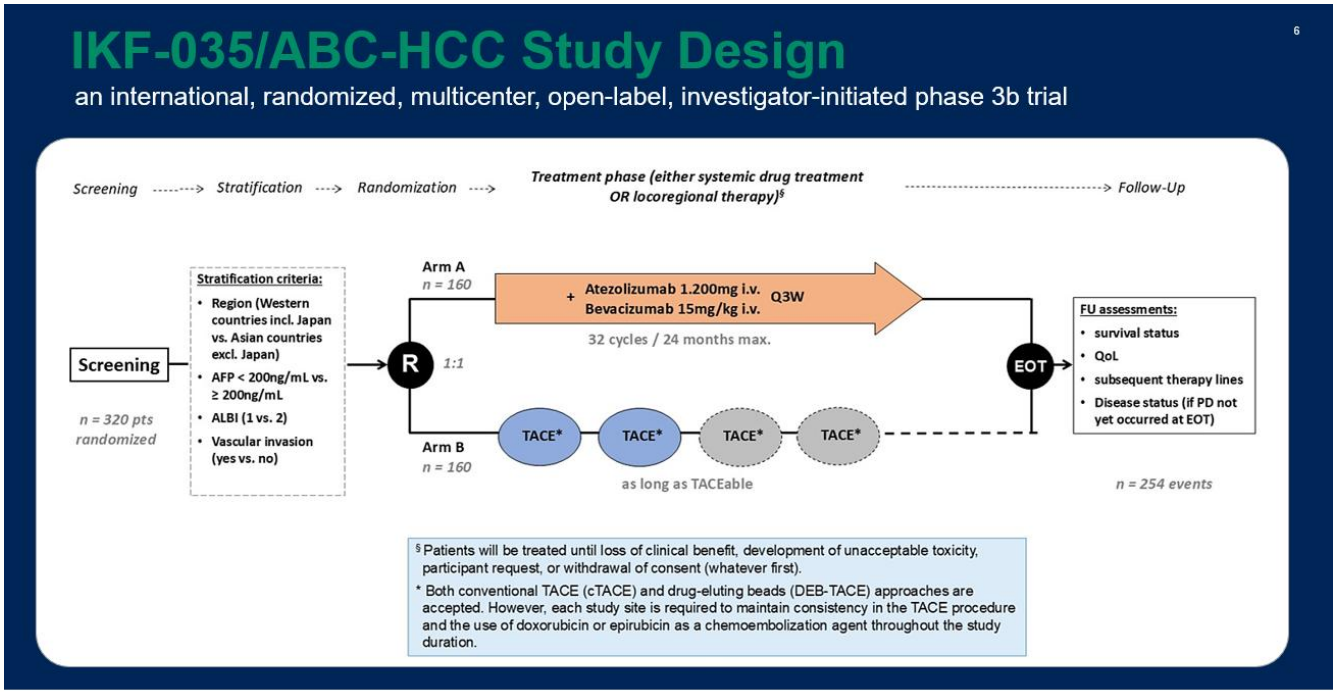
Adjuvant pembrolizumab for patients with HCC and complete radiological response after surgical resection or local ablation. Phase 3 Keynote 937 study

Overall Survival



Chan et al.

INKF/ABC-HCC: A pase IIIb, randomized, multicenter, open-label trial of atezolizumab plus bevacizumab versus TACE in intermediate-stage HCC



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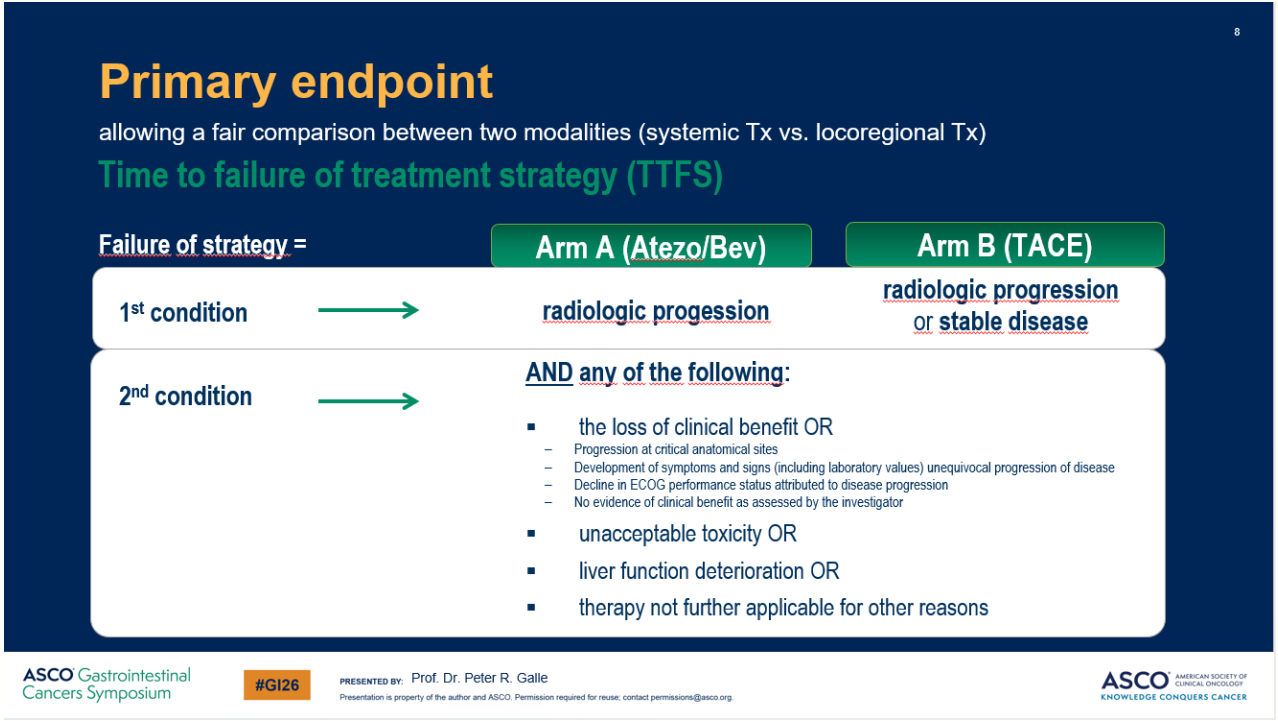

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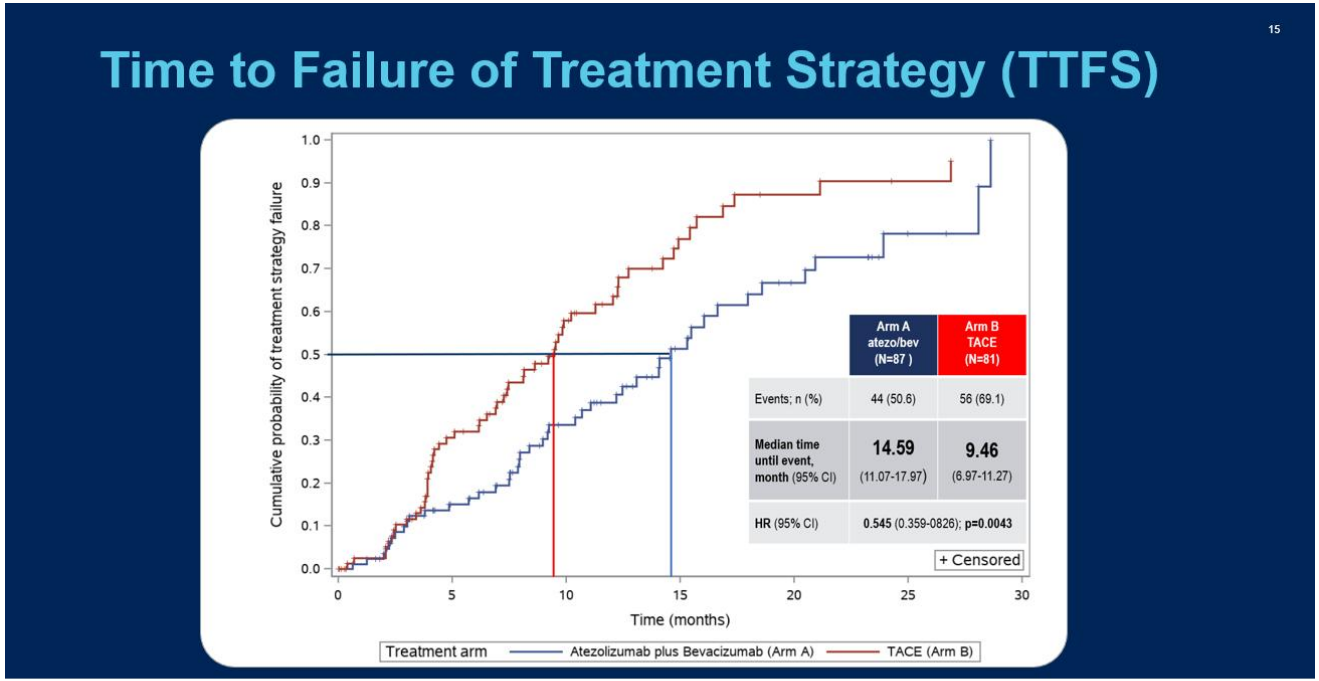
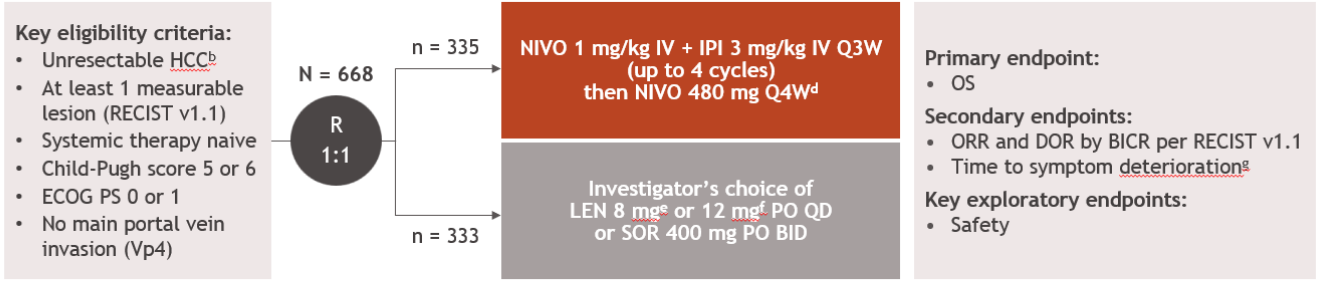


Nivolumab plus ipilimumab vs lenvatinib or sorafenib as a first line treatment for unresectable HCC: 4 years follow-up of CheckMate 9DW.

CheckMate 9DW

CheckMate 9DW study design

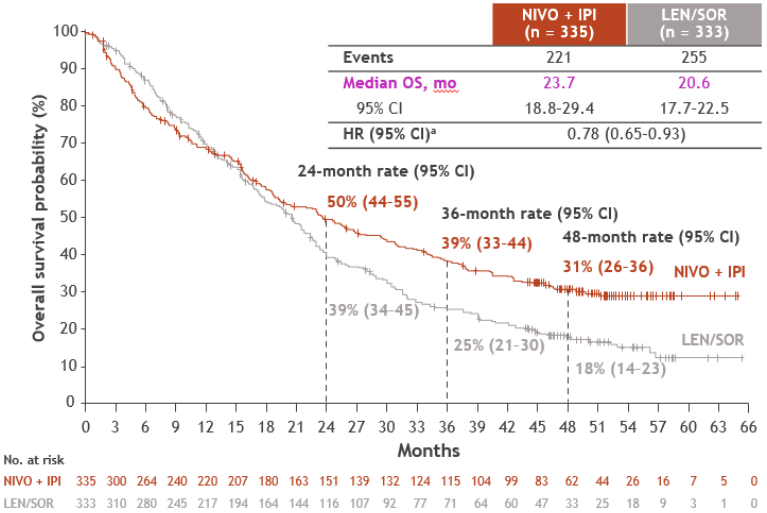
- CheckMate 9DW is a global, phase 3, randomized, open-label trial of NIVO in combination with IPI compared with LEN or SOR as 1L treatment in patients with unresectable HCC[a]



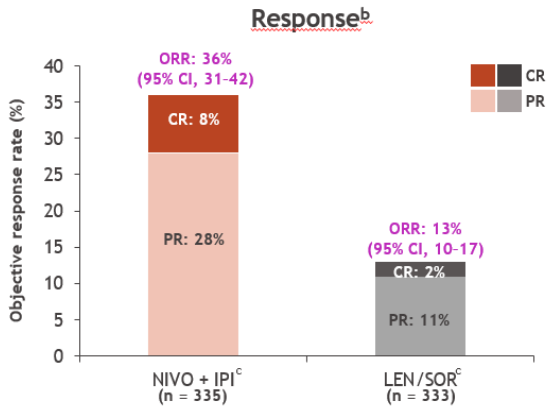
- At data cutoff (July 9, 2025), median (range) follow-up[h] was 52.5 (44.0-66.1) months

Nivolumab plus ipilimumab vs lenvatinib or sorafenib as a first line treatment for unresectable HCC: 4 years follow-up of CheckMate 9DW.

Overall survival, response, and duration of response



	NIVO + IPI (n = 335)	LEN/SOR (n = 333)
Events	221	255
Median OS, mo	23.7	20.6
95% CI	18.8-29.4	17.7-22.5
HR (95% CI)[a]	0.78 (0.65-0.93)	



	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)

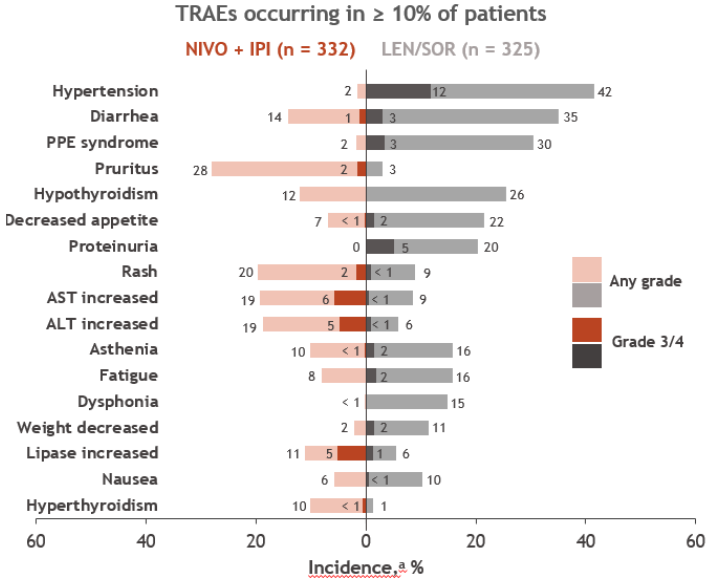
- Sustained OS benefit with NIVO + IPI vs LEN/SOR with longer follow-up, and higher 48-month OS rates
- Continued ORR benefit with NIVO + IPI vs LEN/SOR, with a higher CR rate and durable responses

Nivolumab plus ipilimumab vs lenvatinib or sorafenib as a first line treatment for unresectable HCC: 4 years follow-up of CheckMate 9DW.

Safety summary

All treated patients, n (%)	NIVO + IPI (n = 332)	LEN/SOR (n = 325)
Median (range) duration of treatment, mo	4.7 (< 0.1 to 24.4)	6.9 (< 0.1 to 50.6)

All treated patients, n (%)	NIVO + IPI (n = 332)		LEN/SOR (n = 325)	
	Any grade	Grade 3/4	Any grade	Grade 3/4
TRAEs[a]				
Any TRAEs	277 (83)	136 (41)	297 (91)	138 (42)
Serious TRAEs	94 (28)	83 (25)	47 (14)	42 (13)
TRAEs leading to discontinuation	59 (18)	44 (13)	34 (10)	21 (6)
Treatment-related deaths[b]	12 (4)[c]		3 (< 1)[d]	



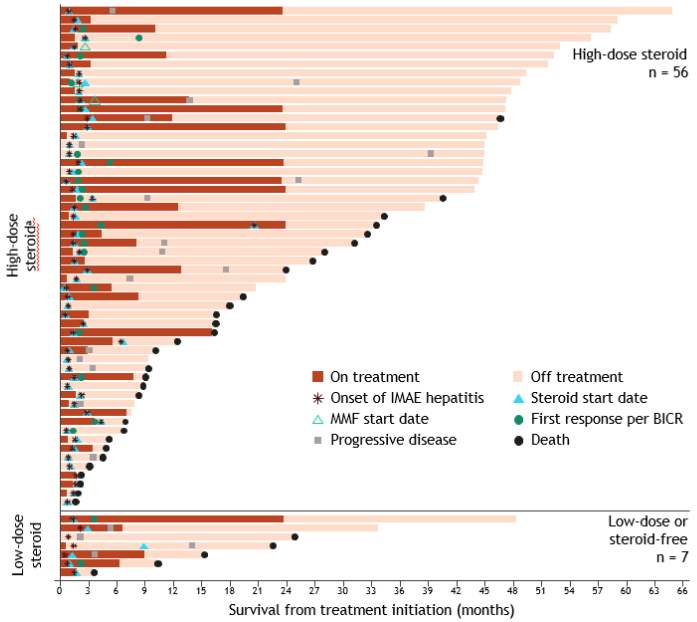
- Safety was consistent with previous follow-up,[1] with no new safety signals

Nivolumab plus ipilimumab vs lenvatinib or sorafenib as a first line treatment for unresectable HCC: 4 years follow-up of CheckMate 9DW.

Immune-mediated hepatitis with NIVO + IPI

All NIVO + IPI treated patients, n (%)	NIVO + IPI (n = 332)			
	Any grade	Grade 3/4	Received high-dose steroids[a]	Leading to D/C
Hepatitis IMAEs[b]	63 (19)	51 (15)	56 (17)	19 (6)

- Median time to onset of any-grade immune-mediated hepatitis was 6.0 (range, 0.9-88.9) weeks; these events resolved in 47 of 63 (75%) patients with a median time to resolution of 10.3 (range, 0.9-129.3+) weeks
- Hepatitis IMAEs continued to be manageable using established algorithms and most did not result in treatment discontinuation



Muchas gracias por su atención

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