



# Survival benefit of TACE combined with sorafenib for hepatocellular carcinoma patients with portal vein tumor thrombus

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*Response to:* Lehman JM, Horn L. Targeted therapy in small cell lung cancer: can DLL3 notch up a victory? *Transl Cancer Res* 2017;6:S453-6.

Submitted Aug 06, 2017. Accepted for publication Sep 04, 2017.

doi: 10.21037/tcr.2017.09.12

**View this article at:** <http://dx.doi.org/10.21037/tcr.2017.09.12>

Hepatocellular carcinoma (HCC) is the most common primary hepatic malignant tumor and the world's fifth most common tumor. Portal vein tumor thrombosis (PVTT) have been appeared about 10–40% for HCC patients (1,2). PVTT predicted a dismal prognosis, because they promoted HCC recurrence and metastasis, impaired hepatic reserves, raised portal vein pressure, and reduced portal vein flow. The median survival time (MST) of HCC and PVTT patients is obviously decreased compared to those without PVTT. According to the invading location in portal vein of the PVTT, the studies from our group proposed “Cheng’s classification” to divided the PVTT into four types (type I, being segmental/sectoral branches of portal vein; type II, being left and/or right portal vein; type III, being main portal vein trunk, and type IV, being superior mesenteric vein) (3,4). According to the guidelines from Barcelona Clinic Liver Cancer (BCLC), HCC with PVTT was classified as advanced HCC (BCLC stage C). They recommended sorafenib as the standard treatments for patients with advanced HCC. However, some studies have shown that some treatment modalities like transarterial chemoembolization (TACE), radiotherapy (RT), transarterial radioembolization (TARE), and resection-based multimodal treatments in some selected HCC and PVTT patients may prefer better outcomes than sorafenib (5-7). Our comments were responded to “editorial

on combination treatment beyond sorafenib alone for HCC with portal vein tumor thrombosis”, and indicated that the new advances treatments were applied for HCC patients with PVTT.

## Combination treatment for HCC with PVTT

In recent years, diverse treatments like TACE, RT, hepatic arterial-infusion chemotherapy (HAIC), hyperthermia (CERT), external beam RT, or a combination of modalities have been used for HCC and PVTT patients. Correspondingly, there are lots of combination treatment strategies like TACE in combined with sorafenib, sorafenib plus RT, TACE with RT, RT and arterial infusion chemotherapy. TACE is generally controversial as it can lead to the liver necrosis and worsen liver function. However, recent technical progress in the form of super-selective TACE and improved advanced HCC patients’ selection based on good liver functional reserve, basic conditions of HCC and PVTT patients, and the presence of collateral circulation following PVTT. What’s more, external beam radiation applied in PVTT due to the sensitivity of the HCC, especially in PVTT. Recently, one meta-analysis evaluated the benefits of TACE combined with sorafenib and demonstrated that the combination treatment achieved a great improvement of OS for PVTT patients (8).

TACE is recommended in some selected HCC patients with PVTT and achieves quality-of-life advantages. Some HCC patients with PVTT under sorafenib alone may benefit from the combination treatment like TACE plus sorafenib, TACE plus RT, and some more aggressive treatment strategies can be carried out in HCC patients with PVTT.

### Individualized and multi-disciplinary treatment for different patients

A Chinese expert consensus on multi-disciplinary treatment for HCC with PVTT (2016 edition) (9) led in Eastern Hepatobiliary Surgical Hospital from our group had published online last year. This is the first expert consensus focused on treating HCC and PVTT patients in the world, and could provide guidance on treatment of these patients. From this article, TACE combined sorafenib may lead to a longer overall survival (OS) for HCC patients with PVTT. In other words, a complete multi-disciplinary liver tumor board include hepatobiliary surgeons, hepatologists, interventional radiologists, pathologist, oncologists, radiologists, and primary care physicians (10). Furthermore, additional consultative services can be obtained based on the individual needs of different patients. A multi-disciplinary liver tumor group needs to employ the ability to determine the most appropriate management of some individualized patients with PVTT. And the group should make prompt diagnosis with the help of different board members and expertise, then provide a platform to promptly and optimally deliver any form of therapy following the diagnosis of HCC. With the platform of a multi-disciplinary liver tumor group, many cases of HCC that have the potential to grow rapidly can be identified and individualized therapy will be offered to the particular patient. Indeed, future research should focus on combinations of different established treatment modalities for PVTT in HCC and the formation of a perfect multi-disciplinary liver tumor board.

### Conclusions

Despite the fact that the standard treatment strategy for HCC patients with PVTT was sorafenib according to BCLC Stage C (11), many studies indicated that the possibility of other treatment modalities like surgical resection, TACE, TARE, radiation therapy including external RT or selective internal radiation therapy (SIRT) of the liver lesions, and systemic agents, and the combination

treatment is a very promising strategy for some selected HCC patients with PVTT. It may improve the management of patients through comprehensive and efficient counsel and offer specific treatment strategy to different PVTT patients. Future research should be geared towards the generation of high-level evidence of the combinations of novel treatments and establish an effective and efficient multidisciplinary liver tumor group.

### Acknowledgments

*Funding:* This work was supported by grants from the National Key Basic Research Program “973 project” (No. 2015CB554000); the Science Fund for Creative Research Groups (No. 81521091); the China National Funds for Distinguished Young Scientists (No. 81125018); the ChangJiang Scholars Program (2013) of the Chinese Ministry of Education; the Shanghai Science and Technology Committee (No. 134119a0200, SHDC12015106); the National Natural Science Foundation of China (No. 8160110271) and the SMMU Innovation Alliance for Liver Cancer Diagnosis and Treatment (2012).

### Footnote

*Provenance and Peer Review:* This article was commissioned by the editorial office, *Translational Cancer Research*. The article did not undergo external peer review.

*Conflicts of Interest:* All authors have completed the ICMJE uniform disclosure form (available at <http://dx.doi.org/10.21037/tcr.2017.09.12>). The authors have no conflicts of interest to declare.

*Ethical Statement:* The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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**Cite this article as:** Luo B, Chen ZH, Zhang XP, Wang M, Cheng SQ. Survival benefit of TACE combined with sorafenib for hepatocellular carcinoma patients with portal vein tumor thrombus. *Transl Cancer Res* 2017;6(Suppl 7):S1293-S1295. doi: 10.21037/tcr.2017.09.12