BERLIN 2025 ESMO congress

LBA11

Neoadjuvant toripalimab plus lenvatinib and GEMOX in resectable, high-risk intrahepatic cholangiocarcinoma: A randomized, multicenter, open-label phase II-III clinical trial

G. Shi[1], J. Fan[1], J. Zhou[1], X. Huang[1], F. Liang[2], X. Liang[3], R. Dong[4], Q. Ye[1], Q. Gao[1], Z. Yu[5], W. Zhai[6], J. Lu[1], Y. Ji[7], X. Li[8], F. Liu[9], K. Wang[10], W. Yang[11], J. Zhang[12], S. Qiu[1], J. Zou[13]

[1] Department of Hepatobiliary Surgery and Liver Transplantation, Zhongshan Hospital Affiliated to Fudan University, Shanghai, China, [2] Department of Biostatistics, Zhongshan Hospital Affiliated to Fudan University, Shanghai, China, [3] Department of General Surgery, Sir Run Run Shaw Hospital, Zhejiang University, School of Medicine, Hangzhou, China, [4] Department of General Surgery, Tangdu Hospital, The Fourth Military Medical University, Xi'an, China, [5] Department of Hepatobiliary Surgery, The First Affiliated Hospital of Wenzhou Medical University - Gongyuanlu Site, Wenzhou, China, [6] Hepatobiliary and Pancreatic Surgery, The First Affiliated Hospital of Zhengzhou University, Zhengzhou, China, [7] Department of Pathology, Zhongshan Hospital Affiliated to Fudan University, Shanghai, China, [8] Department of Hepatobiliary Surgery, Shenzhen General Hospital of Shenzhen University, Shenzhen, China, [9] Department of General Surgery, The First Affiliated Hospital Of Anhui Medical University, Hefei, China, [10] Hepatology Dept., Shanghai Eastern Hepatobiliary Surgery Hospital, Shanghai, China, [11] Department of Hepatobiliary Surgery, The First Affiliated Hospital of Xi'an Jiaotong University, Xi'an, China, [12] Department of Hepatobiliary Surgery, The First Hospital of China Medical University, Shenyang, China[13] Research and Development Department, Shanghai Junshi Biosciences Co., Ltd., Shanghai, China

Background

Previous clinical trials demonstrated that the GOLP (GEMOX in combination with Lenvatinib and anti-PD1 antibody) regimen exhibited robust antitumor activity and manageable safety in both advanced iCCA and biliary tract cancer. These findings provide a strong rationale for investigating this regimen as neoadjuvant therapy in resectable high-risk iCCA.

Methods

This randomized, multicenter, open-label phase II-III trial (ZSAB-neoGOLP) evaluated neoadjuvant GOLP regimen in patients (pts) with resectable iCCA exhibiting high-risk features for recurrence. Eligible pts were randomly assigned 1:1 to receive GEMOX*3 cycles, Lenvatinib 8 mg for 9 weeks, and Toripalimab *3 doses followed by resection (neoadjuvant arm [neo arm]) or traditional surgical resection (control arm [ctrl arm]). All pts received adjuvant capecitabine Q3W for 8 cycles after curative resection. The primary endpoint was event-free survival (EFS). Secondary endpoints included OS, major pathologic response (MPR), pathological complete response (pCR), R0 resection rate, ORR according to RECIST v1.1, recurrence-free survival (RFS), and safety. An interim analysis was planned upon 70% of pre-specified events or after surgery in the last patient.

Results

At data cutoff (April 30, 2025), 178 pts underwent randomization (neo arm: n=88; ctrl arm: n=90). At the prespecified interim analysis after a median follow-up of 16.9 months (mo), the neo arm demonstrated significantly longer median EFS than that of the ctrl arm. OS favored the neo arm, though not meeting interim significance threshold (two-sided α=0.0019). During neoadjuvant therapy, all-grade treatment-related adverse events (TRAEs) occurred in 92% of pts (grade ≥3: 26.4%).Table: LBA11

Efficacy summary

	Neo arm (n=88)	Ctrl arm (n=90)
Median EFS, mo	18.0	8.7
	HR 0.48 (95% CI 0.31-0.74; p=0.0006)	
Median OS, mo	NR	31.4
	HR 0.43 (95% CI 0.23-0.79; p=0.0050)	
Median RFS, mo	15.4	9.7
	HR 0.69 (95% CI 0.45-1.06)	
ORR, n (%)	48 (54.5)	-
MPR, n (%)	17 (19.3)	0
pCR, n (%)	4 (4.5)	0
R0 resection rate, n (%)	84 (95.5)	84 (93.3)

Conclusions

For resectable high-risk iCCAs, neoadjuvant GOLP regimen demonstrated statistically significant improvement in EFS compared with traditional resection, with manageable safety.

Clinical trial identification

NCT04669496.

Legal entity responsible for the study

Zhongshan Hospital of Fudan University.

Funding

Clinical Research Plan of SHDC (SHDC-2020CR1003A).

Disclosure

All authors have declared no conflicts of interest.