

# AHCC Trials Group

Newsletter 2020

*Making a difference together*

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Welcome to our AHCC Trials Group yearly newsletter.

As we welcome 2021, we looked back on 2020 which has been one of the most challenging periods. Though the AHCC Trials Group meeting planned for May 2020 was postponed, the Trials Group has progressed despite the adversity and uncertainty surrounding the current health crisis. The PLANet Study, AHCC07 study, the Translational and Clinical Research (TCR) Flagship Program in Liver Cancer has its latest results were published in Cell and Nature Communications. The HCC Registry in Asia (AHCC08) Steering Committee met virtually on 19 June 2020 and the AHCC08 study was concluded.

The AHCC Trials Group moved swiftly to remote working and we have successfully secured grants and is preparing for 1 clinical trial and 2 prospective studies under the Trials Group. AHCC10 Study is projected to start recruitment in the 1<sup>st</sup> quarter of 2021 and this is a brief introduction of the study in this newsletter.

As the AHCC Trials Group continues to grow to include more partners from the Asia Pacific and new members from China, Japan and United States, we like to thank all the members for their commitments. Maintaining the close working relationship as a group for 24 years is one of the greatest feats of the AHCC Trials Group, and this is made possible with all the dedications, support and hard work of our members and study team. Thank you for pulling the AHCC Trials Group through all these years!

Trial Coordinating Centre:



## AHCC07

### Precision Medicine in Liver Cancer across an Asia-Pacific Network

Clinicaltrials.gov identifier: NCT03267641

**Protocol chair:** Prof Pierce Chow

**Number of participating centres:** 7 recruiting sites from 5 countries (Malaysia, Philippines, Singapore, Thailand and USA)

**Status:** As of 31 Dec 2020, recruited 83 patients out of the target recruitment of 103 patients.

**Project start and end date:** 16 May 2016 to 15 May 2022

**Abstract:** Hepatocellular carcinoma (HCC) is the 6th most common cancer in the world but the 2nd most important cause of cancer death. Because of its highly heterogeneous nature, the current approach to identifying druggable targets have not delivered efficacious systemic therapies in HCC and is a main reason for the high case fatality. Even when surgical resection is potentially curative in early disease, tumour recurrence remains high and long term survival poor because of the absence of useful adjuvant therapy. To address these unmet needs, this prospective study aims to investigate the genomic heterogeneity and immunological profile of surgically resected HCC, and relate them to the subsequent clinical trajectory. Genomic and immunological studies are subsequently repeated when tumours recur, to validate clonally dominant driver mutations and immunological processes that are targetable.

**Study objective:** To evaluate the clinical trajectory of a cohort of patients who has undergone surgical resection of HCC in terms of time to recurrence (TTR) in relation to the genomics and immunomics profile of the primary tumour.

#### Recent Publications:

1. Nguyen PHD, Ma S, Phua CZJ, Kaya NA, Lai HLH, Lim CJ, Lim JQ, Wasser M, Lai L, Tam WL, Lim TKH, Wan WK, Loh T, Leow WQ, Pang YH, Chan CY, Lee SY, Cheow PC, Toh HC, Ginhoux F, Iyer S, Kow AWC, Young Dan Y, Chung A, Goh BKP, Albani S, Chow PKH, Zhai W, Chew V. **Intratumoural immune heterogeneity as a hallmark of tumour evolution and progression in hepatocellular carcinoma.** *Nat Commun.* 2021 Jan 11;12(1):227. doi: 10.1038/s41467-020-20171-7. PMID: 33431814. (Impact factor: 12.124)
2. Sharma A, Seow JJW, Dutertre CA, Pai R, Blériot C, Mishra A, Wong RMM, Singh GSN, Sudhagar S, Khalilnezhad S, Erdal S, Teo HM, Khalilnezhad A, Chakarov S, Lim TKH, Fui ACY, Chieh AKW, Chung CP, Bonney GK, Goh BK, Chan JKY, Chow PKH, Ginhoux F, DasGupta R. **Onco-fetal Reprogramming of Endothelial Cells Drives Immunosuppressive Macrophages in Hepatocellular Carcinoma.** *Cell.* 2020 Oct 15;183(2):377-394.e21. doi: 10.1016/j.cell.2020.08.040. Epub 2020 Sep 24. PMID: 32976798 (Impact factor: 38.637)



## AHCC08

### Hepatocellular Carcinoma Registry in Asia

Clinicaltrials.gov identifier: NCT03233360

**Protocol chair:** Prof Pierce Chow

**Status:** Completed recruitment of 2,533 patients from 33 sites in 9 countries in 31 Dec 2019 and patient follow-up in 30 June 2020. Publication is in progress.

**Abstract:** Hepatocellular carcinoma is the 6<sup>th</sup> most common cancer in the world and the 2<sup>nd</sup> most common cause of cancer deaths, and afflicts approximately 800,000 people yearly. However, there is great geographical variation in the distribution of HCC, and approximately 80% of this cancer is found in Asia and central-western Africa. In Asia, it is the third most common cancer. Overall survival in HCC patients is dependent on the pathological stage of the cancer and underlying liver function at diagnosis as well as the treatment modality received. However, there is a lack of data to inform health policy makers on the current burden of HCC in the Asia-Pacific. Currently available data from clinical trial reports describe a very specific and narrow group of carefully selected patients treated by specific protocol therapies in a controlled regime. Isolated case series reported by academic hospitals in the Asia-Pacific similarly do not reflect real-world practices or clinical outcomes. Evidence suggests that use of newer pharmacological agents for the treatment of HCC is increasing. This study developed a registry of HCC patients, with the aim of providing a better understanding of the current real-world treatment patterns, patient characteristics, and outcomes among HCC patients drawn from the Asia-Pacific.

**Study objective:** To provide a complete longitudinal picture of the HCC patient journey in several representative Asian countries.

#### **Preliminary results Presentations:**

1. **Online publication at ASCO 2018, Chicago**  
*Differences in presentation and management patterns in patients with hepatocellular carcinoma (HCC) between China and Singapore: Initial data from the HCC Registry in Asia Results on 174 patients from China (4 sites) and Singapore (2 sites) until 31 Dec 2017*
2. **Poster presentation at ASCO GI 2019, San Francisco and**
3. **E-poster presentation at ILCA 2018, London**  
*Differences in presentation and management patterns in patients with hepatocellular carcinoma (HCC) between China and Singapore: Initial data from the HCC Registry in Asia Results on 174 patients from China (4 sites) and Singapore (2 sites) until 31 Dec 2017*
4. **Poster presentation at ASCO GI 2019, San Francisco**  
*Differences in Presentation and Management Patterns in Patients with Hepatocellular Carcinoma (HCC): Data from HCC Registry in Asia Results on 657 patients from China (5 sites), South Korea (4 sites), Singapore (3 sites) and Japan (2 sites) until 30 Aug 2018*
5. **Poster presentation at 10<sup>th</sup> APPLE Congress 2019, Aug 29-31, 2019, Hokkaido, Japan**  
*Variations in cancer stages at diagnosis and management strategies in Hepatocellular Carcinoma (HCC): Data from the HCC Registry in Asia (AHCC08) Results on 951 patients from Australia (2 sites), China (6 sites), Japan (4 sites), South Korea (6 sites), Singapore (3 sites) and Taiwan (4 sites) until Apr 2019*

## Online Survey

### Changes in the Management of Hepatocellular Carcinoma (HCC) during the COVID-19 pandemic

#### Study Team:

##### Chairman:

Professor Pierce Chow Singapore/ National Cancer Centre

##### Members:

A/Prof Simone Strasser Australia/ Royal Prince Alfred Hospital

Prof Zhu Xu China/ Beijing Cancer Hospital

Prof Masatoshi Kudo Japan/ Kindai University Hospital

Prof Lee Joon Hyeok South Korea/ Samsung Medical Centre

Prof Chen Chien-Hung Taiwan/ National Taiwan University Hospital

Dr Rawisak Chanwat Thailand/ National Cancer Institute

Asst Prof Mihir Gandhi Singapore/ Singapore Clinical Research Institute

**Abstract:** The World Health Organization (WHO) declared a pandemic of the coronavirus disease SARS-CoV-2 (COVID-19). The pandemic impacted on healthcare institutions worldwide and most prioritised the management of COVID-19 and adapted their practices for non-COVID diseases. Many countries in the Asia-Pacific undertook such precautionary measures even before the pandemic was declared as a result of the experience of previous outbreaks such as SARS and MERS. Oncology services are variably impacted either by changes in the time to diagnosis and treatment or to the modality of treatment. There is also concern that treatment may predispose the patients to the complications of COVID-19. Hepatocellular carcinoma (HCC) is endemic in the Asia-Pacific, which carries more than 70% of the global burden of the disease. It is essential to understand the impact COVID-19 has on the management of HCC in the real world so that appropriate remedies to gaps may be planned.

**Study objective:** To provide an understanding of how the management of HCC has been modified during the COVID-19 pandemic.

**Method:** The study team designed a multi-country online survey to evaluate the impact of the pandemic on diagnosis and treatment of HCC patients. The survey was sent to all the AHCC members to provide in-depth data on pre and during pandemic for HCC diagnosis, treatment, outcomes, pandemic control measures and proposals for the future course to minimise the impact on HCC patient care.

**Outcome:** A total of 27 sites from 14 countries responded to the first survey. A second survey was sent to these 27 sites to request for more details. With the data collected, the study team is currently analysing the data to evaluate the impact on each aspect of patient care. The results will be submitted for publication.

## AHCC10

### Early detection of HCC: miRNA, microbiome and imaging biomarkers in the evolution of chronic liver disease in a high-risk prospective cohort

**Protocol chair:** Prof Pierce Chow

**Number of participating centres:** 14 recruiting sites in Singapore

**Status:** Pending award of grant and ethics approval. Recruitment is projected to start in the 1<sup>st</sup> quarter of 2021.

#### **Abstract:**

HCC is the 6th most common cancer and the 4th leading cause of cancer death worldwide. In Singapore, HCC is the 3rd leading cause of cancer death in male and 4th in female. A major reason for its lethality is the absence of diagnostic modalities with high accuracy for the detection of early stage HCC. Currently only 20% of HCC are diagnosed in the early stage when curative treatment is possible. The inability to diagnose HCC earlier for the majority of patients is thus an urgent unmet need. In this study, we aim to develop the 1<sup>st</sup> miRNA in-vitro diagnostic (IVD) kit for HCC with higher accuracy and better ease of use compared with the extant combination of AFP and US. Separately, we aim to develop an AI algorithm with MRI to predict individual risks of HCC within a specific timeline. We will also work to examine changes in the microbiome and metabolome in the build-up to HCC development. The aim is to identify potential therapeutic targets in the microbiome and metabolome where intervention can prevent HCC development and slow the progression of liver diseases. This protocol leverages on data uncovered by the AHCC07 study which has identified miRNA and metabolomic biomarkers for HCC. These findings require validation in a prospective cohort of high-risk patients. This is the first cohort study with circulating miRNA, predictive MRI (LiverMultiScan), metabolome and microbiome in chronic liver disease.

#### **Study Design:**

This study will recruit a prospective cohort of 2,000 patients at high-risk of developing HCC and a parallel 100 HCC patient cohort scheduled for surgical resection. The cohorts will be followed up to 3 years. The study will focus on the roles of circulating miRNA, predictive MRI algorithm, metabolome and microbiome in high-risk patients who eventually develop HCC versus those who don't. The study is in collaboration with 3 industrial partners, 2 academic institutions and 6 hospitals and 8 SingHealth Polyclinics in Singapore.



*The Investigators at the 4<sup>th</sup> AHCC08 Steering Committee Meeting held virtually on 19<sup>th</sup> June 2020. From top left, Ms Lynette Lai, Dr Senthil Sockalingam, Dr Chien-Hung Chen, Asst Prof Mihir Gandhi, Prof Pierce Chow, Ms Swizzle Ko, Prof Masatoshi Kudo, Dr Rawisak Chanwat and A/Prof Simone Strasser.*

The Asia-Pacific Hepatocellular Carcinoma (AHCC) Trials Group is a collaborative group formed in 1997 by clinicians treating HCC in major medical centres in the Asia-Pacific region. The aims of the trials group are to conduct preventive and therapeutic trials in HCC, to carry out basic and translational research in this field and to develop training and educational programmes pertaining to HCC. With these objectives, the AHCC Trials Group holds annual general meetings and symposia that bring together international experts to create opportunities to network and share updates and research ideas.

The last meeting was held in May 2019 and we could not have a meeting in 2020 due to the COVID-19 pandemic. Nevertheless, the Trials Group has stayed strong and achieved greater heights. We hope to be able to meet either in person or virtually in the new year, 2021.

We hope all the investigators and their families a great 2021 ahead!

## Contact Details

For further queries, please contact the AHCC Trials Group at

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Read more about all trials  
under AHCC Trials Group at  
<http://www.scri.edu.sg>