Prof. Shukui Qin: strategy on liver cancer treatment for Asian population

Submitted Nov 10, 2013. Accepted for publication Nov 21, 2013.
doi: 10.3978/j.issn.2304-3865.2013.11.06
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Prof. Shukui Qin is the deputy director of People's Liberation Army (PLA) 81 Hospital (Nanjing, China), director of Cancer Center of Chinese PLA, and director of National Drug Clinical Trial Agency of PLA 81 Hospital. He serves as the executive member of the Asian Clinical Oncology Society (ACOS), chair of Chinese Society of Clinical Oncology (CSCO), council member of PLA Medical Science Commission (and the executive member of its oncology society), member of the Oncology Branch of Chinese Medical Association.

After decades of clinical practice and scientific research, Prof. Qin has accumulated rich experiences in the medical treatment of gastrointestinal cancers and their bone metastases. Prof. Qin has published over 400 articles in peer-reviewed journals and 44 scientific books. He has been granted numbers of professional awards at the ministerial and provincial levels (including four first-class prizes, two second-class prizes, seven third-class prizes, and two fourth-class prizes). Currently he is the editor-in-chief of two highly rated journals (Journal of Clinical Oncology and Clinical Oncology Tribune) in China (Figure 1).

The 16th Annual Meeting of Chinese Society of Clinical Oncology (CSCO) was held at Xiamen International Conference Center from Sep 25 to 29, 2013. Prof. Shukui Qin shared his professional view on Strategy on liver cancer treatment for Asian population.

Figure 1 Prof. Shukui Qin, MD, PHD.

CCO: What are the major characteristics of Asian hepatocellular carcinoma (HCC) patients, especially Chinese patients?

Prof. Qin: More than 75% of HCC occur in the Asia-Pacific region. When compared with patients in the rest of the world, the prognosis is worse and survival time is shorter in Asian patients, which owes to the heterogeneity of HCC between East and West. And the etiology, the staging, the malignant biological behaviors (clinical manifestations), clinical treatment strategies are quite different between the West and Asia. Even some researchers think HCC is really (actually) two diseases.

For example, chronic infection with hepatitis B virus (HBV) remains the dominant risk factor in China, while the cause of 75% HCC in America, Europe, Japan and Indonesia is hepatitis C infection (HCV). In addition, in Asia area especially in China, other risk factors include water pollution (blue-green algae), excessive alcohol consumption and food pollution (aflatoxins). But HCC usually associated with liver metabolic disease (non-alcoholic steatohepatitis), autoimmune diseases, cryptogenic hepatitis or cryptogenic cirrhosis in America, Europe and Japan, and this trend goes more and more obviously.

More specifically in China, HCC has significantly Chinese characteristics with about 55% of the global new cases of HCC and 45% to 50% deaths in the world occurred in China. HCC has been the second leading cause of death caused by cancer in China. In addition, most (85%) of the patients has been diagnosed with the mid or late-stage HCC according to Barcelona clinic liver cancer staging system (BCLC staging system) when first diagnosed, and 78% of the patients associate with other liver diseases (mainly HBV and liver cirrhosis) in China.

CCO: In your opinion, how to make appropriate treatment strategies based on characteristics of Chinese HCC patients?

Prof. Qin: Just like the treatments for other cancers, it is important to advocate multidisciplinary collaboration and multimodality treatment approaches in the management of HCC. In terms of curative treatment, surgical operation is the preferred option, including hepatectomy and liver transplantation, and we can also perform focal ablation for early stage HCC. As for the palliative treatment, focal ablation and interventional therapy, we have made significant progress in systemic treatment especially in molecular targeted treatment and systemic chemotherapy in recent years. Furthermore, we have also made some beneficial exploration in precise radiotherapy.

The main characteristics of Chinese HCC patients: first diagnosed with the mid or late-stage HCC and most of the patients associate with HBV and liver cirrhosis. Since there are two different diseases (the highly malignant tumor and chronic liver disease) in the same organ in one patient at the same time, they may influence each other and reinforce a vicious cycle.

The specificity and complexity of HCC bring some considerable difficulties to the treatment strategy formulation, so we should emphasize thinking comprehensively and reasonable to beware of attend to one thing and loses another. We believe that medical treatment strategies for HCC should be the combination of antitumor and antiviral treatment as well as the combination of controlling of cancer and protecting liver and gall bladder. Therefore, the management of HCC should cover various treatments including molecular targeted therapy, systemic chemotherapy, biological therapy, antiviral treatment and symptomatic treatment to release the tumor load, improve the patients' symptoms, extend survival time and improve the quality of life.

CCO: You've been emphasized the systemic chemotherapy of HCC, could you please make a detailed analysis?

Prof. Qin: Systemic chemotherapy means the chemotherapy drugs are given by oral administration, intramuscular injection, and intravenous administration and can reach cancer cells throughout the body. Systemic chemotherapy has been used for advanced HCC treatment in the 1950s and then gradually become a common method of palliative care.

In fact, HCC is a kind of systemic disease or local manifestation on the basis of systemic diseases. It cannot be cured with surgery and other local treatments alone and both radical resection and liver transplantation cannot prevent its recurrence. From the previous clinical practice, HCC is not sensitive enough to chemotherapy drugs and its objective response rate (ORR) fluctuated greatly (0-25%) and none of the chemotherapy regimens can make the five-year survival rate of advanced HCC over 5%.

In recent years, many new cytotoxic chemotherapy drugs have come out, and they have significantly better curative effects and are safer compared with traditional drugs. The emergence of such drugs create new space for systemic chemotherapy of HCC, which challenges and questions the traditional view that systemic chemotherapy is not suitable for liver cancer.

On that basis, I organized Phase I, II study of FOLFOX 4 systemic chemotherapy in advanced HCC patients. And the results have been presented. I have conducted a randomized controlled multicenter Phase III clinical trial (EACH study) in patients who had locally advanced or metastatic HCC and were ineligible for complete resection or local treatment and researchers from 38 different cancer centers have involved in this study since 2007. And the results have been published in the *Journal of Clinical Oncology*.

CCO: You mentioned the EACH study just now, so could you talk about details and results of it?

Prof. Qin: This study was designed for Chinese patients that (since) Chinese patients are the overwhelming majority of the participators (75%) and they account for the major part of the observation group in EACH study. In addition, considering the relevant regulations for clinical research in China and the clinical need for HCC from other Asian countries, the study also conducted patients from South Korea and Thailand.

The EACH study was designed to evaluate the efficacy and safety of FOLFOX4 (oxaliplatin plus infusional 5-fluorouracil and folinic acid) *vs.* doxorubicin as palliative systemic chemotherapy in advanced HCC. The primary endpoint was overall survival (OS) and the secondary endpoints included progression-free survival (PFS), response rate (RR) and safety.

Although this study didn't reach the primary endpoint, the trend of OS improvement and the results of PFS and RR improvement with FOLFOX4 demonstrated it may benefit patients with advanced HCC in Asian.

This study confirmed systemic chemotherapy used for

patients with advanced HCC can obtain objective response as well as a significant survival benefit, which prompted treatments based on the containing OXA regimen and would occupy the important position. It could provide useful experience and important basis for the future HCC clinical trials with patients in China and other Asian-Pacific region.

Cite this article as: Zhang S. Prof. Shukui Qin: strategy on liver cancer treatment for Asian population. Chin Clin Oncol 2014;3(1):10. doi: 10.3978/j.issn.2304-3865.2013.11.06

CCO: Thank you very much!

Acknowledgements

Disclosure: The author declares no conflicts of interest.

(Science Editor: Shannon Zhang, CCO, editor@thecco.net)

