Professor Yongqian Shu: advances in the treatment of advanced pancreatic cancer

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For public awareness of the standards for the diagnosis and treatment of pancreatic cancer and up-to-date information, and to improve the level of practice in this field in China, Chinese Anti-Cancer Association held an expert meeting on new advances in the treatment of pancreatic cancer on April 20, 2013 in Shanghai. DXY took the chance to interview Professor Yongqian Shu, director of oncology at Jiangsu Provincial People's Hospital, about the development of treatment for advanced pancreatic cancer.

DXY: Welcome, Professor Shu! Thank you for accepting our interview. Advanced pancreatic cancer is difficult to treat and known as one of the tumors with the lowest survival rates. According to reports, the relative 5-year survival rate is as low as 5.5% in pancreatic cancer patients. The incidence of the condition has also shown an increasing trend in recent years. Current treatment of pancreatic cancer include surgery, adjuvant therapy, palliative and supportive care. Could you please describe the characteristics and status quo of the treatment for advanced pancreatic cancer in China?

Prof. Shu: Thank you. I am very honored to be interviewed today. Consistent with the global trend, the morbidity and mortality rates of pancreatic cancer are increasing in China year by year. Currently, the mortality rates of male and female patients are ranked sixth and seventh in all malignancies, respectively. Anatomically, the pancreas is located posterior to the stomach in the body, making the lesions hard to find before they appear to be somewhat symptomatic at an advanced stage, when the window for surgery is missed.

Globally, only 10-15% patients are detected early enough and operable, while most of the others are not diagnosed until the condition is advanced. So, the situation of treatment for advanced pancreatic cancer is very grim. Even the five-year survival rate is very low after surgery. For those receiving non-surgical care, such as radiotherapy and chemotherapy, survival is about 5.8 months, with a median survival of about 6 months. This is the general picture of the diagnosis and treatment of pancreatic cancer in China.

DXY: At the expert meeting on new advances in the treatment of advanced pancreatic cancer, Professor Ramesh Ramanathan from the University of Arizona College of Medicine presented the current situation of the diagnosis and treatment for this condition in the United States. Could you compare the differences in this respect between China and the United States?

Prof. Shu: China is not making a considerable progress in the treatment of pancreatic cancer. We have been behind our foreign peers in clinical research based on large sample sizes. In the last few weeks, they just announced a protocol called CA046, which was the result of the research presented by Professor Ramanathan and his team from the University of Arizona College of Medicine at the meeting. Their result has rewritten the NCCN guidelines for the treatment of pancreatic cancer.

China has been learning from western countries in terms of the treatment of pancreatic cancer, including the fluorouracil-based chemotherapy before 1996, and then Gemzar (gemcitabine) since 1996 because of its superiority in treating advanced pancreatic cancer in three

large multicenter randomized clinical studies, which was a major update in the treatment guidelines. From 1996 to 2013, we are able to have the opportunity to discuss with the U.S. experts on the results of a large-scale, randomized international multi-center Phase III clinical trial comparing nab-paclitaxel plus gemcitabine with gemcitabine alone in patients with advanced pancreatic cancer. The results have altered the recommendation from monotherapy to nab-paclitaxel combined with gemcitabine for advanced pancreatic cancer in this year's NCCN treatment guidelines. This will undoubtedly change the direction of future treatment for this condition, enabling increased objective response rate and significantly improved median survival, which may be close to or more than one year.

Previously, the median survival is often very short in patients with advanced pancreatic cancer—not long ago, as reported at the American Society of Clinical Oncology (ASCO) meeting, the survival did not exceed one year even in patients with advanced pancreatic cancer who had highly favorable performance status (PS) scores and received a combination therapy with three agents (fluorouracil + oxaliplatin + CPT). The professor and his team's findings presented at today's meeting is undoubtedly an efficient and controlled option for clinical treatment. It benefits those whose PS scores are 0-1, or even 2, and extends the survival time for patients with advanced pancreatic cancer.

I believe that a multi-center clinical study will definitely be carried out in China to verify whether such protocol is applicable for Asians. I look forward to its initiation and the subsequent benefits to Chinese patients with pancreatic cancer.

DXY: The slow progress in the treatment of pancreatic cancer and limited long-term survival of patients has made us concerned. The encouraging results of the recent MPACT study showed that ABRAXANE® (nab-paclitaxel) in combination with gemcitabine significantly prolonged overall survival as compared with those receiving gemcitabine monotherapy. That has surely brought a new dawn for patients with pancreatic cancer. Based on the information and discussion at this meeting. What is the role of MPACT study in clinical practice?

Prof. Shu: I believe MPACT, or the CA046 protocol, produced informative results for our Chinese specialists in the clinical treatment of advanced pancreatic cancer. Before that, a number of foreign multicenter open-label trials had had negative findings with various chemotherapy regimens for advanced pancreatic cancer, including gemcitabine plus oxaliplatin, gemcitabine plus fluorouracil, and gemcitabine plus capecitabine, as well as gemcitabine plus molecular targeted drugs. They strongly discouraged Chinese investigators from getting a positive result in a clinical trial regarding the treatment of pancreatic cancer. We should have continued our exploration and efforts, but based on existing evidence, we felt hopeless and were thus pessimistic, for a long period of time, in finding a regimen to effectively extend the survival for patients with advanced pancreatic cancer.

The MPACT protocol laid out the direction for our clinical research in the future. In the past, for potentially resectable borderline tumors, which are relatively large lesions that the surgeons believe there may be a risk of incomplete resection, neoadjuvant therapy is generally not advised. Now that the MPACT protocol allows tumor regression with a very high effectiveness at about 30% to 50%, a high response rate can be achieved even when the patient's condition is not ideal. Academically, we call it complete response and partial response (CR plus PR). With higher effectiveness of tumor regression than all of the previous options, we are able to include neoadjuvant chemotherapy in the treatment of patients with resectable pancreatic cancer, which is performed in two cycles before surgery.

In his presentation, Professor Ramanathan has demonstrated their follow-up treatment visits, and they expect a high rate of tumor response. We saw radiological evidence of tumor regression and postoperative pathological findings of necrosis in more than 90% of tumor tissues, which is the response after chemotherapy. Their results definitely opened a new path for the upcoming treatment of cancer. Before the discussion with them today, however, the vast majority of experts traditionally suggest that neoadjuvant therapy is of no value to the treatment of pancreatic cancer, but we have got some great take-home messages today. Besides that, we see the hopeful future of the fundamental nab-paclitaxel and gemcitabine-based regimen plus molecular targeted drugs, or maintenance therapy with nab-paclitaxel for patients benefited from the six courses of treatment, rather than the gemcitabine plus molecular targeted therapy in the past. That is because it has low toxicity and high efficiency—it provides an alternative option of pancreatic cancer as a component in the maintenance therapy, and ultimately prolongs progression-free survival (PFS), so that the survival time of a patient can be further extended. Through this meeting, we have learned that SPARC, a protein targeted by nab-paclitaxel, is expressed in nearly 68% of patients with

pancreatic cancer. This has undoubtedly provided a new therapeutic target for the treatment of pancreatic cancer.

DXY: We have noticed that albumin paclitaxel has been listed as a class 1 recommendation for first-line treatment of metastatic pancreatic in the NCCN Guidelines 2013 updated last week. Do you think the MPACT findings are applicable to Chinese patients?

Prof. Shu: I work long hours as a first-line clinician. Nab-paclitaxel has been applied in clinical settings for many years, and we have accumulated a wealth of experience, not only in those with pancreatic cancer, but also in other cancer patients. Clinicians always want to provide effective treatment for patients with advanced cancer. I believe the MPACT study will obtain a positive result in China and benefit Chinese patients. There are differences between Asians and Caucasians, but in fact many antineoplastic agents registered in China have shown similar effectiveness to their foreign counterparts, especially cytotoxic drugs (i.e., chemotherapy drugs). There is no obvious difference between our clinical trial results and those done in foreign countries. There may be some slight difference in the dosage. I think the MPACT findings should benefit Chinese patients with pancreatic cancer.

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DXY: Is there a need for modification or specific attention regarding the clinical use of albumin paclitaxel in Chinese patients?

Prof. Shu: I have my personal advice, but I also think that China's State Food and Drug Administration (SFDA) will follow its basic principle for auditing the protocol, because the MPACT obtains a positive result using a fixed dose, and has been approved by SFDA. I hope to conduct a study with a small sample size (20-30 cases) in China, clinically known as the preliminary study, to explore the tolerability among Chinese patients with pancreatic cancer whose physical rating is favorable (0-1 points). If the dose is well tolerated in this study, I believe few modifications or adjustments would be needed following large-scale clinical trial. That is because our current task is to reduce the toxicity of the chemotherapy drugs so that the regimen can be fully implemented. China's cancer experts have been doing a good job in this area, so I believe the MPACT protocol may be able to continue in China, though the indications should be observed.

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