A single-arm, open-label, Phase II study of tislelizumab combined with lenvatinib and GEMOX regimen for conversion therapy of potentially resectable locally advanced biliary tract cancers

Liu Dongming, Zhang Xihao, Mu Han, Liu Changfu, Zhang Weihao, Cui Yunlong, Wu Qiang, Zhu Xiaolin, Fang Feng, Zhang Wei, Xing Wenge, Li Qiang, Song Tianqiang, Lu Wei, Li Huikai
Department of Hepatobiliary, Liver Cancer Research Center for Prevention and Therapy Clinical Laboratory, Tianjin Medical University Cancer Institute and Hospital, National Clinical Research Center for Cancer, Key Laboratory of Cancer Prevention and Therapy, Tianjin, Tianjin's Clinical Research Center for Cancer, Tianjin, China

Background

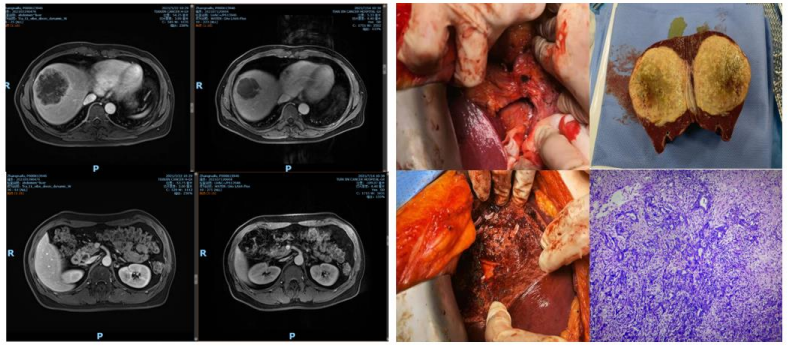
Surgery remains the only curative treatment for biliary tract cancers, and conversion therapy helps to convert locally unresectable patients to resectable patients to improve overall survival. Tislelizumab, a PD-1 monoclonal antibody, shows promising antitumor activity and safety in the treatment of advanced HCC when combined with lenvatinib. This study aimed to explore the efficacy and safety of tislelizumab combined with lenvatinib and GEMOX in potentially resectable advanced BTC.

Methods

In this prospective, single-center, single-arm phase II study (NCT05036798), major eligible criteria were potentially resectable locally advanced BTC, no previous systemic treatment, Child-Pugh A or B, ECOG PS 0 or 1. Patients received GEMOX, followed by intravenous tislelizumab (200mg, D1, Q3W) and lenvatinib (8mg/kg, PO, QD)≤7 cycles. Patients who remain unable to receive surgery would receive tislelizumab combined with lenvatinib for maintenance therapy. Primary endpoint was R0 resection rate. Secondary endpoints were progression free survival(PFS), objective response rate(ORR), and disease control rate(DCR) (RECIST 1.1).

Results

Between May 22, 2021 and January 24, 2022, 25 patients were enrolled with a median age of 59.7 years (range 33-77).11 males(44%),14 females(56%); Child-Pugh class A(n=23,92%) or B(n=2,8%); ECOG PS 0(n=25,100%). The median tumor size was 5.3 cm (range, 1.57-11.06), 36% pts had intrahepatic metastases, 12% had extrahepatic metastases, and 60% had lymph node metastases. As of 27 April 2022, 13 pts (52%) received R0 resection, 2 patient received intraoperative radiotherapy.1 patient (4%) achieved complete pathological response(pCR). The median duration of therapy before surgery was 3.44 cycles(range 2-8). ORR and DCR were 56% and 92% respectively(PR, n=14; SD, n=9). There were no severe complications, 3 patient developed the complication of leukopenia and thrombocytopenia, 2pts observed diarrhea and hypertension.



Figur. A male patient diagnosed with TMN IIIb stage ICC with Lymph node metastasis. The patient was treated with GEMOX (Gemcitabine 1800mg, D1, D8; Oxaliplatin 150mg, D1, Q3W) + Tislelizumab (200mg, D1, Q3W) + Lenvatinib (8mg/kg, PO, QD). After 2 months of treatment, the patient was evaluated based on the mRECIST criteria, partial response was achieved and was subsequently surgically resected.

Baseline characteristic (n=25)	
Median age, year (Range)	59.7 (33-77)
Sex, n% (Male)	44%
ECOG PS Score, n (%)	
0	0 (0%)
1	25 (100%)
Child-Pugh, n (%)	
A	23 (92%)
B	2 (8%)
Hepatitis, n (%)	
None	19 (76%)
B	5 (20%)
C	0 (0%)
Both	0 (0%)
Liver cirrhosis, n (%)	1 (4%)
CA19-9＞37 U/ml	20 (80%)
Extrahepatic metastasis, n (%)	3 (12%)
Lymph node metastasis, n (%)	15 (60%)
After treatment	
CA19-9＞37 U/ml	15 (60%)
Clinical/pathological outcome	
ORR	56%
DCR	92%
pCR	4%
Conversion rate	84%
Surgery rate	60%

Table. Baselin、Treatment、outcome

Conclusion

Tislelizumab in combination with lenvatinib and GEMOX achieved a promising ORR and R0 resection conversion rate with manageable safety profile in potentially resectable locally advanced BTC. The curative effect of gallbladder cancer and intrahepatic cholangiocarcinoma is better than that of hilar cholangiocarcinoma and extrahepatic cholangiocarcinoma. Further follow-up is ongoing.