AZIENDA SANITARIA LOCALE DI BIELLA

Nuove frontiere applicative

Carcinoma pancreas e vie biliari

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Disclosure

as of June 8th 2026

In the last 3 years I received:

- Personal honoraria for acting as consultant or participating to advisory boards:
  - AstraZeneca, Servier, Merck Serono, MSD, BMS, GSK, Pierre Fabre, Daiichi Sankyo, Takeda

ESMO
GOOD SCIENCE
BETTER MEDICINE
BEST PRACTICE

ESMO OPEN SCIENCE FOR OPTIMAL CANCER CARE

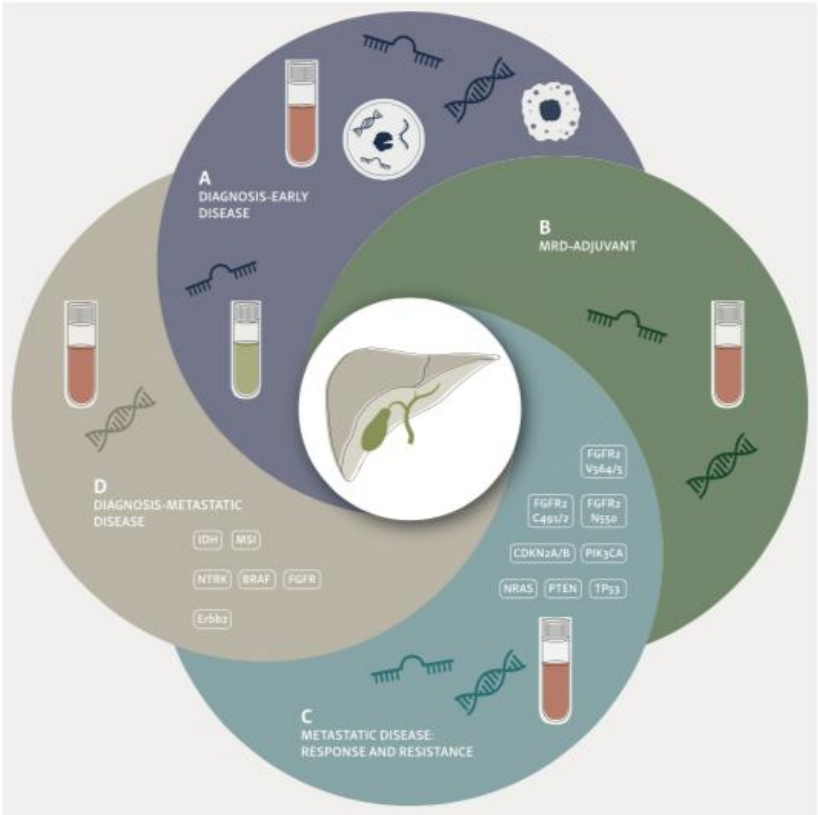
Volume 10 - Issue 5 - 2025

REVIEW

Precision oncology in biliary tract cancer: the emerging role of liquid biopsy

M. de Scordilli[1,2], M. Bortolot[1,2], S. Torresan[1,2], C. Noto[2,3], S. Rota[1,2], P. Di Nardo[1], A. Fumagalli[1], M. Guardascione[1], E. Ongaro[1], L. Foltran[1*] & F. Puglisi[1,2]

[1]Department of Medical Oncology, Centro di Riferimento Oncologico di Aviano (CRO), IRCCS, Aviano; [2]Department of Medicine, University of Udine, Udine; [3]Medical Oncology, ASUGI, Ospedale Maggiore, Trieste, Italy



ESMO guideline

Liquid biopsies using **cfDNA** may be considered, if not enough tumour tissue is available for NGS.

The gene panel should include **IDH1**, **HER2/neu**, and **BRAF** to test for hotspot mutations.

Voget A et al, Ann Oncol 2023

Recommendations for the use of next-generation sequencing (NGS) for patients with metastatic cancers: a report from the ESMO Precision Medicine Working Group

F. Mosele[1], J. Remon[2], J. Mateo[3], C. B. Westphalen[4], F. Barlesi[1], M. P. Lolkema[5], N. Normanno[6], A. Scarpa[7], M. Robson[8], F. Meric-Bernstam[9], N. Wagle[10], A. Stenzinger[11], J. Bonastre[12,13], A. Bayle[1,12,13], S. Michiels[12,13], I. Bièche[14], E. Rouleau[15], S. Jezdic[16], J-Y. Douillard[16], J. S. Reis-Filho[17], R. Dienstmann[18] & F. André[1,19,20*]

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Available online 24 August 2020

Table 10. List of genomic alterations level I/II/III according to ESCAT in advanced cholangiocarcinoma (CC)

Gene	Alteration	Prevalence	ESCAT	References
IDH1	Mutations	20%	IA	Abou-Alfa G. K, et al. *Ann Oncol.* 2019[129]
FGFR2	Fusions	15%	IB	Vogel A, et al. *Ann Oncol.* 2019[130]
	MSI-H	2%	IC	Marabelle A, et al. *J Clin Oncol.* 2020[131]
NTRK	Fusions	2%	IC	Doebele RC, et al. *Lancet Oncol.* 2020[50]
BRAF^{V600E}	Mutations	5%	IIB	Wainberg Z, et al. *J Clin Oncol.* 2019[132]
ERBB2	Amplifications Mutations	10% 2%	IIIA	Javle MM, et al. *J Clin Oncol.* 2017[133]
PIK3CA	Hotspot mutations	7%	IIIA	André F, et al. *N Engl J Med.* 2019[72]
BRCA 1/2	Mutations	3%	IIIA	De Bono J, et al. *N Engl J Med.* 2020[93]
MET	Amplifications	2%	IIIA	Camidge D, et al. *J Clin Oncol.* 2018[52]

ESCAT, European Society for Medical Oncology (ESMO) Scale for Clinical Actionability of molecular Targets

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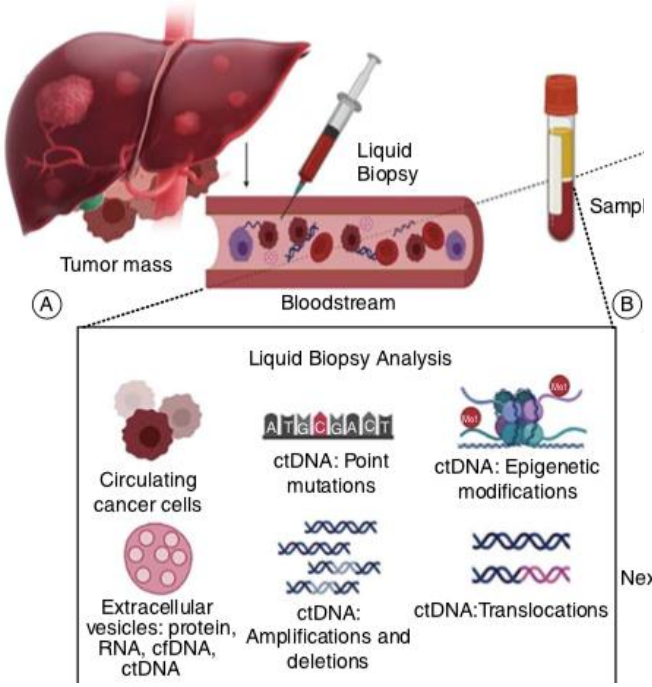

Table 1. Studies that evaluated the utility of plasma ctDNA in BTC.

	Year	Study design	Method	Sample size (n)	Mutation detection rate in plasma (%)	Tissue-plasma ctDNA concordance (%)
Berchuck et al.	2022	Retrospective	NGS -70–73 gene panel	1671	84% -44% targetable	87% for *IDH1* mutations; 100% for *BRAFV600E* and 18% for *FGFR2* fusions
Zill et al.[a]	2015	Prospective	NGS -54 gene panel	26	85%	90.3% in 17 of the 26 patients
Ettrich et al.	2019	Prospective	NGS -15 gene panel	23	61%	74% -92% in iCCA cohort
Okamura et al.	2021	Retrospective	NGS -68–73 gene panel	71	76%	68–90% in 40patients analyzed
Chen et al.	2021	Prospective	NGS -150 gene panel	154	94.8%	*TP53* (35.1 in ctDNA vs. 40.4% tissue DNA) and *KRAS* (20.1 ctDNA vs. tissue DNA 22.6%)
Guo et al.	2021	Prospective	NGS -520 gene panel	28	53.6%	Not matched
Ohyama et al.	2023	Prospective	NGS -60 gene panel	38	24% -18% targetable	Not matched
Csoma et al.	2022	Prospective	NGS -67 gene panel	25	68%	SNVs were proven in 84% of cases

Awosika JA et al, Hep Oncol 2024

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Trends in
Cancer

Forum

Circulating tumor DNA in biliary tract cancers: challenges, opportunities, and clinical readiness

Francheska Cadacio[1,2,#], Anthony Turpin[3,#], Pedro M. Rodrigues[4,5,6], Florian Castet[7,8,9], Angela Lamarca[10,11,12], John Bridgewater[13], Jesús M. Bañales[4,5,6,14], Teresa Macarulla[2,7,8,9,*], and Tian V. Tian[7,8,9,*]

Table 1. Recent trials on biliary tract cancers and their possible ancillary part with the use of liquid biopsy

Study	Authors	Drug or combination	Matched molecular alteration	Available data from LB ancillary part	No. of patients with evaluable ctDNA data	LB sequencing platform	Main key LB findings
TOPAZ-1 (Phase 3)	Oh [4]	CIS/GEM–Durva	No	Yes	419	Guardant Infinity ctDNA	Tissue-LB concordance (≥93%) in simple genetic alterations. Low tissue-LB concordance in complex alterations (52% for *ERBB2* amplification and 47% for *FGFR2* fusions).
KEYNOTE 966 (Phase 3)	Kelley (2023)	CIS/GEM–Pembro	No	Not yet	n/a	n/a	n/a
FOENIX-CCA2 (Phase 2)	Goyal [6]	Futibatinib	FGFR alteration	Yes	95	Illumina TruSight Oncology 500	Positive tissue-LB concordance (87%) in *FGFR2* fusions or rearrangements in 83 out of 95 patients.
ClarIDHy (Phase 3)	Abou-Alfa (2020) and Zhu X (2021)	Ivosidenib	*IDH1* mutation	Yes	18	PGDx elio plasma complete	Most mutations that were found exclusively to end-of-treatment and not in baseline samples were associated to MAPK pathway in 6 out of 18 patients (33%).
KCSG-HB19-14 (Phase 2)	Lee CK (2023)	FOLFOX–Trastuzumab	HER2 positive	Not yet	n/a	n/a	n/a
MyPathway (Phase 2)	Javle [7]	Trastuzumab–Pertuzumab	HER2 positive	Yes	15	FoundationOne Liquid CDx	Positive tissue-LB concordance (67%) via HER2 copy number ratios, with ratios decreasing or remaining stable in patients with partial or stable disease, but increasing in the patient with progressive disease over the course of the treatment.
SGNTUC-019 (Phase 2)	Nakamura (2023)	Trastuzumab–Tucatinib	HER2 positive	Yes	29	Guardant360	Positive tissue-LB concordance (75.9%) in HER2 amplification.
HERIZON-BTC-01 (Phase 2)	Harding (2023)	Zanidatamab	HER2 positive	Yes	25	Guardant360	Positive tissue-LB concordance (59%) in HER2 amplification. Decrease in ctDNA levels from baseline observed in 72% of the patients with over 90% of them having partial response or stable disease.

cells

MDPI

Review

Liquid Biopsy Frontiers in Pancreatic Cancer: Insights from Circulating Cell-Free Nucleic Acids

Maria Latiano [1,†], Maria De Angelis [1,†], Anna Latiano [1], Orazio Palmieri [1], Tiziana Pia Latiano [2], Marco Donatello Delcuratolo [2], Matteo Tardio [3], Francesca Bazzocchi [3], Marco Gentile [4], Fulvia Terracciano [4], Grazia Anna Niro [4] and Francesca Tavano [1,*]

Published: 14 May 2026

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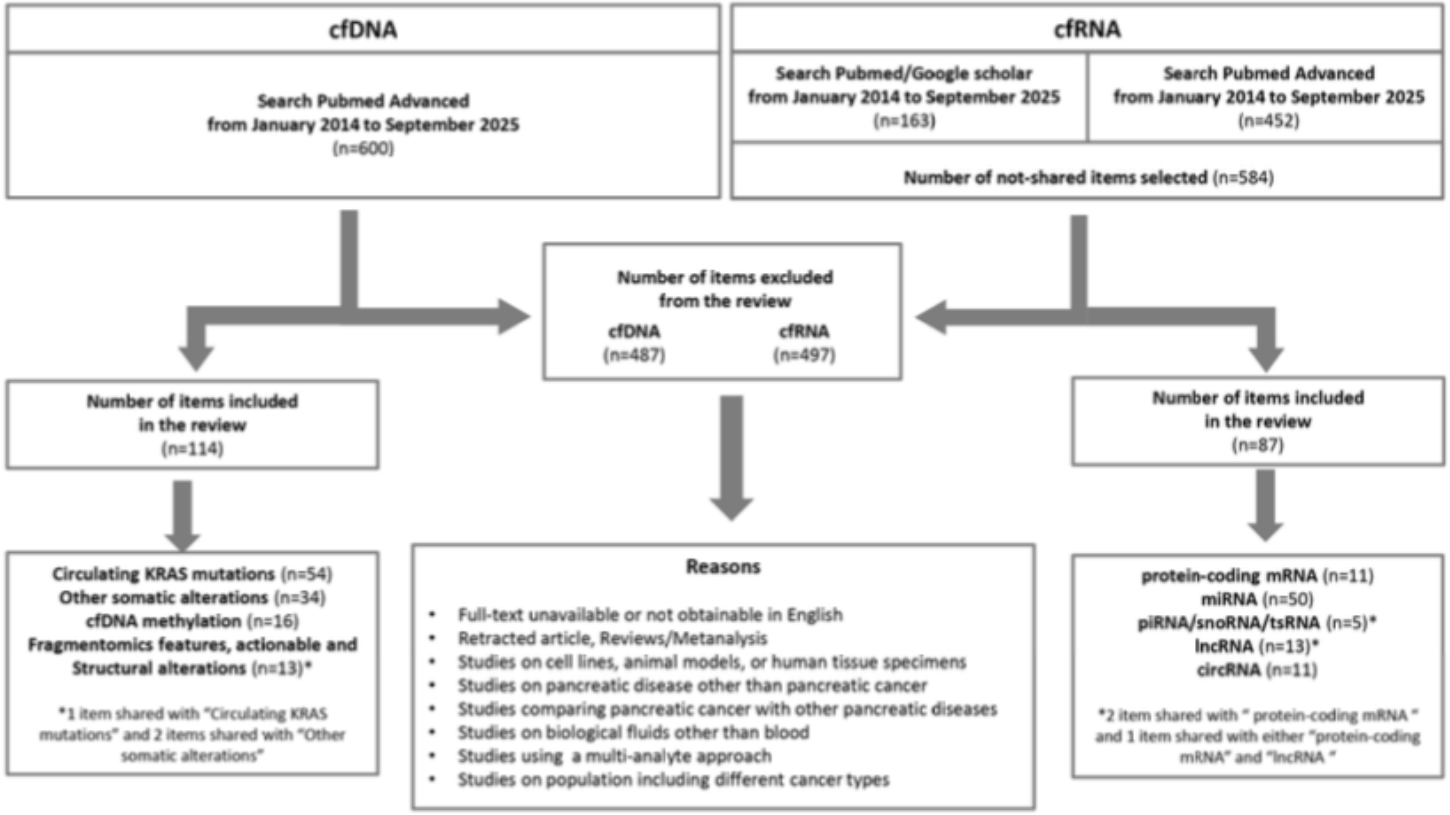
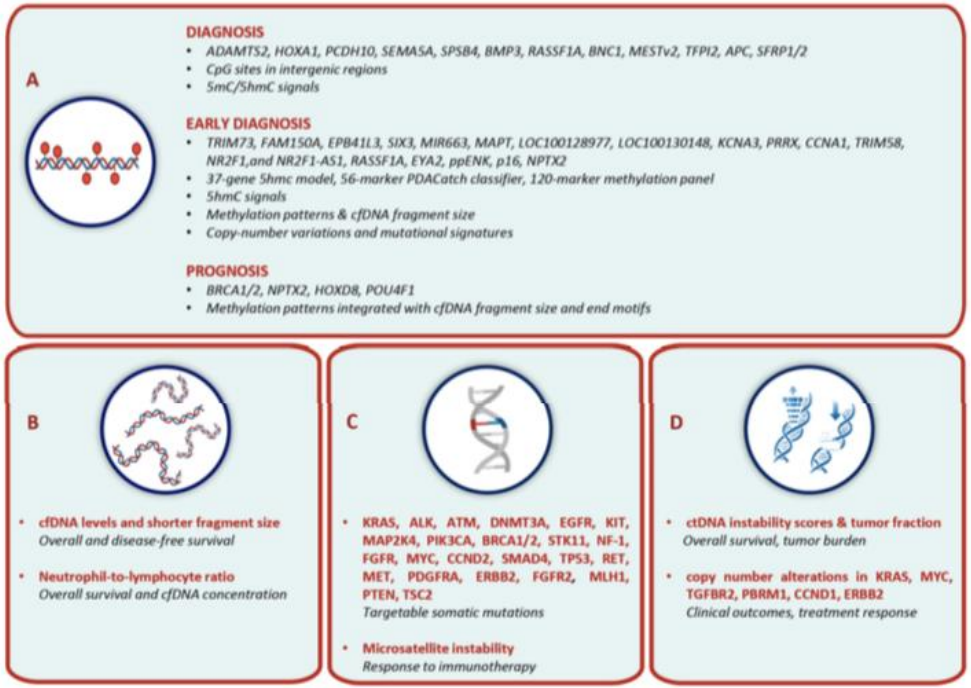




- Current findings are limited by **small cohort** sizes, heterogeneous study designs, and **variability** in analytical methods and platforms often based on non-standardized gene panels and **cut-off values** for ctDNA positivity.
- There is a lack of **large prospective validation** studies.
- These findings should be considered **hypothesis-generating** rather than practice-changing and require confirmation in larger, well-defined studies with uniformly treated populations.

Figure 3. Liquid biopsy insights in pancreatic cancer: cfDNA methylation (**A**), fragmentomics/ systemic inflammatory markers (**B**), actionable mutations (**C**), and structural alterations (**D**).

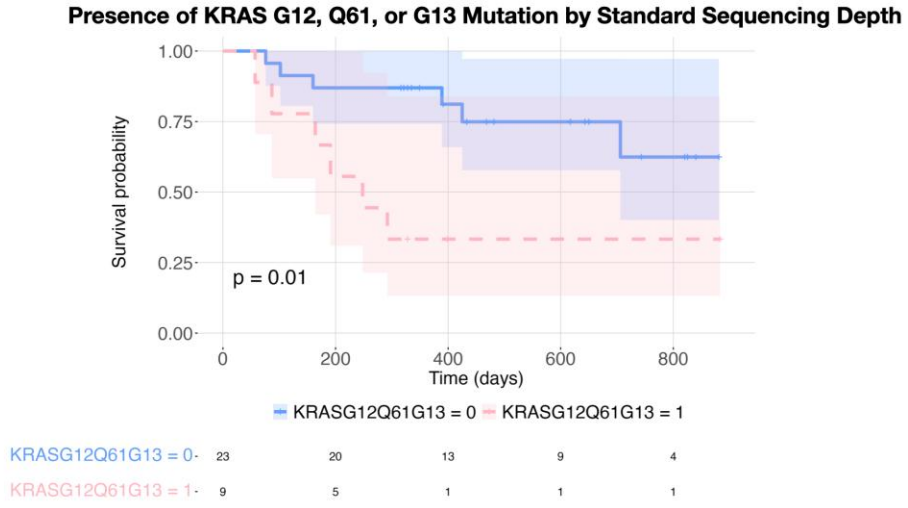
frontiers | Frontiers in Oncology

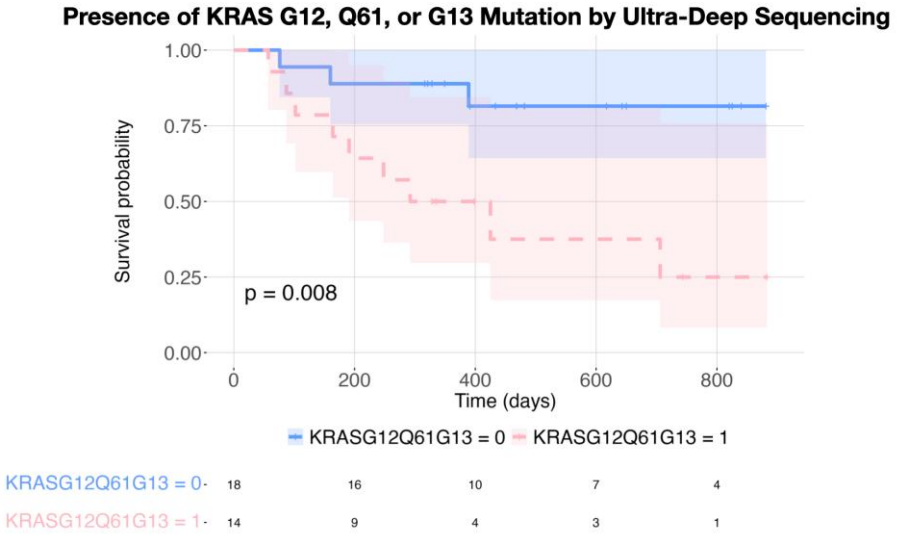
Ultra-sensitive detection of mutant *KRAS* in circulating tumor DNA predicts survival in resectable pancreatic adenocarcinoma

Madison Cox[1,2*], Amy Wells[1,2], Dominic Vitello[1], Larissa Masnyk[1], Lauren M. Janczewski[1], Vishvetha Rengaraju[1], Chengwei Peng[2,3,4], John Abad[1,2,3], Qiang Zhang[3,4], Shidong Jia[5*], Pan Du[5*] and Akhil Chawla[1,2,3,4*]

PUBLISHED 04 May 2026

- Plasma samples were collected from 45 patients with non-metastatic PDAC prior to treatment start.
- Baseline ctDNA was analyzed for KRAS G12/G13/Q61 mutations using the **PredicineCARE liquid biopsy assay** (20,000x sequencing depth) and the **PredicineCare ULTRA assay** (≥100,000x sequencing depth), providing full KRAS gene coverage.





Standard depth sequencing identified pathogenic KRAS mutations (G12/ G13/Q61) in 11 patients.

Ultra-deep sequencing identifying mutant KRAS in these same 11 patients and an additional 7 patients.

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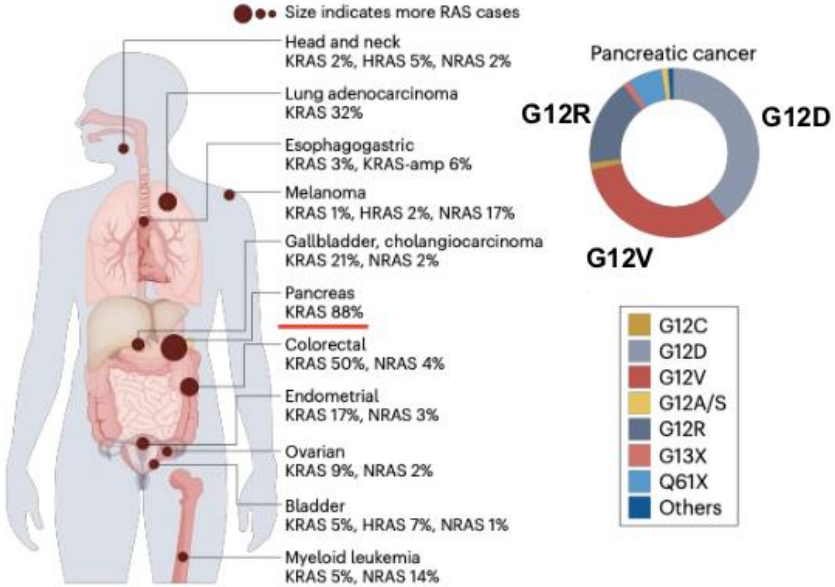


Singhal A, et al. Nat Medicine 2024
Merz V, et al. Front Onc 2023

2026 ASCO ANNUAL MEETING

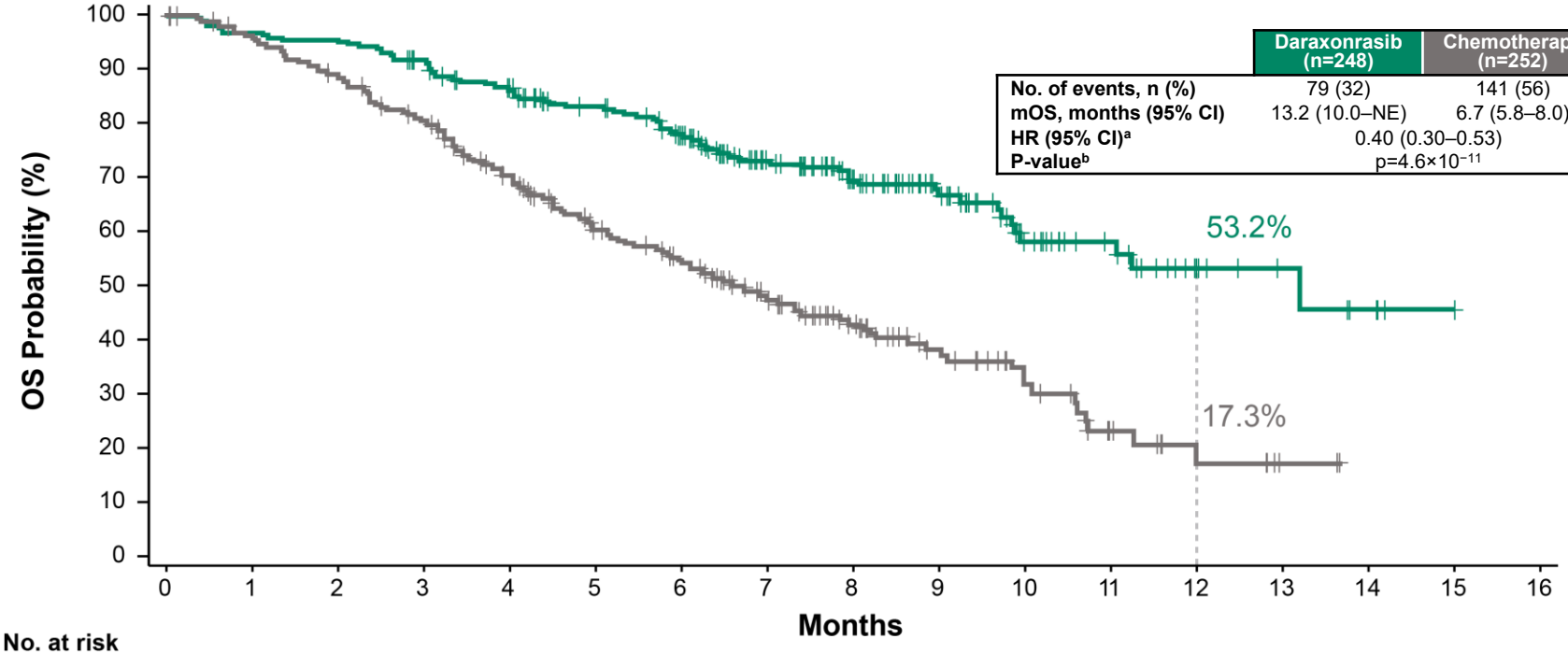
Daraxonrasib, a RAS(ON) multi-selective inhibitor vs chemotherapy in previously treated metastatic pancreatic adenocarcinoma (mPDAC): Primary and final analysis from the Phase 3 RASolute 302 study

Brian M. Wolpin,[1] Zev A. Wainberg, Andrew E. Hendifar, Mitesh J. Borad, Filippo Pietrantonio, Shubham Pant, Pascal Hammel, Chiara Cremolini, Gulam A. Manji, Paul E. Oberstein, Ignacio Garrido-Laguna, Christoph Springfeld, Nilofer S. Azad, Makoto Ueno, Stephen Y. Chui, Ying Zhang, Hina Patel, Yeonju Lee, Zeena Salman, Eileen M. O'Reilly

On behalf of RASolute 302 investigators

[1]Hale Family Center for Pancreatic Cancer Research; Dana-Farber Cancer Institute, Boston, MA, USA

Key Secondary Endpoint: Overall Survival in the Overall Population



	Daraxonrasib (n=248)	Chemotherapy (n=252)
No. of events, n (%)	79 (32)	141 (56)
mOS, months (95% CI)	13.2 (10.0–NE)	6.7 (5.8–8.0)
HR (95% CI)[a]	0.40 (0.30–0.53)	
P-value[b]	$p=4.6\times10^{-11}$	

No. at risk																	
Daraxonrasib	248	240	237	225	208	188	165	125	90	62	37	24	11	7	4	1	0
Chemotherapy	252	235	217	193	161	126	108	78	53	35	21	10	5	2	0		

Data cutoff: 10 Feb 2026. Median (range) follow-up time was 8.5 (3.2−15.9) months.

m, median; NE, not estimable; OS, overall survival.

[a]HRs and 95% CIs were based on the stratified Cox model with Efron's method of tie handling. [b]P-values were calculated using the stratified log-rank test.

PRESENTED BY: Brian M. Wolpin, MD, MPH

Conclusions

- Liquid biopsy tests are rapidly being integrated into clinical care for patients with PC and BTC
- Early detection remains challenging (tests are more accurate in advanced stages)
- Their main use probably will be when tissue is unavailable or when urgent therapeutic decisions are required
- They could allow the identification of actionable alterations that qualify patients for targeted therapies

Grazie!

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