Prof. Jun Ma and Prof. Jin-Ching Lin: clinical trials: the vital key to NPC progress

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Editor's note

The 2017 Taiwan Society for Therapeutic Radiology and Oncology Conference "Bring Insight into Impacts" and Both Sides across the Strait Forum was held at Taipei Medical University on 16th, 17th of December 2017. An army of world-renowned experts in the fields of radiology and oncology was invited to share and study a number of clinical cases via this highly-effective academic exchange platform. Discussed topics widely covered precision medicine, proton therapy, nasopharyngeal carcinoma, head and neck cancers and so on. At this conference, *Therapeutic Radiology and Oncology* (*TRO*) had the great honor to invite Prof. Jun Ma, the Key Laboratory of Multidisciplinary Diagnosis and Treatment of Nasopharyngeal Carcinoma, Guangzhou, China and Prof. Jin-Ching Lin, Department of Radiation Oncology, Taichung Veterans General Hospital, Taiwan to have an exclusive interview with us.

Figure 1 Prof. Jun Ma.

Experts' introduction

Prof. Jun Ma (*Figure 1*) is the Director of the Key Laboratory of Multidisciplinary Diagnosis and Treatment of Nasopharyngeal Carcinoma, Guangzhou, China. His main research interests include nasopharyngeal cancer, prognosis prediction and comprehensive treatment of nasopharyngeal carcinoma. As we know, NPC is a unique type of head and neck cancer, which has a high incidence in Southern China. His research group has been involved in the investigation of NPC for more than 15 years, and they have identified vital prognostic factors and explored the optimal schedule and chemotherapy regimens combined with radiotherapy in patients with locoregionally advanced NPC.

Prof. Jin-Ching Lin (*Figure 2*), currently serves as the Chief of the Department of Radiation Oncology, Taichung Veterans General Hospital, Taiwan. He is well-experienced in nasopharyngeal carcinoma. His research focuses are on combined chemoradiotherapy of various cancers, head and neck cancers, and especially nasopharyngeal

Figure 2 Prof. Jin-Ching Lin.

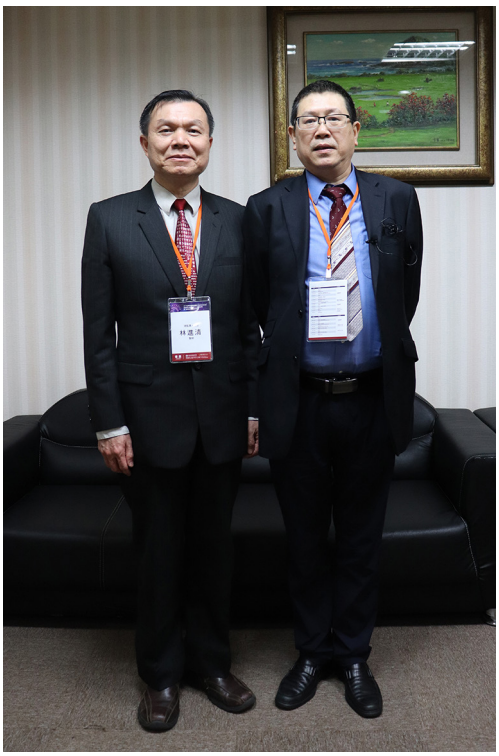

Figure 3 Prof. Jin-Ching Lin (left) and Prof. Jun Ma (right).

carcinoma and tumor biomarkers. He gave a presentation on "The Role of Systemic Therapy in Nasopharyngeal Carcinoma" and received a lot of attention in the conference.

TRO: Could you (Figure 3) briefly explain the treatment of induction chemotherapy with docetaxel, cisplatin, and fluorouracil (TPF)?

Prof. Ma: Concurrent chemoradiotherapy (CCRT) is the standard treatment for locoregionally advanced NPC; however, about 20% of patients still develop distant metastasis and 10% of them will experience locoregional recurrence after CCRT. Adding induction chemotherapy to CCRT might be a promising treatment strategy to further improve the prognosis and distant control. Docetaxel, cisplatin, and fluorouracil (TPF) induction chemotherapy are the effective regimens for locoregionally advanced head and neck cancer, but the efficacy of this regimen in NPC remained unclear at that time. Thus, we did a phase 3 randomized trial to compare adding 3 cycles of TPF induction chemotherapy to CCRT with CCRT alone in locoregionally advanced NPC. The results of this 3-year trial have been published in *Lancet Oncology* last year, and the TPF plus CCRT group showed a significantly better 3-year failure-free survival (80% *vs.* 72%), OS (92% *vs.* 86%), and distant failure-free survival (90% *vs.* 83%) than the CCRT alone group.
Prof. Lin: I agree with Dr. Ma. The induction chemotherapy followed by CCRT is one of the standard treatments for locoregionally advanced NPC in recent years.

TRO: Are there any disadvantages of TPF?

Prof. Ma: The main disadvantage of TPF induction chemotherapy is the toxicity, especially the neutropenia. In our trials, about 45% of patients experienced grade 3–4 adverse events. Grade 3 or 4 neutropenia occurred in 35% of patients, followed by leucopenia (27%), diarrhea (8%), and stomatitis (6%); 2% of patients experienced neutropenic fever. One patient died of septic shock due to grade 4 neutropenia and lack of timely medical care. However, the toxicity of TPF is generally manageable and acceptable, and I consider that TPF induction chemotherapy is safe under close follow-up and timely medical care.
Prof. Lin: Basically, I share the same view with Prof. Ma. TPF is a very effective and manageable toxin treatment. Compared to other kinds of chemotherapy, higher symptoms like leucopenia may occur but TPF is still a manageable treatment. In the future trials, I suggest using different kinds of combination chemotherapy. It may show a similar effect but with less toxicity.

TRO: You and your team had spent 7 years on the clinical trial of TPF induction chemotherapy in nasopharyngeal carcinoma. Have you and your team met any unforgettable frustrations or difficulties?

Prof. Ma: The biggest challenge we have met during the TPF trials is the optimal dose of the TPF regimen. In some famous clinical trials from Western countries, the TPF dosage was usually higher. For TAX 323 and TAX 324, the dose of TPF regimen was 75 mg/m^2 d1, 75 mg/m^2 d1, 750 mg/m^2 d1–5. However, 70–80% of patients would experience grade 3–4 neutropenia during TPF induction chemotherapy. Moreover, this conventional regimen was based on the data of Western patients, whether it is safe and tolerable for Asian patients remain unknown. Thus, we started the preliminary clinical trials to study the optimal TPF dosage for Asian patients. When we designed the TPF trials, there was a big problem for us as the optimal dose of TPF for Asian patients was unclear. To solve this problem, we searched a lot of literature and consulted with many chemotherapy experts, and we finally used

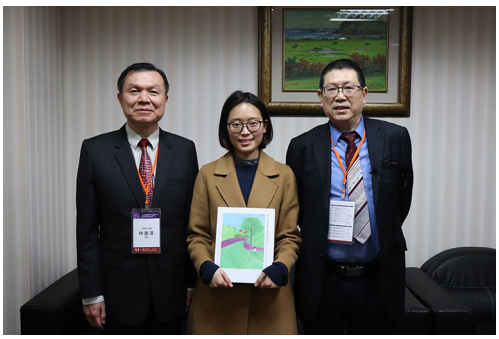

Figure 4 Prof. Jin-Ching Lin, Prof. Jun Ma and AME Science Editor.

the TPF regimen (docetaxel 60 mg/m^2 d1, cisplatin 60 mg/m^2 d1, and fluorouracil 600 mg/m^2/day d1–5) based on the previous phase 1 studies done at our Cancer Center, which was 20% lower than the conventional regimen. The positive results of our study suggested that this modified TPF regimen was well-tolerated and produced encouraging results in Asian patients with NPC.

Prof. Lin: TPF dosage used in Western countries is not suitable for Asian patients with NPC. From my personal experience, the optimal dosage for Asian patients with NPC or other cancers should reduce about 20% of TPF.

TRO: Please give some suggestions to young doctors or medical school students who would like to specialize in radiation oncology?

Prof. Ma: My suggestion is to involve yourself in research as soon as possible. Don't just read or recite the medical books. Science and technology are advancing with each passing day; thus, research skills are essential for doctors specializing in oncology. They can start by asking a small question, and try to answer the question by searching the literature. Then they would know more about the current status, progress, and study methods of this topic, and eventually they can become an expert in this field. Young doctors can build up self-confidence from their research during this process, and they will find more good questions to answer in the future.

Prof. Lin: For young radiation oncologists, please review the current literature more and spend more time on clinical practices. They should keep improving their clinical skills by observing and taking care of patients. Furthermore, they can take an active part in the study group to learn more about the research process and try to improve themselves.

From their final answering, we could know that Dr. Ma and Dr. Lin are both practical and hard-working people. We feel honored to have the opportunity to share their expertise and thoughts by having such a in-depth interview (*Figure 4*).

Acknowledgments

Many thanks to Dr. Ma and Dr. Lin for sparing some time to have an exclusive interview with us even if they had a busy schedule.

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