CONNECT TO WIN 2026

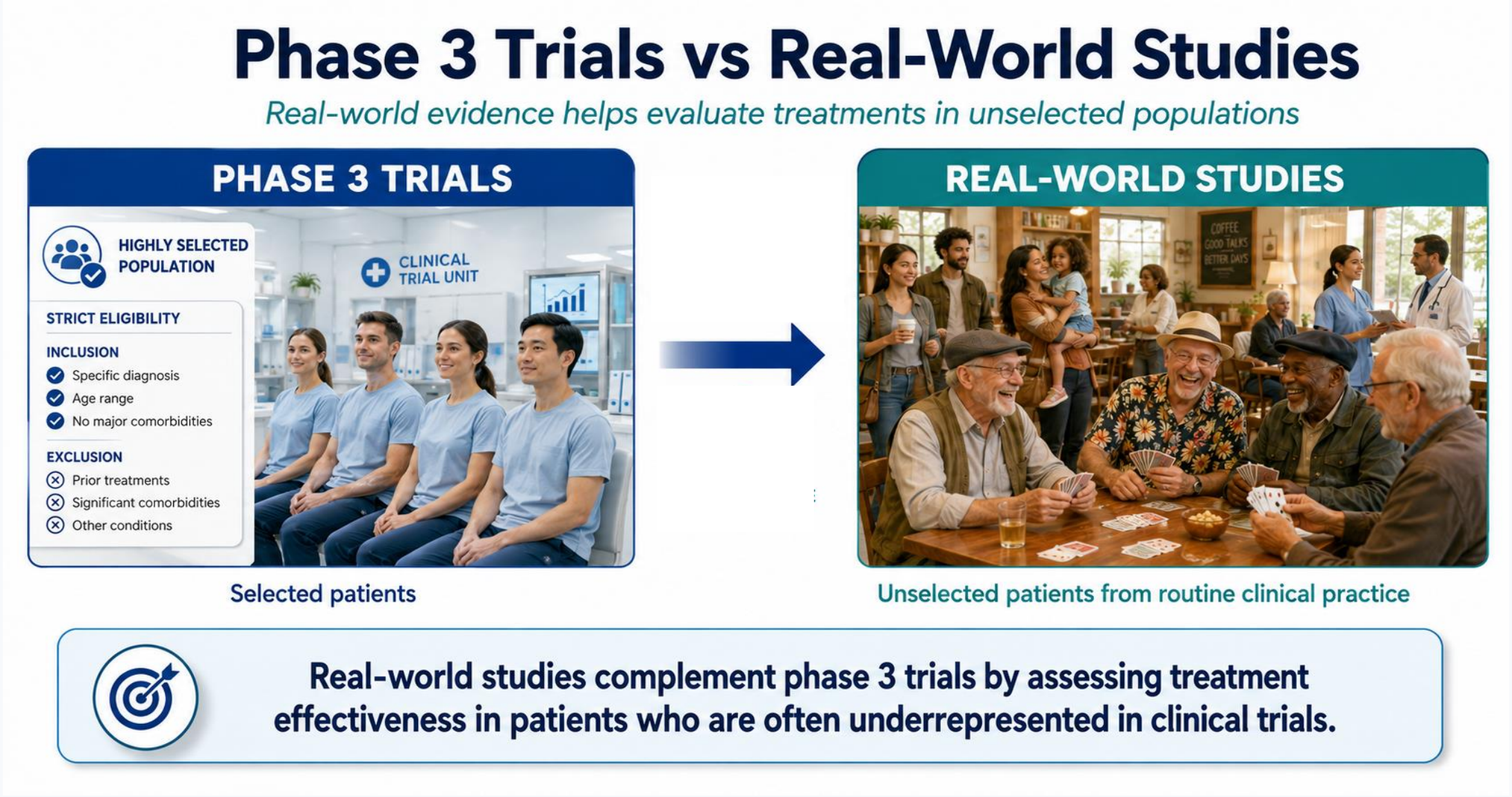
Value of RWE in Liver Cancer Research

From data to clinical pathways

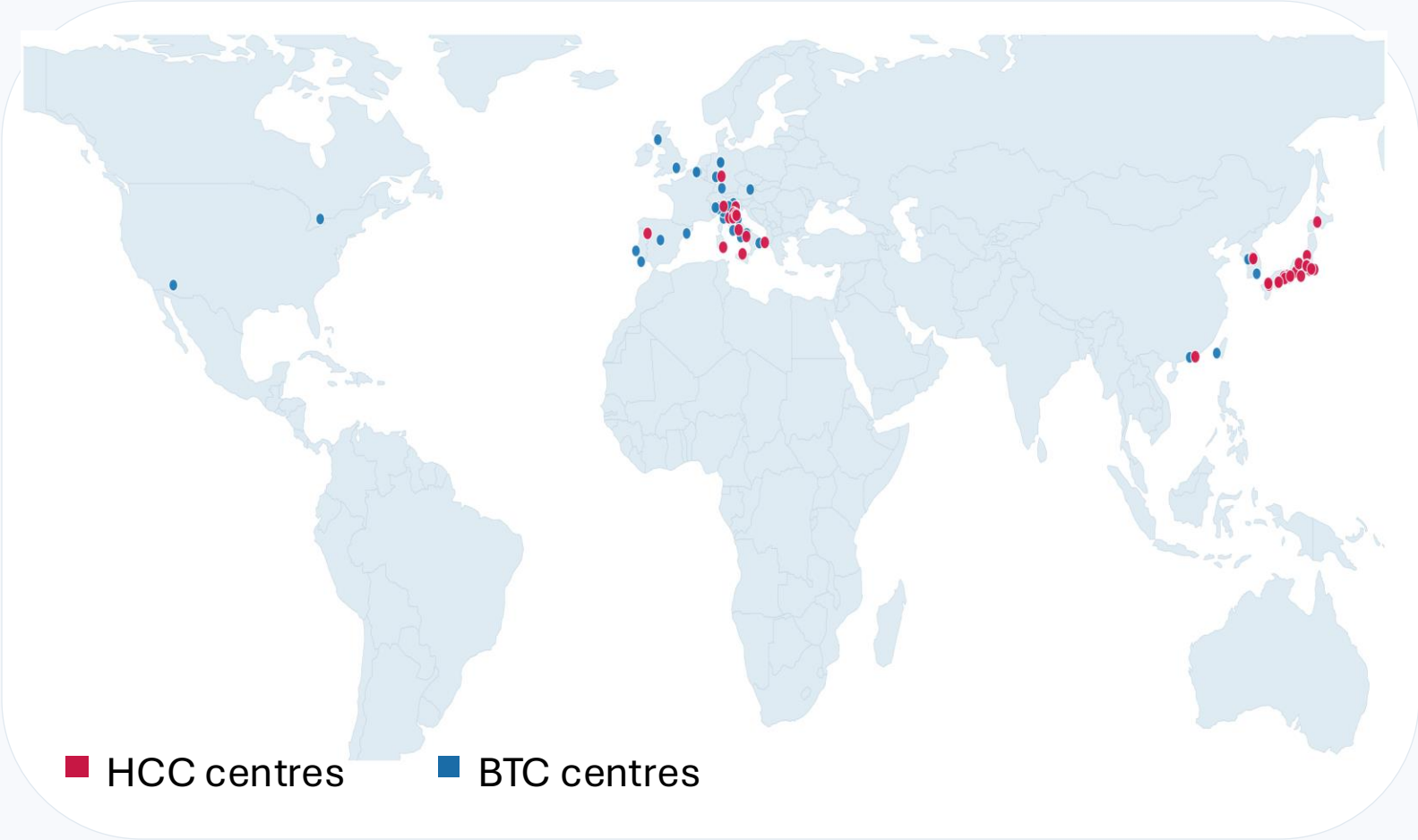
Mara Persano

IRCCS San Raffaele Hospital, Milan

Clinical trials and real-world evidence: complementary views



An international network behind the evidence



HCC DATABASE

2,205 patients

46 centres, 6 countries

BTC DATABASE

1,358 patients

55 centres, 12 countries

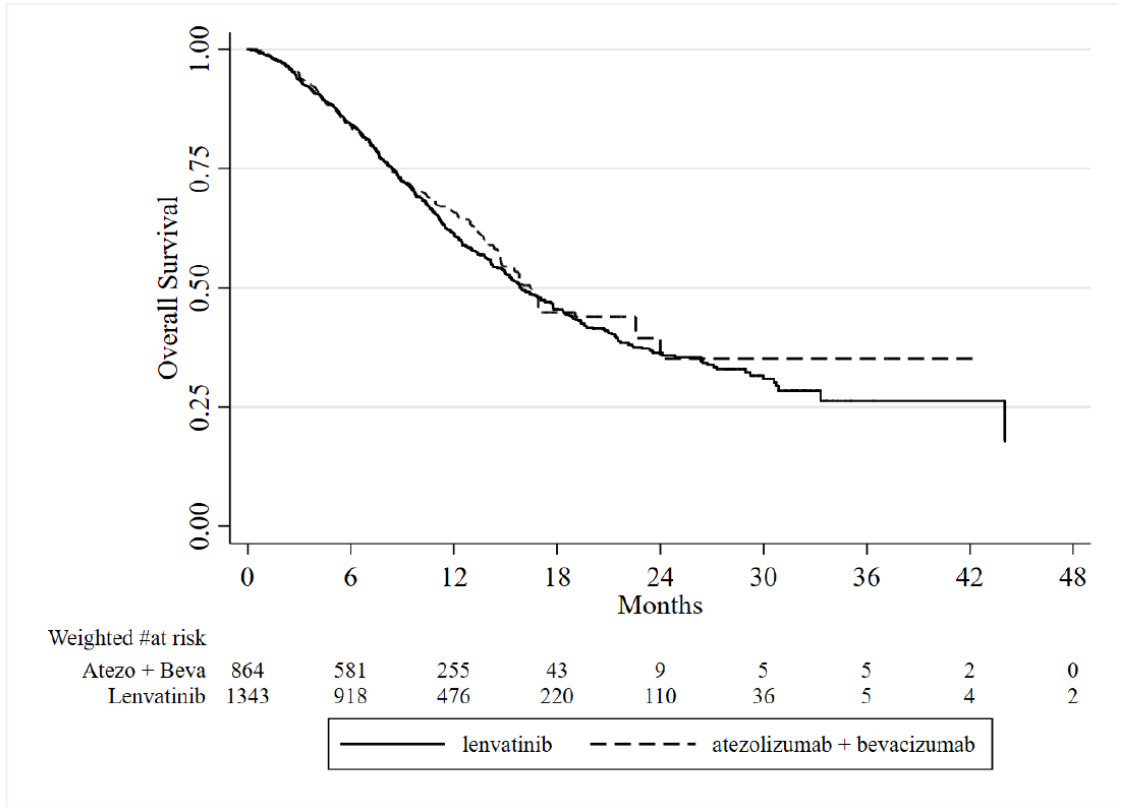
BTC registry: Rimini et al. Liver Int 2025;45:e70428; manuscript collaborators, 2026.

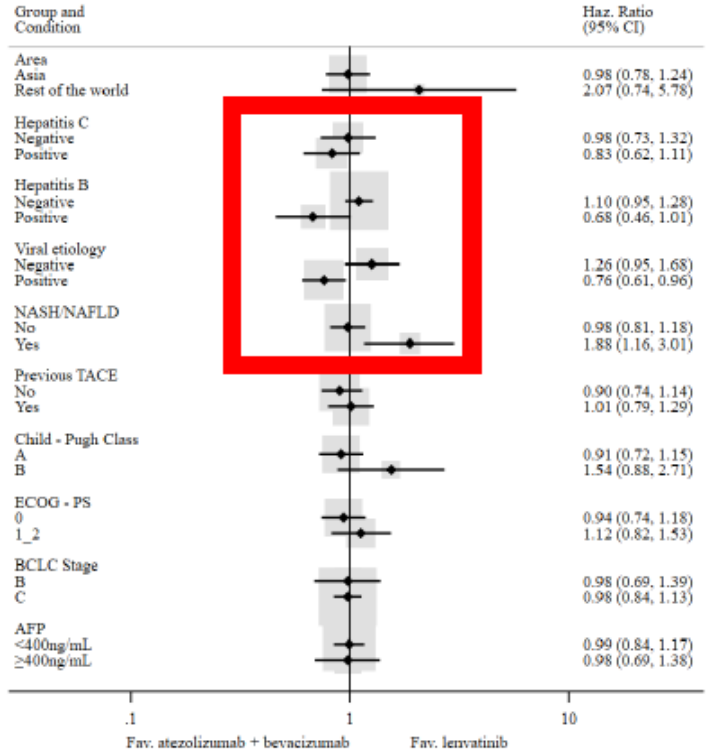
Advanced HCC: the randomized evidence

2008	2018	2020	2022	2025
SHARP	**REFLECT**	**IMbrave150**	**HIMALAYA**	**CheckMate 9DW**
Sorafenib vs placebo	Lenvatinib vs sorafenib	Atezo + bev vs sorafenib	STRIDE vs sorafenib	Nivo + ipi vs lenva/sora
mOS 10.7/7.9	mOS 13.6/12.3	mOS 19.2/13.4	mOS 16.4/13.8	mOS 23.7/20.6
HR 0.69	HR 0.92	HR 0.66	HR 0.78	HR 0.79

SHARP: Llovet et al. NEJM 2008 | REFLECT: Kudo et al. Lancet 2018 | IMbrave150: Finn et al. NEJM 2020 (updated OS) | HIMALAYA: Abou-Alfa et al. NEJM Evid 2022 | 9DW: Yau et al. Lancet 2025.

Atezo + bev vs Lenvatinib in RWE



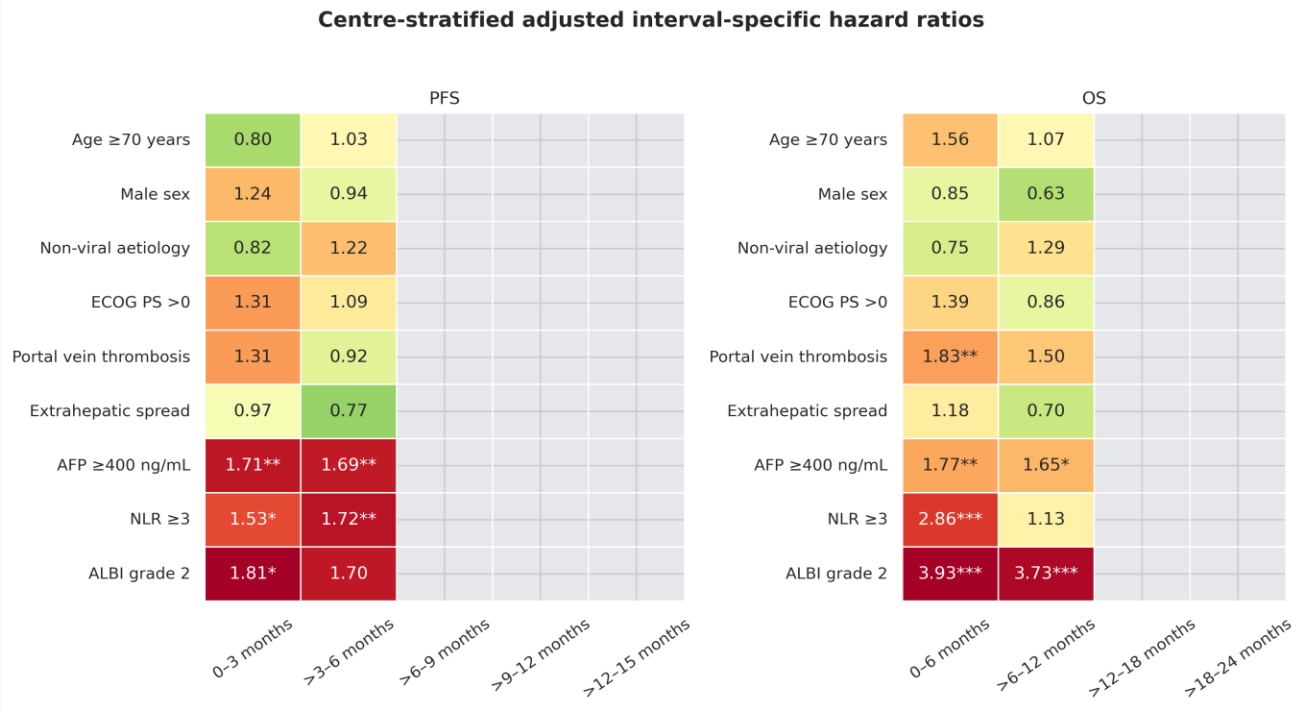


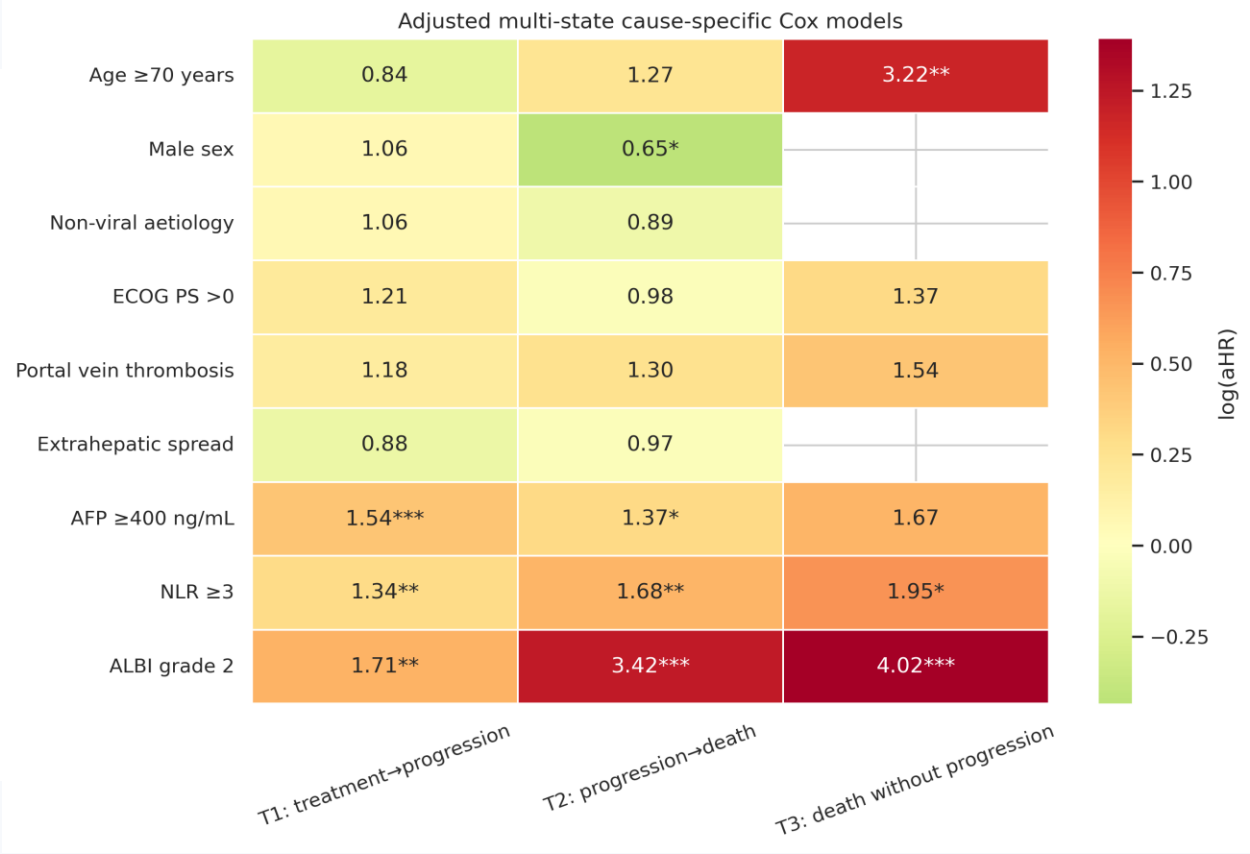
2,205 patients

Adjusted OS HR 0.97 (95% CI 0.80–1.17)

Casadei-Gardini A et al. Eur J Cancer 2023;180:9–20. doi:10.1016/j.ejca.2022.11.017.

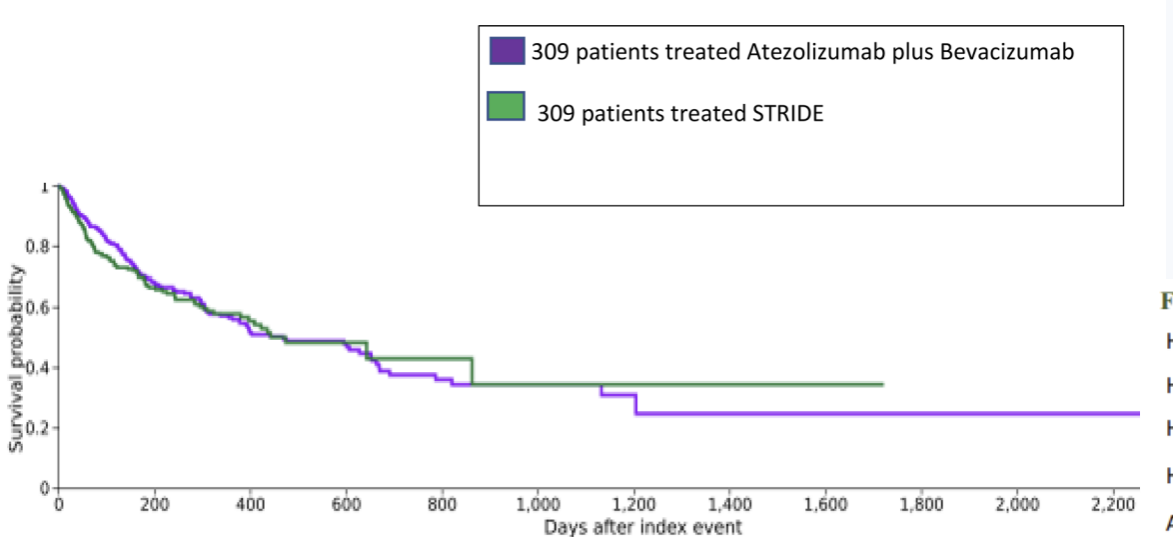
From a single HR to time-dependent clinical risk





Persano M et al. Dynamic Prognostic Effects Across the Disease Trajectory in HCC. Unpublished manuscript, 2026.

Atezo + Bev vs STRIDE: a TriNetX matched comparison



What is TriNetX?

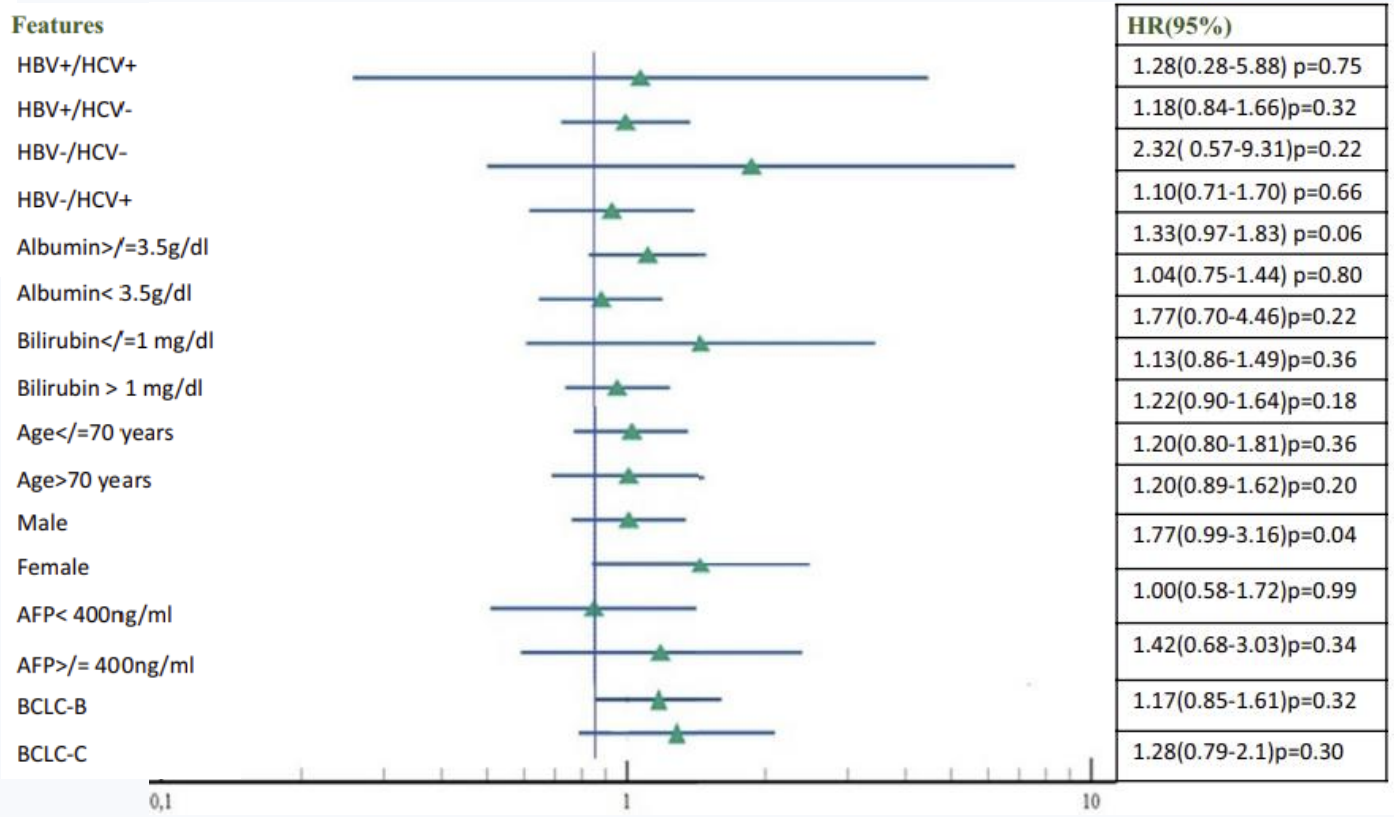
TriNetX is a global federated health research network, which aggregates de-identified electronic health records from over 127 healthcare organizations worldwide

Retrospective BCLC B/C cohort

2,307 patients: 1,998 **Atezo + Bev**/309 **STRIDE**

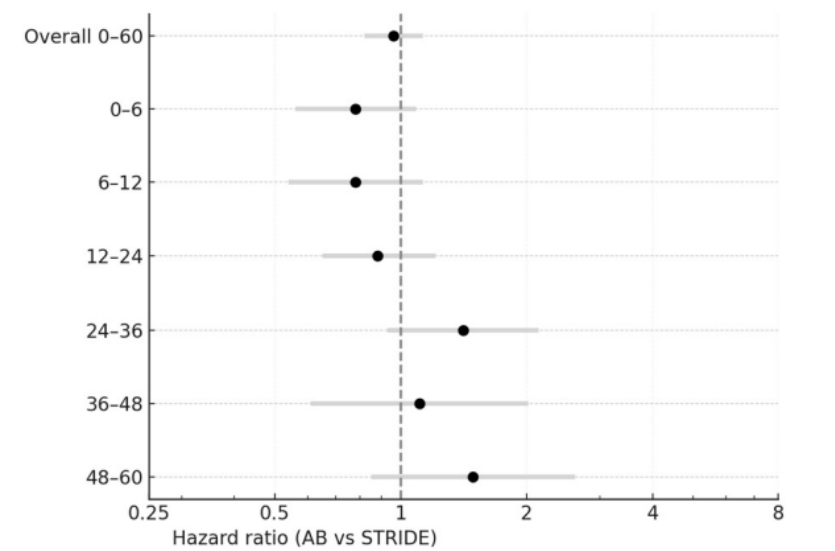
1:1 propensity-score matching: 309 vs 309

OS HR 0.94 (95% CI 0.73–1.22); p=0.67

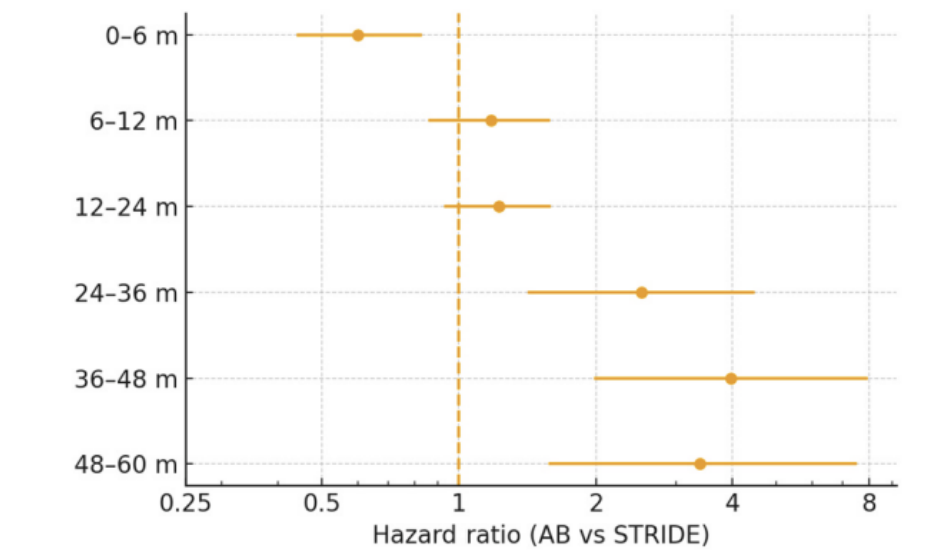


Lo Prinzi F et al. Target Oncol 2025;20:707–713. doi:10.1007/s11523-025-01161-5.

Atezo + Bev vs STRIDE: an anchored indirect comparison

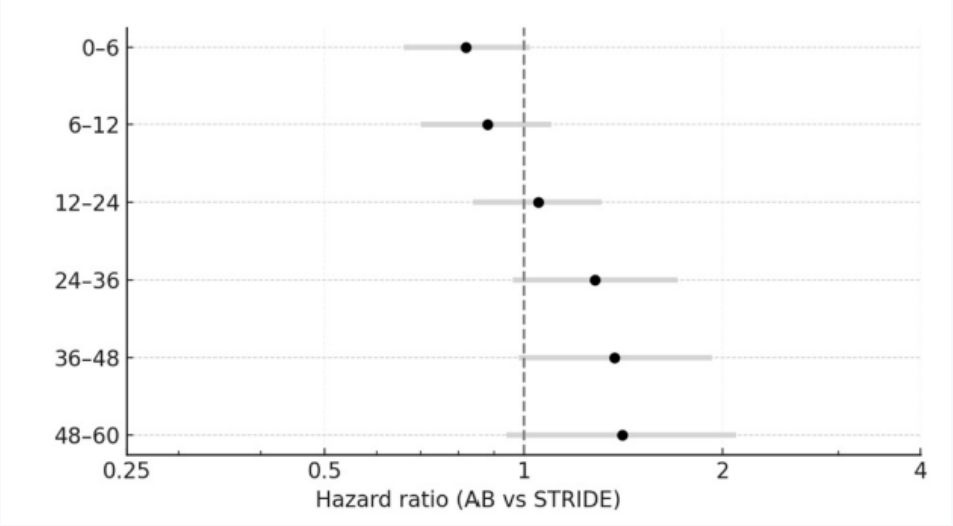


Trial anchored analysis



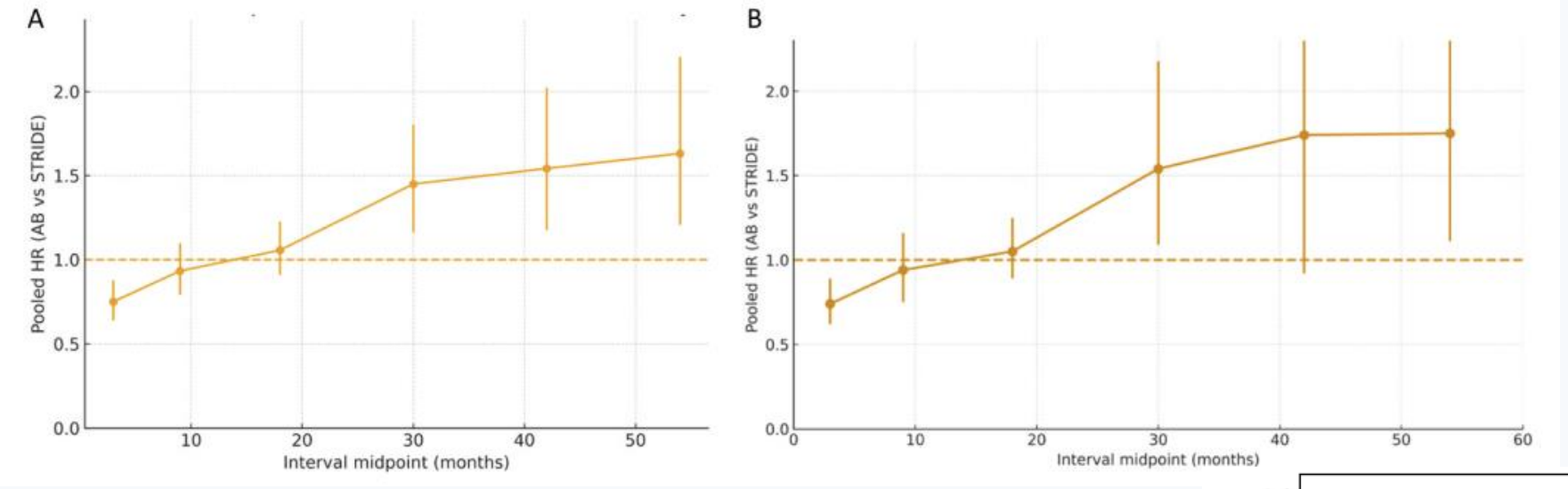
RW MAIC-weighted analysis

TriNetX matched RW analysis



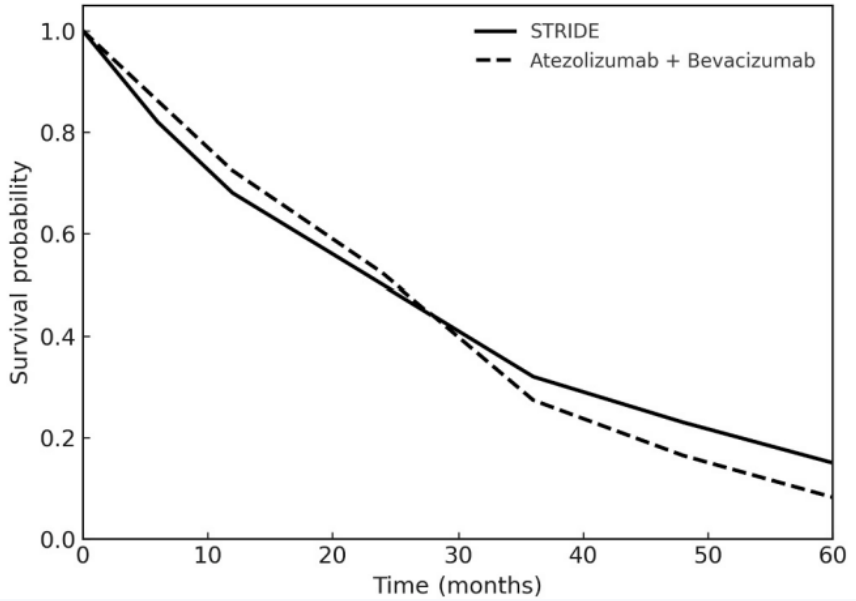
Casadei Gardini A et al. EJC 2026

Atezo + Bev vs STRIDE: an anchored indirect comparison



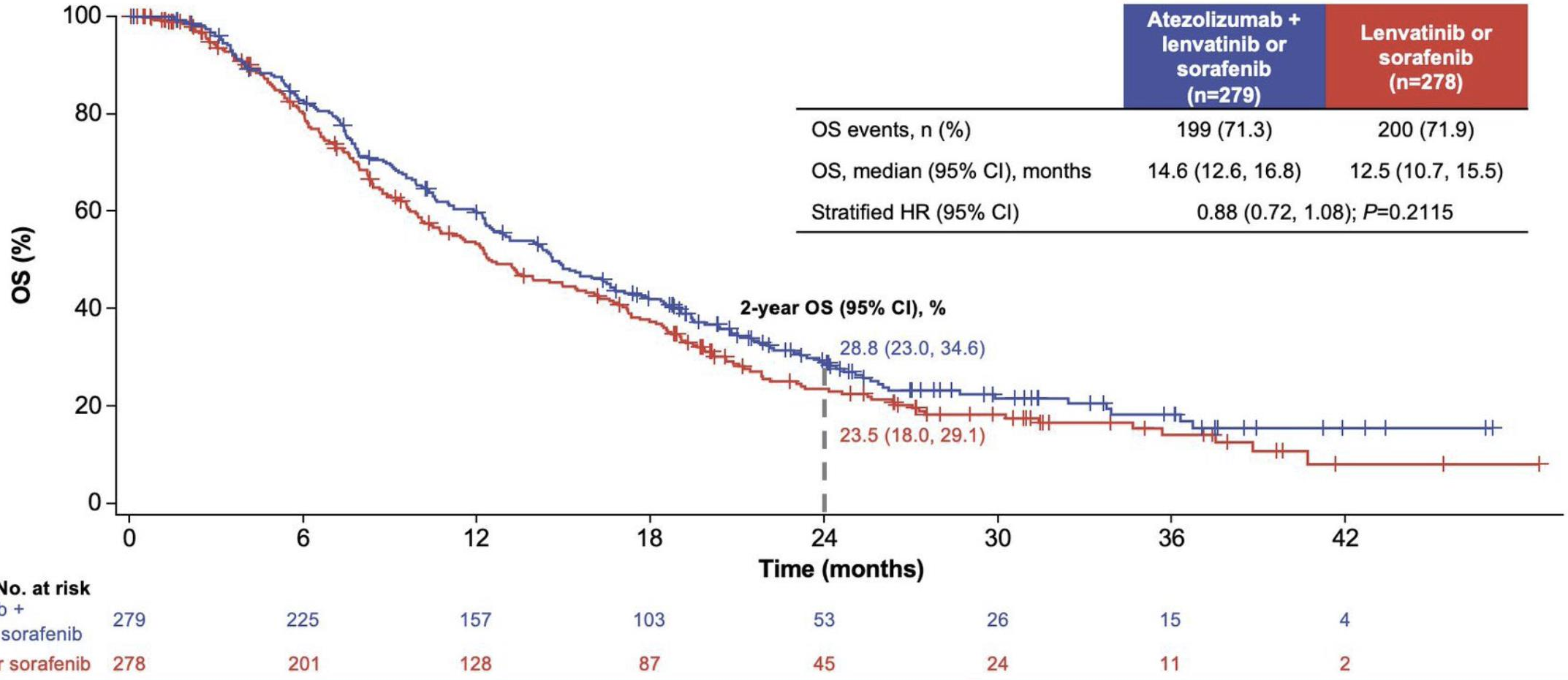
Pooled interval-specific hazard ratios for A+B versus STRIDE across analytic frameworks.

Interval (months)	HR (Fixed)	95% CI	HR (Random)	95% CI
0–6	0.75	0.63 – 0.89	0.74	0.62 – 0.89
6–12	0.95	0.80 – 1.12	0.96	0.78 – 1.15
12–24	1.05	0.90 – 1.22	1.05	0.87 – 1.25
24–36	1.45	1.17 – 1.80	1.54	1.05 – 2.21
36–48	1.55	1.20 – 2.00	1.74	0.98 – 3.30
48–60	1.65	1.25 – 2.20	1.75	1.05 – 2.90



Casadei Gardini A et al. EJC 2026

What after immunotherapy first-line?

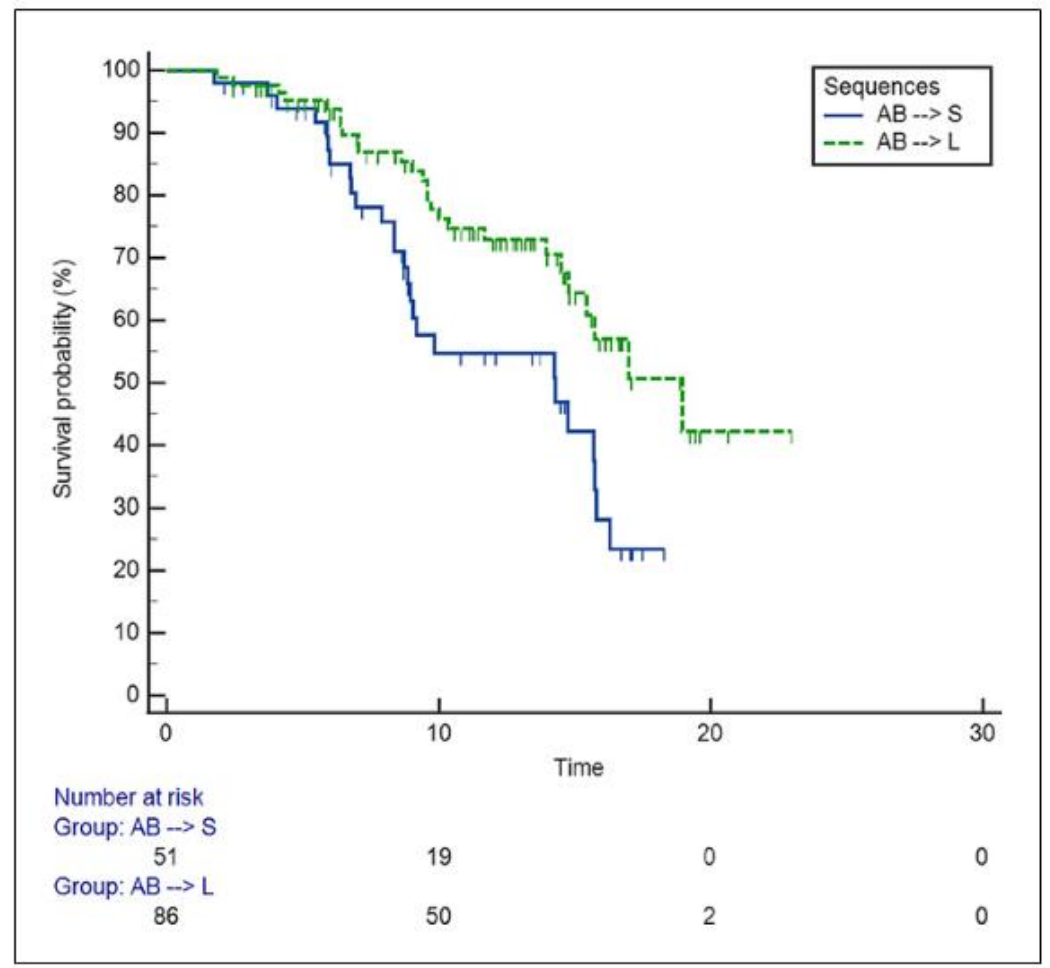


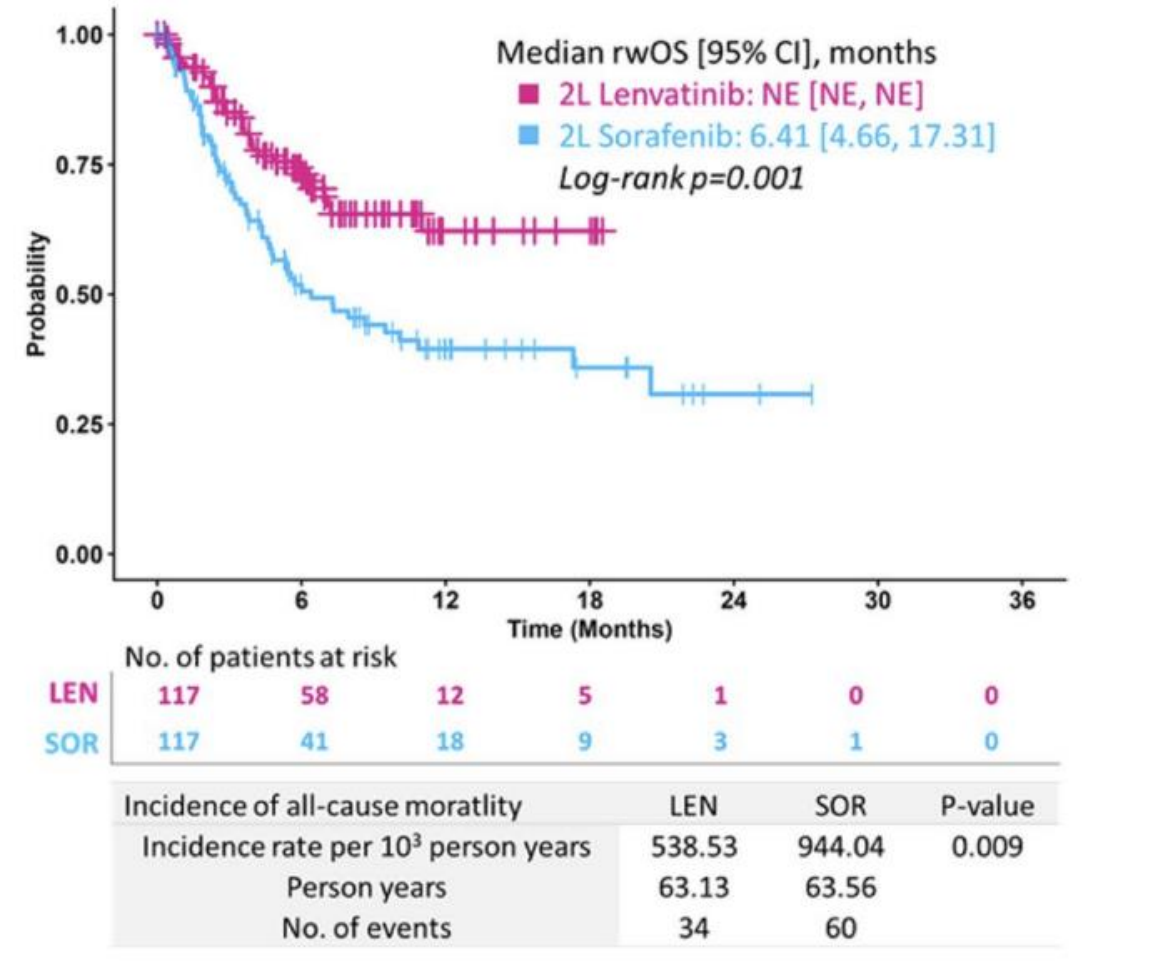
	Atezolizumab + lenvatinib or sorafenib (n=279)	Lenvatinib or sorafenib (n=278)
OS events, n (%)	199 (71.3)	200 (71.9)
OS, median (95% CI), months	14.6 (12.6, 16.8)	12.5 (10.7, 15.5)
Stratified HR (95% CI)	0.88 (0.72, 1.08); *P*=0.2115	

The addition of atezolizumab to TKI resulted in a numerical improvement in OS vs TKI alone; however, the improvement was not statistically significant

Vogel A et al. IMbrave251 final analysis. J Clin Oncol 2026;44(suppl):4002. doi:10.1200/JCO.2026.44.16_suppl.4002.

What after immunotherapy first-line?





Incidence of all-cause moratlity	LEN	SOR	P-value
Incidence rate per 10^3 person years	538.53	944.04	0.009
Person years	63.13	63.56	
No. of events	34	60	

Persano M et al. Eur J Cancer 2023;189:112933; Oncology 2025;103:456–468. • Lee MJ et al. Hepatol Int 2026. doi:10.1007/s12072-026-11142-z.

Advanced BTC: the randomized evidence

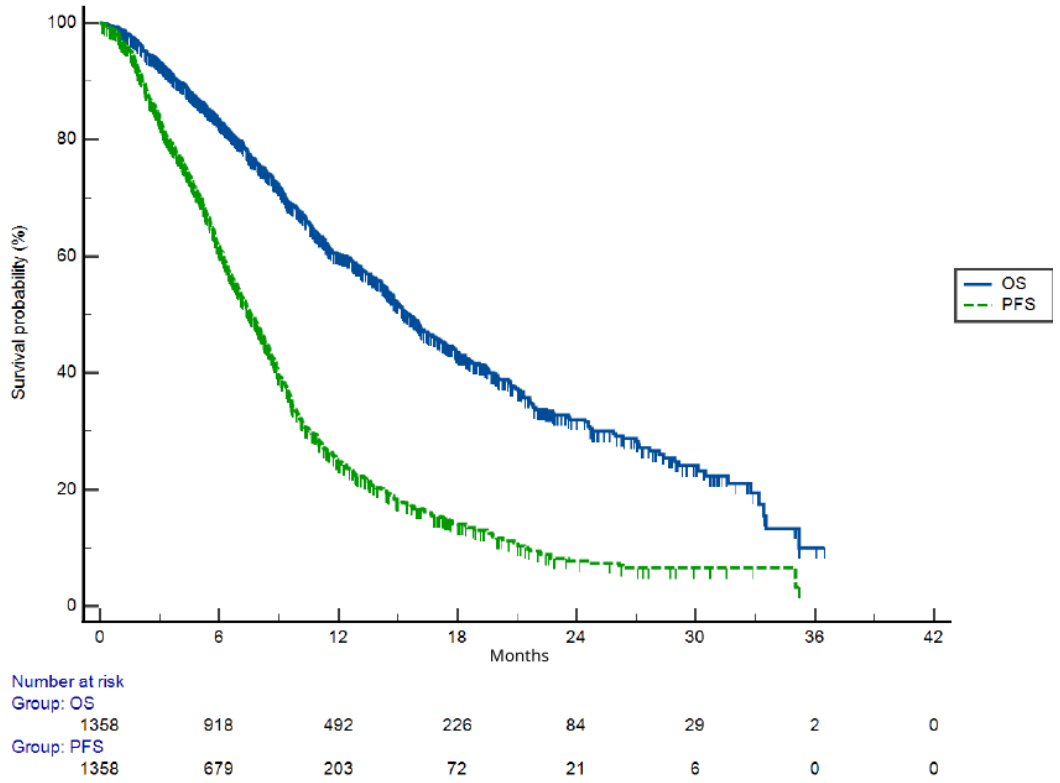
2010	2021	2022	2023
ABC-02	**ABC-06**	**TOPAZ-1**	**KEYNOTE-966**
Gem + cis vs gem	FOLFOX + ASC vs ASC alone	Durva + gem + cis vs gem + cis	Pembro + gem + cis vs gem + cis
mOS 11.7/8.1	mOS 6.2/5.3	mOS 12.8/11.5	mOS 12.7/10.9
HR 0.64	**HR 0.69**	**HR 0.80**	**HR 0.83**

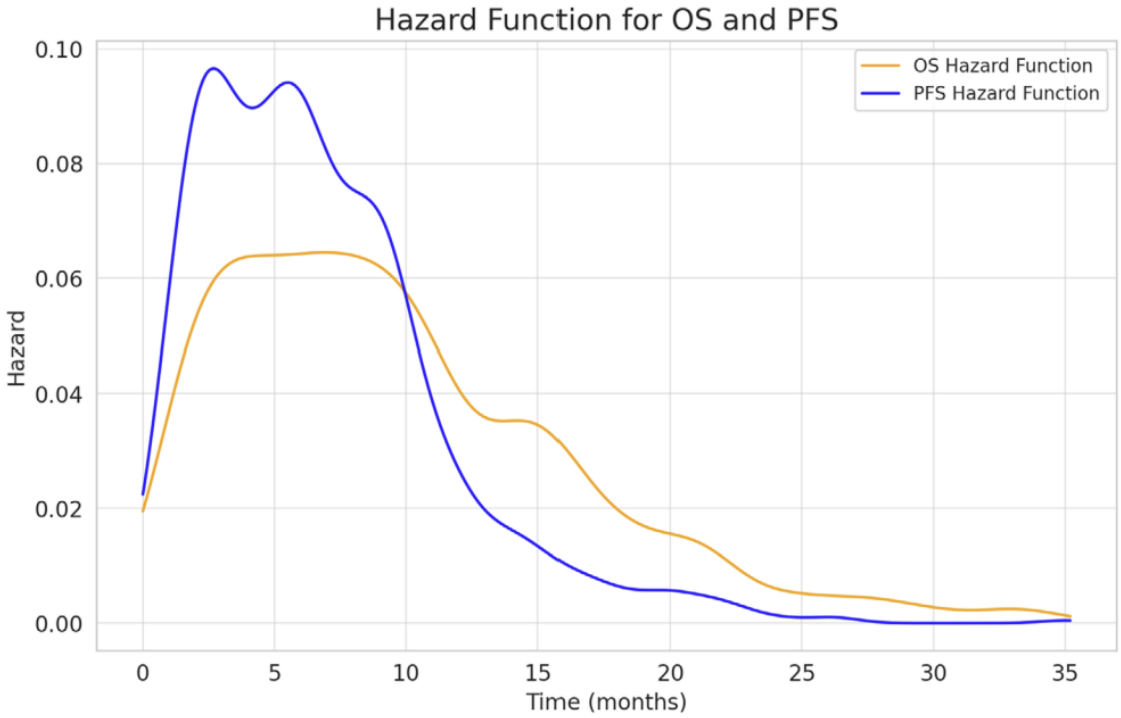
ABC-02: Valle et al. NEJM 2010 | ABC-06: Lamarca et al. Lancet Oncol 2021 | TOPAZ-1: Oh et al. NEJM Evid 2022 / FDA review 2024 | KEYNOTE-966: Kelley et al. Lancet 2023.

Chemoimmunotherapy outcomes across 55 centres

1,358 patients

median OS 15.6 months

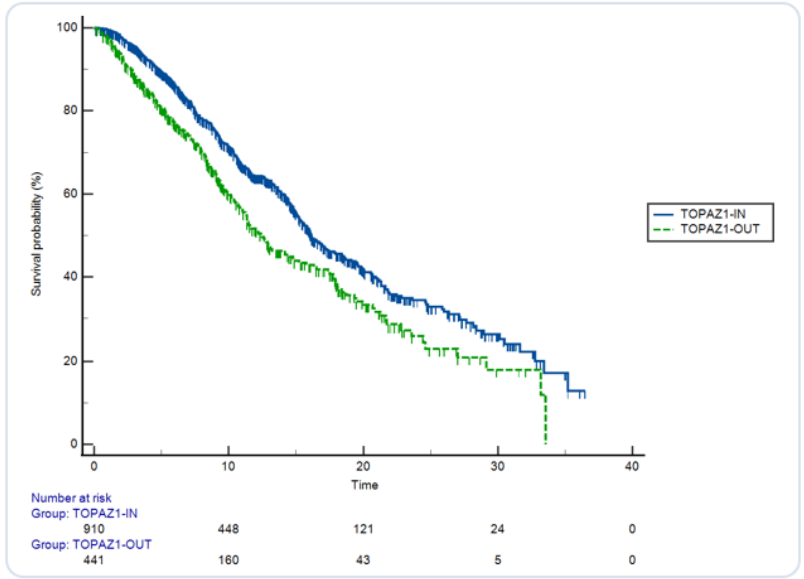




Rimini M et al. Liver Int 2025;45:e70428. doi:10.1111/liv.70428.

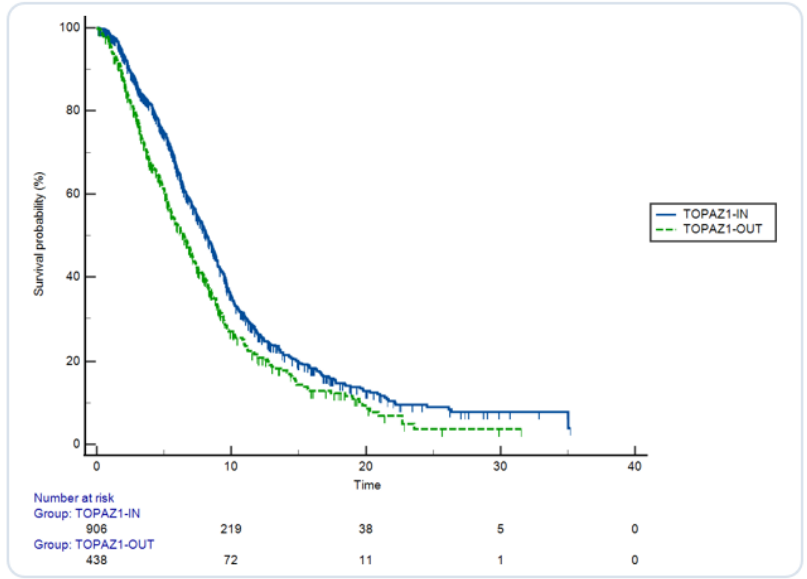
Beyond the inclusion/exclusion criteria

Overall survival in RWD



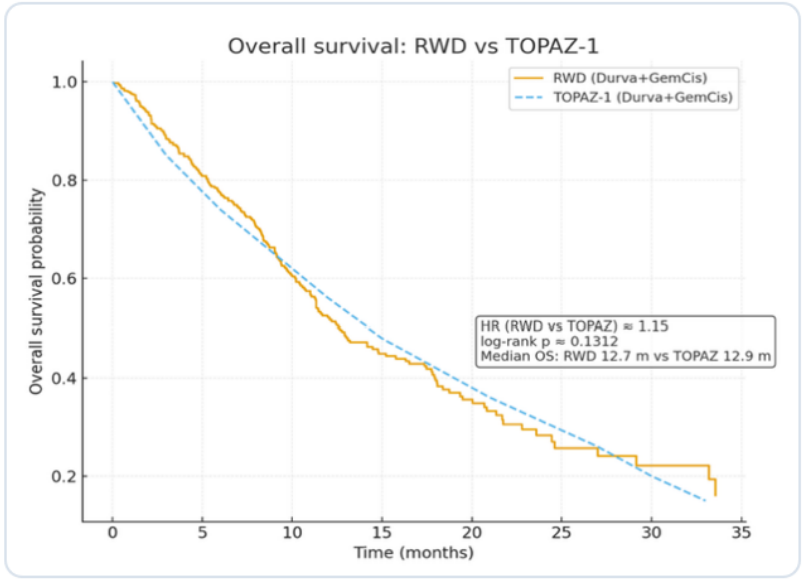
16.1 vs 12.5 mo HR 0.69 · p=0.0001

Progression-free survival in RWD



8.2 vs 6.5 mo HR 0.73 · p<0.0001

OS: TOPAZ-1-out vs TOPAZ-1

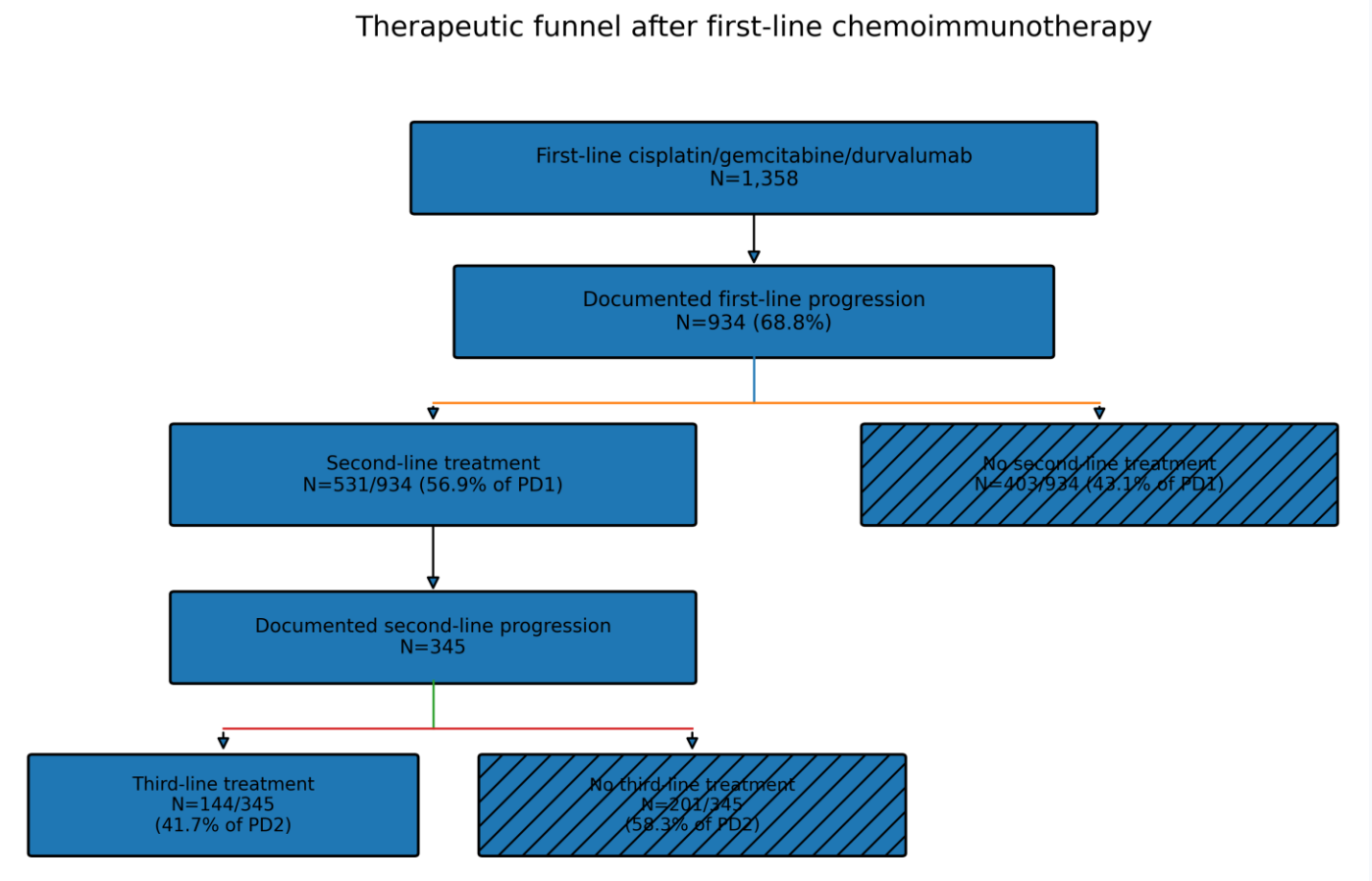


OS 12.7 vs 12.9 mo
HR 1.15 · p=0.13

Lo Prinzi F, Rimini M et al. Int J Cancer 2026 (online 12 Aug). doi:10.1002/ijc.70699.

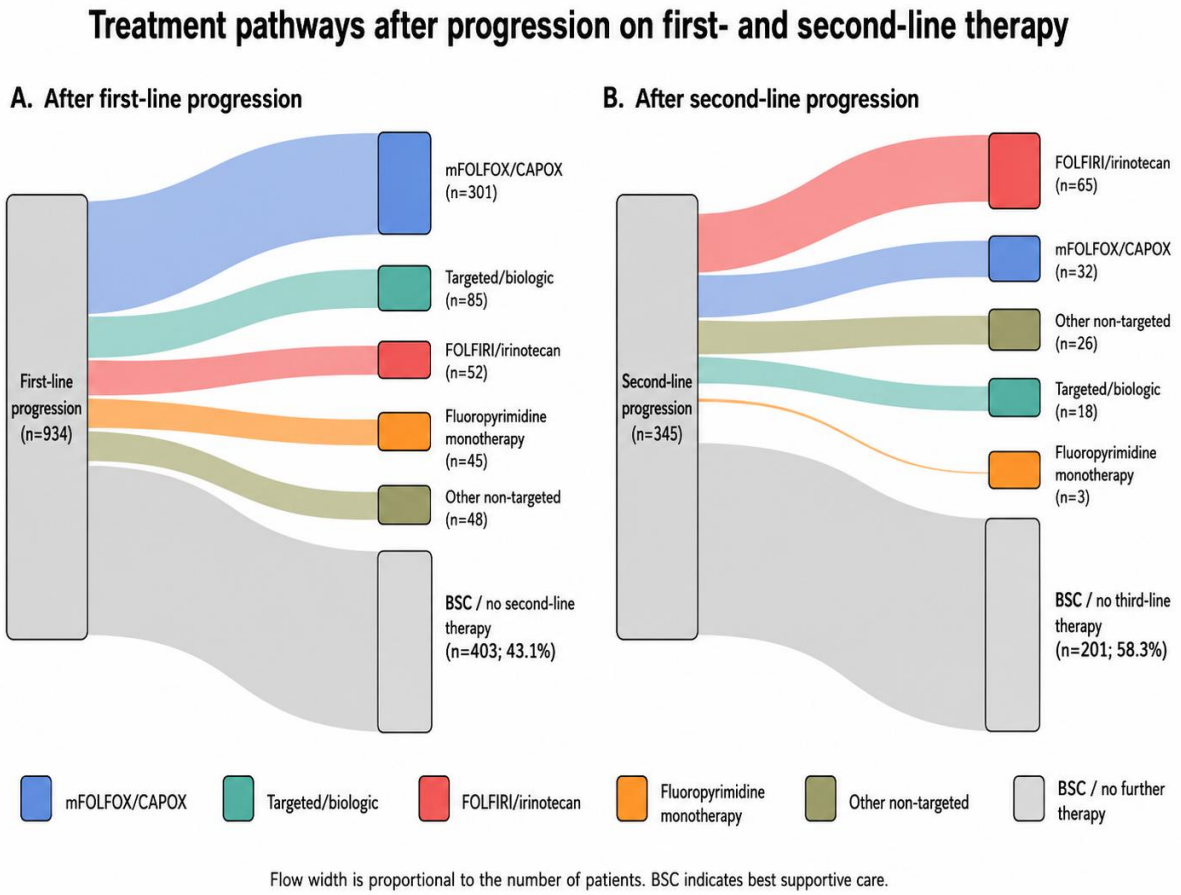
Progression is a major point of treatment attrition

403/934 (43.1%)
No 2L after documented progression



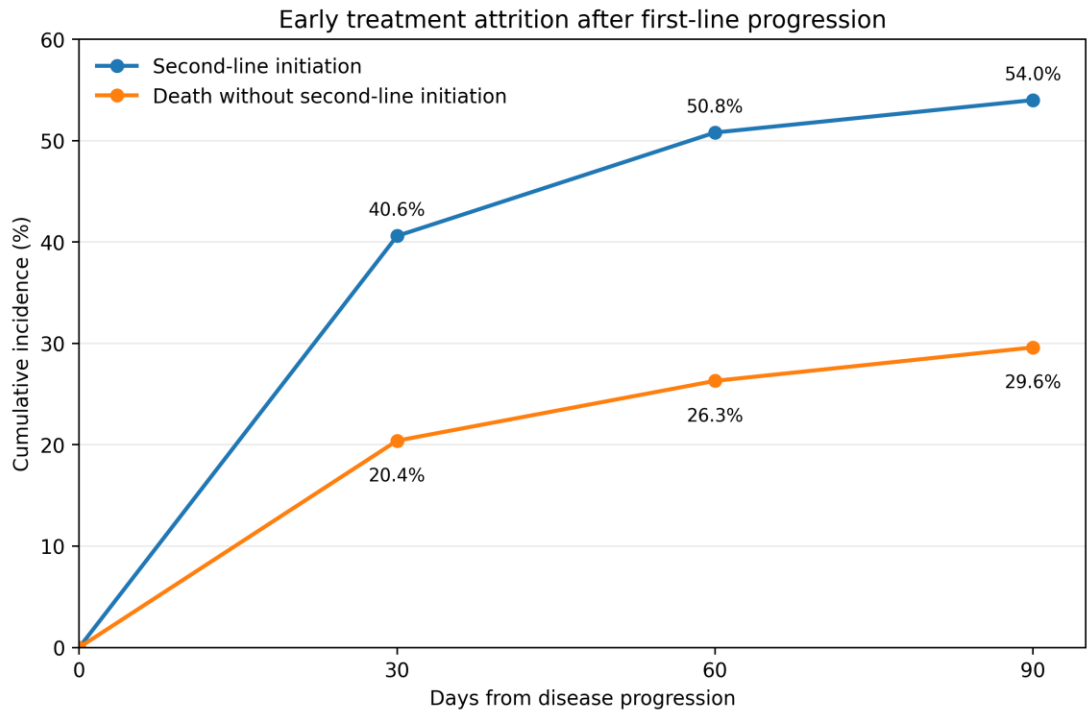
Rimini M et al. Treatment Attrition and Longitudinal Care Pathways in Advanced BTC. Unpublished manuscript, 2026; Figs 1 and 4B.

Attrition increases with each treatment transition

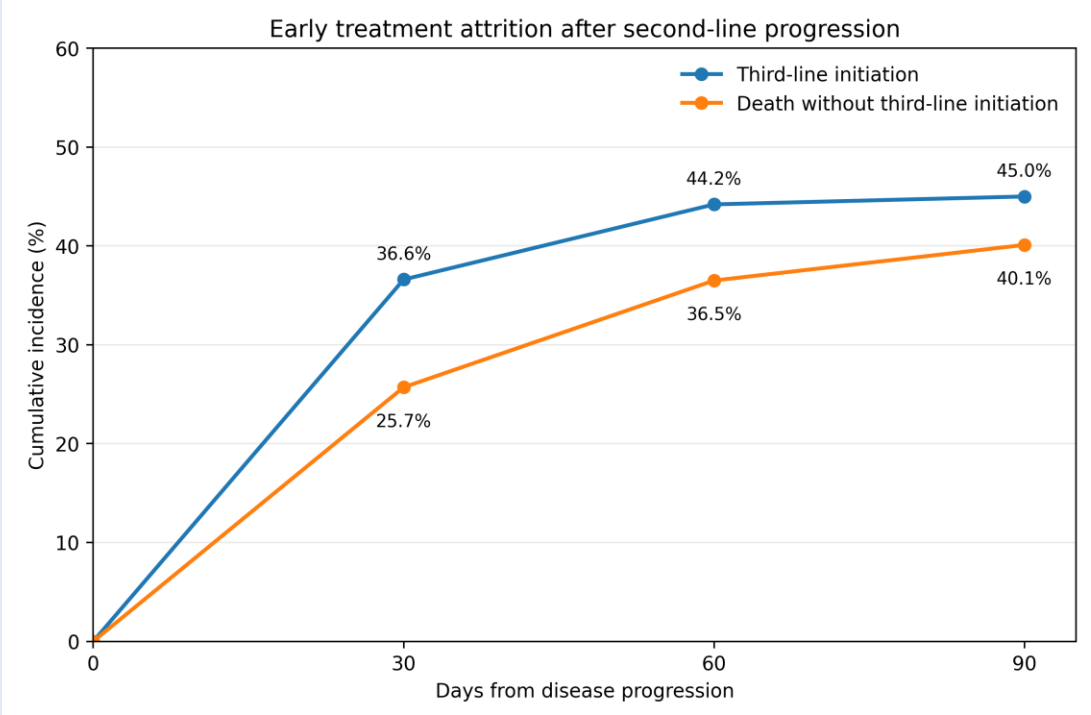


Rimini M et al. Treatment Attrition and Longitudinal Care Pathways in Advanced BTC. Unpublished manuscript, 2026.

A narrow window after progression



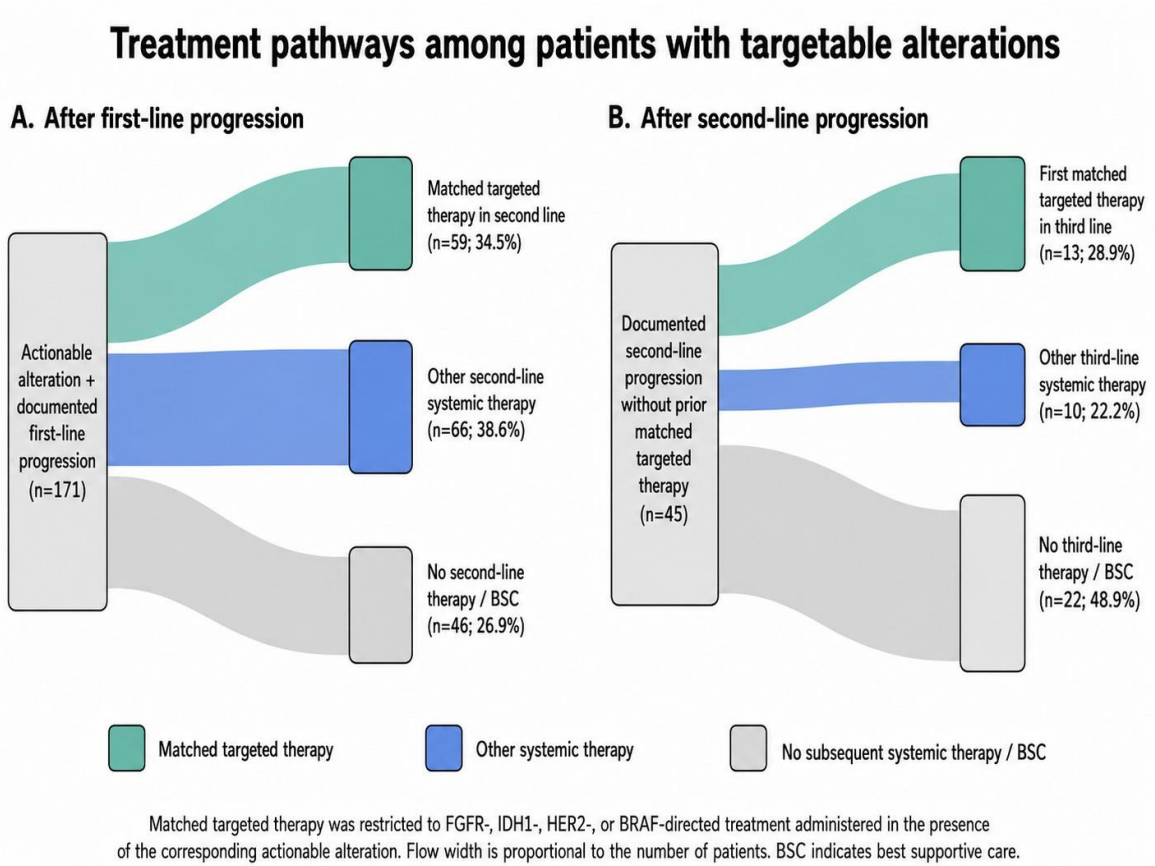
29.6% died without 2L at day 90



40.1% died without 3L at day 90

Rimini M et al. Treatment Attrition and Longitudinal Care Pathways in Advanced BTC. Unpublished manuscript, 2026.

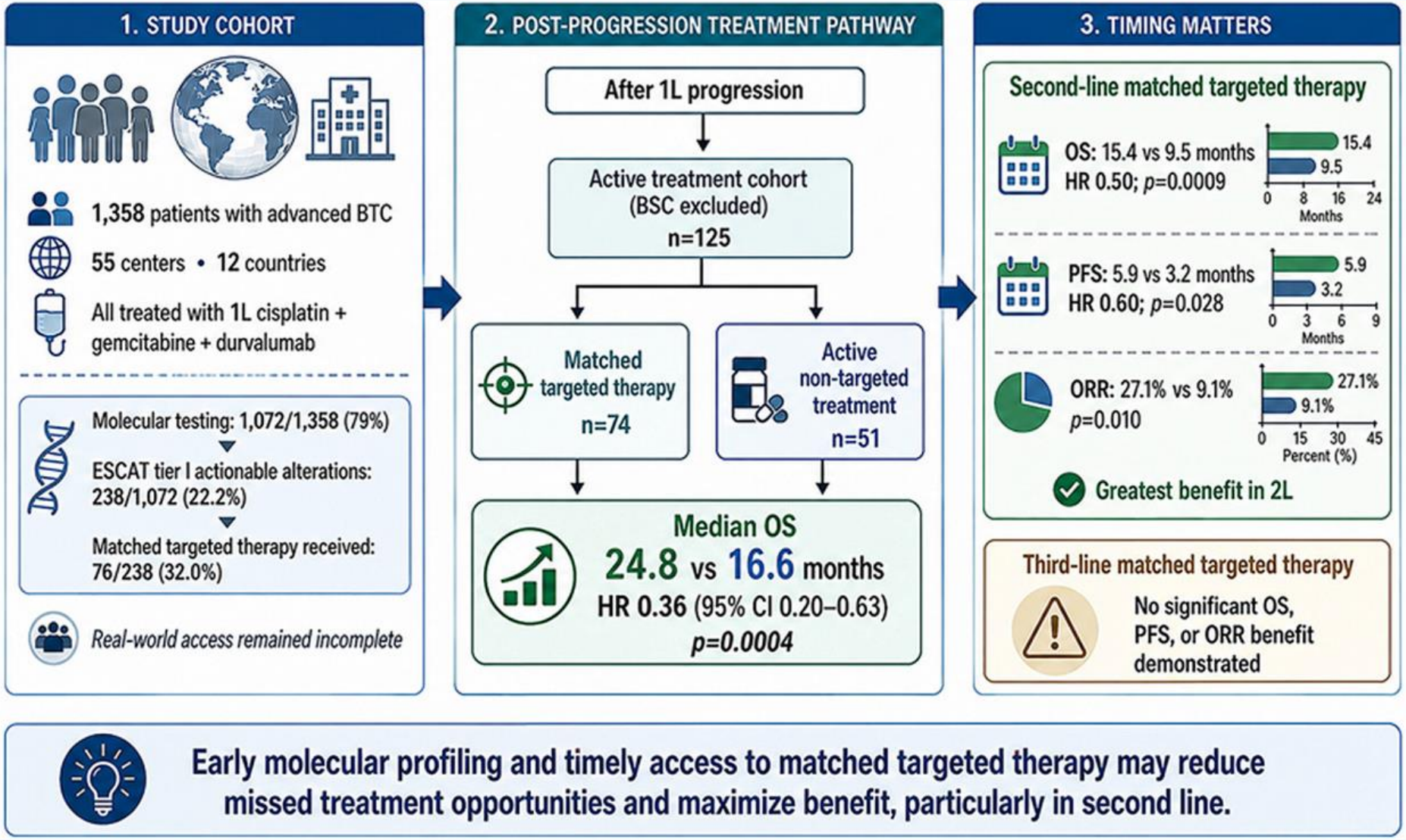
Actionable biology ≠ access to matched therapy



31.9% of patients with an actionable alteration received matched treatment

Rimini M et al. Treatment Attrition and Longitudinal Care Pathways. Unpublished manuscript, 2026; Supplementary Figure 1.

Timing matters

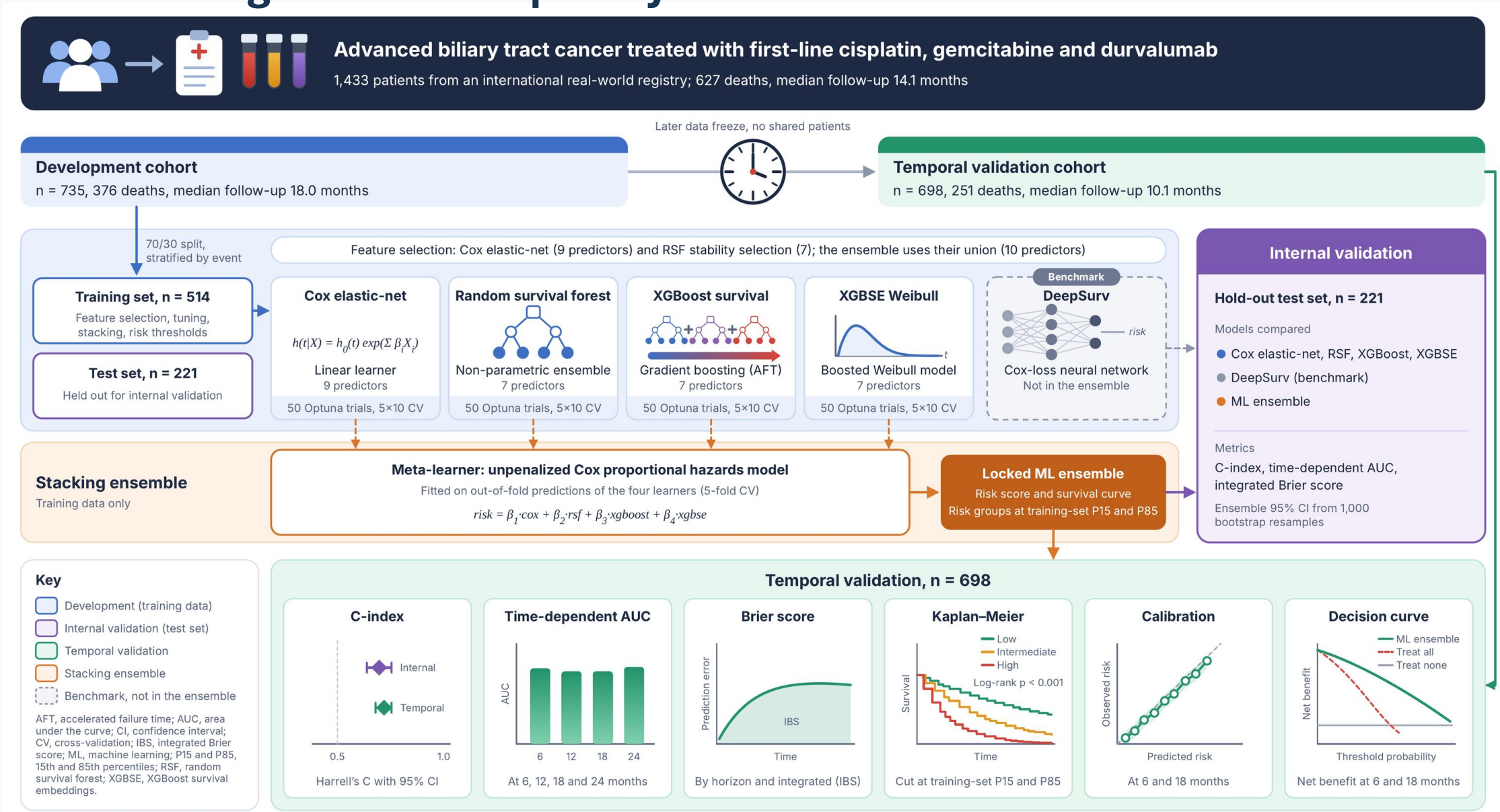


Rimini M et al. J Hepatol 2026. doi:10.1016/j.jhep.2026.09.012. PMID:42800681.

RWE: turning clinical complexity into better care

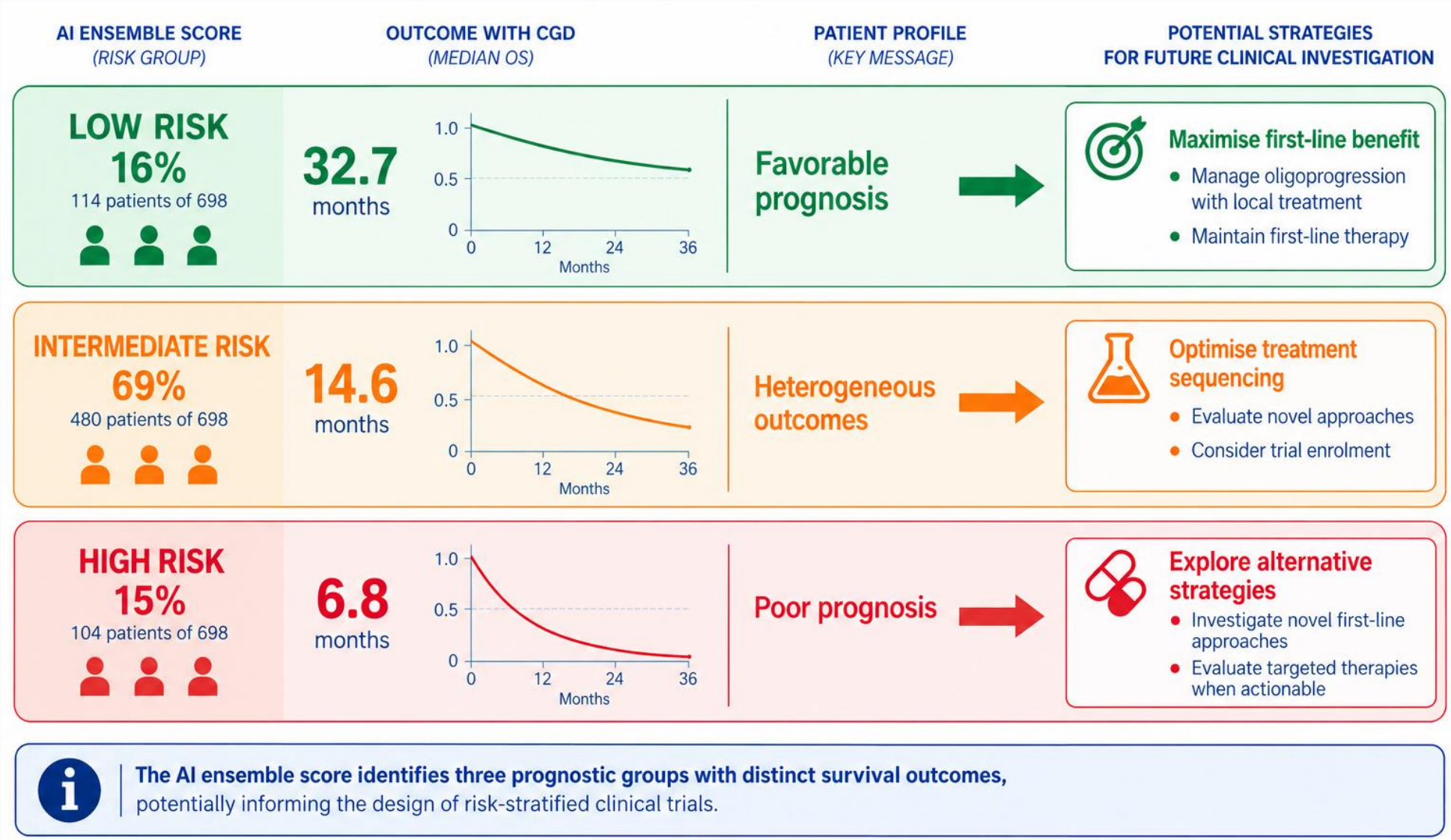


RWE: turning clinical complexity into better care



Rimini M et al. Unpublished manuscript

RWE: turning clinical complexity into better care



Rimini M et al. Unpublished manuscript

Thank You!