THE Asia-Pacific Hepatocellular Carcinoma Trials Group

2025

THE AHCC TRIALS GROUP NEWSLETTER

2025 has been yet another remarkable year for the AHCC Trials Group. On 21st August, we came together for the 15th AHCC Trials Group General Meeting held in conjunction with 7th Singapore Liver Cancer Consortium (SLCC) Scientific Symposium, marking another successful gathering of our vibrant community of collaborators and researchers.

Throughout the year, the Trials Group has been actively expanding its reach, initiating new sites, and enrolling patients into our ongoing studies: (i) AHCC10 ELEGANCE; (ii) AHCC11 PROSECT; (iii) AHCC09 STRATUM; (iv) PLANET 2.0 AHCC12 EMPHASIS; and (v) AHCC13. In addition to that, we have also continuously generated high-level scientific findings and research publications from our completed studies: (i) AHCC07 PLANet 1.0 and (ii) AHCC08 INSIGHT.

With the progression of the AHCC09 STRATUM multinational Phase II randomized controlled clinical trial, the AHCC Trials Group has gone on to establish deeper collaborations with several overseas academic centers and healthcare institutions. This expansion has brought our network to an impressive 64 centers across 17 countries in the Asia-Pacific region—a testament to the Trials Group's growth since its establishment 28 years ago.

Fostering strong partnerships and camaraderie amongst members of the Trials Group has always been a cornerstone of our mission. Together, we strive to create a collaborative platform for meaningful scientific and medical discussions aimed at developing innovative treatment strategies for HCC.

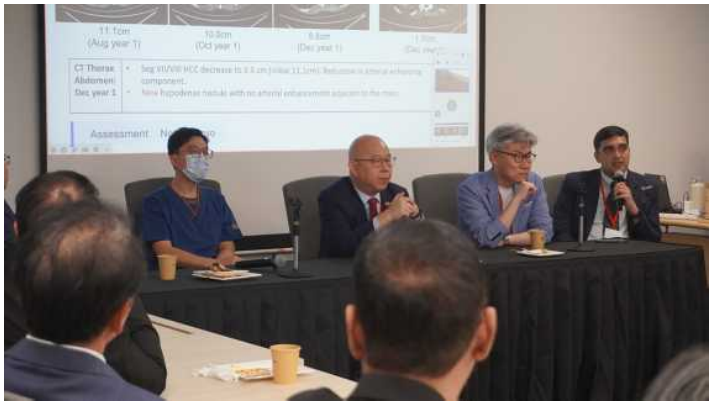
We would like to extend our heartfelt gratitude to every member of the Trials Group for your unwavering support and dedication, especially during the challenging years when in-person gatherings were not possible. Your contributions have been instrumental in driving the growth and success of the Group. Here's to continued progress and exciting milestones ahead!

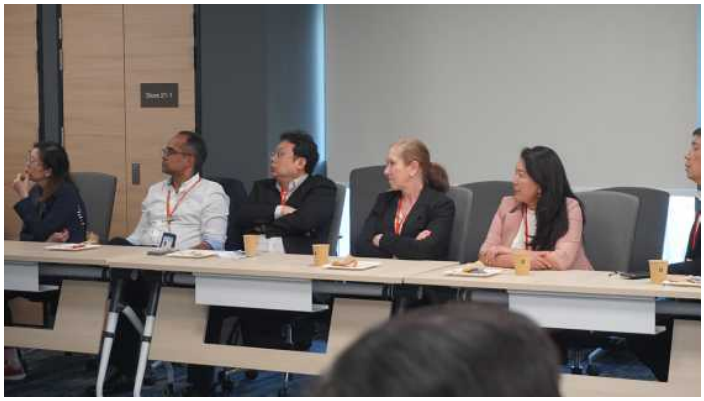
CONTENTS

HAPPENINGS

AHCC TRIALS GROUP 15TH GENERAL MEETING & 7TH SCIENTIFIC SYMPOSIUM OF SLCC

The AHCC Trials Group held its annual General Meeting on 21st August 2025, bringing together over 40 Trials Group members from across the region, marking this year the 15th AHCC Trials Group General Meeting since its inception. In conjunction with the Trials Group General Meeting, the 7th Symposium of the Singapore Liver Cancer Consortium (SLCC) also took place with over 150 researchers, clinicians, healthcare professionals and industry collaborators in attendance. An annual affair, this year's meeting and symposium took place at the new National Cancer Centre Singapore (NCCS) building, which also houses the AHCC Trials Group secretariat.





During the symposium, members and collaborators shared insights into the latest clinical advancements in HCC treatment and presented scientific findings from translational research based on our ongoing studies. The vibrant discussions and exchange of knowledge underscored the value of in-person collaborative platforms in driving impactful clinical research and fostering meaningful partnerships.

UPDATES – ONGOING STUDIES

AHCC09 STRATUM

A multi-national, double-blind, placebo-controlled, parallel randomized arms, phase II trial to compare the safety and efficacy of SIRT-Y90 followed by atezolizumab plus bevacizumab versus SIRT-Y90 followed by placebo in patients with locally-advanced HCC

Clinicaltrials.gov identifier: NCT05377034

Participating sites: 15 recruiting sites from Singapore, South Korea, Taiwan and China

Singapore
- National Cancer Centre Singapore (NCCS)
- National University Hospital (NUH)

Taiwan
- National Taiwan University Cancer Centre
- National Taiwan University Hospital
- Taipei Veterans General Hospital
- Taichung Veterans General Hospital
- Kaohsiung Chang Gung Memorial Hospital

South Korea
- Seoul National University Hospital (SNUH)
- Severance Hospital, Yonsei University Health System
- Samsung Medical Center

China
- Beijing Tsinghua Changgung Hospital
- West China Hospital, Sichuan University
- (new) People's Liberation Army General Hospital (301 and 6th Medical Centre)
- (new) Shandong Cancer Hospital

STUDY STATUS

The study has been enrolling patients from all 4 participating countries, with 13 sites actively recruiting. In 2025, the trial saw the inclusion of 3 new sites from China. While remaining negotiations and approvals are underway, the AHCC Trials Group is excited to warmly welcome our additional members onboard the study to boost recruitment rates.

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.

As of December 2025, 132 patients have been screened, of which 72 have received Y-90 and have been randomised. This would not have been possible without the efforts of all recruiting sites. With their continued support, the study is slated to end recruitment in the upcoming year. Additionally, a few major changes were implemented in the study. Firstly, the original target recruitment of 176 has been updated to 100 in view of our industry partner's interests. With the same considerations, some endpoints of interest have been revised to include 9-month analysis as demonstrated in the study aims on page 4. In terms of safety, the 3rd Data Safety Monitoring Board meeting is scheduled for January 2026 to ensure the trial's continued adherence to safety standards, safeguarding all study patients' interest.

UPDATES – ONGOING STUDIES

AHCC09 STRATUM

STUDY DESIGN

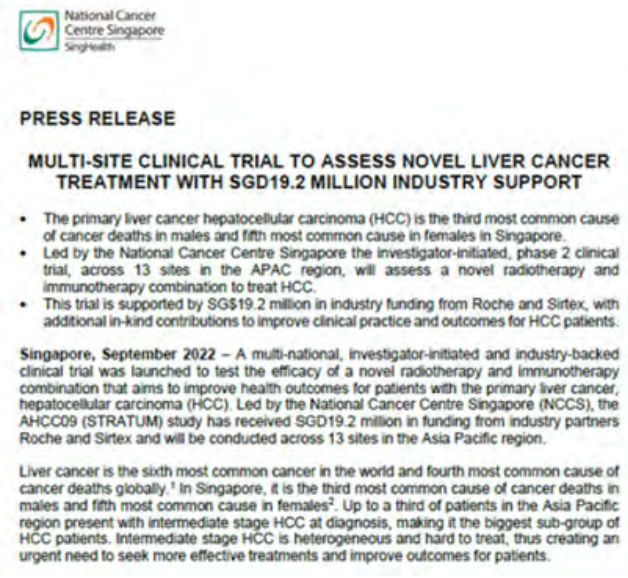
This is a phase II randomized placebo-controlled clinical trial, enrolling an estimated 100 locally advanced HCC patients from up to 15 sites from the Asia-Pacific Hepatocellular Carcinoma (AHCC) Trials Group. Proposed sites include those in Singapore, China, South Korea, and Taiwan. All 100 patients 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.

STUDY AIMS

To compare the best overall response rate (BORR) at 9-, 12- and 18-months post-randomization

- **To investigate the sustained response and disease control rate at 9-, 12- and 18- months post-randomization**
- **To investigate the time to response and progression**
- **To investigate the progression-free survival (PFS), overall survival (OS) and health-related quality of life at 12- and 18-months post-randomization**
- **To investigate the quality-adjusted life years at 18m**
- **To elucidate the safety profile of atezolizumab plus bevacizumab in a systemic setting after loco-regional therapy**

MEDIA RELEASE



National Cancer Centre Singapore
SingHealth

PRESS RELEASE

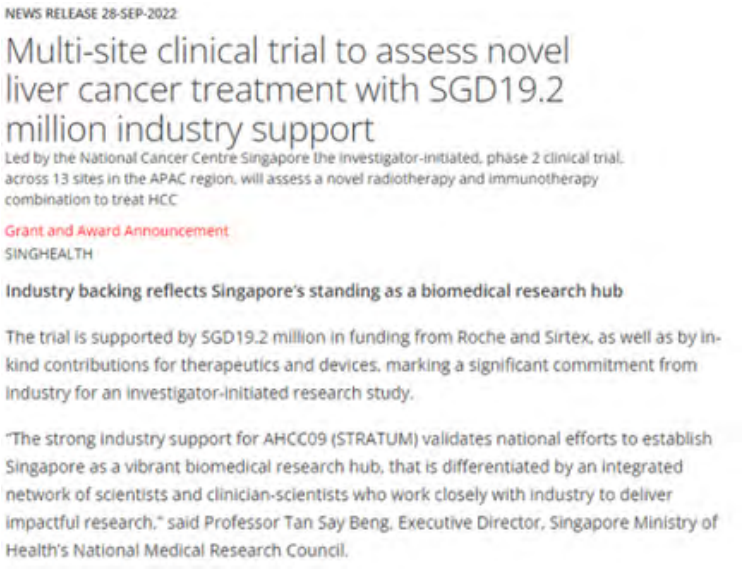
MULTI-SITE CLINICAL TRIAL TO ASSESS NOVEL LIVER CANCER TREATMENT WITH SGD19.2 MILLION INDUSTRY SUPPORT

- 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

UPDATES – ONGOING STUDIES

AHCC10 ELEGANCE

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

Participating sites:

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

STUDY STATUS

As of March 2025, the study has completed recruitment, with a final cohort of 2002 patients.

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 early HCC patients scheduled for surgical resection, thereby acting as a parallel surgical arm and a positive control to the ELEGANCE cohort.

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 as well.

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 – ONGOING STUDIES

AHCC10 ELEGANCE

STUDY DESIGN

The study recruits 2,002 high-risk patients that harbor any of the following: (1) cirrhosis; (2) hepatitis B; (3) hepatitis C; (4) 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.

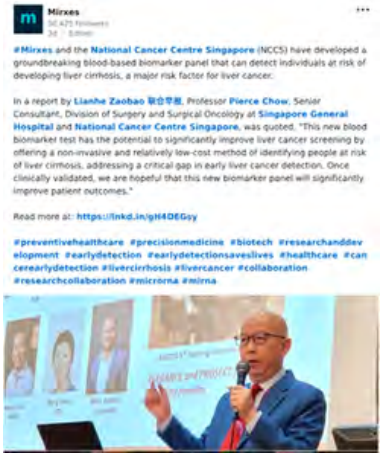
PRESENTATIONS

- **Multi-parametric MRI (mpMRI) identified chronic hepatitis B patients with subclinical liver inflammation, 28 Mar 2024, Asian Pacific Association for the Study of the Liver (APASL) 2024**
-
- **Diagnostic accuracy of microRNAs as non-invasive biomarkers for the diagnosis of liver cirrhosis, 30 Mar 2024, Asian Pacific Association for the Study of the Liver (APASL) 2024**
- **Microbiome in Development of HCC, 21 August 2025, 7th Singapore Liver Cancer Consortium (SLCC) Scientific Symposium 2025, Lee. J**
- **Integrative Metagenomic and Metabolomic Profiling Reveals Potential Biomarkers for Early Detection of Hepatocellular Carcinoma (HCC), 19-20 September 2025, SingHealth DUKE-NUS Scientific Congress 2025**
- **From Biopsy to Biomarkers: The Past, Present and Future of Non-invasive Quantitative Imaging Biomarkers, 20 November 2025, Asia Pacific Digestive Week (APDW) Perspectum Breakfast Symposium 2025**

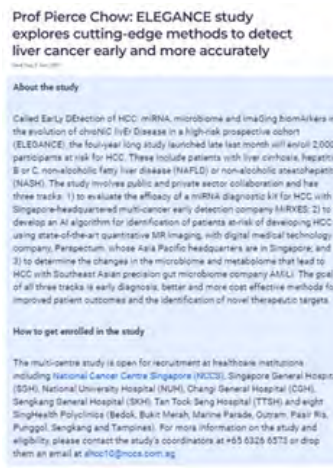
ABSTRACT SUBMISSION

- **Quantifying increased confidence in ruling out HCC using liver function tests and quantitative MRI, APASL 2025 Wang Y.C., Brady M., Chow P.K.H., et al**
- **qMRI enhances standard-of-care for hepatocellular carcinoma detection: proof-of-concept using Bayesian networks, ISMRM 2025 Wang Y.C., Wong Y.J., Brady M., Chow P.K.H., et al**

MEDIA RELEASE



A new blood-based biomarker panel is under development by Mirxes and NCCS such that liver cirrhosis can be identified and treated in its earliest stages.



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

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

UPDATES – ONGOING STUDIES

AHCC11 PROSECT

Prospective cohort study of changes in circulatory miRNA after surgical resection of HCC.

Clinicaltrials.gov identifier: NCT05148572

Participating sites:

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

STUDY STATUS

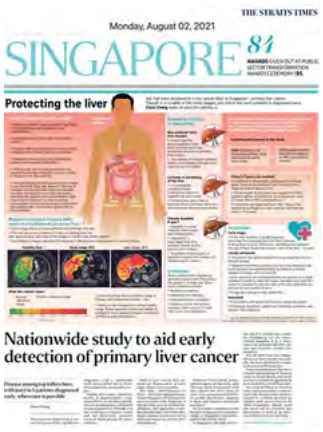
As of April 2025, the study has completed recruitment, with a final cohort of 101 patients.

The study serves as a positive control to validate the findings in the AHCC10 ELEGANCE study, where 101 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.

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**

MEDIA RELEASE


THE STRAITS TIMES

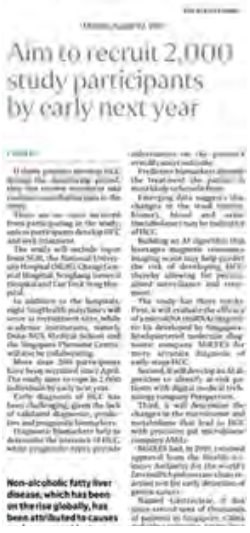
Monday, August 02, 2021

SINGAPORE 81

Protecting the liver

Nationwide study to aid early detection of primary liver cancer

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


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

Non-alcoholic fatty liver disease, which has been on the rise globally, has been attributed to causes

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

STUDY DESIGN

101 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.

UPDATES – ONGOING STUDIES

AHCC12 EMPHASIS & AHCC13: PRECISION MEDICINE IN LIVER CANCER ACROSS ASIA-PACIFIC NETWORK 2.0

Clinicaltrials.gov identifier: NCT05516628

Participating sites:

- Singapore General Hospital (SGH)
- Changi General Hospital (CGH)
- National Cancer Centre Singapore (NCCS)
- National University Hospital (NUH)
- Sengkang General Hospital (SKH)

Participating institutes:

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

PLANet 2.0 was 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 needs in HCC currently, which 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. Previously in the NMRC TCR PLANet 1.0 (AHCC07) which was the predecessor of the current PLANET 2.0 programme that we are now reporting on, we have banked a large amount of prospectively collected biosamples with very granularly curated clinical and multi-omics data from a cohort of 147 patients. These patients had surgical resection for hepatocellular carcinoma (HCC) and were closely followed-up after surgery. Consistent with the standard of care for HCC after surgical resection they did not receive adjuvant treatment after resection. We were thus able to explore the correlation between molecular phenotype and the natural clinical trajectory of surgically resected HCC. These patients (and samples) now serve as a control group and provide a solid basis for the renewal programme PLANet 2.0 where biosamples and multi-omics data are similarly collected in two prospective clinical trials which now receive best in-class therapies. These clinical studies serve as proof-of-concept to our translational findings. PLANet 2.0 focuses on spatial –omics which aims to lead to improved and nuanced understanding of the tumour microenvironment (TME).

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 Prof TOH Han Chong (NCCS)
- **Theme 4**: Pre-Clinical Disease Modelling and Target Discovery – Led by Dr TAM Wai Leong (GIS) and Dr Polly Chen (CSI, NUS)
- **Theme 5:** Data Architecture, Data Security and Data Science Applications – Led by A/Prof Liu Nan (Duke-NUS)

UPDATES – ONGOING STUDIES

AHCC12 EMPHASIS & AHCC13: PRECISION MEDICINE IN LIVER CANCER ACROSS ASIA-PACIFIC NETWORK 2.0

The AHCC12 EMPHASIS, which mirrors the IMbrave050 randomised, open-label, phase 3 study, enrolls patients with histologically-proven HCC scheduled for surgical resection, and who are at a high risk of recurrence. During surgery, multi-region sampling of the tumour is collected, and patients will be treated with atezolizumab (anti-PD-L1) and bevacizumab (anti-VEGF) in an adjuvant setting thereafter. On the basis of the updated IMbrave050 data announced in ESMO 2024 Barcelona, which reported that the initial RFS benefit with atezolizumab + bevacizumab vs active surveillance was not sustained over time, the team is currently amending the protocol to tighten the target population to include only patients with higher tumour burden (i) exceeding 'up-to-7' criteria HCC (ii) with macrovascular invasion (Vp1/Vp2).

The AHCC13 study leverages on the patient pool of 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 (SIRT-Y90) followed by systemic therapy (atezolizumab and bevacizumab) or placebo. Throughout both the AHCC12 and AHCC13 studies, patient biosamples (blood, urine and stool) will 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 for opportunity that enables patient stratification and selection to improve HCC treatment outcomes.

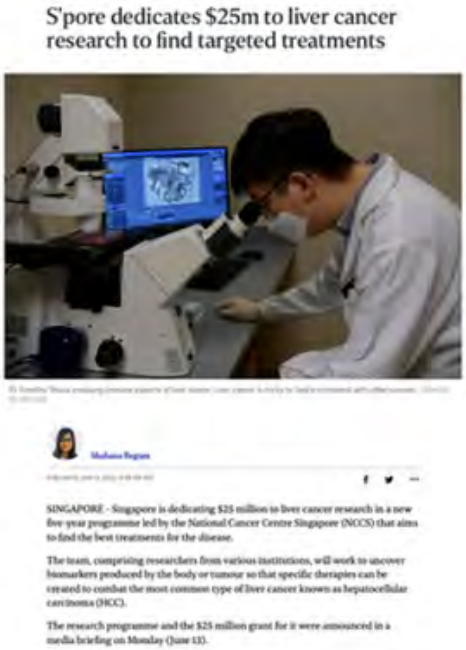
STUDY STATUS

As of December 2025, all 5 sites have been initiated for the AHCC12 EMPHASIS adjuvant atezolizumab plus bevacizumab trial. 37 patients have been screened and 7 patients have been enrolled into the adjuvant trial. For the AHCC13 translational study which leverages on the AHCC09 STRATUM study, 72 patients have been randomized and received the Y90 with or without atezolizumab plus bevacizumab. The longitudinal biosamples of these patients have been collected for translational investigation. As the study progresses, manuscript plans are underway with some in the review process - we look forward to a fruitful year ahead.

UPDATES – ONGOING STUDIES

AHCC12 EMPHASIS & AHCC13: PRECISION MEDICINE IN LIVER CANCER ACROSS ASIA-PACIFIC NETWORK 2.0

MEDIA RELEASE



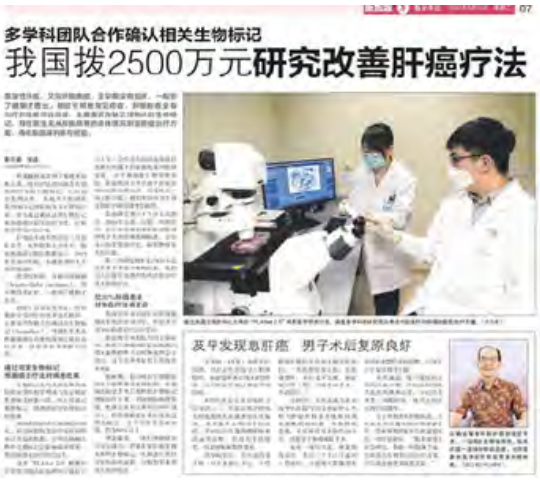
S'pore dedicates $25m to liver cancer research to find targeted treatments

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

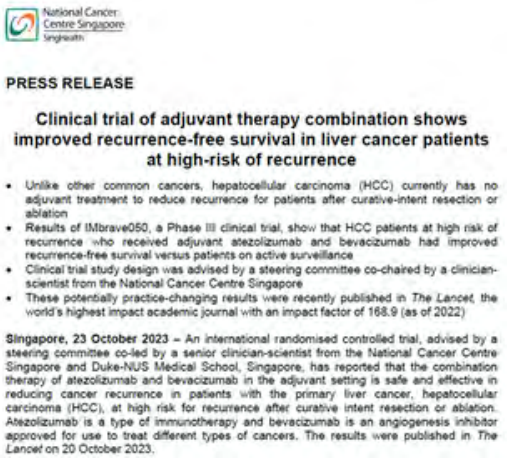


多学科团队合作确认相关生物标记

我国拨2500万元研究改善肝癌疗法

及早发现息肝癌　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



National Cancer Centre Singapore
Singhealth

PRESS RELEASE

Clinical trial of adjuvant therapy combination shows improved recurrence-free survival in liver cancer patients at high-risk of recurrence

- Unlike other common cancers, hepatocellular carcinoma (HCC) currently has no adjuvant treatment to reduce recurrence for patients after curative-intent resection or ablation
- Results of IMbrave050, a Phase III clinical trial, show that HCC patients at high risk of recurrence who received adjuvant atezolizumab and bevacizumab had improved recurrence-free survival versus patients on active surveillance
- Clinical trial study design was advised by a steering committee co-chaired by a clinician-scientist from the National Cancer Centre Singapore
- These potentially practice-changing results were recently published in *The Lancet*, the world's highest impact academic journal with an impact factor of 168.9 (as of 2022)

Singapore, 23 October 2023 – An international randomised controlled trial, advised by a steering committee co-led by a senior clinician-scientist from the National Cancer Centre Singapore and Duke-NUS Medical School, Singapore, has reported that the combination therapy of atezolizumab and bevacizumab in the adjuvant setting is safe and effective in reducing cancer recurrence in patients with the primary liver cancer, hepatocellular carcinoma (HCC), at high risk for recurrence after curative intent resection or ablation. Atezolizumab is a type of immunotherapy and bevacizumab is an angiogenesis inhibitor approved for use to treat different types of cancers. The results were published in *The Lancet* on 20 October 2023.

Media Release: AHCC12 study closely mirrors the positive IMbrave050 trial published on *The Lancet* with Prof Pierce Chow listed as senior author

UPDATES – COMPLETED STUDIES

AHCC07 PRECISION MEDICINE IN LIVER CANCER ACROSS ASIA-PACIFIC NETWORK

Clinicaltrials.gov identifier: NCT03267641

STUDY 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).

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:

1. 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
2. Most driver mutations are non-truncal and display high ITH which explains current poor therapeutic efficacies in HCC
3. There is a co-existence of multiple transcriptomic sub-types in HCC where the worst subtype drives clinical trajectory and outcome
4. Distinct immunological microenvironments exist in HepB related HCC versus non-B-non-C HCC

RECENT PUBLICATIONS

- **Histone-lysine N-methyltransferase EHMT2 (G9a) inhibition mitigates tumorigenicity in Myc-driven liver cancer (2023); Mol Oncol**
  Thng DKH, Chow PKH, Chow EK, et al.
- **Multi-region sampling with paired sample sequencing analyses reveals sub-groups of patients with novel patient-specific dysregulation in Hepatocellular Carcinoma (2023); BMC Cancer**
  Jeon AJ, Foo RSY, Chow PKH, et al.
- **Splice-switch oligonucleotide-based combinatorial platform prioritizes synthetic lethal targets CHK1 and BRD4 against MYC-driven hepatocellular carcinoma (2022); Bioeng Transl Med**
  Thng DKH, Chow PK, Chow EK, et al.
- **IFNγ-IL-17+ CD8 T cells contribute to immunosuppression and tumor progression in human hepatocellular carcinoma (2022); Cancer Lett**
  Lee YH, Chow PKH, Chew V et al.

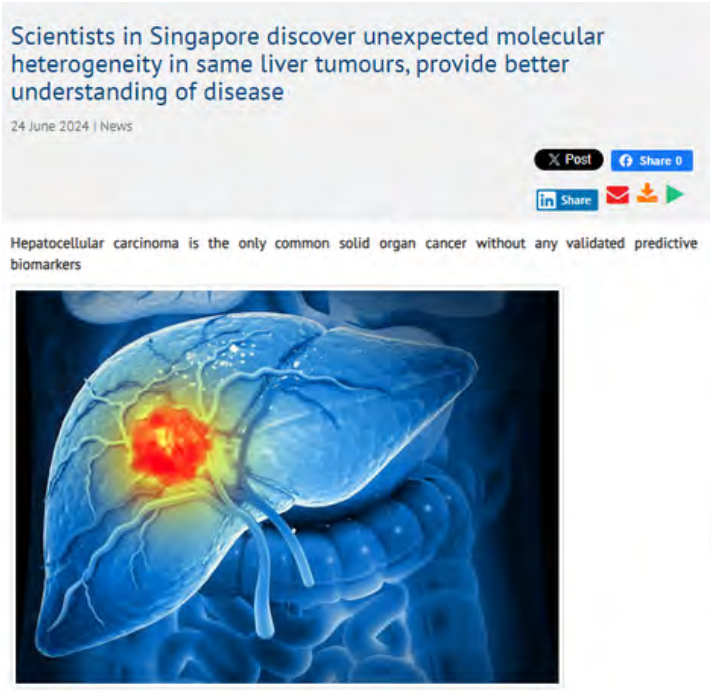
UPDATES – COMPLETED STUDIES

AHCC07 PRECISION MEDICINE IN LIVER CANCER ACROSS ASIA-PACIFIC NETWORK

Clinicaltrials.gov identifier: NCT03267641

PLANET

MEDIA RELEASE


Scientists in Singapore discover unexpected molecular heterogeneity in same liver tumours, provide better understanding of disease

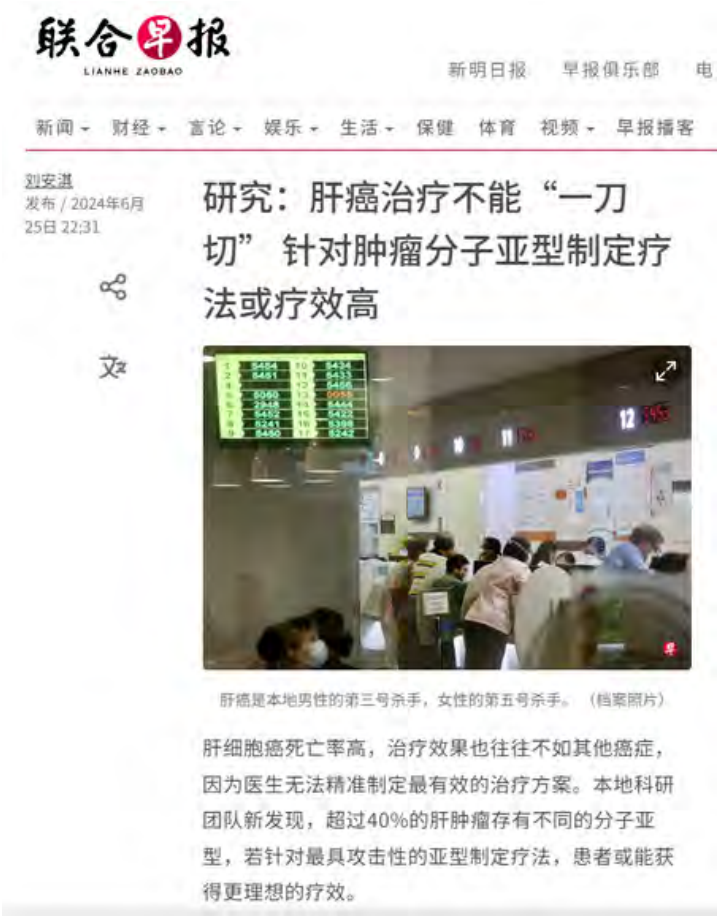
24 June 2024 | News

Post Share 0 Share

Hepatocellular carcinoma is the only common solid organ cancer without any validated predictive biomarkers

Media Release: Scientists in Singapore discover unexpected molecular heterogeneity in same liver tumours, provide better understanding of disease.
Published on BioSpectrum Asia on 24 June 2024

Media Release: “One size fits all" treatment for liver cancer insufficient, developing therapies targeting tumour molecular subtypes may be more effective 研究：肝癌治疗不能“一刀切” 针对肿瘤分子亚型制定疗法或疗效高 Published in Lianhe Zaobao on 25 June 2024


联合早报 LIANHE ZAOBAO

新明日报 早报俱乐部 电

新闻 财经 言论 娱乐 生活 保健 体育 视频 早报播客

刘安淇
发布 / 2024年6月25日 22:31

研究：肝癌治疗不能“一刀切” 针对肿瘤分子亚型制定疗法或疗效高

肝癌是本地男性的第三号杀手，女性的第五号杀手。（档案照片）

肝细胞癌死亡率高，治疗效果也往往不如其他癌症，因为医生无法精准制定最有效的治疗方案。本地科研团队新发现，超过40%的肝肿瘤存有不同的分子亚型，若针对最具攻击性的亚型制定疗法，患者或能获得更理想的疗效。

UPDATES – COMPLETED STUDIES

AHCC08 INSIGHT

Insight into real-world practice of management of HCC in Asia-Pacific

Clinicaltrials.gov identifier: NCT03233360

STUDY STATUS

Completed recruitment of 2533 participants in December 2019. Pending publications.

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

- **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**

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)**
- **Presentation at APPLE 2024, Honolulu, USA**
- **Presentation at EASL 2024, Milan, Italy**
- **Presentation at APPLE 2025, Kobe, Japan**

RECENT PUBLICATIONS

- **Real-World Data on the Diagnosis, Treatment, and Management of Hepatocellular Carcinoma in the Asia-Pacific: The INSIGHT Study (2023); Liver Cancer**
  Sim YK, Chong MC, Chow PKH, et al.

Participating sites from 9 countries:

Australia
- Royal Adelaide Hospital
- Royal Prince Alfred Hospital

Singapore
- National Cancer Centre Singapore (NCCS)
- National University Hospital (NUH)
- Singapore General Hospital (SGH)

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

Thailand
- National Cancer Institute
- Siriraj Hospital, Mahidol University

Taiwan
- China Medical University Hospital
- National Taiwan University Hospital
- Taipei Veterans General Hospital
- Taichung Veterans General Hospital
- Kaohsiung Chang Gung Memorial 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

South Korea
- Asan Medical Centre
- Korea University Anam Hospital
- Seoul National University Hospital (SNUH)
- Severance Hospital, Yonsei University Health System
- Samsung Medical Center
- St. Mary's Hospital
- St. Vincents Hospital
- Ajou University Hospital

LIST OF COMPLETED STUDIES

AHCC08 THE INSIGHT STUDY

Clinicaltrials.gov identifier: NCT03233360

- ***Protocol Chair: Prof Pierce Chow***
- ***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. First publication in October 2023, other publications 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

Clinicaltrials.gov identifier: NCT03267641

- ***Protocol Chair: Prof Pierce Chow***
- ***Status: Completed recruitment of 147 patients in January 2021. Main publications in Gut, Nat Comm, 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

Clinicaltrials.gov identifier: NCT01135056

- ***Protocol Chair: Prof Pierce Chow***
- ***Status: Completed recruitment of 147 patients in January 2021. Main publications in Gut, Nat Comm, Proc Natl Acad Sci and Biomaterials.***
- ***Number of participating centres: 7 centres from Singapore, Malaysia, Philippines and United States of America***

AHCC05 PHASE I/II STUDY OF SIR-SPHERES PLUS SORAFENIB (CHEMO-RADIOTHERAPY) AS FIRST LINE TREATMENT IN PATIENTS WITH NON-RESECTABLE PRIMARY HEPATOCELLULAR CARCINOMA

Clinicaltrials.gov identifier: NCT007127901

- ***Protocol Chair: Prof Pierce Chow***
- ***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***

LIST OF COMPLETED STUDIES

AHCC04 PHASE II DOSE ESCALATING TRIAL OF INTRA-TUMORAL BRACHYSIL IN UNRESECTABLE HEPATOCELLULAR CARCINOMA

Clinicaltrials.gov identifier: NCT00247260

- ***Protocol Chair: Prof Pierce Chow***
- ***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

Clinicaltrials.gov identifier: NCT00027768

- ***Protocol Chair: Prof London Ooi***
- ***Status: Completed recruitment of 103 patients in March 2007. Published in World J Surg 6 March 2013: 1-6.***
- ***Number of participating centres: 4***

AHCC02 RANDOMIZED DOUBLE BLIND TRIAL OF MEGESTROL ACETATE VERSUS PLACEBO FOR THE TREATMENT OF INOPERABLE HEPATOCELLULAR CARCINOMA

Clinicaltrials.gov identifier: NCT00041275

- ***Protocol Chair: Prof Pierce Chow***
- ***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

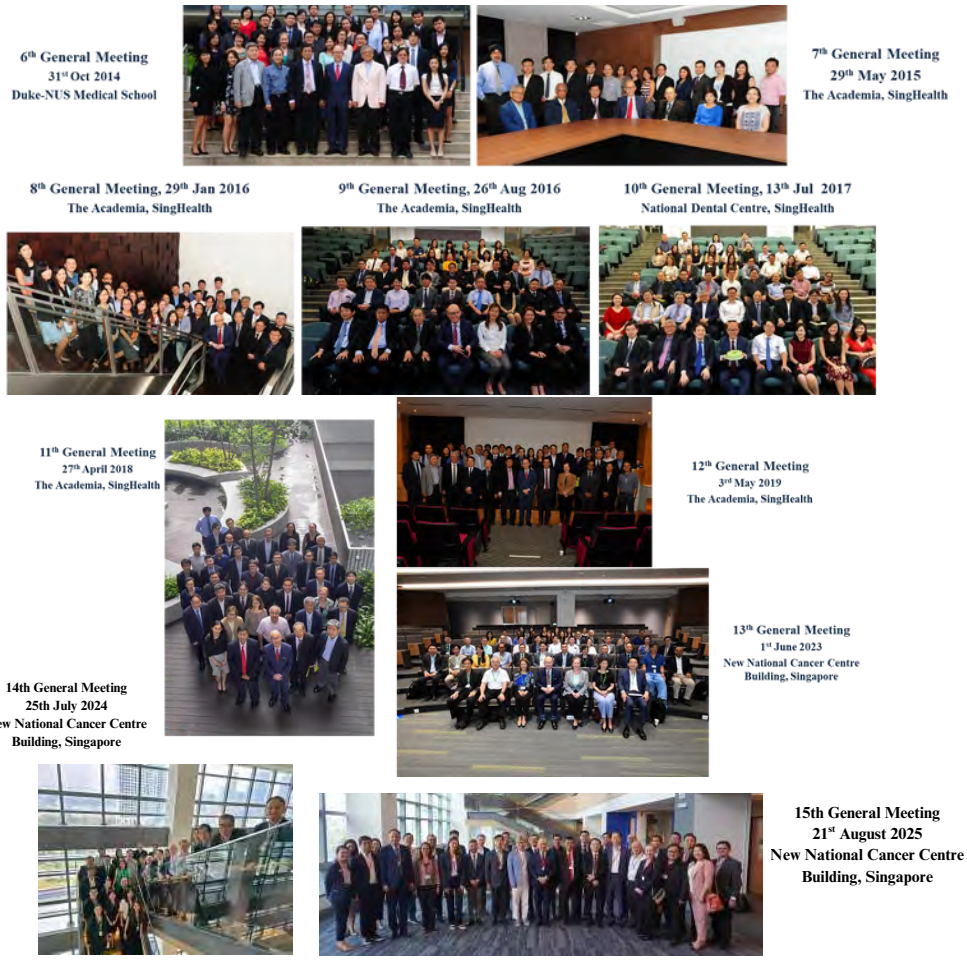
Clinicaltrials.gov identifier: NCT000034241

- ***Protocol Chair: Prof Pierce Chow***
- ***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 clinical research network formed in 1997 by clinicians from major medical centres in the Asia-Pacific region. These clinicians recognised the urgency and necessity for a collaborative platform for the initiation of clinical studies to develop novel treatment strategies for HCC.

The first randomised controlled trial of the group was initiated by the Singapore General Hospital as a single centre prospective HCC clinical trial which later expanded rapidly to a multi-centre trial in the Asia-Pacific region. This was the start to the development of more trials with the support from government funding agencies like the National Medical Research Council (NMRC) and collaborations with industry. The Trials Group has since launched 13 multi-centre trials and 1 real-world registry study with more than 60 participating centres from 17 countries.



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 this vision, the Trials Group holds annual general meetings and symposia to bring together international experts for the exchange of research ideas, clinical study proposals and networking.

With nearly 28 years of experience, the AHCC Trials Group comprises of clinicians, scientists, academics, coordinators, and related professionals with significant expertise in:

- Protocol development and feasibility evaluation;
- Budget allocation and contract negotiation;
- Managing ethical, regulatory and administrative procedures for clinical studies in various countries,
- Initiating, executing and maintenance of clinical and translational studies; and
- Data collection and analyses for studies.

THE AHCC TEAM

[From left to right, top to bottom]
Jia Ying Han, Evelyn Chiew, Dr Chen Gao Bin, Dr Ang Chow Hiang Alex, Dr Chew Sin Chi, Zhang Boya (Student), Dr Toh Qin Kane, Royston Liew (Student), Sekar Karthik, Carine Lim, Sim Yu Ki, Rachel Teo, Dr Chen Xinyu, Jacelyn Chua, Dr Wu Ling Yan, Ong Xiao Quan, Jade Goh, Chong Shay Lee, Prof Pierce Chow, Chew Suet Li, Weng Yuqi, Vennese Low, Ashley Ng, Yeo Zhi Hui, Fiona Ni Ni Moe

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 28 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 US

For further queries, please contact the AHCC Trials Group at Network Secretariat:
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