2023 APPLE
The 13th Asia-Pacific Primary Liver Cancer Expert Meeting
Novel Insights into the Evolution of Liver Cancer Management
July 6-8, 2023 | Grand InterContinental Seoul Parnas, Seoul, Korea

广西医科大学第一附属医院
THE FIRST AFFILIATED HOSPITAL OF GUANGXI MEDICAL UNIVERSITY

A single-center prospective randomized controlled clinical study of the safety and efficacy of cadonilimab versus cadonilimab combined with transhepatic arterial perfusion chemotherapy (HAIC) for neoadjuvant therapy with sequential resection in patients with CNLC Ⅰb/Ⅱa multinodular hepatocellular carcinoma (CAR_Hero)

Yongguang Wei; Zhiming Zeng; Guangzhi Zhu; Zili Lv; Xinping Ye; Hao Su; Chuangye Han; Jilong Wang; Ming Su; Shuiping Yu; Ning Peng; Kun Zhao; Xiwen Liao; Wei Qin; Chengkun Yang; Kaiyin Xiao; Liling Long; Jie Ma; Peng Tao*

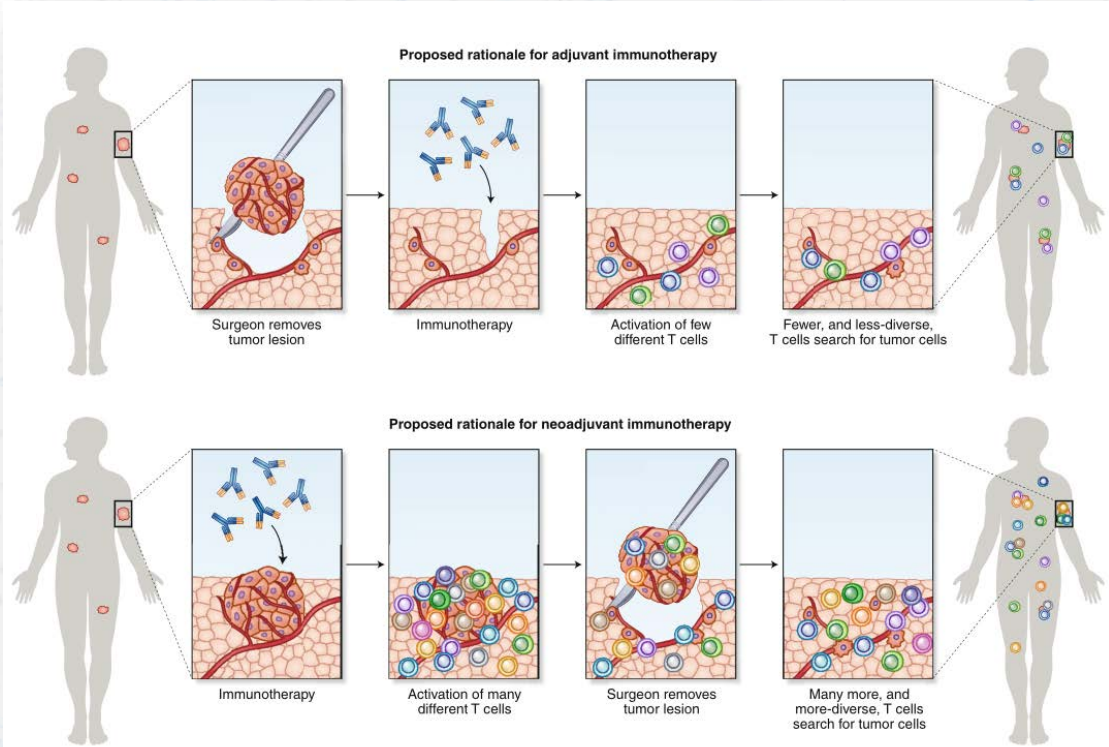
Department of Hepatobiliary Surgery, The First Affiliated Hospital of Guangxi Medical University
Guangxi Key Laboratory of Enhanced Recovery after Surgery for Gastrointestinal Cancer and
Key Laboratory of High-Incidence-Tumor Prevention & Treatment (Guangxi Medical University), Ministry of Education, 530021, Nanning, People's Republic of China

*Contact: Professor Tao Peng; *E-mail*: pengtaogmu@163.com

#97

Background and Aims

- The recurrence rate of hepatocellular carcinoma (HCC) is high after surgery. However, there are no approved standard-of-care neoadjuvant or adjuvant therapies.
- Progress has been made in a number of neoadjuvant therapies for HCC [1].
- Cadonilimab is a first-in-class bispecific, humanized IgG1 anti body targeting PD-1 and CTLA-4, which has potential anti-tumor activity in HCC [2].
- HAIC plus immunotherapy has synergistic antitumor effect [3].



- This trial is to evaluate the safety and efficacy of cadonilimab plus FOLFOX-HAIC as a neoadjuvant management for the resectable multinodular CNLC Ib/IIa HCC.

1. Oh DY, et al. NEJM Evidence. 2022;1(8). doi:10.1056/EVIDoa2200015.
2. Xu Q, et.al. J Clin Oncol. 2022; 40(16). doi: 10.1200/JCO.21.02091.
3. 2021 ASCO abs#e16146
4. Picture source: NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®)

Methods

Resectable multinodular CNLC Ib/IIa HCC

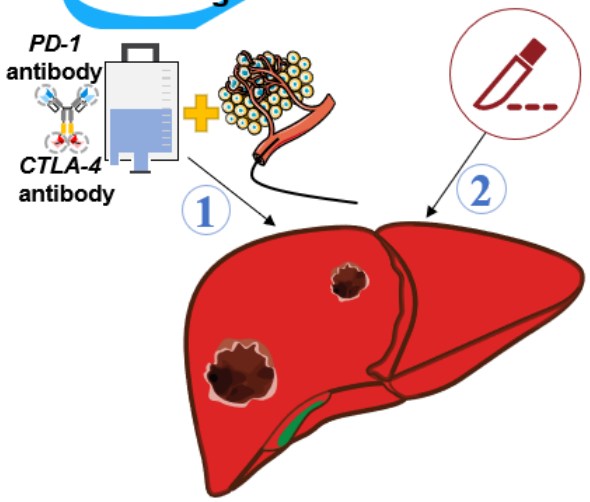
A: 2 cycels Cadonilimab (6mg/kg Q2W)

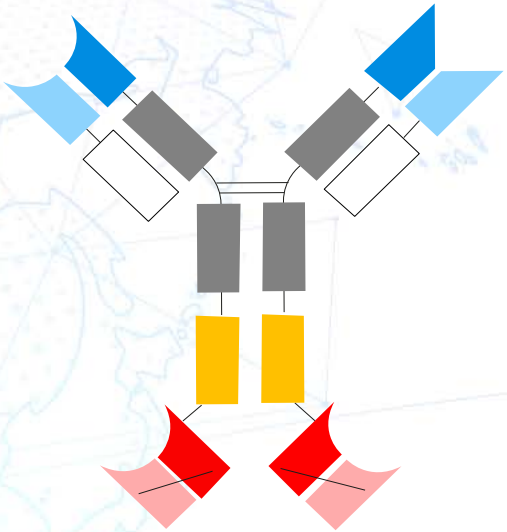
B: Once FOLFOX-HAIC + 2 cycels Cadonilimab

C: Once FOLFOX-HAIC

→ Hepatectomy → Once FOLFOX-HAIC (depend on high-risk recurrence factors) → Follow-up

Screening — 3-4 weeks — 4 weeks





Cadonilimab (AK104)

primary endpoints

- MPR (major pathologic response; ≥ 50% tumor necrosis in resected tissue)
- 1-year RFS (recurrence free survival) rate

secondary endpoints

- ORR (overall response rate, per RECIST 1.1)
- DCR (disease control rate)
- AEs (adverse events)

Key Eligibility Criteria:

① Patients with resectable CNLCIb/IIa multinodular HCC;

② Previously, patients has not received systematic therapy for HCC;

③ Histologically, cytologically or imageo-logically documented HCC;

④ Child-Pugh grade A; PS=0-1.

Phase Results

Table 1. Patients baseline characteristics.

Characteristic (N=12)		No. of patients	%
Age(years)	Median(range)	63(51-71)	/
Gender	Male	16	100
ECOG PS	0	16	100
HBV	infection	13	81.5
Tumor stage	CNLC Ⅰb	6	37.5
	CNLC Ⅱa	10	62.5
BMI	Median(range)	22.5(21.3-24.5)	/
Greatest tumor diameter	≥ 5 cm	5	31.3
PIVKA-II(mAU/ml)	positive	13	81.5
AFP (ng/ml)	positive	12	75
	≥ 400 ng/ml	6	37.5

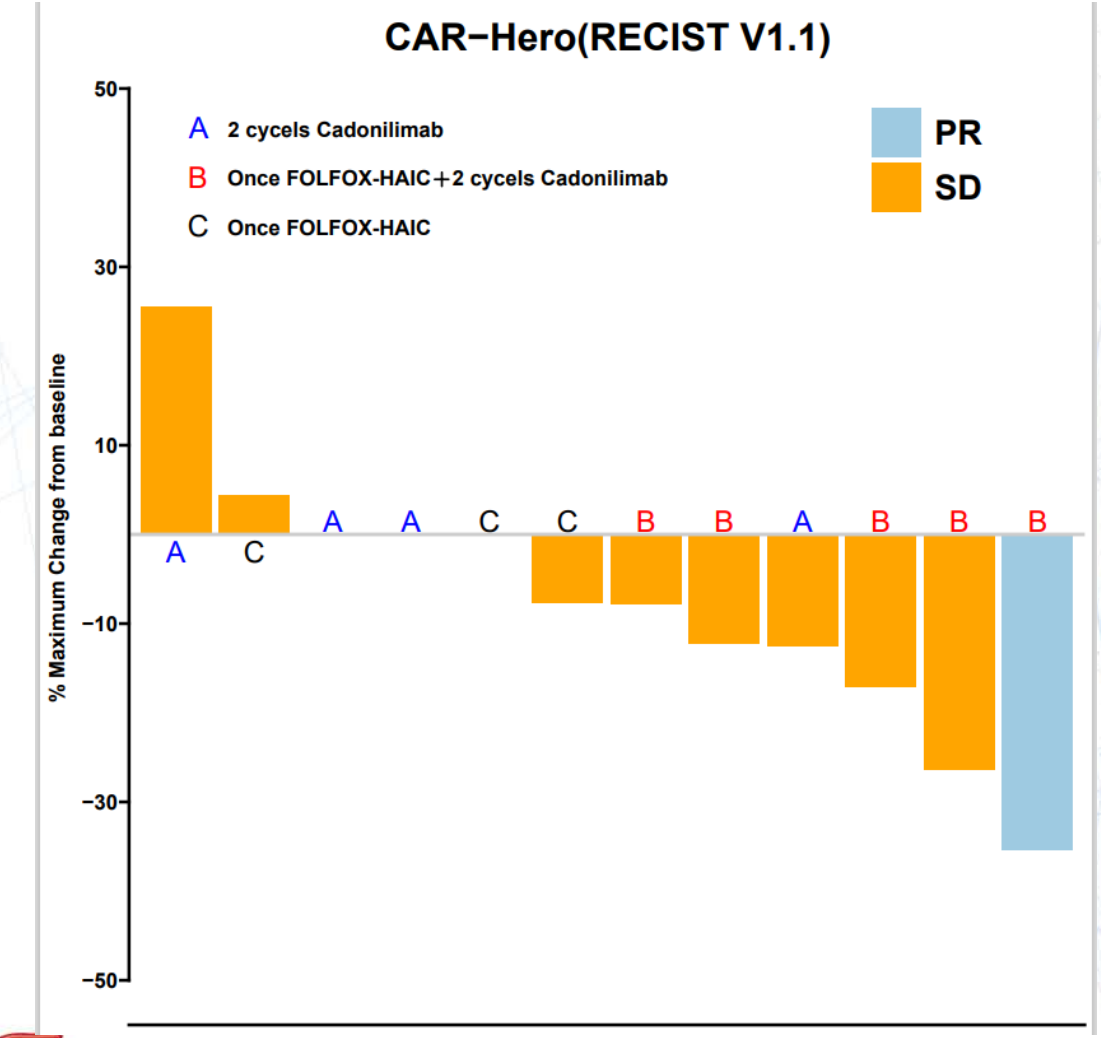
Table 2. The response outcomes of patients.

NO.	Group	RECIST v1.1	Living tissue	tumor necrosis	Fibrosis and inflammatory infiltration area	MVI	Ishak grade
1	A	SD	70%+80%	30%+20%		M0	G1S4
2	B	SD	0%+100%	100%+0%		M0	G2S3
3	A	SD	60%+90%	0%	40%+10%	M0	G1-2S4
4	C	SD	85%+60%	0%	15%+40%	M0+M1	G1S4
5	B	PR+SD	0%+90%	100%+0%	0%+10%	M0	G2S4
6	A	SD	60%+80%	40%+20%		M1+M0	G2S4
7	B	PR+SD	0%+30%	100%+0%	0%+70%	M0	-
8	A	SD	80%+90%	0%	20%+10%	M1+M0	G2S4
9	C	SD	90%	0%	10%	M0	-
10	C	SD	Drop out				
11	B	PR+SD	0%+30%	100%+70%		M1	G1S4
12	B	PR+SD	Possible pCR; AFP and PIVKA-II decreased to normal range				
13-16	B	neoadjuvant therapy phase					

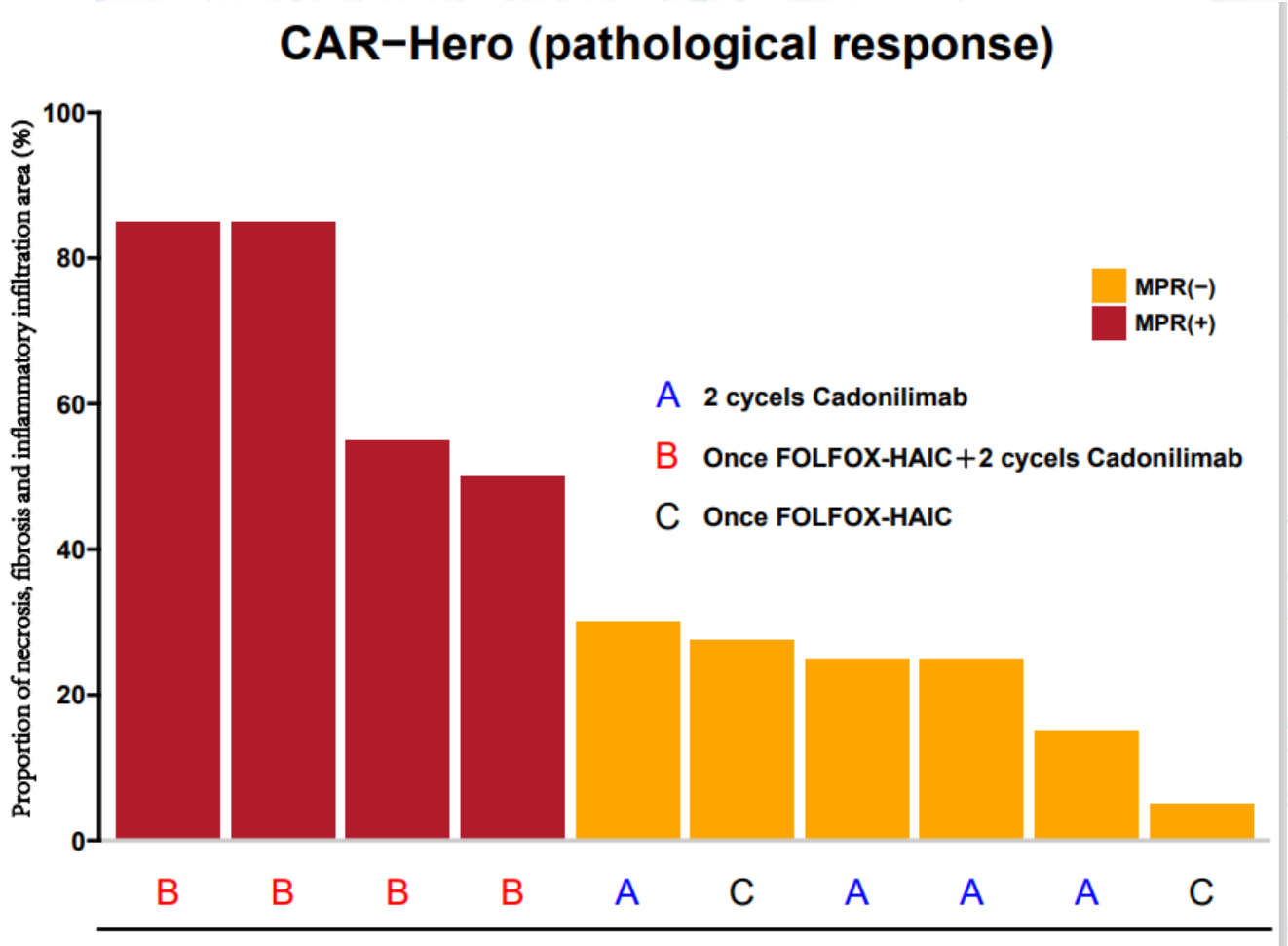
- Imaging evaluation of individual lesions was based on RICIST v1.1 criteria.
- The content before and after "+" indicates the results of different lesions.

Phase Results

Radiographic evaluation



Pathological evaluation



- MPR means significant pathological response: defined as the proportion of residual tumor active cells in the tumor bed ≤ 50%.

Phase Results

Safety evaluation

- The main common Treatment Related Adverse Events (TRAEs) in the neoadjuvant phase were list in Table 3. No grade 3 or worse TEAEs occurred and delayed surgery.
- No additional postoperative complications were significantly associated with preoperative neoadjuvant therapy.
- The most common surgical complications were ALT and AST increase (100%), bilirubin increase (60%), serum amylase increase (40%) and significant pleural effusion (20%).

Table 3. TRAEs in the preoperative phase.

group	TRAE (grade)	n (%)
A (n=4)	Bilirubin increase (1)	1 (33.4)
	Triiodothyronine decrease (1)	1 (33.4)
B (n=9)	ALT, AST increase (1-2)	7 (77.8)
	Bilirubin increase (1)	4 (23.1)
	asthenia (1)	3 (44.5)
	proteinuria (2)	1 (11.1) [b]
C (n=3)	ALT, AST increase (1)	2 (66.7)
	Bilirubin increase (1)	1 (33.4)

[b] This patient has type 2 diabetes mellitus and his blood glucose control is mediocre.

Phase Conclusions

This study preliminarily demonstrated that neoadjuvant cadonilimab plus HAIC show promising antitumor activity with manageable safety for HCC. This trail is ongoing.

Acknowledgement and Disclosure

The authors thank all of the participating pts and their families, as well as the investigators, study coordinators and the whole project team. The authors acknowledge to Akeso Biopharma Ltd. for their drugs supports. Conflict of interest: None.