

Immune Checkpoint Inhibitors in Advanced Cholangiocarcinoma: A Systematic Review of Efficacy, Safety, and Emerging Biomarkers

Faiz Un Nisa, Moeez Ali, Talha Khan, Muskan Lohana, **Aniba Asif**, Nandni Kumari, Maaz Ali

Presenting author: **Aniba Asif**
Isra University | aniba87121@gmail.com

BACKGROUND

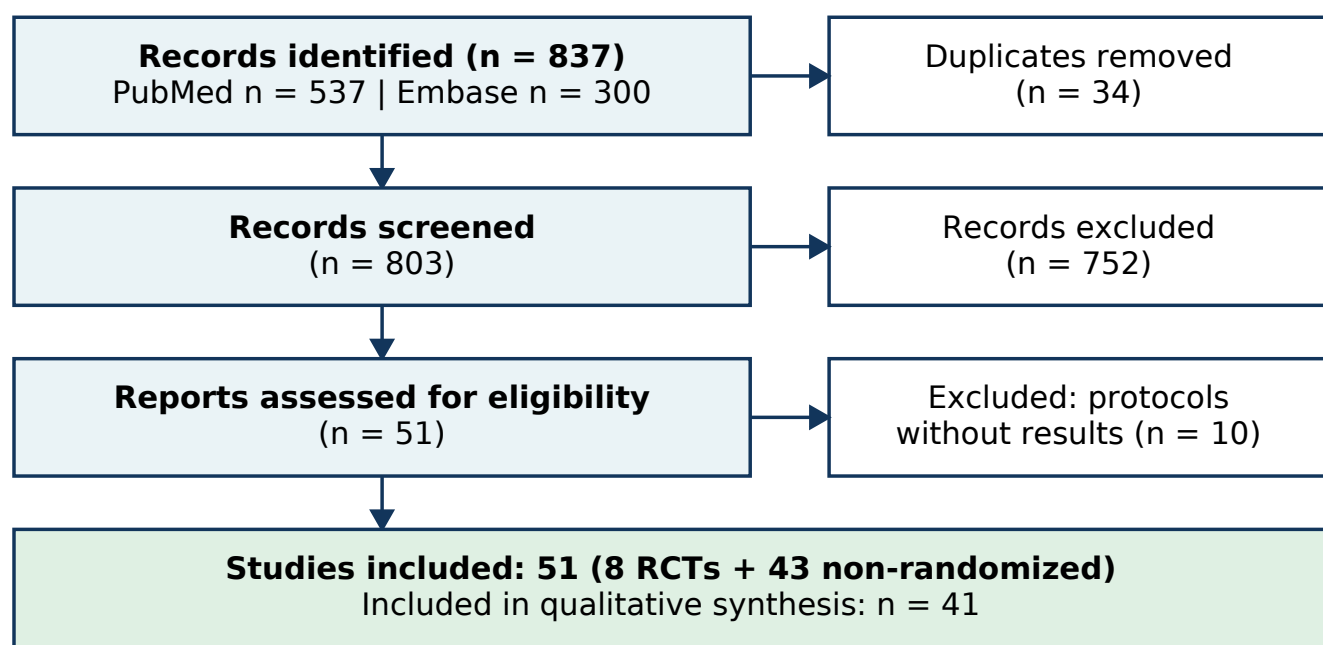
- Cholangiocarcinoma (CCA) is aggressive and usually diagnosed at an advanced stage.
- Gemcitabine-cisplatin (GemCis) was standard care for over a decade, with limited benefit.
- Immune checkpoint inhibitors (ICIs) may improve outcomes, but results vary.

Aim: assess efficacy, safety and biomarkers of ICIs in advanced CCA.

METHODS

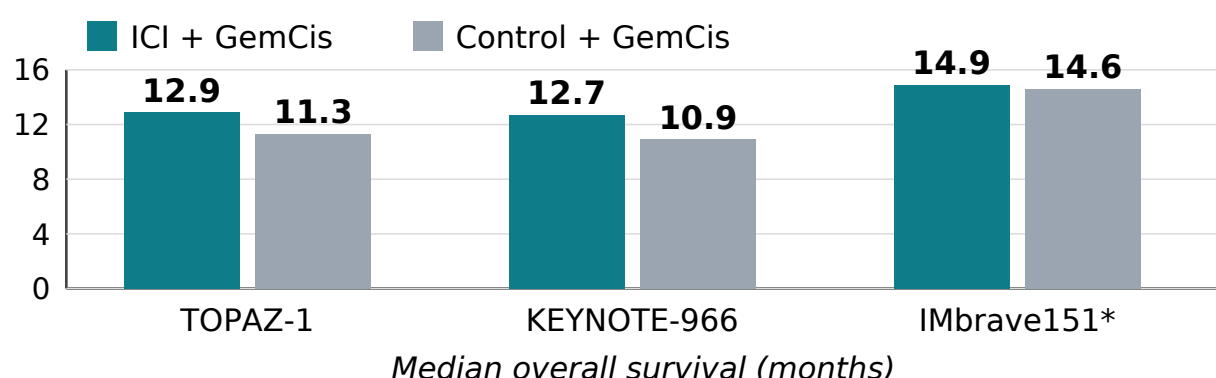
- PRISMA 2020 systematic review (not registered).
- PubMed and Embase, inception to Dec 2024.
- Adults with CCA on PD-1/PD-L1/CTLA-4 inhibitors in prospective trials.
- ROBINS-I and Cochrane RoB 2; narrative synthesis.

STUDY SELECTION



About 4,800 patients. 72.7% of non-randomized studies had moderate risk of bias.

FIRST-LINE RESULTS



*IMbrave151 (phase II): HR 0.97, not significant.

- TOPAZ-1** (durvalumab): HR 0.76; 24-month OS 23.6% vs 11.5%.
- KEYNOTE-966** (pembrolizumab): HR 0.83.

SECOND-LINE AND NOVEL REGIMENS

- ICI monotherapy: ORR 3–22%, mOS 4.3–14.2 months.
- ICI + TKI: ORR 9–28%, mOS 6.4–16.0 months.
- Triplet (toripalimab + lenvatinib + GEMOX): ORR 80%, mOS 22.5 months.
- Radiotherapy + camrelizumab: ORR 61.1%, mOS 22.0 months.
- ICI + HAIC: 15.4% surgical conversion.

SAFETY (GRADE ≥3 TRAEs)

Treatment class	Grade ≥3 TRAEs
ICI monotherapy	10–17%
Chemo-ICI (first-line)	70–75%
ICI + TKI	30–60%
Triplet	17–57%
Radiotherapy + ICI	8–14%

No unexpected toxicity signals.

BIOMARKERS

- PD-L1:** not predictive of OS benefit.
- HRD/DDR mutations:** ORR 71.4% vs 33.3%; PFS HR 0.43.
- ctDNA clearance:** ORR 66.7% vs 12.5%; PFS 8.9 vs 2.4 months.

Small, non-randomized data; need validation.

DISCUSSION

- Adding ICIs to GemCis moved mOS beyond the 11.7-month plateau of the GemCis era.
- No biomarker is yet validated for routine selection.

LIMITATIONS

- Mostly single-arm studies; ORR may be overestimated.
- Heterogeneous regimens; no meta-analysis.

CONCLUSIONS

Chemo-immunotherapy (durvalumab or pembrolizumab + GemCis) is first-line standard for advanced CCA. Triplet and HAIC combinations and biomarker-guided selection (HRD/DDR, ctDNA) need validation.