THE Asia-Pacific Hepatocellular Carcinoma Trials Group

2022

THE AHCC TRIALS GROUP NEWSLETTER

As 2022 comes to a close, we look back on the year with gratitude as it marked another successful year for the AHCC Trials Group. Despite the impact that COVID-19 has made on the daily lives and routines of many, the Trials Group has maintained great resilience, and continually sought to generate high scientific outputs in studies that have concluded and has been consistently recruiting patients for its ongoing trials. The Trials Group has also recently initiated a few studies, including renewing its funding for the continuation of the PLANet 1.0 AHCC07 study (now continued as the PLANet 2.0 study) (the Translational and Clinical Research (TCR) Flagship Program in Liver Cancer). All of which is done with the aim of improving prognosis and the clinical outcomes of patients with hepatocellular carcinoma (HCC).

The Trials Group is actively screening and enrolling patients for (i) AHCC10 ELEGANCE; (ii) AHCC11 PROSECT; (iii) newly-initiated AHCC09 STRATUM as well as (iv) & (v) newly-initiated AHCC12 EMPHASIS and AHCC13 studies, both of which fall under the PLANet 2.0 programme.

Despite the challenges and travel restrictions imposed by the pandemic, the Trials Group has also successfully initiated its multi-national study, the AHCC09 STRATUM, involving 13 sites from 4 countries around Asia Pacific. This international study is also fully supported by industry, a reflection of the importance of the Asia-Pacific region to endeavors in HCC.

Additionally, the AHCC10 ELEGANCE study has also recruited more than 1,400 patients thus far and we continue to push for increased enrolment so that more patients who are at high risk of developing HCC can benefit from this surveillance study. We have commenced the preliminary analysis phase with our industrial partners in AHCC10, and are now looking forward to novel discoveries. With these new discoveries and new studies initiated that span the whole spectrum of HCC patients, the Trials Group continues to persevere through the current difficult time.

As the AHCC Trials Group continues to grow and include more partners and scientific institutes across the globe, we would like to take this opportunity to thank all members for their unwavering support and commitment to the Trials Group. Maintaining the close working relationship and camaraderie amongst members of the group for the past 25 years is one of the greatest accomplishments of the AHCC Trials Group, and it could not have been done without your dedication, support and hardwork. Thank you for supporting the AHCC Trials Group through these years!

CONTENTS

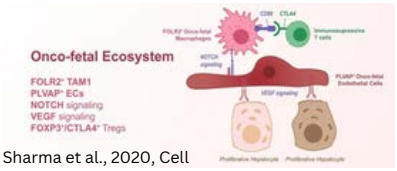
UPDATES COMPLETED STUDIES

AHCC07 Precision Medicine in Liver Cancer across an Asia-Pacific Network

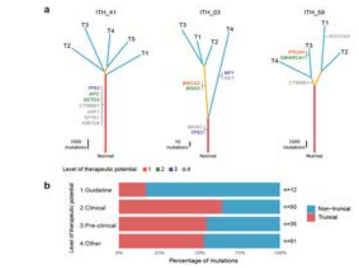
Clinicaltrials.gov Identifier: NCT03267641

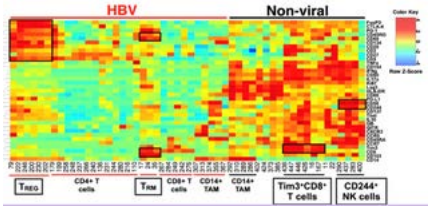
Status: Study concluded in May 2022, and was renewed in June 2022 as PLANet 2.0

This is a multi-national, multi-disciplinary study whose strategy is based on the multi-region sampling of tumors, where solid tumors and their metastases are intrinsically complex. The importance of multi-region sampling is due to the high-intratumoral heterogeneity (ITH) present in tumors, where a single biopsy often only reflects a part of the tumor. Understanding the existence of high ITH can provide a more holistic picture of the tumor, and this forms the basis of the AHCC07 study. From the study, we have recruited 147 patients across 6 sites in 4 Asia Pacific countries (Malaysia, Philippines, Thailand and Singapore) and 1 site in Durham, USA. From these 147 patients, we have generated a wide array of data, ranging from genomics to epigenomics, metabolomics, translational immunomics, and patient derived models. Of the 147 patients, 132 patients have reached the study end-point (as defined by recurrence, death or completion of 2 year follow-up from date of surgery).



Sharma et al., 2020, Cell


Zhai et al., 2021, Natl Sci Rev



Chew et al., 2019, Gut

This study has allowed us to delineate the multi-omics landscape of HCC, and confirmed the presence and importance of recognizing the high ITH in HCC tumors. From this study, we have made a few significant discoveries including:

- Oncofetal re-programing in HCC confers immuno-suppressive and immune-escape mechanisms mediated by VEGF/NOTCH signaling with a niche co-localization of cells and molecular pathways
- Most driver mutations are non-truncal and display high ITH which explains current poor therapeutic efficacies in HCC
- There is a co-existence of multiple transcriptomic sub-types in HCC where the worst subtype drives clinical trajectory and outcome
- Distinct immunological microenvironments exist in HepB related HCC versus non-B-non-C HCC

PARTICIPTING SITES

Malaysia
University Malaya Medical Center

Philippines
The Medical City

Thailand
National Cancer Institute

Singapore
National Cancer Centre
National University Hospital
Singapore General Hospital

USA
Duke University School of Medicine

AHCC Trials Group Website: http://www.scri.edu.sg/crn/asia-pacific-hepatocellular-carcinoma-ahcc-trials-group/about-ahcc/

UPDATES COMPLETED STUDIES

AHCC07 PLANET CONTINUED

PUBLICATIONS

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UPDATES COMPLETED STUDIES

AHCC07 PLANET CONTINUED

- 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. (2021) Intratumoural immune heterogeneity as a hallmark of tumour evolution and progression in hepatocellular carcinoma. *Nat Commun.*
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- Lee YH, Chuah S, Nguyen PHD, Lim CJ, Lai HLH, Wasser M, Chua C, Lim TKH, Leow WQ, ..., Chow PKH, Albani S, Liu H, Chew V (2022) IFNγ–IL-17+ CD8 T cells contribute to immunosuppression and tumor progression in human hepatocellular carcinoma. *Cancer Letters*
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UPDATES COMPLETED STUDIES

AHCC08 The Insight Study - Insight into Real-world Practice of Management of HCC in Asia-Pacific

Clinicaltrials.gov Identifier: NCT03233360

Status: Completed recruitment of 2533 participants in December 2019. Pending publication

The study has successfully concluded and achieved recruitment target of 2500 patients in December 2019. Through this study, we have obtained one of the largest real-world HCC patient dataset, where patients from Singapore, Australia, China, Hong Kong, Japan, New Zealand, South Korea, Taiwan and Thailand are recruited. The aim of the study is to understand how the management of HCC varies between the participating countries, and to work with academic partners to determine possible underlying variables that could result in such variation observed. Data analysis is in progress and papers are pending publication.

PUBLICATIONS IN PROGRESS

- Real-world Data of the Diagnosis, Treatment and Management of Hepatocellular Carcinoma in Asia-Pacific: The INSIGHT study
- Post-study analysis and the development of suitable analytic models for the AHCC08 Registry Data
- Survival and cost-effectiveness and impact of positive clinical trials in the management of Hepatocellular Carcinoma (HCC) in Asia: The HCC Registry in Asia between 2013 and 2019

Participating Sites

Australia
- Royal Adelaide Hospital
- Royal Prince Alfred Hospital

China
- Guangxi Medical University Cancer Center
- Second Affiliated Hospital Zhejiang University School of Medicine
- Zhongshan Hospital, Fudan University
- Beijing Cancer Hospital
- Harbin Medical University Cancer Hospital
- Nanjing Bayi Hospital

Hong Kong
- Queen Mary Hospital

Japan
- Kindai University Hospital
- Kyorin University School of Medicine
- National Cancer Centre
- University of Tokyo
- National Center of Global Health and Medicine

New Zealand
- Auckland City Hospital

Singapore
- National Cancer Centre
- National University Hospital
- Singapore General Hospital

South Korea
- Asan Medical Centre
- Korea University Anam Hospital
- Samsung Medical
- Seoul National University Hospital
- St Vincents Hospital
- St. Mary's Hospital
- Ajou University Hospital
- Severance Hospital, Yonsei University College of Medicine

Tawian
- China Medical University Hospital
- Taipei Veterans General Hospital
- KS-Chang Gung Memorial Hospital
- National Cheng Kung University Hospital
- National Taiwan University Hospital

Thailand
- National Cancer Institute
- Siriraj Hospital, Mahidol University

AHCC Trials Group Website: http://www.scri.edu.sg/crn/asia-pacific-hepatocellular-carcinoma-ahcc-trials-group/about-ahcc/

UPDATES COMPLETED STUDIES

AHCC08 INSIGHT STUDY CONTINUED

PRESENTATIONS

Results on all 2,533 patients from China, Thailand, Hong Kong, Singapore, Taiwan, New Zealand, Australia, South Korea and Japan until June 2020:

- Lecture at 4th EWALT Meeting 2022, Tokyo, Japan (virtual)
- Lecture at APASL 2022, Seoul, Korea (virtual)

Subset of Registry Results:

- Online publication at ASCO 2018, Chicago – 174 patients from China and Singapore until Dec 2017
- Poster presentation at ASCO GI 2019, San Francisco – 174 patients from China and Singapore until Dec 2017
- E-poster presentation at ILCA 2018, London – 174 patients from China and Singapore until Dec 2017
- Poster presentation at ASCO GI 2019, San Francisco – 657 patients from China, South Korea, Singapore and Japan until Aug 2018
- Poster presentation at 10th APPLE Congress 2019, Hokkaido, Japan – 951 patients from Australia, China, Japan, South Korea, Singapore and Taiwan until Apr 2019

UPDATES CURRENT STUDIES

AHCC09 Multinational Phase II Trial to Compare Safety and Efficacy of SIRT (Y-90 Resin Microspheres) Followed by Atezolizumab Plus Bevacizumab, vs SIRT (SIRT-Y90) Followed by Placebo in Locally Advanced HCC Patients

Clinicaltrials.gov Identifier: NCT05377034

Participating Sites

Up to 13 recruiting sites from:

- Singapore
- Taiwan
- South Korea
- China

Participating sites: Including up to 13 recruiting sites from Singapore, South Korea, Taiwan and China

Study status: The study has started enrolling patients from Singapore, with remaining participating centres to be initiated in the first half of 2023

Being a highly complex internal organ, it is difficult to identify cancer of the liver until a later stage. As a result, almost half of the patients present with locally advanced disease at the time of diagnosis, where the standard of care is loco-regional therapy. Selective Internal Radiation therapy (SIRT) with Yttrium-90 (Y90) has been observed to deliver sustained therapeutic effects beyond its half-life and minimal adverse events were seen with its usage. This phenomenon is attributed to the ability of SIRT-Y90 to induce an immunological response in the tumor microenvironment (TME), where an increase in cytotoxic immune cells has been observed in the TME after SIRT-Y90 administration. The creation of such proinflammatory environment is significant as majority (55%) of HCC tumors display either the immune desert or excluded phenotype, in which the tumors lack cytotoxic T cells, thereby allowing for tumor immune escape. We hypothesize that that the administration of SIRT-Y90 followed by interval treatment with immunomodulating drugs such as Atezolizumab together with anti-VEGF Bevacizumab will create a synergistic effect on the infiltration of T cells into tumors, thereby enhancing anti-tumor immunological outcomes.

STUDY AIMS

- To compare the best overall response rate (BORR) of SIRT-Y90 followed by atezolizumab plus bevacizumab (study arm) versus SIRT-Y90 followed by placebo (control arm) in patients with locally advanced HCC 12 months post-randomization
- To investigate the sustained response and disease control rate at 12 and 18 months post-treatment randomization
- To identify the time to and duration of response
- To uncover the time to progression – Progression-free survival (PFS) and overall survival (OS) at 12- and 18-months post-randomization
- To elucidate the safety profile of Atezolizumab plus Bevacizumab in systemic setting after loco-regional therapy

UPDATES CURRENT STUDIES

AHCC09 STRATUM CONTINUED

STUDY DESIGN

This is a phase II randomized placebo-controlled clinical trial, enrolling an estimated 176 locally advanced HCC patients from up to 13 sites from the Asia-Pacific Hepatocellular Carcinoma (AHCC) Trials Group. Proposed sites include those in Singapore, China, South Korea, and Taiwan. All 176 patients will be given SIRT-90 loco-regional therapy as standard of care, followed by either placebo or a combination of Atezolizumab and Bevacizumab (Atezo-Bev) in a 1:1 ratio. The safety and clinical efficacy of Atezo-Bev as a systemic therapy after administration of loco-regional therapy will be assessed.

MEDIA

National Cancer Centre Singapore
SingHealth

PRESS RELEASE

MULTI-SITE CLINICAL TRIAL TO ASSESS NOVEL LIVER CANCER TREATMENT WITH SGD19.2 MILLION INDUSTRY SUPPORT

- The primary liver cancer hepatocellular carcinoma (HCC) is the third most common cause of cancer deaths in males and fifth most common cause in females in Singapore.
- Led by the National Cancer Centre Singapore the investigator-initiated, phase 2 clinical trial, across 13 sites in the APAC region, will assess a novel radiotherapy and immunotherapy combination to treat HCC.
- This trial is supported by SG$19.2 million in industry funding from Roche and Sirtex, with additional in-kind contributions to improve clinical practice and outcomes for HCC patients.

Singapore, September 2022 – A multi-national, investigator-initiated and industry-backed clinical trial was launched to test the efficacy of a novel radiotherapy and immunotherapy combination that aims to improve health outcomes for patients with the primary liver cancer, hepatocellular carcinoma (HCC). Led by the National Cancer Centre Singapore (NCCS), the AHCC09 (STRATUM) study has received SGD19.2 million in funding from industry partners Roche and Sirtex and will be conducted across 13 sites in the Asia Pacific region.

Liver cancer is the sixth most common cancer in the world and fourth most common cause of cancer deaths globally.[1] In Singapore, it is the third most common cause of cancer deaths in males and fifth most common cause in females[2]. Up to a third of patients in the Asia Pacific region present with intermediate stage HCC at diagnosis, making it the biggest sub-group of HCC patients. Intermediate stage HCC is heterogeneous and hard to treat, thus creating an urgent need to seek more effective treatments and improve outcomes for patients.

Media Release: Study aim to recruit patients with locally advanced HCC, and is supported by industry, 21 September 2022

NEWS RELEASE 28-SEP-2022

Multi-site clinical trial to assess novel liver cancer treatment with SGD19.2 million industry support

Led by the National Cancer Centre Singapore the investigator-initiated, phase 2 clinical trial, across 13 sites in the APAC region, will assess a novel radiotherapy and immunotherapy combination to treat HCC

Grant and Award Announcement
SINGHEALTH

Industry backing reflects Singapore's standing as a biomedical research hub

The trial is supported by SGD19.2 million in funding from Roche and Sirtex, as well as by in-kind contributions for therapeutics and devices, marking a significant commitment from industry for an investigator-initiated research study.

"The strong industry support for AHCC09 (STRATUM) validates national efforts to establish Singapore as a vibrant biomedical research hub, that is differentiated by an integrated network of scientists and clinician-scientists who work closely with industry to deliver impactful research," said Professor Tan Say Beng, Executive Director, Singapore Ministry of Health's National Medical Research Council.

Media Release: Industry backing of SGD19.2 million reflects Singapore's standing as a biomedical research hub, Published in EurekaAlert, 28 September 2022

AHCC Trials Group Website: http://www.scri.edu.sg/crn/asia-pacific-hepatocellular-carcinoma-ahcc-trials-group/about-ahcc/

UPDATES CURRENT STUDIES

AHCC10 Early detection of HCC: miRNA, microbiome and imaging biomarkers in the evolution of chronic liver disease in a high-risk prospective cohort

Clinicaltrials.gov Identifier: NCT04965259

Status: As of November 2022, the study has recruited over 1500 patients. The study aims to recruit of 2,000 patients by Q3 of 2023.

Hepatocellular Carcinoma (HCC) is the 7th most common cancer and 4th most important cause of cancer-related death in the world, afflicting almost a million people annually. A large geographical variation exist in the distribution of HCC, with 80% of the burden shouldered within Asia-Pacific due to the significant prevalence of Hepatitis B in the region. While potentially curative therapies (in the form of surgical resection, transplantation and radiofrequency ablation) offers patients with early HCC a notable survival advantage, only around 20% of patients are diagnosed early enough to be eligible for such procedures due to the low sensitivity of current screening methods in detecting early HCC. Through the AHCC07 PLANet 1.0 study, a suite of miRNA signatures has shown to be promising biomarkers at detecting early HCC, but these results require further validation in a large prospective cohort of high-risk patients. Bearing that in mind, the ELEGANCE study aims to be the world's 1st prospective cohort study that explores the potential of miRNA, microbiome, metabolome and imaging biomarkers to be used as diagnostic biomarkers for the early detection of HCC in 2,000 high-risk patients. In addition, the ELEGANCE study will also conduct a first-in-the-world investigation on the possibility of these biomarkers to monitor the progression of chronic liver disease, with the goal of providing heightened surveillance to patients who are most at risk of developing HCC. Furthermore, the AHCC11 PROSECT study enrolls 100 earl HCC patients scheduled for surgical resection, thereby acting as a parallel surgical arm and a positive control to the ELEGANCE cohort.

Participating Sites

- Singapore General Hospital (SGH)
- Changi General Hospital (CGH)
- National Cancer Centre Singapore (NCCS)
- National University Hospital (NUH)
- Sengkang General Hospital (SGH)
- Tan Tock Seng Hospital (TTSH)
- Singhealth Polyclinics (SHP)
  - Bedok
  - Bukit Merah
  - Marine Parade
  - Outram
  - Pasir Ris
  - Punggol
  - Sengkang
  - Tampines

Moreover, CT and MRI scans are the only available imaging modality to detect early HCC thus far. Of which, CT scans involve radiation and MRI scans with gadolinium contrast involves high costs and potential harmful accumulation in the brain. Thus a better imaging modality is urgently needed for early HCC detection.

STUDY AIMS

- To develop the 1st miRNA in-vitro diagnostic (IVD) kit for HCC with higher sensitivity and better ease of use compared with the extant standard of care surveillance: combination of serum AFP and US
- To develop an AI algorithm with MRI to predict individual risks of HCC within a specific timeline
- To stratify individual patient risks of disease progression and the development of HCC
- To identify microbiome and metabolome that can predict HCC development
- To identify potential therapeutic targets in the microbiome and metabolome where intervention can prevent HCC development and slow the progression of liver diseases.

UPDATES CURRENT STUDIES

AHCC10 ELEGANCE CONTINUED

STUDY DESIGN

The study recruits 2,000 high-risk patients that harbor any of the following: (i) cirrhosis; (ii) hepatitis B; (iii) hepatitis C and (iv) NASH/NAFLD. The cohort will be followed up 6 monthly for up to 3 years. To meet the stated robust aims of the study, the AHCC Trials Group is in collaboration with various academic and industrial partners.

MEDIA

THE STRAITS TIMES

Monday, August 02, 2021

Aim to recruit 2,000 study participants by early next year

FROM B1

If these patients develop HCC during the monitoring period, they can receive treatment and continue contributing data to the study.

There are no costs incurred from participating in the study, unless participants develop HCC and seek treatment.

The study will include input from SGH, the National University Hospital (NUH), Changi General Hospital, Sengkang General Hospital and Tan Tock Seng Hospital.

In addition to the hospitals, eight SingHealth polyclinics will serve as recruitment sites, while academic institutions, namely Duke-NUS Medical School and the Singapore Phenome Centre, will also be collaborating.

More than 200 participants have been recruited since April. The study aims to reach 2,000 individuals by early next year.

Early diagnosis of HCC has been challenging, given the lack of validated diagnostic, predictive and prognostic biomarkers.

Diagnostic biomarkers help to determine the presence of HCC, while prognostic types provide information on the patient's overall cancer outcome.

Predictive biomarkers identify the treatment the patient is most likely to benefit from.

Emerging data suggests that changes in the stool (microbiome), blood and urine (metabolome) may be indicative of HCC.

Building an AI algorithm that leverages magnetic resonance imaging scans may help predict the risk of developing HCC, thereby allowing for personalised surveillance and treatment.

The study has three tracks. First, it will evaluate the efficacy of a microRNA (miRNA) diagnostic kit developed by Singapore-headquartered molecular diagnostic company MiRXES for more accurate diagnosis of early-stage HCC.

Second, it will develop an AI algorithm to identify at-risk patients with digital medical technology company Perspectum.

Third, it will determine the changes in the microbiome and metabolome that lead to HCC with precision gut microbiome company AMiLi.

MiRXES had, in 2019, received approval from the Health Sciences Authority for the world's first miRNA polymerase chain reaction test for early detection of gastric cancer.

Named Gastroclear, it has since served tens of thousands of patients in Singapore, China and other countries, saving lives by identifying early-stage gastric cancer in asymptomatic patients, said Dr Zhou Lihan, co-founder and chief executive of MiRXES.

"We are very excited to be part of this study and look forward to making this innovation accessible to millions of at-risk individuals," he added.

Associate Professor Dan Yock Young, a senior consultant in the division of gastroenterology and hepatology at NUH, said: "Liver

Non-alcoholic fatty liver disease, which has been on the rise globally, has been attributed to causes such as a more Western diet.

Some experts believe that an increased consumption of fructose (such as in soft drinks and cookies) has contributed significantly to this condition, Prof Chow said.

Media Release: Aim to recruit 2,000 study participants by early next year, Published in The Straits Times, 2 Aug 2021

Prof Pierce Chow: ELEGANCE study explores cutting-edge methods to detect liver cancer early and more accurately

Cara Yap, 5 July 2021

About the study

Called EarLy DEtection of HCC: miRNA, microbiome and imaGing biomArkers in the evolution of chroNiC livEr Disease in a high-risk prospective cohort (ELEGANCE), the four-year long study launched late last month will enroll 2,000 participants at risk for HCC. These include patients with liver cirrhosis, hepatitis B or C, non-alcoholic fatty liver disease (NAFLD) or non-alcoholic steatohepatitis (NASH). The study involves public and private sector collaboration and has three tracks: 1) to evaluate the efficacy of a miRNA diagnostic kit for HCC with Singapore-headquartered multi-cancer early detection company MiRXES; 2) to develop an AI algorithm for identification of patients at-risk of developing HCC using state-of-the-art quantitative MR imaging, with digital medical technology company, Perspectum, whose Asia Pacific headquarters are in Singapore; and 3) to determine the changes in the microbiome and metabolome that lead to HCC with Southeast Asian precision gut microbiome company AMiLi. The goal of all three tracks is early diagnosis, better and more cost effective methods for improved patient outcomes and the identification of novel therapeutic targets.

How to get enrolled in the study

The multi-centre study is open for recruitment at healthcare institutions including National Cancer Centre Singapore (NCCS), Singapore General Hospital (SGH), National University Hospital (NUH), Changi General Hospital (CGH), Sengkang General Hospital (SKH), Tan Tock Seng Hospital (TTSH) and eight SingHealth Polyclinics (Bedok, Bukit Merah, Marine Parade, Outram, Pasir Ris, Punggol, Sengkang and Tampines). For more information on the study and eligibility, please contact the study's coordinators at +65 6326 6573 or drop them an email at ahcc10@nccs.com.sg

Media Release: ELEGANCE Study aims, Published in Oncoshot Online, 4 Jul 2021

跨机构四年肝癌研究 招募2000高风险患者参与

订户

来自 / 联合早报

文 / 王颖卿

发布 / 2021年5月5日 5:00 AM

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新加坡国立癌症中心自上月底展开为期四年的肝癌研究，计划下来10个月内招募2000名肝细胞癌高风险患者参与，研究如何更准确地诊断出早期肝细胞癌及评估个人患肝细胞癌的可能性。

Media Release: Introduction to the ELEGANCE Study, Published in Lianhe Zaobao, 5 May 2021

THE STRAITS TIMES

Monday, August 02, 2021

SINGAPORE 84

Protecting the liver

Nationwide study to aid early detection of primary liver cancer

Media Release: Nationwide study to aid early detection of primary liver cancer, Published in The Straits Times, 2 Aug 2021

UPDATES CURRENT STUDIES

AHCC11 Prospective Cohort Study of Changes in Circulatory MicroRNA after Surgical Resection of HCC

Clinicaltrials.gov Identifier: NCT05148572

Status: As of November 2022, the study has enrolled more than 15 patients out of the targeted 100.

The study serves as a positive control to validate the findings in the AHCC10 ELEGANCE study, where 100 histologically-proven HCC patients who are scheduled for surgical resection are enrolled. Progressive changes in the profiles of miRNA signatures pre- and post-surgical resection will be determined in hopes to identify signatures that could predict recurrence. Additionally, the study also aims to uncover key metabolites predictive of recurrence.

PARTICIPATING SITES

- Changi General Hospital (CGH)
- National Cancer Centre (NCC)
- National University Hospital (NUH)
- Singapore General Hospital (SGH)
- Sengkang General Hospital (SKH)
- Tan Tock Seng Hospital (TTSH)

STUDY AIMS

- To investigate whether the miRNA biomarkers predictive of HCC in a high-risk cohort (AHCC10 ELEGANCE patients) will revert back to non-HCC signatures post-surgical resection
- To determine if the same miRNA signatures that are used to predict HCC occurrence in a high-risk cohort (AHCC10 ELEGANCE patients) can also be used to predict HCC recurrence
- To identify novel signatures that can predict HCC recurrence
- To discover key metabolites that can predict recurrence of HCC and to correlate changes in choline, bile acid and tryptophan metabolic pathways with changes in the composition and function of gut microbiota

STUDY DESIGN

100 patients histologically diagnosed with early HCC and scheduled for surgical resection will be enrolled from 6 hospitals in Singapore. Patients will have their pre and post-surgical resection biosamples (plasma, urine and stool) collected for research purposes.

MEDIA


THE STRAITS TIMES

Monday, August 02, 2021

SINGAPORE 84

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Nationwide study to aid early detection of primary liver cancer

Media Release: Nationwide study to aid early detection of primary liver cancer, Published in The Straits Times, 2 Aug 2021

UPDATES CURRENT STUDIES

AHCC12 EMPHASIS and AHCC13 Precision Medicine in Liver Cancer across an Asia-Pacific Network 2.0

Clinicaltrials.gov Identifier: NCT05516628

Study status: Recruitment is projected to start in the 1st quarter of 2023

PLANet 2.0 is awarded the National Medical Research Council Open Fund – Large Collaborative Grant (NMRC OF-LCG) on 1 June 2022. This is a whole-of-nation, multi-disciplinary collaboration comprising of experts from different scientific fields (epigenomics, genomics, immunomics, metabolomics, proteomics, clinical trials and data science) from renown research institutes in Singapore (Genome Institute of Singapore (GIS), Institute of Molecular and Cell Biology (IMCB), Cancer Science Institute (CSI) and Duke-NUS Medical School).

The lack of validated predictive biomarkers remains as one of the most pressing unmet clinical need in HCC currently, that prevents better clinical outcomes for patients. The absence of predictive biomarkers can be attributed to the lack of useful adjuvant therapy after potentially curative therapies such as resection, radiofrequency ablation and transplantation, as well as the existence of a highly heterogeneous genome in HCC. In fact, the high intra-tumoral heterogeneity (ITH) was validated in the PLANet 1.0 programme (AHCC07), who's study strategy is based on the multi-region sampling of resected HCC. The PLANet 1.0 programme revealed many insights into the landscape of HCC tumors, including the onco-fetal immune evasion pathway adopted in HCC tumors and indeed the presence of a highly heterogeneous genome, where a single biopsy is not sufficient to provide a holistic picture of the tumor.

As such, the renewed PLANet 2.0 programme serves as a natural progression of scientific inquiries, and builds on the insights gained from PLANet 1.0. PLANet 2.0 leverages on two prospective therapeutic studies – the AHCC12 EMPHASIS study and AHCC13 (leveraging on AHCC09 STRATUM) – with these 2 studies covering the entire spectrum of HCC.

The AHCC12 EMPHASIS study enrolls patients with histologically-proven HCC scheduled for surgical resection, and who are at a high risk of recurrence. During surgery, multiple sections of the tumor will be collected for sampling in light of the high ITH in HCC as established in PLANet 1.0, and patients will be given Atezolizumab (anti-PD-L1) and Bevacizumab (anti-VEGF) in an adjuvant setting thereafter.

Participating Sites

- Singapore General Hospital (SGH)
- Changi General Hospital (CGH)
- National Cancer Centre Singapore (NCCS)
- National University Hospital (NUH)
- Sengkang General Hospital (SGH)
- Tan Tock Seng Hospital (TTSH)

Participating Institutes

- Genome Institute of Singapore (GIS)
- Institute of Molecular and Cell Biology (IMCB)
- Cancer Science Institute (CSI)
- Duke-NUS Medical School

UPDATES CURRENT STUDIES

PLANET 2.0 CONTINUED

The AHCC13 study leverages on the patient pool in AHCC09 STRATUM, which enrolls patients with locally advanced HCC, who are no longer eligible for surgical resection. These patients will be given loco-regional radiation (SRIT-Y90) followed by systemic therapy (Atezolizumab and Bevacizumab) or placebo. Throughout both the AHCC12 and AHCC13 studies, patient biosamples will also be collected longitudinally. This highly integrated and multi-orthogonal approach adopted in PLANet 2.0 provides us with an opportunity to elucidate and definitively validate predictive biomarkers, and also uncover cellular mechanisms and interactions that underpins recurrence, response and resistance to treatment. All of which opens a window of opportunity that enables patient stratification and selection to improve HCC patient prognosis

5 RESEARCH THEMES UNDER PLANET 2.0

- Theme 1: Deep Phenotyping and Correlation with Clinical Responses to Therapy – Led by Pierce CHOW Kah-Hoe (NCCS) and Prof Patrick TAN (GIS)
- Theme 2: Elucidating Spatial Distribution of Biomarkers at single-cell resolution – Led by Prof Vinay TERGAONKAR (IMCB)
- Theme 3: Translational and Functional Immunomics – Led by A/Prof TOH Han Chong (NCCS)
- Theme 4: Pre-Clinical Disease Modelling and Target Discovery – Led by Dr TAM Wai Leong (GIS) and Dr Edward CHOW Kai-Hua (CSI, NUS)
- Theme 5: Data Architecture, Data Security and Data Science Applications – Led by Prof Roger D. VAUGHAN (Duke-NUS)

MEDIA

S'pore dedicates $25m to liver cancer research to find targeted treatments

Shabana Begum

SINGAPORE - Singapore is dedicating $25 million to liver cancer research in a new five-year programme led by the National Cancer Centre Singapore (NCCS) that aims to find the best treatments for the disease.

The team, comprising researchers from various institutions, will work to uncover biomarkers produced by the body or tumour so that specific therapies can be created to combat the most common type of liver cancer known as hepatocellular carcinoma (HCC).

The research programme and the $25 million grant for it were announced in a media briefing on Monday (June 13).

Media Release: S'pore dedicates $25m to liver cancer research to find targeted treatments, Published in The Straits Times, 14 Jun 2022

多学科团队合作确认相关生物标记

我国拨2500万元研究改善肝癌疗法

及早发现患肝癌 男子术后复原良好

Media Release: 我国拨2500万元研究改善肝癌疗法, Published in Lianhe Zaobao, 14 Jun 2022

PAST MULTI-CENTRE TRIALS OF THE AHCC TRIALS GROUP

AHCC08 The Insight Study (NCT03233360)

- Status: Completed recruitment of 2533 patients in December 2019. Preliminary results were presented at ASCO 2018, ILCA 2018, ASCO GI 2019, APPLE 2019, EWALT 2019 and APASL 2022. Publication in progress.
- Number of participating centres: 33 centres from Singapore, Australia, China, Hong Kong, Japan, New Zealand, South Korea, Taiwan and Thailand

AHCC07 Precision Medicine in Liver Cancer across an Asia-Pacific Network (NCT03267641)

- Status: Completed recruitment of 147 patients in January 2021. Two main publication Gut, Nat Commu, Proc Natl Acad Sci and Biomaterials.
- Number of participating centres: 7 centres from Singapore, Malaysia, Philippines and United States of America

AHCC06 Phase III Multi-Centre Open-Label Randomized Controlled Trial of Selective Internal Radiation Therapy (SIRT) Versus Sorafenib in Locally Advanced Hepatocellular Carcinoma (NCT01135056)

- Status: Completed recruitment of 360 patients in May 2016. Published in Journal of Clinical Oncology 2 March 2018. doi: 10.1200/JCO.2017.76.0892 and BMC 7 November 2016 doi: 10.1186/s12885-016-2868-y.
- Number of participating centres: 29 centres from Singapore, Brunei, Indonesia, Malaysia, Mongolia, Myanmar, New Zealand, Philippines, South Korea, Taiwan and Thailand

AHCC05 Phase I/II Study of SIR-Spheres plus Sorafenib (Chemo-Radiotherapy) as First Line Treatment in Patients with Non-Resectable Primary Hepatocellular Carcinoma (NCT00712790)

- Status: Completed recruitment of 35 patients in June 2009. Published in PLoS ONE 2014 9(3):e90909. doi: 10.1371/journal.pone.0090909.
- Number of participating centres: 5
-

AHCC04 Phase II Dose Escalating Trial of Intra-Tumoral BrachySil in Unresectable Hepatocellular Carcinoma (NCT00247260)

- Status: Completed. Results Published in International Journal of Radiation Oncology *Biology* Physics Vol. 67, Issue 3, 1 March 2007; 786-792.
- Number of participating centres: 6

AHCC03 Randomised Trial of Adjuvant Intra-Arterial Radio-Active Iodine after Curative Resection of Hepatocellular Carcinoma (NCT00027768)

- Status: Completed recruitment of 103 patients in March 2007. Published in World J Surg 6 March 2013: 1-6.
- Number of participating centres: 4

PAST MULTI-CENTRE TRIALS OF THE AHCC TRIALS GROUP

AHCC02 Randomized Double Blind Trial of Megestrol Acetate versus Placebo for the Treatment of Inoperable Hepatocellular Carcinoma (NCT00041275)

- Status: Completed recruitment of 204 patients in 2007. Results published in Br J Cancer 2011 September 27;105(7): 945–952.
- Number of participating centres: 8

AHCC01 Randomised Trial of Tamoxifen versus Placebo for the Treatment of Inoperable Hepatocellular Carcinoma (NCT00003424)

- Status: Completed recruitment of 324 patients in June 2000. Results published in Hepatology 2002 36:1221-1226.
- Number of participating centres: 11

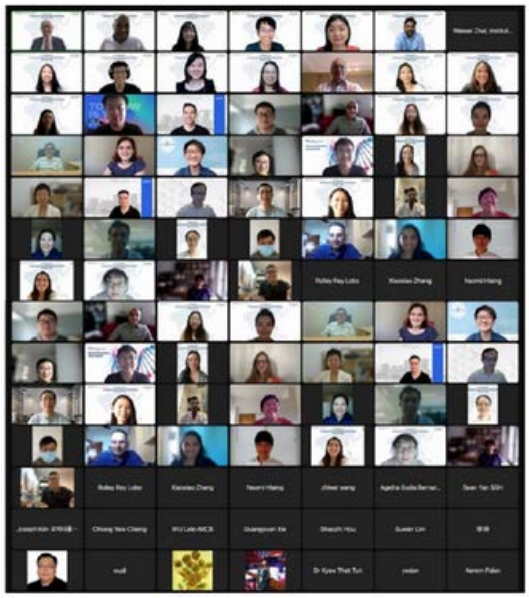
ABOUT THE AHCC TRIALS GROUP

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. These clinicians share a common goal of seeking novel treatments for HCC and recognised the urgency and necessity for collaboration so that more efficacious therapies can be developed for the large number of HCC patients. Together with the strong alliances formed with both industry and academia, the mission of the AHCC network is to conduct preventive and therapeutic trials in HCC, carry out translational research in this field and develop training and educational programs pertaining to HCC. With these objectives, the 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 next general meeting and symposia will be coming your way in Q2 of 2023.

By maintaining a close working relationship with academic researchers and industry partners, the AHCC Trials Group and members within it can leverage on complementary strengths and work together to design and plan clinical trials and studies that lead to better HCC patient prognosis and clinical outcomes.

Since the conception of the AHCC Trials Group in 1997, the AHCC Trials Group Secretariat led by Prof Pierce Chow has been involved in the general administration and management of the AHCC Trials Group network. The Secretariat has been maintaining the network registry, website, social media sites and the publishing of the periodic Trials Group newsletters to keep the group abreast of any developments and happenings across the network. Lastly, the AHCC Trials Group will like to thank all the members and collaborators for their support throughout the year as well as a good, fruitful and successful 2023 ahead!

The 3th Symposium of the SLCC and the AHCC Trials Group 12th General Meeting on 3 May 2019



The 4th SLCC Symposium held on 26 March 2022, despite the ongoing COVID-19 situation

AHCC Trials Group Website: http://www.scri.edu.sg/crn/asia-pacific-hepatocellular-carcinoma-ahcc-trials-group/about-ahcc/

THE AHCC TEAM

[From left to right]
Jacelyn Chua, Chen Gao Bin, Sekar Karthik, Ling Wen Huan, Dr Chen Kaina, Chew Sin Chi, Prof Pierce Chow, Chong Shay Lee, Cheryl Chua, Fiona Ni Ni Moe, Kyra Yeo, Aileen Tay, Seshachalam Pratap, Ong Xiao Quan, Han Qingguang, Sim Yu Ki, Evelyn Chiew, Jade Goh, Ashley Ng, Wu Ling Yan

The strength of the AHCC Trials Group lies in its spread of collaborating centres and its track record of successfully completed trials. We would like to thank all our AHCC Trials Group members, the study team members and our collaborators for the support and trust in the past 25 years. We look forward to another exciting year ahead as we continue to strive to improve the clinical landscape in HCC through the AHCC09, AHCC10, AHCC11, AHCC12 and AHCC13 studies.

CONTACT DETAILS

For further queries, please contact the AHCC Trials Group at

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