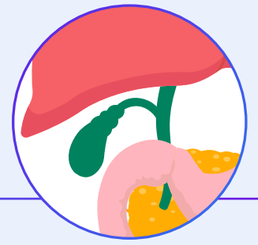
The Evolving Standard of Care in Advanced Biliary Tract Cancers:
Three-Year Survival Data Supports Durvalumab + gem-cis in First-Line Treatment

The publication of this infographic was supported by **AstraZeneca**. This content is intended for **US Healthcare Professionals only**.

Oncol AMJ. 2025;2[1]:98-99. https://doi.org/10.33590/oncolamj/RRYL1738

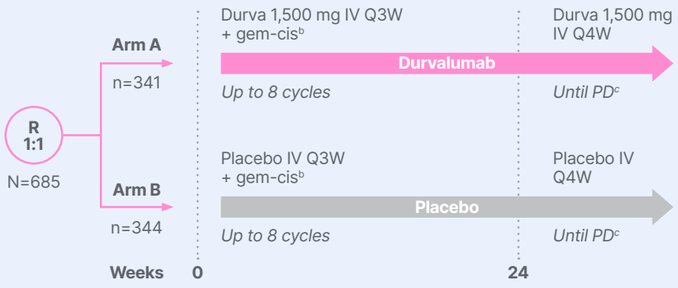
Introduction

TOPAZ-1 is a Phase III, randomized, double-blind, placebo-controlled, multi-center, global study for 1L treatment with durvalumab + gem-cis[a] in adult patients with advanced biliary tract cancers (BTC).[1]



Study population

- Previously untreated, unresectable, locally advanced or metastatic BTCs at initial diagnosis, including intrahepatic or extrahepatic cholangiocarcinoma and gallbladder carcinoma
- Recurrent disease >6 months after curative surgery or completion of adjuvant therapy[a]
- ECOG PS of 0 or 1



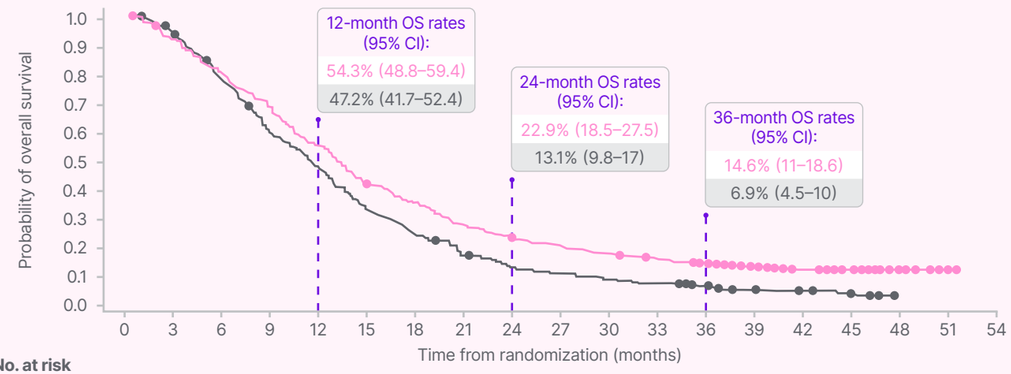
The primary analysis demonstrated statistically significant improvements in OS and PFS and a higher ORR with durvalumab + gem-cis versus placebo + gem-cis, as well as a tolerable safety profile.[1]

This demonstration of the addition of durvalumab to gem-cis was the first advancement in the 1L setting for advanced BTCs in over 10 years.[1]

		Durvalumab + gem-cis (n=341)	Placebo + gem-cis (n=344)
Primary endpoint	Median OS, months (95% CI)	12.8 (11.1–14.0)	11.5 (10.1–12.5)
	HR (95% CI)	0.80 (0.66–0.97); p=0.021	
Key secondary endpoints[d]	Median PFS, months (95% CI)	7.2 (6.7–7.4)	5.7 (5.6–6.7)
	HR (95% CI)	0.75 (0.63–0.89); p=0.001	
	ORR, %	(n=341) 26.7	(n=343) 18.7
	Safety, %	(n=338)	(n=342)
	TRAEs	92.9	90.1
	Serious TRAEs	15.7	17.3
	TRAEs leading to discontinuation	8.9	11.4
	Any immune-mediated AE	12.7	4.7

In the post-hoc 3-year analysis of TOPAZ-1:

2x more patients were estimated to be alive in the **durvalumab arm compared to placebo arm** (14.6% and 6.9%, respectively); a greater OS rate ratio compared with previous data cut-off points.[2*]



No. at risk																			
Durvalumab + gem-cis	341	309	268	227	184	140	118	92	75	67	58	50	43	31	21	15	7	1	0
Placebo + gem-cis	344	316	260	199	159	110	82	59	43	37	30	25	18	11	8	4	0	0	0

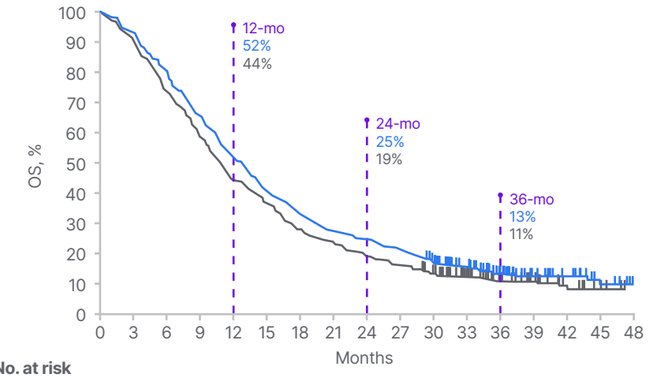
*The 3-year OS analysis was conducted post hoc and not powered for statistical significance.

Data cut off was October 23, 2023. At the 3-year analysis, OS maturity was 89%. Median duration of follow-up was 42.9 months in the durvalumab arm and 41.8 months in the placebo arm.

- The safety profile of durvalumab + gem-cis remained consistent with previous analyses, with no new signals detected.[1,2]
- Among extended long-term survivors (patients alive ≥30 months after baseline; n=88), patients treated with durvalumab + gem-cis were more likely to be extended long-term survivors (n=58/88). No individual subgroup drove long-term survival.[2]

Three-year follow-up data from KEYNOTE-966

KEYNOTE-966 was a similar study comparing **gem-cis with or without pembrolizumab**; however, unlike TOPAZ-1,[†] it continued gemcitabine beyond 8 cycles.[3*]



No. at risk																			
Pembro + gem-cis	553	496	430	350	275	217	176	147	131	113	86	64	39	21	15	6	0		
Placebo + gem-cis	536	483	394	313	236	195	149	125	102	86	63	43	27	20	10	4	0		

*The 3-year OS analysis was not powered for statistical significance.

Data cut off was November 14, 2023. Median duration of follow-up was 36.6 months.

[†]We cannot draw any definitive conclusions from indirect comparisons, as the study design, demographics and other criteria may differ between trials.

Additional analyses conducted for TOPAZ-1:*

*These analyses were not powered for statistical significance.

Patient subgroups
Consistent OS results across various patient subgroups, including regional subgroups,[4] primary tumor location,[5] and disease status.[6]

Additional safety analysis
Durvalumab + gem-cis was associated with an OS benefit versus placebo, irrespective of imAE occurrence.[1,7]

QoL
No detriment in QoL as assessed by TTD in the durvalumab group compared with placebo.[8]

Mutation status
Benefit consistently observed with durvalumab, including in patients with clinically actionable alterations.[9]

Antibiotics
No meaningful difference in OS for patients who received antibiotics during the study period compared with those who did not.[10]

Prognostic factors
Analysis supports this regimen in patients with previously untreated advanced BTCs, irrespective of baseline demographics, disease characteristics, clinical or laboratory factors.[11]

SAT use
Median duration of first SAT was similar for both arms, suggesting that durvalumab does not impact the efficacy of SAT.[3] Longer time to first subsequent anti-cancer therapy in the durvalumab arm compared to the placebo arm (median: 18.7 months [95% CI: 13.2–42.2] and 12.3 months [95% CI: 11.3–24.1]).[2]

Conclusion

TOPAZ-1 is the first global Phase III study to evaluate an immuno-oncology-based regimen in the 1L advanced BTC setting, with numerous secondary analyses that support its use in a broad population[1]

Data from the 3-year follow-up analysis of TOPAZ-1 supports the use of durvalumab + gem-cis as SoC in patients with locally advanced or metastatic BTCs[2,13]

Footnotes:

[a]Chemotherapy and/or radiation; [b]Cisplatin (25 mg/m^2) followed by gemcitabine (1,000 mg/m^2), each administered on Days 1 and 8, Q3W for up to 8 cycles (SoC chemotherapy); [c]Until confirmed PD, withdrawal of consent, or another discontinuation criteria is met. [d]PFS and ORR were measured according to RECIST v1.1 using investigator assessments.

Abbreviations:

1L: first line; AE: adverse event; BTC: biliary tract cancer; Durva: durvalumab; ECOG PS: Eastern Cooperative Oncology Group performance status; gem-cis: gemcitabine + cisplatin; imAE: immune-mediated adverse event; IV: intravenous; ORR: objective response rate; OS: overall survival; PD: progressive disease; pembro: pembrolizumab; PFS: progression-free survival; QnW: every n weeks; R: randomization; SAT: subsequent anti-cancer therapy; SoC: standard of care; TRAE: treatment-related adverse event; TTD: time to deterioration.

1. Oh et al. NEJM Evid 2022;1(8):EVIDoa2200015.
2. Oh et al. J Hepatol. 2025;DOI:10.1016/j.jhep.2025.05.003.
3. Finn RS et al. ASCO Annual Meeting; May 31-June 4, 2024.
4. Vogel A et al. J Clin Oncol 2022;40(Suppl 16):4075.
5. He AR et al. Poster O-1. World Congress on Gastrointestinal Cancer (World GI), June 29-July 2, 2022.
6. Okusaka T et al. Ann Oncol 2022;33(Suppl 9):S1471.
7. Antonuzzo L et al. Ann Oncol 2022;33(Suppl 7):S566-7.
8. Burris H et al. J Clin Oncol 2023;40(suppl 16):4070.
9. Valle JW et al. European Society for Medical Oncology (ESMO) Asia Congress, December 2-4, 2022.
10. He AR et al. J Clin Oncol 2023;41(Suppl 4):550.
11. He AR et al. Ann Oncol 2023;34(Suppl 2):S220.
12. Vogel A et al. Ann Oncol 2024;35(Suppl 2):S233-4.
13. AstraZeneca UK Ltd. IMFINZI (duvalumab). FDA prescribing information. February 2025. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2025/761069s051lbl.pdf. Last accessed 12 March 2025.