

## Options and survival benefits of conversion therapy for unresectable hepatocellular carcinoma

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### Abstract

In the study by Wu *et al*, patients with unresectable hepatocellular carcinoma were subjected to transarterial chemoembolization (TACE) as a conversion therapy in order to render their tumors suitable for resection. A nomogram was devised and shown to be effective in predicting the survival of these patients. Generalization of the results, however, is questionable since the study subjects consisted of patients who had resection after TACE while excluding patients with the same disease but not suitable for TACE. Immunotherapy can be considered to be an option for conversion therapy. However, markers for determining responses to a conversion therapy and for guiding the decision between TACE and sequential immunotherapy have been lacking. The question of whether effective conversion therapy can truly enhance overall survival remains unanswered.

**Key Words:** Conversion therapy; Immunotherapy; Liver resection; Survival; Transarterial chemoembolization; Unresectable hepatocellular carcinoma

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**Core Tip:** In addition to transarterial chemoembolization (TACE), immunotherapy should also be among the options for conversion therapy for rendering unresectable hepatocellular carcinoma suitable for resection. For patients unsuitable for TACE, immunotherapy can be an alternative.

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## TO THE EDITOR

We read with interest the article “Inflammation-related nomogram for predicting survival of patients with unresectable hepatocellular carcinoma received conversion therapy” by Wu *et al*[1]. Some points in the article are noteworthy, and the authors are to be complimented for their insightful reporting.

The authors reported the results of a nomogram for predicting the survival of patients with unresectable hepatocellular carcinoma (HCC) who had received transarterial chemoembolization (TACE) as a conversion therapy before liver resection. The results were promising as they would help predict survival after liver resection following a successful conversion therapy. However, a few points are to be noted. The selected group for analysis consisted of patients who had undergone liver resection. As previously reported in the literature, only 9.5% to 28.8% of patients receiving TACE were able to undergo conversion therapy[2,3]. Therefore, it remains questionable whether the survival data of this group of patients can also represent the survival of patients with the same disease who intend to receive conversion therapy but are unable to do so.

The Up-to-seven criteria have been proposed as a predictor for tumor response to TACE as a conversion therapy[4]. TACE is considered effective in patients with a low tumor burden, but it is considered ineffective in those with a high tumor burden. Therefore, for patients with a high tumor burden, alternative conversion therapies may be considered instead of TACE.

Recently, several treatments for unresectable HCC have shown promising results, including those in the HIMALAYA [5] and Imbrave150 trials[6]. Immunotherapy-such as that featuring anti-programmed death ligand 1 antibody (atezolizumab) or that featuring anti-vascular endothelial growth factor antibody (bevacizumab)-is in emerging use. It should be considered to be a treatment option in conversion therapy, particularly as an alternative for patients who are not suitable for TACE[7,8].

Lastly, the selection of patients is worth mentioning. Unfortunately, markers for determining responses to a conversion therapy and for guiding the decision between TACE and sequential immunotherapy have been lacking. The question of whether effective conversion therapy can truly enhance overall survival remains unanswered, particularly when considering the efficacy of emerging types of agents in treating selected patients. In this study, conversion therapy allowed for resection of HCC and consequently achieved better survival outcomes compared to conventional palliative treatment for initially unresectable HCC. Data from studies like this are crucial for refining guidelines and guiding further research to identify parameters for predicting survival.

## FOOTNOTES

**Author contributions:** She WH performed the research and wrote the manuscript; Cheung TT provided supervision. All authors have read and approved the final manuscript.

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## REFERENCES

- 1 Wu JL, Luo JY, Jiang ZB, Huang SB, Chen GR, Ran HY, Liang QY, Huang MS, Lai LS, Chen JW. Inflammation-related nomogram for predicting survival of patients with unresectable hepatocellular carcinoma received conversion therapy. *World J Gastroenterol* 2023; **29**: 3168-3184 [PMID: 37346152 DOI: 10.3748/wjg.v29.i20.3168]
- 2 Kim Y, Stahl CC, Makramalla A, Olowokure OO, Ristagno RL, Dhar VK, Schoech MR, Chadalavada S, Latif T, Kharofa J, Bari K, Shah SA. Downstaging therapy followed by liver transplantation for hepatocellular carcinoma beyond Milan criteria. *Surgery* 2017; **162**: 1250-1258 [PMID: 29033224 DOI: 10.1016/j.surg.2017.08.007]
- 3 Li B, Qiu J, Zheng Y, Shi Y, Zou R, He W, Yuan Y, Zhang Y, Wang C, Qiu Z, Li K, Zhong C. Conversion to Resectability Using Transarterial Chemoembolization Combined With Hepatic Arterial Infusion Chemotherapy for Initially Unresectable Hepatocellular Carcinoma. *Ann Surg Open* 2021; **2**: e057 [PMID: 37636551 DOI: 10.1097/AS9.000000000000057]
- 4 Yasui Y, Tsuchiya K, Kurosaki M, Takeguchi T, Takeguchi Y, Okada M, Wang W, Kubota Y, Goto T, Komiyama Y, Higuchi M, Takaura K, Hayashi T, Takada H, Tamaki N, Nakanishi H, Itakura J, Takahashi Y, Asahina Y, Enomoto N, Himeno Y, Izumi N. Up-to-seven criteria as a useful predictor for tumor downstaging to within Milan criteria and Child-Pugh grade deterioration after initial conventional transarterial

- chemoembolization. *Hepatol Res* 2018; **48**: 442-450 [PMID: 29278654 DOI: 10.1111/hepr.13048]
- 5 **Kelley RK**, Sangro B, Harris W, Ikeda M, Okusaka T, Kang YK, Qin S, Tai DW, Lim HY, Yau T, Yong WP, Cheng AL, Gasbarrini A, Damian S, Bruix J, Borad M, Bendell J, Kim TY, Standifer N, He P, Makowsky M, Negro A, Kudo M, Abou-Alfa GK. Safety, Efficacy, and Pharmacodynamics of Tremelimumab Plus Durvalumab for Patients With Unresectable Hepatocellular Carcinoma: Randomized Expansion of a Phase I/II Study. *J Clin Oncol* 2021; **39**: 2991-3001 [PMID: 34292792 DOI: 10.1200/JCO.20.03555]
  - 6 **Finn RS**, Qin S, Ikeda M, Galle PR, Ducreux M, Kim TY, Kudo M, Breder V, Merle P, Kaseb AO, Li D, Verret W, Xu DZ, Hernandez S, Liu J, Huang C, Mulla S, Wang Y, Lim HY, Zhu AX, Cheng AL; IMbrave150 Investigators. Atezolizumab plus Bevacizumab in Unresectable Hepatocellular Carcinoma. *N Engl J Med* 2020; **382**: 1894-1905 [PMID: 32402160 DOI: 10.1056/NEJMoa1915745]
  - 7 **Kudo M**, Han KH, Ye SL, Zhou J, Huang YH, Lin SM, Wang CK, Ikeda M, Chan SL, Choo SP, Miyayama S, Cheng AL. A Changing Paradigm for the Treatment of Intermediate-Stage Hepatocellular Carcinoma: Asia-Pacific Primary Liver Cancer Expert Consensus Statements. *Liver Cancer* 2020; **9**: 245-260 [PMID: 32647629 DOI: 10.1159/000507370]
  - 8 **Kudo M**, Kawamura Y, Hasegawa K, Tateishi R, Kariyama K, Shiina S, Toyoda H, Imai Y, Hiraoka A, Ikeda M, Izumi N, Moriguchi M, Ogasawara S, Minami Y, Ueshima K, Murakami T, Miyayama S, Nakashima O, Yano H, Sakamoto M, Hatano E, Shimada M, Kokudo N, Mochida S, Takehara T. Management of Hepatocellular Carcinoma in Japan: JSH Consensus Statements and Recommendations 2021 Update. *Liver Cancer* 2021; **10**: 181-223 [PMID: 34239808 DOI: 10.1159/000514174]



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