ISSN 1948-5204 (online)

World Journal of *Gastrointestinal Oncology*

World J Gastrointest Oncol 2024 December 15; 16(12): 4532-4781

Published by Baishideng Publishing Group Inc

World Journal of Gastrointestinal Oncology

Contents

Monthly Volume 16 Number 12 December 15, 2024

EDITORIAL

REVIEW

ORIGINAL ARTICLE

Case Control Study

Retrospective Cohort Study

World Journal of Gastrointestinal Oncology

Monthly Volume 16 Number 12 December 15, 2024

Contents

World Journal of Gastrointestinal Oncology

Monthly Volume 16 Number 12 December 15, 2024

Contents

LETTER TO THE EDITOR

World Journal of Gastrointestinal Oncology

Monthly Volume 16 Number 12 December 15, 2024

Contents

ABOUT COVER

AIMS AND SCOPE

The primary aim of *World Journal of Gastrointestinal Oncology* (*WJGO*, *World J Gastrointest Oncol*) is to provide scholars and readers from various fields of gastrointestinal oncology with a platform to publish high-quality basic and clinical research articles and communicate their research findings online.

WJGO mainly publishes articles reporting research results and findings obtained in the field of gastrointestinal oncology and covering a wide range of topics including liver cell adenoma, gastric neoplasms, appendiceal neoplasms, biliary tract neoplasms, hepatocellular carcinoma, pancreatic carcinoma, cecal neoplasms, colonic neoplasms, colorectal neoplasms, duodenal neoplasms, esophageal neoplasms, gallbladder neoplasms, *etc*.

INDEXING/ABSTRACTING

The *WJGO* is now abstracted and indexed in PubMed, PubMed Central, Science Citation Index Expanded (SCIE, also known as SciSearch®), Journal Citation Reports/Science Edition, Scopus, Reference Citation Analysis, China Science and Technology Journal Database, and Superstar Journals Database. The 2024 edition of Journal Citation Reports® cites the 2023 journal impact factor (JIF) for *WJGO* as 2.5; JIF without journal self cites: 2.5; 5-year JIF: 2.8; JIF Rank: 72/143 in gastroenterology and hepatology; JIF Quartile: Q3; and 5-year JIF Quartile: Q2. The *WJGO*'s CiteScore for 2023 is 4.2 and Scopus CiteScore rank 2023: Gastroenterology is 80/167; Oncology is 196/404.

RESPONSIBLE EDITORS FOR THIS ISSUE

Production Editor: *Si Zhao*; **Production Department Director:** *Xiang Li*; **Cover Editor:** *Jia-Ru Fan*.

NAME OF JOURNAL
World Journal of Gastrointestinal Oncology

ISSN
ISSN 1948-5204 (online)

LAUNCH DATE
February 15, 2009

FREQUENCY
Monthly

EDITORS-IN-CHIEF
Monjur Ahmed, Florin Burada

EDITORIAL BOARD MEMBERS
https://www.wjgnet.com/1948-5204/editorialboard.htm

PUBLICATION DATE
December 15, 2024

INSTRUCTIONS TO AUTHORS
https://www.wjgnet.com/bpg/gerinfo/204

GUIDELINES FOR ETHICS DOCUMENTS
https://www.wjgnet.com/bpg/GerInfo/287

GUIDELINES FOR NON-NATIVE SPEAKERS OF ENGLISH
https://www.wjgnet.com/bpg/gerinfo/240

PUBLICATION ETHICS
https://www.wjgnet.com/bpg/GerInfo/288

PUBLICATION MISCONDUCT
https://www.wjgnet.com/bpg/gerinfo/208

ARTICLE PROCESSING CHARGE
https://www.wjgnet.com/bpg/gerinfo/242

STEPS FOR SUBMITTING MANUSCRIPTS
https://www.wjgnet.com/bpg/GerInfo/239

ONLINE SUBMISSION
https://www.f6publishing.com

World Journal of Gastrointestinal Oncology

Submit a Manuscript: https://www.f6publishing.com

World J Gastrointest Oncol 2024 December 15; 16(12): 4757-4761

DOI: 10.4251/wjgo.v16.i12.4757

ISSN 1948-5204 (online)

LETTER TO THE EDITOR

Advancing hepatocellular carcinoma treatment with hepatic arterial infusion chemotherapy

Eda Caliskan Yildirim, Yakup Ergun

Specialty type: Oncology

Provenance and peer review: Invited article; Externally peer reviewed.

Peer-review model: Single blind

Peer-review report's classification

Scientific Quality: Grade B, Grade C

Novelty: Grade A, Grade C

Creativity or Innovation: Grade B, Grade C

Scientific Significance: Grade A, Grade C

P-Reviewer: Amante MF; Hashim Z

Received: July 19, 2024

Revised: October 9, 2024

Accepted: October 18, 2024

Published online: December 15, 2024

Processing time: 115 Days and 23.6 Hours

Eda Caliskan Yildirim, Department of Medical Oncology, Sincan Training and Research Hospital, Ankara 06100, Türkiye

Yakup Ergun, Department of Medical Oncology, Bower Hospital, Diyarbakır 21100, Türkiye

Corresponding author: Yakup Ergun, MD, Associate Professor, Department of Medical Oncology, Bower Hospital, Yenisehir, Elazıg Street, Diyarbakır 21100, Türkiye. dr.yakupergun@gmail.com

Abstract

Hepatocellular carcinoma (HCC) remains a major challenge in oncology, being a leading cause of cancer-related mortality worldwide. Early-stage HCC is typically treated with surgical resection, transplantation, or ablation, while advanced-stage HCC relies on systemic therapies like sorafenib and newer combinations such as atezolizumab-bevacizumab. Despite these advancements, there is still a need for effective treatments for unresectable HCC, especially in cases with macroscopic vascular invasion. Hepatic arterial infusion chemotherapy (HAIC) has demonstrated promising outcomes in Asia for the treatment of unresectable HCC, yet its application in Western countries has been relatively limited. This letter reviews the recent meta-analysis by Zhou *et al* published in the *World Journal of Gastrointestinal Oncology*, which demonstrates the efficacy and safety of HAIC *vs* sorafenib. The analysis includes 9 randomized controlled trials and 35 cohort studies, highlighting significant improvements in overall survival, progression-free survival, and objective response rates with HAIC and its combinations. The editorial explores the reasons behind the limited use of HAIC in Western countries. It underscores the potential of HAIC to enhance treatment outcomes for advanced HCC and calls for more research and broader adoption of HAIC in clinical practice globally.

Key Words: Hepatocellular carcinoma; Hepatic arterial infusion chemotherapy; Tyrosine kinase inhibitors; Immunotherapy; Survival

Core Tip: Hepatic arterial infusion chemotherapy (HAIC) is shown to be a highly effective and safer treatment for advanced hepatocellular carcinoma. Despite its success in Asia, HAIC is underutilized in western countries. Further research and clinical trials in diverse populations are essential to validate HAIC's benefits and integrate it into global oncology practices.

Citation: Caliskan Yildirim E, Ergun Y. Advancing hepatocellular carcinoma treatment with hepatic arterial infusion chemotherapy. *World J Gastrointest Oncol* 2024; 16(12): 4757-4761
URL: https://www.wjgnet.com/1948-5204/full/v16/i12/4757.htm
DOI: https://dx.doi.org/10.4251/wjgo.v16.i12.4757

TO THE EDITOR

Hepatocellular carcinoma (HCC) remains a formidable challenge in oncology, representing the sixth most commonly diagnosed cancer and the fourth leading cause of cancer-related mortality globally[1]. In the early stages, curative approaches such as surgical resection, transplantation, and ablation are treatment options depending on the patient's status. For intermediate-stage HCC, locoregional treatment approaches like transarterial chemoembolization (TACE) or transarterial radioembolization (TARE) are prioritized. In advanced-stage HCC, systemic therapies are the first choice of treatment, as recommended by international guidelines[2]. Recently, there have been significant advancements in the treatment of unresectable HCC. The evolution of systemic therapy that began with sorafenib has led to a considerable improvement in HCC survival outcomes with the introduction of combination regimens such as atezolizumab-bevacizumab, and durvalumab-tremelimumab. However, there remains an unmet need to optimize treatment for unresectable HCC with macroscopic vascular invasion.

Hepatic arterial infusion chemotherapy (HAIC) has recently emerged as a prominent treatment method for unresectable HCC, particularly in Asia. Although it has not yet been included in European and American guidelines, it is recognized in Japanese guideline as a treatment option for HCC with portal vein thrombosis that is unsuitable for other local treatments[3]. HAIC delivers chemotherapeutic agents directly into the hepatic artery, which supplies blood to the liver and, more importantly, to the HCC tumors. Since HCC tumors derive their blood supply predominantly from the hepatic artery (as opposed to the portal vein, which supplies most of the normal liver), HAIC ensures that a high concentration of the drug reaches the tumor with minimal exposure to the rest of the liver and systemic circulation. This method enhances the effectiveness of the chemotherapy while reducing systemic side effects[4].

This letter aims to provide a critical and comprehensive overview of the recent meta-analysis by Zhou *et al*[5] on the efficacy of HAIC for advanced HCC. The editorial seeks to highlight the significant findings of the study, discuss the potential benefits and drawbacks of HAIC, and explore the reasons behind its limited adoption in western countries despite its demonstrated success in Asia.

HAIC AND COMBINATION THERAPY STRATEGIES

HAIC can be administered as monotherapy or in combination with other treatment modalities. While it is most commonly combined with systemic therapies, there are also examples in the literature where it is used in combination with other locoregional therapies. Among combination therapies, studies evaluating concomitant use with sorafenib are predominant.

There are five randomized controlled trials (RCT) comparing the outcomes of sorafenib with sorafenib + HAIC combination therapy. Among these, only two are phase 3 RCT, and their results are inconsistent. Kudo *et al*[6] conducted a study across 31 centers in Japan, in which adding HAIC to sorafenib treatment showed an effect on progression-free survival (PFS) and objective response rate (ORR) but not on medical overall survival (mOS) [mOS: 11.8 months *vs* 11.5 months; hazard ratio (HR) = 1.009; $P = 0.9$][6]. Conversely, He *et al*[7] carried out a study in five centers from China, and adding HAIC to sorafenib treatment significantly increased mOS (mOS: 13.3 months *vs* 7.1 months; HR = 0.35; $P < 0.001$). This study also found statistically significant improvements in ORR and medical PFS (mPFS) with the HAIC + sorafenib combination[7]. The discrepancies between these two studies could be attributed to differences in HCC etiology and the chemotherapy regimens used in HAIC. The Japanese study included approximately 50% of patients with hepatitis C virus (HCV)-related HCC and 20% with hepatitis B virus (HBV)-related HCC, while the Chinese study had 80% of patients with HBV-related HCC. Pooled analyses of two phase 3 studies evaluating the efficacy of sorafenib indicate that sorafenib is more effective in HCV-related HCC[8]. Additionally, the chemotherapy protocols utilized in HAIC exhibited notable differences. The Japanese study employed a low-dose 5-fluorouracil (5-FU)-cisplatin[6], whereas the Chinese study utilized the FOLFOX regimen[7].

HAIC is being utilized in numerous medical centers employing a multitude of chemotherapy regimens, including low-dose cisplatin, low-dose cisplatin-5-FU, high-dose cisplatin-5-FU, and 5-FU-oxaliplatin(FOLFOX)[9]. Cisplatin-based chemotherapy regimens are frequently utilized in HAIC treatments. In a phase 2 study by Ikeda *et al*[10], patients with advanced-stage HCC were treated with either sorafenib monotherapy or a combination of sorafenib and HAIC with cisplatin. The combination therapy achieved an overall response rate of approximately 20%[10]. The primary advantage of cisplatin monotherapy is the absence of a need for catheter placement. Due to the synergistic antitumoral effects of

cisplatin and 5-FU, they have been tested together in HAIC applications across different dose combinations. Although the use of low-dose cisplatin with 5-FU (FP) is quite heterogeneous, the weekly cisplatin dose is generally 10-20 mg/m², and the 5-FU dose is 200-300 mg/m² for five days each week[9]. In a retrospective study, Nouso *et al*[11] compared HCC patients treated with low-dose FP to those monitored with best supportive care and reported significantly longer survival in the group receiving low-dose FP with HAIC (mOS: 14 months *vs* 5.2 months; $P < 0.0001$)[11]. In one of the few phase 3 trials in this field, Kudo *et al*[6] also used low-dose FP in their study of HAIC + sorafenib. Although no survival difference was demonstrated in the overall population, the subgroup with portal trunk invasion showed better survival compared to sorafenib alone (mOS: 11.7 months *vs* 6.5 months)[6]. Additionally, the Korean Liver Cancer Study Group compared low-dose FP with high-dose FP, finding better ORR rates with the high-dose regimen (16.7% *vs* 0%). The high-dose FP regimen consisted of 60 mg/m² cisplatin and 500 mg/m² 5-FU administered on days 1-3 every four weeks, approximately two to three times the dose used in the low-dose FP regimen[12].

All HAIC studies conducted with the FOLFOX regimen have met their primary endpoints[7,13,14]. In phase 3 randomized trial conducted in patients with intermediate-stage HCC, FOLFOX HAIC was compared with TACE, and it demonstrated superiority in both OS (mOS: 23.1 months *vs* 16.1 months; HR = 0.58; $P < 0.001$) and PFS (mPFS: 9.6 months *vs* 5.4 months; HR = 0.57; $P < 0.001$)[13]. ORRs as high as 50% have been achieved with FOLFOX-HAIC[13,14]. Despite the absence of direct comparisons between different chemotherapy regimens utilized in HAIC, the FOLFOX regimen has exhibited the most favorable outcomes so far, thereby becoming the most widely adopted regimen in clinical practice in Asia.

One of the major drawbacks of HAIC is the lack of a well-established, standardized protocol for its application. Additionally, the need for catheter placement introduces risks of catheter-related infections and thrombosis. The overall frequency of catheter-related complications is reported to be between 5% and 15%[9]. On the other hand, side effects associated with cytotoxic chemotherapy are also observed. The most common adverse events include bone marrow suppression, hypoalbuminemia, anorexia, hyperbilirubinemia, and elevated transaminase levels[15].

A meta-analysis comparing HAIC + sorafenib combination therapy with sorafenib alone in advanced HCC (including five RCTs and two observational studies) found that the combination therapy was associated with significantly better OS (HR = 0.56; $P < 0.01$), PFS (HR = 0.44; $P < 0.01$), and ORR (RR = 3.77; $P < 0.01$). However, grade 3/4 adverse events were more common in the combination arm[16]. Subgroup analysis showed that oxaliplatin-based HAIC resulted in better OS, PFS, and ORR compared to cisplatin-based HAIC, potentially due to oxaliplatin's ability to induce immunogenic tumor cell death[17] and/or achieve higher concentrations in the tumor and its microenvironment[18].

The success of sorafenib + HAIC combination therapy may be attributed to sorafenib breaking the resistance to chemotherapeutic agents and creating a synergistic anticancer effect with HAIC[19]. Sorafenib may also enhance vascular permeability, increasing the concentration of locally administered chemotherapeutic agents[20]. In addition, HAIC administered prior to sorafenib treatment may reduce tumor burden, thereby increasing the efficacy of the drug[8].

In Zhou *et al*'s meta-analysis[5], the effectiveness of HAIC and its combination strategies in advanced HCC was investigated. This meta-analysis included studies on HAIC alone or in combination with other treatment strategies in unresectable HCC [according to the Barcelona Liver Clinic Cancer (BCLC) staging system, BCLC-B and BCLC-C] patients. A total of 9 RCTs and 35 cohort studies were included, comparing HAIC and combination therapies with Sorafenib in terms of OS, PFS, ORR (complete response and partial response), and adverse events. This meta-analysis encompassed a significantly larger number of studies compared to previous meta-analyses. While most included studies investigated HAIC + sorafenib combination therapy, the meta-analysis also evaluated combinations like HAIC + TACE and HAIC + ablation + lenvatinib. According to the meta-analysis, HAIC was deemed a better treatment option than TACE and sorafenib in terms of both efficacy and safety. Although combining HAIC with different treatment modalities appeared more effective than monotherapy, the improvement was marginal. Network meta-analysis of OS and PFS results indicated that HAIC with lenvatinib + ablation and HAIC + ablation combinations were associated with the best OS (HR = 0.12) and PFS (HR = 0.25) outcomes.

According to American and European guidelines, atezolizumab-bevacizumab or durvalumab-tremelimumab combinations are the standard first-line treatment for unresectable RCC. However, Eastern guidelines also include locoregional therapy in addition to systemic therapy. The addition of locoregional therapy to standard treatment for unresectable HCC remains an area of important research. A retrospective small-scale study in China evaluating the addition of HAIC to atezo-beva systemic therapy in advanced HCC reported impressive results with an ORR of 67% and mPFS of 10.3 months. Due to the short follow-up period, mOS was not reached[21]. In another study included in Zhou *et al*'s meta-analysis, the combination of HAIC and an anti-PD-1 inhibitor was compared to HAIC alone without specifying a particular anti-PD-1 inhibitor (90% of patients received toripolimab and sintilimab)[5]. The combination resulted in mOS of 18 months, compared to 14 months with HAIC monotherapy ($P = 0.018$; HR = 0.62). Disease control was also better with the combination (83% *vs* 66%; $P = 0.006$; HR = 0.62)[22]. A retrospective study by He *et al*[23] comparing the HAIC + toripalimab + lenvatinib triplet regimen with lenvatinib monotherapy found that the triplet regimen had superior OS (17.1 months *vs* 10.1 months; HR = 0.50; $P = 0.005$) and ORR (47.2% *vs* 9.2%; $P < 0.001$)[23].

All studies on HAIC are predominantly from East Asia, primarily China. Despite the promising outcomes observed in HAIC studies, the divergence in HCC projections between the East and West fuels skepticism toward HAIC in the western medical community. The etiology of HCC in the eastern population is largely attributed to HBV, with patients frequently diagnosed at advanced stages. In contrast, the west is characterized by a higher prevalence of alcohol- and HCV-related HCC, with patients typically diagnosed at earlier stages. The number of patients in western countries who are not able to undergo locoregional treatments such as TACE and TARE is quite limited.

CONCLUSION

HAIC holds significant potential for improving outcomes in advanced HCC. Continued research and efforts to overcome existing barriers will ensure that patients worldwide can benefit from this advanced treatment option. To facilitate broader adoption of HAIC, more large-scale clinical trials in diverse populations are necessary. These studies should aim to validate the benefits of HAIC and explore optimal combination strategies with other treatments. Additionally, increasing awareness and training in HAIC techniques among Western healthcare providers will be crucial for integrating this promising therapy into global oncology practices.

FOOTNOTES

Author contributions: Caliskan Yildirim E reviewed the literature and wrote the manuscript; Ergun Y contributed to the discussion and design of the manuscript; All authors reviewed, edited, and approved the final manuscript and revised it critically for important intellectual content, gave final approval of the version to be published and agreed to be accountable for all aspects of the work.

Conflict-of-interest statement: The authors declare that they have no conflict of interest.

Country of origin: Türkiye

ORCID number: Yakup Ergun 0000-0003-4784-6743.

S-Editor: Fan M
L-Editor: A
P-Editor: Chen YX

REFERENCES

1 **Sung H**, Ferlay J, Siegel RL, Laversanne M, Soerjomataram I, Jemal A, Bray F. Global Cancer Statistics 2020: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries. *CA Cancer J Clin* 2021; **71**: 209-249 [PMID: 33538338 DOI: 10.3322/caac.21660]

2 **Reig M**, Forner A, Rimola J, Ferrer-Fàbrega J, Burrel M, Garcia-Criado Á, Kelley RK, Galle PR, Mazzaferro V, Salem R, Sangro B, Singal AG, Vogel A, Fuster J, Ayuso C, Bruix J. BCLC strategy for prognosis prediction and treatment recommendation: The 2022 update. *J Hepatol* 2022; **76**: 681-693 [PMID: 34801630 DOI: 10.1016/j.jhep.2021.11.018]

3 **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]

4 **Ueshima K**, Komemushi A, Aramaki T, Iwamoto H, Obi S, Sato Y, Tanaka T, Matsueda K, Moriguchi M, Saito H, Sone M, Yamagami T, Inaba Y, Kudo M, Arai Y. Clinical Practice Guidelines for Hepatic Arterial Infusion Chemotherapy with a Port System Proposed by the Japanese Society of Interventional Radiology and Japanese Society of Implantable Port Assisted Treatment. *Liver Cancer* 2022; **11**: 407-425 [PMID: 36158592 DOI: 10.1159/000524893]

5 **Zhou SA**, Zhou QM, Wu L, Chen ZH, Wu F, Chen ZR, Xu LQ, Gan BL, Jin HS, Shi N. Efficacy of hepatic arterial infusion chemotherapy and its combination strategies for advanced hepatocellular carcinoma: A network meta-analysis. *World J Gastrointest Oncol* 2024; **16**: 3672-3686 [PMID: 39171172 DOI: 10.4251/wjgo.v16.i8.3672]

6 **Kudo M**, Ueshima K, Yokosuka O, Ogasawara S, Obi S, Izumi N, Aikata H, Nagano H, Hatano E, Sasaki Y, Hino K, Kumada T, Yamamoto K, Imai Y, Iwadou S, Ogawa C, Okusaka T, Kanai F, Akazawa K, Yoshimura KI, Johnson P, Arai Y; SILIUS study group. Sorafenib plus low-dose cisplatin and fluorouracil hepatic arterial infusion chemotherapy versus sorafenib alone in patients with advanced hepatocellular carcinoma (SILIUS): a randomised, open label, phase 3 trial. *Lancet Gastroenterol Hepatol* 2018; **3**: 424-432 [PMID: 29631810 DOI: 10.1016/S2468-1253(18)30078-5]

7 **He M**, Li Q, Zou R, Shen J, Fang W, Tan G, Zhou Y, Wu X, Xu L, Wei W, Le Y, Zhou Z, Zhao M, Guo Y, Guo R, Chen M, Shi M. Sorafenib Plus Hepatic Arterial Infusion of Oxaliplatin, Fluorouracil, and Leucovorin vs Sorafenib Alone for Hepatocellular Carcinoma With Portal Vein Invasion: A Randomized Clinical Trial. *JAMA Oncol* 2019; **5**: 953-960 [PMID: 31070690 DOI: 10.1001/jamaoncol.2019.0250]

8 **Bruix J**, Cheng AL, Meinhardt G, Nakajima K, De Sanctis Y, Llovet J. Prognostic factors and predictors of sorafenib benefit in patients with hepatocellular carcinoma: Analysis of two phase III studies. *J Hepatol* 2017; **67**: 999-1008 [PMID: 28687477 DOI: 10.1016/j.jhep.2017.06.026]

9 **Iwamoto H**, Shimose S, Shirono T, Niizeki T, Kawaguchi T. Hepatic arterial infusion chemotherapy for advanced hepatocellular carcinoma in the era of chemo-diversity. *Clin Mol Hepatol* 2023; **29**: 593-604 [PMID: 36775834 DOI: 10.3350/cmh.2022.0391]

10 **Ikeda M**, Shimizu S, Sato T, Morimoto M, Kojima Y, Inaba Y, Hagihara A, Kudo M, Nakamori S, Kaneko S, Sugimoto R, Tahara T, Ohmura T, Yasui K, Sato K, Ishii H, Furuse J, Okusaka T. Sorafenib plus hepatic arterial infusion chemotherapy with cisplatin versus sorafenib for advanced hepatocellular carcinoma: randomized phase II trial. *Ann Oncol* 2016; **27**: 2090-2096 [PMID: 27573564 DOI:

10.1093/annonc/mdw323]

11 **Nouso K**, Miyahara K, Uchida D, Kuwaki K, Izumi N, Omata M, Ichida T, Kudo M, Ku Y, Kokudo N, Sakamoto M, Nakashima O, Takayama T, Matsui O, Matsuyama Y, Yamamoto K; Liver Cancer Study Group of Japan. Effect of hepatic arterial infusion chemotherapy of 5-fluorouracil and cisplatin for advanced hepatocellular carcinoma in the Nationwide Survey of Primary Liver Cancer in Japan. *Br J Cancer* 2013; **109**: 1904-1907 [PMID: 24008659 DOI: 10.1038/bjc.2013.542]

12 **Woo HY**, Bae SH, Park JY, Han KH, Chun HJ, Choi BG, Im HU, Choi JY, Yoon SK, Cheong JY, Cho SW, Jang BK, Hwang JS, Kim SG, Kim YS, Seo YS, Yim HJ, Um SH; Korean Liver Cancer Study Group. A randomized comparative study of high-dose and low-dose hepatic arterial infusion chemotherapy for intractable, advanced hepatocellular carcinoma. *Cancer Chemother Pharmacol* 2010; **65**: 373-382 [PMID: 19763572 DOI: 10.1007/s00280-009-1126-2]

13 **Li QJ**, He MK, Chen HW, Fang WQ, Zhou YM, Xu L, Wei W, Zhang YJ, Guo Y, Guo RP, Chen MS, Shi M. Hepatic Arterial Infusion of Oxaliplatin, Fluorouracil, and Leucovorin Versus Transarterial Chemoembolization for Large Hepatocellular Carcinoma: A Randomized Phase III Trial. *J Clin Oncol* 2022; **40**: 150-160 [PMID: 34648352 DOI: 10.1200/JCO.21.00608]

14 **Lyu N**, Wang X, Li JB, Lai JF, Chen QF, Li SL, Deng HJ, He M, Mu LW, Zhao M. Arterial Chemotherapy of Oxaliplatin Plus Fluorouracil Versus Sorafenib in Advanced Hepatocellular Carcinoma: A Biomolecular Exploratory, Randomized, Phase III Trial (FOHAIC-1). *J Clin Oncol* 2022; **40**: 468-480 [PMID: 34905388 DOI: 10.1200/JCO.21.01963]

15 **He M**, Liu S, Lai Z, Du Z, Li Q, Xu L, Kan A, Shen J, Shi M. Hepatic arterial infusion chemotherapy for patients with hepatocellular carcinoma: Applicability in Western countries. *Curr Opin Pharmacol* 2023; **70**: 102362 [PMID: 36931163 DOI: 10.1016/j.coph.2023.102362]

16 **Long Y**, Song X, Guan Y, Lan R, Huang Z, Li S, Zhang L. Sorafenib plus hepatic arterial infusion chemotherapy versus sorafenib alone for advanced hepatocellular carcinoma: A systematic review and meta-analysis. *J Gastroenterol Hepatol* 2023; **38**: 486-495 [PMID: 36516040 DOI: 10.1111/jgh.16088]

17 **Tesniere A**, Schlemmer F, Boige V, Kepp O, Martins I, Ghiringhelli F, Aymeric L, Michaud M, Apetoh L, Barault L, Mendiboure J, Pignon JP, Jooste V, van Endert P, Ducreux M, Zitvogel L, Piard F, Kroemer G. Immunogenic death of colon cancer cells treated with oxaliplatin. *Oncogene* 2010; **29**: 482-491 [PMID: 19881547 DOI: 10.1038/onc.2009.356]

18 **Dzodic R**, Gomez-Abuin G, Rougier P, Bonnay M, Ardouin P, Gouyette A, Rixe O, Ducreux M, Munck JN. Pharmacokinetic advantage of intra-arterial hepatic oxaliplatin administration: comparative results with cisplatin using a rabbit VX2 tumor model. *Anticancer Drugs* 2004; **15**: 647-650 [PMID: 15205611 DOI: 10.1097/01.cad.0000131684.06390.fe]

19 **Ma SQ**, Cao BR, Zhang H, Luo LP, Ren Y, Hu T, Chen CM. The lack of Raf-1 kinase feedback regulation enhances antiapoptosis in cancer cells. *Oncogene* 2017; **36**: 2014-2022 [PMID: 27841865 DOI: 10.1038/onc.2016.384]

20 **Lewin M**, Fartoux L, Vignaud A, Arrivé L, Menu Y, Rosmorduc O. The diffusion-weighted imaging perfusion fraction f is a potential marker of sorafenib treatment in advanced hepatocellular carcinoma: a pilot study. *Eur Radiol* 2011; **21**: 281-290 [PMID: 20683597 DOI: 10.1007/s00330-010-1914-4]

21 **Xin Y**, Cao F, Yang H, Zhang X, Chen Y, Cao X, Zhou X, Li X, Zhou J. Efficacy and safety of atezolizumab plus bevacizumab combined with hepatic arterial infusion chemotherapy for advanced hepatocellular carcinoma. *Front Immunol* 2022; **13**: 929141 [PMID: 35990634 DOI: 10.3389/fimmu.2022.929141]

22 **Mei J**, Li SH, Li QJ, Sun XQ, Lu LH, Lin WP, Zheng L, Chen MS, Shi M, Wei W, Guo RP. Anti-PD-1 Immunotherapy Improves the Efficacy of Hepatic Artery Infusion Chemotherapy in Advanced Hepatocellular Carcinoma. *J Hepatocell Carcinoma* 2021; **8**: 167-176 [PMID: 33791252 DOI: 10.2147/JHC.S298538]

23 **He MK**, Liang RB, Zhao Y, Xu YJ, Chen HW, Zhou YM, Lai ZC, Xu L, Wei W, Zhang YJ, Chen MS, Guo RP, Li QJ, Shi M. Lenvatinib, toripalimab, plus hepatic arterial infusion chemotherapy versus lenvatinib alone for advanced hepatocellular carcinoma. *Ther Adv Med Oncol* 2021; **13**: 17588359211002720 [PMID: 33854567 DOI: 10.1177/17588359211002720]

Published by **Baishideng Publishing Group Inc**
7041 Koll Center Parkway, Suite 160, Pleasanton, CA 94566, USA
Telephone: +1-925-3991568
E-mail: office@baishideng.com
Help Desk: https://www.f6publishing.com/helpdesk
https://www.wjgnet.com