TOURMALINE: Safety and Efficacy of Durvalumab in Combination with Gemcitabine-Based Chemotherapy in Advanced Biliary Tract Cancer

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Introduction

- Durvalumab plus GemCis was the first immunotherapy-based regimen to be approved as a first-line treatment for aBTC.[1]
- In TOPAZ-1, the OS benefit with durvalumab plus GemCis versus placebo plus GemCis was maintained through 4 years of follow-up.[2]
- Now, the Phase IIIb TOURMALINE study has assessed the safety and efficacy of durvalumab combined with other gem-based chemotherapy treatments, and at a shortened infusion time after the first cycle.[3]

TOPAZ-1

TOPAZ-1 was the first randomized Phase III study to report 4-year OS in aBTC using a combined immunotherapy and chemotherapy approach.[2]

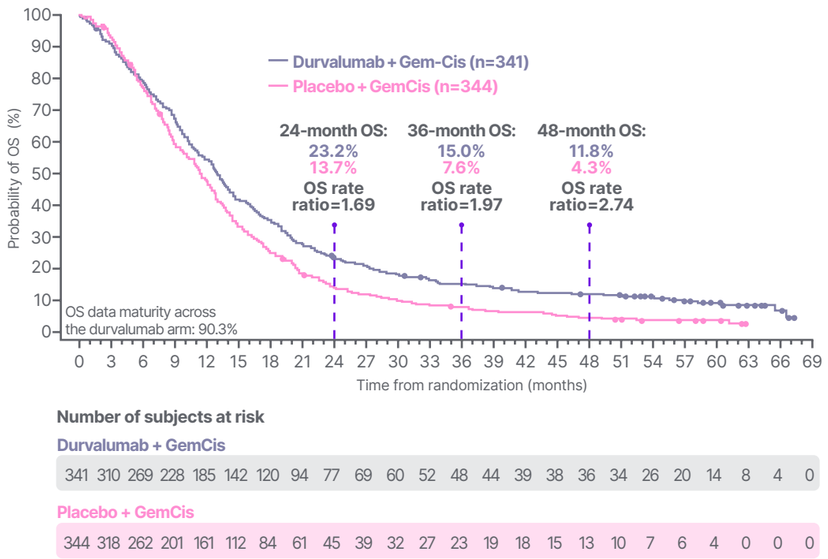
Participants (N=685) were randomized 1:1 to either the durvalumab plus GemCis or the placebo plus GemCis arms.[2]

Key eligibility criteria included:[2]

- Unresectable, locally advanced, or metastatic BTC
- Previously untreated (if unresectable) or metastatic at initial diagnosis
- Recurrent disease >6 months after curative surgery or completion of adjuvant therapy
- ECOG PS 0 or 1

TOPAZ-1: 4-year OS update.[2,3]

	4-year OS analysis DCO: February 28, 2025		Primary analysis DCO: August 11, 2021	
	Durvalumab + GemCis (n=341)	Placebo + GemCis (n=344)	Durvalumab + GemCis (n=341)	Placebo + GemCis (n=344)
Median OS (95% CI), months	13.0 (11.6–14.1)	11.4 (10.1–12.5)	12.8 (11.1–14.0)	11.5 (10.1–12.5)
OS HR (95% CI)	0.75 (0.64–0.88)		0.80 (0.66–0.97; p=0.021)	



TOURMALINE Phase IIIb Study[4]

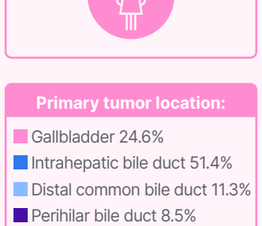
An international, single-arm, open-label study assessed durvalumab combined with a gem-based chemotherapy regimen as first-line treatment for aBTC.

Study Population

- Histologically confirmed locally advanced or metastatic BTC, including iCCA, eCCA, GBC, and AoV
- >18 years of age
- ECOG PS 0–2[a]
- Prior curative treatment is permitted with no minimum time to recurrence, including participants with residual disease

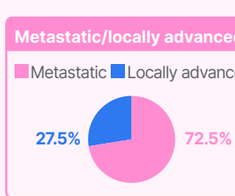
Screening –28 days to –1 day

Durvalumab 1,500 mg Q3W + Gem-based chemotherapy[b] up to eight cycles



Durvalumab 1,500 mg Q4W until disease progression or unacceptable toxicity

Gem maintenance, at investigator's discretion



Durva+Gem (n=20) Durva+Gem+ Cis (n=20) Durva+Gem+ Oxali (n=37) Durva+Gem+ Carbo (n=15) Durva+ Gem+S-1 (n=8) Durva+Gem+ Cis+Nab- paclitaxel (n=13) Durva+Gem+ Cis+S-1 (n=29)

[a]ECOG PS 2 participants were capped at 20% of the overall treated participant population.
[b]Gemcitabine-based chemotherapy regimens were selected by investigator's choice, according to local practice and based on institutional standards.

Unlike in TOPAZ-1, eligibility criteria included WHO/ECOG PS 2, AoV cancer, and recurrent disease <6 months after surgery or adjuvant treatment.[4]

Durvalumab was administered as a 60-minute infusion at Cycle 1, but if well tolerated, subsequent cycles were 30 minutes.[4]

The primary endpoint was the incidence of Grade 3–4 PRAEs within 6 months.[4]

Secondary endpoints included OS rate at 12, 18, and 24 months, ORR, and PFS at 12 and 18 months.[4]

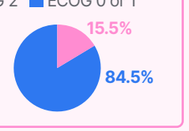
Overall participant demographics and clinical characteristics (N=142).[4]

Median age:
68 (26–92) years

Female sex:
45.1%

Region:

ECOG PS at baseline:

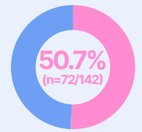


Primary tumor location:
- Gallbladder 24.6%
- Intrahepatic bile duct 51.4%
- Distal common bile duct 11.3%
- Perihilar bile duct 8.5%
- AoV 4.2%

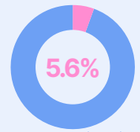
Metastatic/locally advanced:

[c]Italy, Germany, France, Spain, USA.

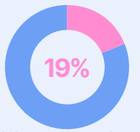
TOURMALINE Findings



Patients experiencing a Grade 3–4 PRAE within 6 months of first durvalumab dose[4]

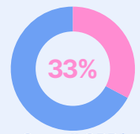


Participants experiencing an IRR[4]



Participants experiencing immune-mediated adverse events[4]

The three most common Grade 3–4 AEs were:[4]
- Anemia: 25.4% (n=36)
- Decreased neutrophil count: 22.5% (n=32)
- Decreased platelet count: 11.3% (n=16)

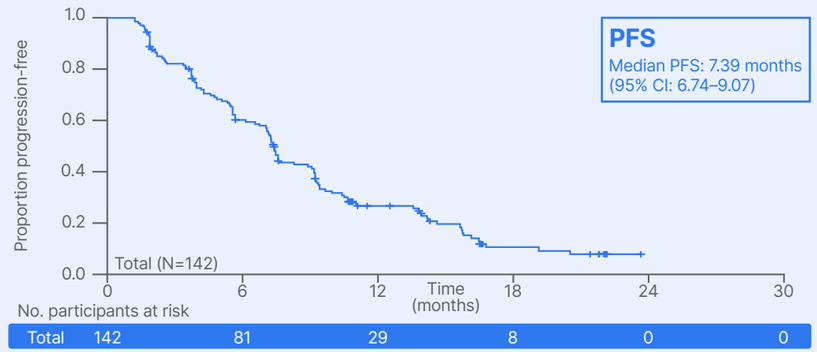


Overall ORR[d] (95% CI: 25.44–41.48)[4]

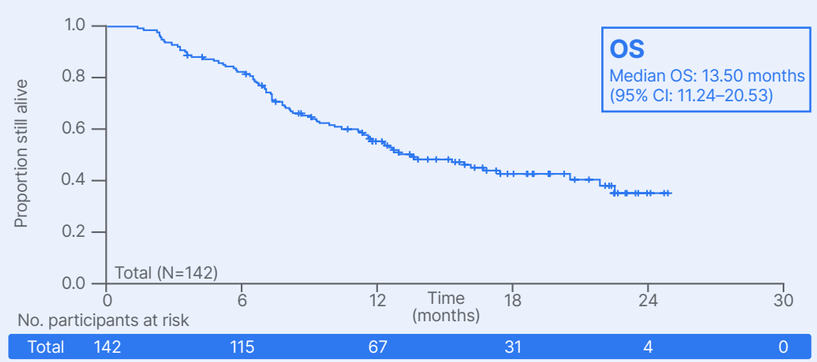
One participant in the Durva+Gem+Oxali cohort experienced a PRAE resulting in death.[4]

[d]Confirmed responses, investigator-assessed per RECIST version 1.1.

Progression-free survival and overall survival Kaplan-Meier curves.[4]



PFS
Median PFS: 7.39 months (95% CI: 6.74–9.07)



OS
Median OS: 13.50 months (95% CI: 11.24–20.53)

Conclusions

No new safety signals were observed.

Reducing the durvalumab infusion to 30 minutes did not increase the number of infusion-related reactions.

One third of participants achieved an objective response.

References: 1. AstraZeneca. 2026. Available at: https://drd9vrdh9yh09.cloudfront.net/50fd68b9-106b-4550-b5d0-12b045f8b184/9496217c-08b3-432b-ab4f-538d795820bd/9496217c-08b3-432b-ab4f-538d795820bd_viewable_rendition__v.pdf. Last accessed: August 19 2026. 2. Oh DY et al. JAMA Oncology. 2026;DOI:10.1001/jamaoncol.2026.2204. 3. Oh DY et al. NEJM Evid. 2022;1(8):EVIDoa2200015. 4. Oh DY et al. J Hepatol. 2026;DOI:10.1016/j.jhep.2026.06.025.

Abbreviations: aBTC: advanced biliary tract cancer; AoV: Ampulla of Vater; BTC: biliary tract cancer; DCO: data cut-off; eCCA: extrahepatic cholangiocarcinoma; Durva+Gem (n=20); Durva+Gem+ Cis (n=20); Durva+Gem+ Oxali (n=37); Durva+Gem+ Carbo (n=15); Durva+ Gem+S-1 (n=8); Durva+Gem+ Cis+Nab- paclitaxel (n=13); Durva+Gem+ Cis+S-1 (n=29); ECOG PS: Eastern Cooperative Oncology Group Performance Status; GBC: gallbladder cancer; Gem: gemcitabine; GemCis: gemcitabine and cisplatin; HR: hazard ratio; iCCA: intrahepatic cholangiocarcinoma; IRR: infusion-related reaction; ORR: objective response rate; OS: overall survival; PFS: progression-free survival; PRAE: possibly-related adverse event; Q2W: once every two weeks; Q3W: once every three weeks; Q4W: once every four weeks; RECIST: Response Evaluation Criteria in Solid Tumors; S-1: tegafur/gimeracil/oteracil.

In the US, durvalumab is approved for use in combination with gemcitabine and cisplatin for the treatment of adults with locally advanced or metastatic biliary tract cancer. The other gemcitabine-based chemotherapy regimens evaluated in TOURMALINE are not approved for use with durvalumab in this setting.