Background

The prognosis of first-line standard chemotherapy for advanced biliary tract cancers (BTCs) is still unsatisfactory. Based on phase III trial TOPAZ-1, chemotherapy plus PD-L1 inhibitor had shown positive survival improvement. Other evidence showed that VEGF inhibitor could modify tumor immune-microenvironment while hepatic arterial infusion chemotherapy (HAIC) could improve the survival in cholangiocarcinoma. Combining these modalities may improve outcomes. Here we conducted a prospective study to evaluate the efficacy and safety of HAIC combined with bevacizumab (VEGF inhibitor) and toripalimab (PD-1 inhibitor) for advanced BTCs.

Study design

This open-label, single-arm, single-center prospective phase II trial was initiated by Peking University Cancer Hospital, China, and registered at clinicaltrials.gov (NCT04217954).

Patients: From October 2019 to December 2021, 32 patients with advanced untreated BTCs were enrolled. The baseline characteristics were listed in Table 1.

Treatments: The combination regimen was composed of hepatic arterial bevacizumab (300 mg for 2h d1), followed by oxaliplatin (40 mg/m² for 2h, days 1-3) and 5-fluorouracil (800 mg/m² for 22h, days 1-3), with intravenous toripalimab (240 mg) on day 1 prior to HAIC, every 4 weeks. A maximum of six consecutive HAIC cycles. Then toripalimab (240 mg) and bevacizumab (300 mg) were intravenously infused every four weeks as maintenance treatment (Figure 1).

Results

Patient characteristics: The baseline characteristics were listed in Table 1.

Endpoints: The primary endpoint was overall survival (OS). Secondary endpoints included objective response rate (ORR), which was evaluated according to Immune-Modified Response Evaluation Criteria In Solid Tumors (imRECIST), progression-free survival (PFS), and safety.

Efficacy: At the cutoff date (July 26, 2022), the median follow-up was 14.9 months. As shown in Table 2, the overall response rate (ORR) was 84.3% (27/32), with 1 complete responses (CR) and 26 partial responses (PR). Stable disease (SD) was observed in 4 patients (12.5%) and progressive disease (PD) occurred in 1 patient (3.1%). Disease control rate (DCR) was 96.9% (31/32). Six-month PFS rate and OS rate were 80.7% and 90.6%, respectively. One-year PFS rate and OS rate were 53.8% and 80.4%, respectively.

Safety: The most common grade 3 or 4 treatment-related AEs (TRAEs) were liver dysfunction (6 [18.8%]), hematotoxicity (4 [12.5%]) and Diarrhea (1 [3.1%]). The Immune-Related Adverse Events (irAEs) occurred in 2 [6.3%] patients. One treatment-related death occurred.

Conclusions

These promising results from HAIC and Bevacizumab in combination with Toripalimab may contribute to a paradigm shift in the first-line treatment for advanced BTC patients. Follow-up for survival is ongoing.

Conflict of interest: None

Endpoints: The primary endpoint was overall survival (OS). Secondary endpoints included objective response rate (ORR), which was evaluated according to Immune-Modified Response Evaluation Criteria In Solid Tumors (imRECIST), progression-free survival (PFS), and safety.

Patient characteristics: The baseline characteristics were listed in Table 1.

Endpoints: The primary endpoint was overall survival (OS). Secondary endpoints included objective response rate (ORR), which was evaluated according to Immune-Modified Response Evaluation Criteria In Solid Tumors (imRECIST), progression-free survival (PFS), and safety.

Results

Patient characteristics: The baseline characteristics were listed in Table 1.

Endpoints: The primary endpoint was overall survival (OS). Secondary endpoints included objective response rate (ORR), which was evaluated according to Immune-Modified Response Evaluation Criteria In Solid Tumors (imRECIST), progression-free survival (PFS), and safety.

Patient characteristics: The baseline characteristics were listed in Table 1.

Endpoints: The primary endpoint was overall survival (OS). Secondary endpoints included objective response rate (ORR), which was evaluated according to Immune-Modified Response Evaluation Criteria In Solid Tumors (imRECIST), progression-free survival (PFS), and safety.

Patient characteristics: The baseline characteristics were listed in Table 1.

Endpoints: The primary endpoint was overall survival (OS). Secondary endpoints included objective response rate (ORR), which was evaluated according to Immune-Modified Response Evaluation Criteria In Solid Tumors (imRECIST), progression-free survival (PFS), and safety.

Patient characteristics: The baseline characteristics were listed in Table 1.

Endpoints: The primary endpoint was overall survival (OS). Secondary endpoints included objective response rate (ORR), which was evaluated according to Immune-Modified Response Evaluation Criteria In Solid Tumors (imRECIST), progression-free survival (PFS), and safety.

Patient characteristics: The baseline characteristics were listed in Table 1.

Endpoints: The primary endpoint was overall survival (OS). Secondary endpoints included objective response rate (ORR), which was evaluated according to Immune-Modified Response Evaluation Criteria In Solid Tumors (imRECIST), progression-free survival (PFS), and safety.

Patient characteristics: The baseline characteristics were listed in Table 1.