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Enhancing Survival of HCC Patients in The New Era - A Multi-disciplinary Team Approach

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In conversation with Singapore's eminent Gastroenterologists, Surgeon, and Oncologist; Prof Lim Seng Gee (NUH), Prof Pierce Chow (SGH and NCCS) and Associate Prof Toh Han Chong (NCCS)

Singapore's Health Sciences Authority (HSA) recently approved an **immunotherapy regimen (Tecentriq + Avastin)** that has been proven to enhance overall and progression-free **survival** in people with unresectable **hepatocellular carcinoma (** HCC) compared to the current standard of care. This approval echoes healthcare professionals ask for innovation within the space, which was left stagnant for a good 13 years. Singapore's multi-disciplinary team (MDT) of specialists**Prof Lim Seng Gee (NUH), Prof Pierce Chow (SGH and NCCS) and Associate Prof Toh Han Chong (NCCS)**are passionate to share more about their role in this novel treatment regimen for hepatocellular carcinoma (liver cancer).

- **In a multi-disciplinary setting, can you share with us what is your involvement and contribution in the diagnosis and treatment process of hepatocellular carcinoma (HCC) and how has your role evolved over the years?**

Prof Lim: The hepatologist is usually the first person to see the patient, and in some situations, diagnosis may not be straightforward. With more sophisticated imaging technology and locoregional therapy, along with better systemic therapy, different specialties bring their expertise to personalize therapy for the individual patient.

Prof Chow: When I first started treating patients with HCC, the only efficacious therapy was surgery and decision making was simple – either surgery or no surgery. Positive RCTs on TACE only came about in 2002, and sorafenib in 2007. Now we have many modalities of therapy including Y90 RE, other TKIs and combination immunotherapy. Decisions have moved on to more than just surgery to include combination strategies like downstaging to curative surgery, combination of surgery and loco-regional therapy and clinical trials in adjuvant therapy. At the National Cancer Centre Singapore, such complex decisions are usually made in the Comprehensive Liver Cancer Clinic in real-time, with the multi-disciplinary tumour board.

Prof Toh: As a medical oncologist, I am involved in weekly multidisciplinary tumour board meetings that include liver surgeons, medical oncologists, radiologists (including interventional radiologists) and nuclear medicine specialists. There have been multiple advances in the clinical management of HCC in just the past few years both in systemic therapies and locoregional therapies. So it is even more crucial to conduct these multidisciplinary meetings to ensure that the best decision is made for every HCC patient – especially when multimodality treatment is considered .

- **What are some key considerations by clinicians/physicians when deciding on the treatment for HCC patients?**

Prof Lim: Treatment options are largely dictated by the stage of disease and the stage of liver disease. A small tumour in a patient with advanced liver disease makes options very limited. Co-morbidities, ECOG status, availability of treatment modalities, expertise (particularly for locoregional therapy), cost of therapy and of course, patient preferences are just some of the many considerations that affect the options for treatment.

Prof Chow: And we also have to consider the availability and efficacy of expertise and therapies at hand (for example, Y90 or atezo-bev is not available in all centers), the therapeutic aim (is the aim curative or palliative?), cost and with an understanding of the possible adverse events (AE) that can manifest in the patient.

Prof Toh: From the point of view of therapeutic intervention , the health and function of the liver would be a very important consideration as HCC is almost always on the background of liver cirrhosis. Advanced HCC patients with poor liver function are much less likely to benefit from therapy and potential side effects carry an increased risk. Other considerations include symptom control and quality of life while on treatment, risk and cost benefit analyses, as well as goals and expectations of treatment.

- **What has been the standard treatment of care for HCC patients? How has that been and what can patients look forward to?**

Prof Lim: The standard of care depends on stage of disease, broadly divided into early, intermediate and advanced HCC. For early HCC, locoregional therapy, resection or liver transplantation are options. For advanced HCC, the only option was sorafenib for many years. The biggest unmet need was advanced HCC where there had been no significant survival advantage till recently.

Prof Chow: From a surgical point of view, it depends on the function of liver, the general fitness of patients and the tumour burden. For those in the early stage, we usually look at surgical resection, radiofrequency ablation (RFA) and transplantation, all of which are potentially curative in early stage HCC. For intermediate or locally advanced stage HCC, common treatment methods are loco-regional therapy such as Y90, TACE – here if the patient is fit the aim should be to downstage to benefit from potentially curative therapies. For those whose tumour has metastasized, systemic therapy with atezolizumab and bevacizumab is recommended.

Prof Toh: To carry on from Prof Lim, in 2018, another targeted therapy – lenvantinib – also positioned itself as the first line treatment of advanced HCC. In 2020, as Prof Chow mentioned, a combination of atezolizumab and bevacizumab demonstrated better survival over sorafenib and became the new standard of care for the first line treatment of stage 4 advanced HCC with good liver function.

- **Tell us more about the newly approved Tecentriq and Avastin immunotherapy regimen. Has this new form of treatment been shown to keep patients in remission and improve their quality of life?**

Prof Lim: The newly approved combination of Tecentriq and Avastin has provided more options for patients with advanced HCC and the results could become the standard of care for those with advanced HCC. Patients are able to tolerate therapy much better and have fewer adverse events, most of which are manageable giving them a higher quality of life. Hence, I would consider this breakthrough therapy based on the article in New England Journal of Medicine.

Prof Toh: This combination is based on rational science where reprogramming and improving the blood vessel system in HCC enhances positive anti-tumour immunity around the cancer, thereby activating the T cells to attack the cancer. The QOL analysis in IMBRAVE150 also proved that atezolizumab + bevacizumab is comparably well tolerated, and ultimately, this combination provides a more favorable overall survival over patients on sorafefnib.

- **Are there any exciting developments around HCC treatment that clinicians/physicians should look out for? Please share what are these developments and why are they the ones to watch.**

Prof Chow: Combination therapies with immunotherapy to improve clinical response and outcomes.

Prof Toh: There are now a number of combination drug trials ongoing, some of which will mature in the next few years. Many of such combinations are immunotherapy based, and there is a sense that the extension of survival of advanced HCC patients will potentially continue to improve over the coming years.

Prof Lim: I agree with Prof Chow and Toh that new combinations may lead to even better outcomes for patients.

Speakers:

Hepatologist*:*

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Surgeon*:*

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