Liver Cancer

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The 8th Asia-Pacific Primary Liver Cancer Expert Meeting (APPLE 2017)

The Art & Science of Conquering Liver Cancer

Singapore, July 14–16, 2017

Abstracts

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Speaker's Lecture Abstracts

Session 1: Epidemiology in Developing and Developed Countries

S1-2

The Challenges of Screening, Control and Management of Liver Cancer in the World's Most Populous Country

Sheng-Long Ye

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Primary Liver Cancer (PLC) is a most common malignancy and the second cause of cancer deaths in China. Hepatocellular carcinoma (HCC) accounts for about 90% of PLC, and high-risk population for HCC include HBV/HCV infection, alcohol abuse, non-alcoholic steatohepatitis (NASH), aflatoxin contamination, cirrhosis from any cause and HCC family history, especially in male patients over the age of 40 years. Routine immunization with HBV vaccination is an approach to decrease the prevalence of HCC. Treatment of hepatitis B and cirrhosis is closely associated to the outcome of HCC. Surveillance by screening with AFP serosurvey and ultrasound in high-risk population at a regular interval of 6 months is a main procedure for early detection of HCC.

The critical challenges for management of HCC in Chinese patients include decompensated cirrhosis, vascular invasion, distant metastasis, low resectability and high recurrence rate. The clinical guideline for management of HCC in China focuses on early diagnosis, multiple modalities of treatment, and prevention of recurrence and metastasis for HCC. A new guideline for pathological diagnosis of liver cancer has recently been published. The clinical diagnosis of HCC is mainly based on imaging assessment. Primovist-enhanced MRI may provide a more valuable diagnosis of focal liver lesions. New biomarkers for clinical diagnosis and outcome prediction are being investigated. Surgery is widely utilized to treat HCC in early and intermediate stages. Recent data indicated that palliative resection for BCLC-B HCC might be more effective to improve prognosis compared to TACE. Novel interventional approaches to treating HCC have been developed in recent years. The local ablation is safe and effective in small HCC ≤3 cm in diameter. Randomized clinical trials indicated similar survival and recurrence rates between surgery and RFA. TACE is suitable for both BCLC-B and C HCC patients. Molecular targeted therapy of sorafenib revealed an encouraging outcome in inoperable and metastatic HCC patients. Intensive studies are investigated to further improve the efficacy of sorafenib combined with other treatment modalities, including surgical resection, ablation, TACE and chemotherapy. Clinical trials with new molecular targeted therapy and chemotherapy in HCC patients are also conducted in China. Portal vein tumor thrombosis (PVTT) is one of the key problems of treatment efficacy and prognosis for HCC patients. Various procedures including surgery, TACE, radiotherapy, molecular targeted therapy and combination therapy are investigated to deal with PVTT in HCC patients. The replication and activation of Hepatitis B/C viruses (HBV/HCV) are closely associated to the recurrence and progression of HCC. An expert consensus has been paid more attention to the indication and application of antiviral therapy on HBV/HCV-related HCC. In summary, multidisciplinary team (MDT) is an optimal approach to personalized treatment with combination therapy of HCC.

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S1-3

The Challenges of Screening, Control and Management of Liver Cancer in the First World Country

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Introduction: Beginning in 1967, the Liver Cancer Study Group of Japan (LCSGJ) started a nationwide prospective registry of patients with HCC. Patients were followed-up after diagnosis with surveys published every two years. In the 18th and most recent follow-up survey for the period 2004–2005, 20,153 patients were newly diagnosed with HCC and 30,677 previously diagnosed patients were being followed-up at 544 institutions, respectively. This follow-up survey showed that, of 17,804 measurable tumors in patients initially diagnosed in the period 2004–2005, 855 (4.80%) were ≤1 cm, 5,106 (28.68%) were 1–2 cm, 4,272 (23.99%) were 2–3 cm, 3,833 (21.53%) were 3–5 cm, and 3,738 (21.00%) were 5–10 cm in diameter, respectively. **Background:** To determine the effectiveness of surveillance and treatment methods longitudinally, we analyzed improvements over time in overall survival (OS) of 173,378 patients with HCC prospectively entered into the LCSGJ registry between 1978 and 2005. **Methods:** All patients from more than 700 institutions throughout Japan with HCC were entered into the LCSGJ registry. Patients were grouped by years of diagnosis, with OS and 5-year OS rates being calculated. We also assessed OS and 5-year OS rates in patients who underwent resection, local ablation, transarterial chemoembolization (TACE), and hepatic arterial infusion chemotherapy (HAIC) and in those with baseline serum alpha-fetoprotein (AFP) levels ≥400 ng/ml. **Results:** The 5- and 10-year OS rates in the cohort of 173,378 patients were 37.9% and 16.5%, respectively. However, over time, the mean maximum tumor size decreased significantly, whereas 5-year OS rates and median survival time increased significantly. Similar findings were observed separately in patients who underwent resection, local ablation, TACE, and HAIC, as well as in patients with AFP levels ≥400 ng/ml. **Conclusion:** The establishment of a nationwide HCC surveillance program in Japan has contributed to longer median OS and increased OS rates in patients diagnosed with this disease. These findings suggest that the establishment of a surveillance program in other countries with patients at risk for HCC may provide significant survival benefits.

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Session 2: Epidemiology & Prevention of HCC – Non Viral Causes of HCC

S2-1

NASH as an Emerging Cause of HCC in Asia Pacific Countries

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Nonalcoholic fatty liver disease (NAFLD) is currently the most common chronic liver disease worldwide and affects around a quarter of the adult population in Asia-Pacific countries. Nonalcoholic steatohepatitis (NASH) is the active form of NAFLD with hepatic necroinflammation, more rapid fibrosis progression, and a higher risk of adverse clinical outcomes. While hepatocellular carcinoma (HCC) only affects a small fraction of NAFLD patients, the total number of cases can still be substantial when one multiplies the risk of HCC and the huge number of patients. As a result, NASH has already become the third most common cause of HCC in the United States. The number of patients undergoing liver transplantation for HCC secondary to NASH has also increased by 4-fold from 2002 to 2012.

Data on NASH-related HCC in Asia are scarce. In a study of 6508 Japanese patients with NAFLD diagnosed by ultrasonography, only 16 (0.25%) developed HCC at a median follow-up of 5.6 years. Although this may suggest that NASH-related HCC is unimportant in Asia-Pacific countries, we should not forget that this problem has only been emerging recently even in western countries. Since it takes decades before chronic liver diseases progress to cirrhosis and HCC, it is possible that there will be a time lag before we witness the wave of NASH-related HCC in Asia.

Although cirrhosis is one of the most important risk factors of HCC for most chronic liver diseases, a number of reports suggest that up to a third of NASH-related HCC develop from non-cirrhotic livers, a figure higher than that in other liver etiologies. There are several possible explanations for this phenomenon. First, there is some overlap in the signaling pathways of NASH and HCC. NASH may thus directly promote HCC development. Second, the proportion of NAFLD patients with cirrhosis is lower than that in other liver diseases. It comes as no surprise that non-cirrhotic HCC is also more common in NAFLD patients. Finally, some patients with NASH-related cirrhosis may be classified as cryptogenic cirrhosis when hepatic steatosis is no longer apparent. In any case, non-cirrhotic HCC has major clinical implications; it would be difficult to define a high risk group for HCC surveillance.

That said, NASH is a preventable disease. Weight reduction through diet and exercise has been shown to reverse NASH and liver fibrosis. Animal and observational studies have also revealed the effect of exercise on HCC prevention. A number of pharmacological agents have also entered phase 2/3 development for NASH. The long-term outcome data from these trials will increase our understanding on the natural history, prevention and treatment of this important disease.

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S2-2

Prevention of HCC in the Asia Pacific – How Can We Do Better?

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Chronic infection with hepatitis B or C virus is the principal cause of hepatocellular carcinoma (HCC) (≥75% of all cases). Of the many non-viral factors relevant to HCC development, obesity and diabetes, and the subsequent development of nonalcoholic steatohepatitis (NASH), are particularly significant risk factors. The most recent report from the USA has shown convincingly that the number of NASH-associated HCC cases is increasing around 9% per annum. Other non-viral causes of HCC include iron overload syndromes, alcohol use, tobacco use, the use of oral contraceptives, and aflatoxin ingestion.

Nonalcoholic fatty liver disease (NAFLD) is considered a hepatic manifestation of metabolic syndrome and is becoming more prevalent worldwide. Patients with active inflammatory NAFLD, termed NASH, are at particular risk of HCC development, even if their livers are not cirrhotic. Although the debate on the relative contributions made by obesity and diabetes to HCC development in the presence and absence of NAFLD continues, several recent publications have addressed HCC developing in NAFLD patients. NASH-associated HCC may be of multi-centric origin, similar to HCC caused by viral hepatitis; both tumor recurrence and de novo HCC should be considered. Also, HCC is difficult to evaluate in NASH patients because histological data are required for NASH diagnosis, which can trigger selection bias. Furthermore, the characteristic features of NASH disappear in the end-stage of disease (the so-called "burned-out" NASH), rendering diagnosis impossible.

The precise mechanisms triggering the development of NASH-associated HCC remain unclear. Genetic susceptibility is likely to be key in determining individual risk, and DNA studies may soon identify biomarkers detecting those at higher risk. Apart from older age and advanced fibrosis, pathophysiological factors associated with the development of NAFLD per se, including insulin-resistance, oxidative stress, and inflammatory cytokine production, are likely to contribute to hepatocarcinogenesis. External factors such as hyper-nutrition and a sedentary lifestyle undoubtedly trigger pathological changes in adipose and liver tissue, but the responses vary greatly from one individual to another; it remains unclear why a minority develops progressive liver disease and HCC. Recently, sarcopenia was reported to be an independent risk factor associated with the development of NAFLD/NASH and (possibly) advanced fibrosis. A role for vitamin D in the development of NAFLD is also emerging.

A multilevel preventative approach will hopefully reduce the incidence of non-viral HCC. There is an urgent need to elucidate the pathogenesis and clinical features of HCC in NASH patients. Further studies are also required to identify patients at high risk of NAFLD/NASH who require more stringent surveillance to prevent HCC, and to establish effective treatments.

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Session 3: Prevention of HCC – Viral Causes of HCC

S3-2
Towards Elimination and Eradication of Hepatitis B – How Close Are We Now?

Seng Gee Lim

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Chronic Hepatitis B leads to one of the largest burdens of chronic liver disease and hepatocellular carcinoma in Asia. With the rapid advances in HCV cure, attention is turning towards cure and eradication of HBV, a far bigger problem in Asia. Estimates place HBV as leading to around 800,000 deaths a year in Asia. How should we approach this problem? There are four pieces of the puzzle that need to be in place to achieve this goal. The first is optimising an already a very effective vaccine that has led to dramatic reductions in HBV prevalence in Asia as well as liver complications in children. However, vaccine coverage is suboptimal in parts of Asia, particularly India and Philippines as well as rural areas. Even with an effective vaccine now 30 years old, it will take another 30 years before a significant impact on liver complications and mortality, as most of these occur in those aged >50 years. The second and probably most important component is screening and linkage to care, as it is estimated that >80% of patients remained undiagnosed. There are no effective or comprehensive screening programs in Asia. Perinatal transmission is the dominant method of transmission in Asia but identifying such patients remains challenging since many patients do not have a family history of HBV. One method that may increase documentation is to follow the Australian method – make viral hepatitis a notifiable disease, as Australia estimates that 57% of their HBV patients are known. The third component is effective therapy that could lead to a cure. Functional cure is the most practical definition featuring HBsAg loss and undetectable viral load. This is still a distant possibility since existing therapies do not generally lead to a cure. While there are now many new strategies that could potentially lead to a cure, they are still in clinical trials and preliminary results do not appear to show a dramatic result in HBV cure. However, it is quite likely a cure will be found. Finally, access to care for effective therapies need to follow a similar pattern as that of HCV and HIV, otherwise the ultimate goal of eradication is unlikely to be achieved. While access to care needs to involve individual health care systems and move towards a univeral health care system, there is much individuals with subject expertise and liver societies, and non governmental organisations can do to promote and strategize to achieve this goal of HBV eradication. A case in point is Mr Charles Gore who singlehandedly formed the World Hepatitis Alliance and contributed to the WHO resolution on viral hepatitis. The 2030 WHO goals for hepatitis elimination remains challenging as all there remains much to be done in the four dimensions to reach this target.

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Session 4: Translational Genomics and Immunomics of HCC

S4-1

Multidimensional Analysis on Immune Microenvironment in HCC – Biomarker and Therapeutic Discovery

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Introduction: Despite recent success in cancer immunotherapies, the dynamics between tumor-microenvironment and the systemic immune system remain elusive. Our immunological analysis aims to identify and characterise important immunological components in hepatocellular carcinoma (HCC) for their potential clinical implications. **Methods:** Our approach consisted of seamless integration of high dimensional mass cytometry by time-of-flight (CyTOF) to identify multiple immune subsets residing in the tumor, its adjacent non-tumor liver tissues and peripheral blood in patients with hepatocellular carcinoma (HCC); next-generation sequencing for deep characterization of these distinct tumor-infiltrating leukocytes and RNA expression analysis of a total of 800 cancer-immune genes in tumor versus its adjacent non-tumor microenvironment. **Results:** We described an immune gradient of progressively more suppressive immune subsets, which includes exhausted T cells, regulatory-T cells, and tumor-associated macrophages, from the periphery, the adjacent non-tumor tissues to tumor. The higher expression of multiple exhaustion markers including PD-1, CTLA-4, Lag-3 and Tim-3 on tumour-infiltrating CD8+CD45RO+ memory T cells demonstrated the preferentially enrichment of these exhausted T cells in the tumor microenvironment. This phenomenon could also served as a immunotherapeutic target using check-point inhibitors immunotherapy in HCC. Further functional characteristics of these cells using RNA sequencing and NanoString showed that their phenotypes are profoundly related to the microenvironment where they reside. **Conclusion:** The current approach provides a holistic analysis of tumor immune microenvironment which mapped the immune landscape of tumor in unprecedented detail. It serves as a platform for the design of immunomonitoring and immunotherapy for cancers.

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S4-2

The Genomic Landscape of Intra-Tumor Heterogeneity and Evolution of Metastasis in HCC

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Tumor heterogeneity lies at the center of treatment response and resistance. Using multi-sectoring approach, we have conducted a genomic study of tumor heterogeneity in nine hepatocellular carcinoma patients with diverse disease etiologies. We found that there is a wide variety of tumor heterogeneity spanning early to late diversification. The genetic lineages show a clear isolation-by-distance pattern where spatially closer sectors are genetically more similar. This is very different from variegated pattern found in colorectal cancers. The sequencing of two intra hepatic metastasis revealed much higher variability than their primary tumours, suggesting that intra-hepatic metastasis is accompanied by rapid diversification at the distant location. Other than classical driver mutations such as TP53 and CTNNB1, many co-occurring mutations in drivers found in other cancer types (e.g. EGFR) offer the possibility of drug repositioning. The studying of tumor heterogeneity provides novel insights into tumor evolution and personalized treatment.

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Session 5: Is Anatomical Pathology in HCC Still Relevant?

S5-1

Is Anatomical Pathology in HCC Still Relevant?

Michiie Sakamoto

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In the era of genome medicine and precision medicine, it is expected to get more detailed and individualized diagnosis of HCC before and after treatment of the patient.

Detailed pathological and clinical study established the concept of early HCC, multistage hepatocarcinogenesis and also multicentric hepatocarcinogenesis. It is not rare to see cases with multiple tumors showing variable stages and cellular differentiation spectra at once in each liver. In such cases, anatomical pathology is essential to give multi-dimensional diagnosis of those multiple tumors.

Moreover, series of molecular markers are available and applicable on routine FFPE tissue sections. Those include molecular markers of early HCC such as HSP70, CAP2, and glutamine synthetase. CAP2 is suggested to be useful to recognize high-grade early HCC. At present, these early HCCs are not definitely diagnosed only by imaging diagnosis or DNA test. By immunohistochemical analyses on biomarkers associated with malignancy, cell signaling features and phenotype, a new subclassification of HCC that reflects the degree of malignancy has been proposed. Additional association with specific pathological subtypes such as scirrhous HCC, MAPK signaling or expression of Glypican 3 as therapeutic target candidates are now under investigation and the subclassification is expected to be applied in the clinical practice.

Studying background lesions and precancerous conditions also still largely depend on pathological and anatomical examinations. Applying computational image analysis techniques to routine pathological diagnosis also will provide more detailed morphological data to be used and analyzed.

Therefore, there is no doubt that anatomical pathology is still relevant and indispensable in HCC practice.

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Session 6: Updates in MIS Surgery in HCC

S6-1
Robotic Hepatectomy for HCC

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The robotic systems have recently been introduced to improve a surgeon's ability in operative field through intuitive hand-control movements, instruments with 7 degrees of freedom, magnified three-dimensional view and stable retraction of a robotic arm. The first robotic liver resection was performed in 2007, the patient was 62-year-old female and had 2.4 cm sized hepatocellular carcinoma (HCC) in the left lateral section.

In 2015, we reported perioperative and oncologic outcomes between minimally invasive liver resection (MILR) and conventional open liver resection (COLR) for hepatocellular carcinoma (HCC) using a propensity-score matched analysis. Ninety-nine patients who received MILR (laparoscopic resection = 83, robotic resection = 16) were matched with 198 patients treated with COLR out of 928 patients with HCC who received curative liver resection from 2002 to 2012. A multivariable logistic model based on factors related to the patient, tumor, and surgical procedure was used to estimate a propensity score. The MILR group experienced significantly less intraoperative blood loss (mean: 389.55 vs. 580.66 mL; P = 0.008), lower complication rates (13.1% vs. 24.7%; P = 0.020), and a shorter length of hospital stay (mean: 8.40 vs. 13.39 days; P < 0.001). The two groups did not differ significantly in disease-free (P = 0.701) or overall survival (P = 0.086). In this study, major liver resections were performed on 17 patients, and 10 of these patients underwent robotic liver resections. Among the patients who received a robotic liver resection, two-thirds underwent major liver resections, and all of these patients except one received an anatomical liver resection.

Recently, we retrospectively reviewed all the cases of robotic and laparoscopic liver resection of hepatocellular carcinoma performed in our center within the period of 2005–2016. One hundred eighty seven patients who received laparoscopic liver resection and 40 patients who received robotic liver resection were included. A multivariable logistic model based on factors related to the patient, tumor and surgical procedure were used to estimate a propensity score. Disease-free survival between the laparoscopic group and robotic group showed no significant difference (median 66 months) vs. median 53 months (p = 0.694). However, the laparoscopic surgery group was noted to undergo more non-anatomic liver resections compared to the robotic surgery group (23% vs. 0, p < 0.001), while the robotic surgery group consisted mostly of major anatomic resections (16% vs. 65%, p < 0.001). In order to compensate for this discrepancy between the two groups, a 1:1 propensity score matching (PSM) was performed. Thirty-eight patients in each group were selected. After PSM, disease-free survival between the groups still showed no significant difference (median 49 months for the laparoscopic group vs. 53 months for the robotic group, p = 0.421). Furthermore, resection margin between the groups showed no significant difference (p = 0.890).

In conclusion, robotic liver resection may show its greatest advantages in conducting major hepatectomies and can produce comparable oncologic outcomes in terms of resection margins and median disease-free survival compared to conventional laparoscopic liver resection in patients with HCC.

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S6-3

Debate: Laparoscopic Liver Resection Is the Standard of Care in HCC

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Laparoscopic liver resection (LLR) is regarded as good optional treatment for hepatocellular carcinoma (HCC). However, there are still several topics to be discussed. The indication on location of the laparoscopic liver resection has been limited to easily accessible lesions previously. Performing laparoscopic liver resection in the posterior and superior parts of the liver has been considered difficult due to inadequate exposure, the poor operative field and the difficulty with parenchymal dissection. However, there are several reports that laparoscopic liver resection is well performed on difficult locations. Anatomic resection has been reported to have advantage over non-anatomic resection. In addition, as the patients with HCC have concomitant liver cirrhosis or chronic liver disease, it is necessary to perform parenchymal sparing liver resection. The type of resections also may depend on the remaining liver's functional capacity. Tailored liver resection can be possible with the use of Glissonian approach. For example, mono-segmentectomy and sub-mono-segmentectomy using the Glissonian pedicle to individual segment has been also reported. Lastly, the oncologic outcome is reported to be comparable to open surgery. The well designed studies may be necessary for generalized acceptance of this surgery.

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Session 7: Controversies in Liver Transplantation for HCC

S7-1

Current Role of Treatment of HCC (TACE / Y90 / RFA) While Awaiting Liver Transplantation

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Liver transplantation (LT) is the ideal treatment for HCC since it can not only cure HCC itself but remove and replace the underling diseased liver. The major problem of LT for HCC is its narrow indication, usually within the Milan criteria, and the absolute scarcity of the donor. To decrease the impact of these disadvantages on the LT candidate with HCC, there are two main strategies for those awaiting LT, the bridging therapy and the downstaging therapy. The former focuses on treating patients within the LT criteria while they are on the waiting list in order to avoid tumor progression outside the criteria and drop out from the waiting list. The latter addresses to treating patients whose HCC status is initially outside the criteria down to within the criteria. However, the efficacy of these strategies to improve the prognosis or to decrease the rate of dropout is still controversial.

There are four major locoregional treatments for the purpose of bridging or downstaging, liver resection (LR), transaretrial chemoembolization (TACE), radiofrequency ablation (RFA), and transarterial radioembolization with Y90 (Y90 TARE). LR, usually performed as the curative intent strategy, is rarely performed for these purposes. TACE, the most common modality, was reported to decrease the dropout rates to 3–13%, however, the adequate necrosis seem difficult to be achieved. RFA is the second widely utilized therapy and can achieve complete eradication of the tumor. It was reported to decrease the dropout rate to 0 to 6%, however, the risk of tumoral seeding may be the critical disadvantage. Y90 TARE was recently introduced for bridging or downstaging therapy for LT candidates with HCC. Although reports were limited, Y90 TARE seems comparable or more effective than TACE, especially for those with the advanced stage HCC. In contrast, the indication of it is limited in terms of liver function.

In Japan where the living donor liver transplantation (LDLT) is the mainstay for LT for HCC patients, bridging or downstaging treatments are not common practice. Rather, the majority of HCC patients have undergone several preceding locoregional therapies before listing for LT, meaning LT is the last defense for those with decompensated cirrhosis precluding the locoregional therapy. Among 139 patients who underwent LDLT for HCC in our institution, 83 patients (60%) had been performed the previous locoregional treatments, TACE as the most frequent therapy (n = 64, 46%) followed by RFA (n = 27, 16%), ethanol injection (n = 21, 15%), LR (n = 13, 10%), and other systemic treatments. The overall recurrence rate was 6% for those within Milan criteria, without the difference between those with and without the preceding treatments. There was no case with the intentional bridging or downstaging treatments.

Here, we will review the current role of locoregional treatments for those awaiting LT, and present our LDLT experience for HCC patients.

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S7-2

Down-Staging HCC Beyond Criteria Followed by Liver Transplantation

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Liver transplantation is now regarded as an effective treatment modality for patients with early hepatocellular carcinoma (HCC). Milan criteria (single nodule up to 5 cm, up to three nodules none larger than 3 cm, with no evidence of extrahepatic spread or macrovascular invasion) have been used as a selection of the ideal candidate of liver transplantation for HCC. But it is sometimes too restrictive to include some good HCC candidate with favorable response with liver transplantation.

Down-staging have been used to make the over the Milan within the Milan and then patients get acceptable criteria to have deceased donor liver. Down-staging can be done any of loco-regional therapy such as transarterial chemoembolization, radiofrequency ablation and even surgical resection. It is frequently confused with the treatment to prevent tumor progression during waiting time. Down-stating is originally designed for patients who have the HCC outside of Milan and so have no priority to get the liver from deceased donor. But recently it is used as a selection tool to find the biologically favorable HCC.

Until now we don't know the down-staging itself has role to reduce the recurrence.

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Session 8: Late Breaking Oral Plenary Session

S8-1

Regorafenib as Second-Line Treatment of Patients with Hepatocellular Carcinoma (HCC) Who Progressed on Sorafenib: Subgroup Analysis of Patients from Asia in the Phase 3 RESORCE Trial

Masatoshi Kudo on behalf of the RESORCE Investigators[3], *Gerold Meinhardt*[1], *Jordi Bruix*[2]

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Introduction: In RESORCE, regorafenib improved overall survival (OS) in patients progressing on sorafenib (HR 0.63; 95% CI 0.50–0.79; one-sided P < 0.0001); median OS was 10.6 vs. 7.8 months. We performed a subgroup analysis of patients from Asian countries. **Methods:** In this double-blind, placebo-controlled trial, adults with HCC who tolerated and had radiological progression on sorafenib, Child–Pugh A liver function, and ECOG PS 0–1 were randomized 2:1 to regorafenib 160 mg/day or placebo, 3 weeks on/1 week off. Primary endpoint was OS. **Results:** A total of 216/573 (38%) patients from Asia were randomized and treated (regorafenib n/N = 143/379; placebo n/N = 73/194). Median age was 56 years, 87% were male, ECOG PS 0/1 was 71%/29%, and 85% were BCLC stage C. Median (range) treatment duration was 3.0 months (0.1–29.4) (regorafenib) and 1.6 months (0.3–24.9) (placebo). Regorafenib improved survival with a 35% reduction in risk of death (HR 0.65; 95% CI 0.46–0.92); median OS (regorafenib vs. placebo) was 9.1 vs. 5.2 months. Median PFS (mRECIST; regorafenib vs. placebo) was 2.8 vs. 1.4 months (HR 0.34; 95% CI 0.25–0.47); median TTP (mRECIST) was 2.8 vs. 1.4 months (HR 0.34; 95% CI 0.24–0.47). Grade ≥3 treatment-emergent adverse events (TEAEs) were 80% (regorafenib) and 59% (placebo). Grade ≥3 TEAEs most commonly associated with regorafenib vs. placebo included hand–foot skin reaction (13% vs. 0), hypertension (10% vs. 1%), hypophosphatemia (8% vs. 3%), fatigue (3% vs. 1%), and diarrhea (1% vs. 0). Drug-related grade 5 TEAEs occurred in 3% (regorafenib) and 1% (placebo) patients. **Conclusion:** Consistent with RESORCE overall results, regorafenib improved OS, PFS, and TTP in the subgroup of patients from Asian countries. Safety was generally similar to that in the overall cohort. The safety profile of regorafenib in HCC was similar to the known safety profile in Asian patients with CRC and GIST.

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Session 9: Updates in Imaging in HCC – Can Imaging Do More than Diagnosis?

S9-1

Role of Hepatocyte Specific Contrast Agent

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Early diagnosis of hepatocellular carcinoma (HCC) is crucial for optimizing treatment outcome. Ongoing advances are being made in imaging of HCC regarding detection, grading, staging, and also treatment monitoring. Considering the process of hepatocarcinogenesis, it is important to evaluate sequential changes via imaging which would help to differentiate HCC from premalignant or benign lesions. Recent state-of-the-art techniques including fast scanning acquisitions, diffusion weighted imaging and new MR imaging contrast agents such as hepatocyte specific agents enable improvements in detection and characterization of focal liver lesions in cirrhotic liver. The clinical use of liver-specific contrast agents allows the physician to obtain morphologic and vascular-related information, thanks to the dynamic study, as well as functional information, thanks to the hepatocyte-selective phase of enhancement. These newly developed hepatocyte specific contrast agents have shown great possibilities not only for improved HCC diagnosis and but also for solving the diagnostic dilemma associated with small or borderline hepatocellular lesions. Furthermore, hepatocyte specific CM-enhanced MRI shows promise in regional functional assessment and patient monitoring. In this lecture, I would like to shed some light on liver imaging reporting and data system(LIRADS), and future MRI techniques.

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S9-2

Beyond Anatomic Imaging with Diffusion Weighted MRI

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Hepatocellular carcinoma (HCC) is widely known for its association with chronic hepatitis and liver cirrhosis. The classic imaging features of HCC can be explained by its unique histological characteristics. This enables patients to proceed to definitive treatment without lesion biopsy, provided that specific criteria for imaging diagnosis are met. However, due the heterogeneous nature of HCC, non-classical imaging findings are frequently encountered. Furthermore, uncommon variants of HCC may demonstrate unusual imaging features. Diffusion weighted MRI (DWI) may assist in increasing specificity for diagnosis, assessing tumor biology, and guide prediction of treatment outcomes.

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S9-3

Positron Emission Tomography (PET) Imaging in HCC

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The advent of hybrid-Positron Emission Tomography (PET) imaging modalities have provided unprecedented opportunities for imaging to play a key role in the advancement of molecular medicine towards optimal, personalized diagnosis and therapy. Molecular imaging allows the non-invasive characterization and quantitation of molecules and molecular events in cells and tissue that are fundamental to the pathophysiology of human disease. In oncology, targeted probes are developed to unravel tumour biology, develop predictive biomarkers, identify therapeutic targets and advance the use of theranostics.

Based on clinical PET studies of HCC, it is well-recognized that 18F-Fluorodeoxyglucose (FDG), by far the most commonly used radiotracer in clinical practice, lacks sensitivity for primary HCC lesion detection (≈50%) [1, 2]. This is attributed to the relatively high glucose-6-phosphatase in liver cells and some HCC tumors. K4, the rate constant for dephosphorylation by glucose 6-phosphatase, is similar to the surrounding liver tissue in 45% of HCCs. The uptake of FDG in HCC is depends on the relative ratio of k3 and k4, k3 being the rate constant for phosphorylation of FDG by Hexokinase, which is upregulated in many cancers [3]. In experimental studies on HCC, hexokinase activity increases during carcinogenesis and glucose 6-phosphatase activity decreases finally to zero. Hence, the degree of differentiation of HCC may be assessed using k3 and k4 as indices, and 18F-FDG has a unique role in prognostication by the ability of tracer avidity to predict HCC recurrence and survival [4–6].

On the other hand, 11C-acetate has been found superior in sensitivity (≈90%) [1, 2]. Translational studies have found that HCC tumors utilize exogenous Acetate by upregulation of acetyl-co-A synthetase 1 (ACSS1) and ACSS2, and one study found in particular, ACSS1 was associated with tumor growth and malignancy under hypoxic conditions in human HCC [7].

Based on our experience in the clinics, we have found combined dual-tracer PET scans to provide the highest sensitivity (93%) compared to 18F-FDG and 11C-Acetate alone (51.2% and 81.4% respectively). However, the specificity was poor (46.2%). Moreover, the utilization of 11C-Acetate is limited by the requirement of an on-site cyclotron due to its short half-life, and radiation dose and costs are important considerations.

Understanding the role of dual-tracer PET scans in HCC and the complementary patterns of FDG and Acetate uptake, their respective metabolic pathways and how they interact, are important in patient management and to further the understanding of cancer metabolism with therapeutic implications.

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Session 10: Local/Regional Therapy in HCC (Radiation)

S10-1

Loco-Regional Therapy of Liver Cancer with Y90 Radioembolization

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Treatment of patients with different stages of hepatocellular carcinoma (HCC) with intra-arterial yttrium-90 microspheres has emerged as a promising new therapeutic option. Several trials provide robust evidence of the survival achieved with radioembolization. However, the current data base is composed of retrospective and uncontrolled trials and in the case of prospective studies limited by small numbers.

A consensus meeting to develop practice guidelines and to recommend future clinical trials for radiation therapy and selective internal radiation therapy (SIRT) in HCC was held at the 5th annual meeting of the Asia-Pacific Primary Liver Cancer Expert consortium. There was agreement that SIRT can be considered in patients with early, intermediate and advanced stage HCC [1]. Because of the lack of randomized phase III trials, studies evaluating the efficacy and safety of sequential combination of EBRT and SIRT were strongly recommended. Similarly, the European (EASL) and American (AASLD) societies have appreciated that there are signals of efficacy and a fair safety profile but uncertainties remain about its comparative effectiveness. Thus, SIRT cannot yet be recommended as standard therapy in patients with HCC.

The existing data base provides preliminary data on outcome. Survival depends on BCLC stage and varies from 10 months in BCLC C to 24.4 months in BCLC A [2].

In addition, preliminary data exist comparing SIRT vs. TACE. Patients with HCC treated by chemoembolization or radioembolization with Yttrium-90 microspheres had similar survival times. Radioembolization may result in longer time-to-progression and less toxicity than chemoembolization [3]. In our Mainz series no significant differences were found in median PFS, OS, and TTP [4]. A lower rate of tumor progression in the SIRT group was nullified by a greater incidence of liver failure.

An ongoing phase II trial (SORAMIC) compares radioembolization followed by sorafenib with sorafenib alone. Initial assessment suggests the combination to be as well tolerated as sorafenib alone [5].

Two important phase III trials are ongoing and results will be available soon – SARAH and SIRveNIB:

SARAH (SorAfenib Versus RADIOEMBOLIZATION in Advanced Hepatocellular Carcinoma; NCT01482442) investigates in almost 500 patients whether SIRT is more effective than sorafenib on overall survival in advanced Hepatocellular carcinoma (HCC) with or without portal venous obstruction and no extrahepatic extension.

SIRveNIB (Study to Compare SIRT Versus Sorafenib; NCT01135056) aims to assess the efficacy of SIRT as compared with Sorafenib in patients with locally

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advanced liver cancer in terms of overall survival in locally advanced HCC in 360 patients.

The available data on SIRT in HCC will be presented.

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S10-2

Proton Beam Therapy for HCC

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Liver is an organ with poor tolerance to radiation damage, especially on patients with viral carrier or cirrhotic liver. X-ray emitted by a linear accelerator is the most common radiotherapy (RT) modality, but difficult to deliver a curative dose for medium- to large-size HCC due to high penetration power of X-ray into normal liver tissue. The physical advantage of proton beam lies on that it has a relatively lower entrance dose before tumor, but releases large amounts of energy when reaching the desired depth (the Bragg peak) and deposits no dose to normal tissues behind the tumor. This advantage protects normal tissues after the treatment target from radiation damage.

Several proton centers in Japan have demonstrated the efficacy of proton therapy on the local tumor control of HCC. The local control from Japanese series ranged from 81 to 95% when tumor size is <10 cm. A recent phase II trial reported from three leading proton centers in USA also showed 2-year and 5-year local control rate was 94% for HCC (median tumor size: 5 cm; range: 1.9–12 cm). Proton therapy was also shown to improve the progression-free survival for patients whose tumor had portal vein thrombosis. The treatment protocol for proton beam on HCC varied between centers, but hypofractionated schedule is a general principle. The fraction number ranges from 5 fractions for small liver tumors to 35 fractions for tumors next to the bowel. In general, most centers administer 10–22 fractions, 3.3–6.6 GyE (Gray equivalent) per fraction, and from 63 to 76 GyE for the total dose.

Potential complications might occur after proton treatment; some are similar to those in X-ray, but others are unique for proton. Radiation pneumonitis in the lowest portion of the right lung might occur when tumor is located close to the diaphragm. Chest wall pain could happen when tumor is large and close to chest wall. Damage to the bowel is possible when tumor attaches stomach, small bowel or colon. More severe skin reaction will occur in proton than X-ray treatment because it has no skin-sparing effects.

Proton and Radiation Therapy Center of Chang Gung Memorial Hospital at Linkou started proton treatment service in 2015–11, and 160 patients with liver tumors were treated at the end of 2017–01; ninety three of them were HCC. Our initial date showed that proton therapy is not only an effective life-prolonging modality, but even provide a life-saving potential for some HCC patients.

Based on the clinical evidence, proton therapy is a highly effective modality for a localized HCC. Even though cost-effectiveness is taken into account, it is well justified to use proton therapy in a localized tumor could not be well controlled by RFA and/or TACE or patient is not a good candidate for invasive procedure. Proton therapy is supplemental to the existing local treatment modalities and should be included in an integrated HCC treatment program.

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S10-3

SBRT for HCC

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Recently, stereotactic body radiotherapy (SBRT) has been recognized as one of the treatment modalities for small hepatocellular carcinoma (HCC). Several investigators have reported a 90%–100% three-year local control rate of SBRT for small tumors (≤3 cm) without an increase in severe adverse effects in patients with Child-Pugh score of ≤7. This excellent result suggested that SBRT could be a competitor of radiofrequency ablation (RFA). However, according to several guidelines, such as the Barcelona Clinic Liver Cancer classification (BCLC) and Japanese guidelines, resection and ablative therapies are the first choice for the treatment of early stage HCC. Radiotherapy, including SBRT or particle therapy, can be considered alternative treatment modalities for patients with HCC who were ineligible for resection or ablation therapies.

The reasons are as follows: 1) Low evidence level. Although the level of evidence for RFA is 2A (Level 2, Non-randomized controlled clinical trials; A, the strength of evidence according to endpoints is total mortality), according to the BCLC, the level of evidence for external three-dimensional conformal radiotherapy, including SBRT is 3A (Level 3, Case series; A, the strength of evidence according to endpoints is total mortality). There is no evidence to support SBRT for therapeutic management of HCC. 2) The lack of results on long-term survival. Several prospective trials have demonstrated that the 3-year overall survival (OS) of RFA is almost 60–70% and that of SBRT is almost 50–70%. The 5-year OS of RFA is almost 50–60%. However, there are no available data on SBRT. 3) Damage to the normal liver after SBRT is relatively higher than that after RFA. Therefore the ablative area is clear and limited with RFA, and damage to the normal liver is also limited. On the other hand, focal liver reaction in the area that receives moderate to high degree of irradiation on CT/MRI after SBRT. Moreover, the area surrounding the focal liver reaction on CT/MRI receives some amount of low to moderate dose of irradiation; implying that damage to the normal liver tissue possible after SBRT.

Therefore, further prospective trials, especially comparison of OS between SBRT and other modalities for untreated HCC patients, are needed before SBRT can become a competitor of the other modalities, such as RFA and resection. In Japan, the STRSPH study, a multicenter prospective study of SBRT for untreated solitary primary HCC, is on-going, and is yet to publish its findings. In addition, a retrospective study comparing SBRT with RFA suggested a 2-year local progression-free survival of about 80% for both modalities. The author concluded that both RFA and SBRT were effective local treatment options for inoperable HCC (JCO 34: 452–459, 2016). In the future, prospective randomized phase III trials that compare SBRT and RFA or resection are ideal. Likewise, it is important to establish SBRT as a modality that compensates for the weak points of RFA or resection, rather than as a competitor.

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Session 11: Local/Regional Therapy in HCC (Ablative)

S11-2

Safety and Effectiveness of Radioembolization for HCC with Portal Vein Thrombosis

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Hepatocellular carcinoma (HCC) is currently the second most common cause of cancer-related death worldwide [1]. In case of early-to-intermediate cases, surgery and locoregional treatments (LRT) are able to efficaciously treat the tumors; on the opposite, in advanced HCCs [portal vein tumor thrombosis (PVTT) or extrahepatic spread], only the palliative use of sorafenib is recommended.

Cho et al. [2] reported HCC patients with PVTT who underwent radioembolization achieved comparable survival to patients who received sorafenib, even after application of inverse probability weighting (IPW). The radioembolization group also experienced fewer severe adverse effects.

Yin et al. [3] stressed the previous study of Im and colleagues [4] conducting that patients with HCC and PVTT can be effectively treated with multimodal treatment comprehending radiotherapy. We read with great interest their manuscript underlying the potential benefit of combining radiotherapy plus LRT for the increasing the overall survival.

However, some major concerns arise in the routine introduction of external beam radiotherapy for the HCC management, mainly in terms of patient quality of life and logistic issues. Radiotherapy protocols typically require multiple sessions: the median daily and total radiation doses were 2.5 and 45 Gray respectively, thus leading to a maximum of nearly 30 applications. As a consequence, such a heavy protocol should increase patient discomfort, eventually limiting his compliance and ending in high overall costs.

Starting from these considerations, we should like to further underline the role of yttrium-90 radioembolization (Y90-RE). Y90-RE has been recently described as a safe procedure in HCC patients, consenting to deliver high radiation dose (>100 Gray) during a single session, appearing to be well-tolerated and effective for patients with advanced HCC patients with cirrhosis, and increasing overall survivals. Moreover, Y90-RE is nowadays used patchy worldwide in the treatment of HCC with PVTT: Y90-RE has been described to be safe also in this setting as downstaging to liver transplantation (LT) [5]. Furthermore, Y90-RE had been reported to have a better response rate compared to transarterial chemoembolization (TACE) in patients with advanced HCC stages: time to progression in patients treated with Y90-RE was superior to TACE in a prospective, randomized phase 2 study (>26 vs. 6.8 months; p=.0012)[6]. In conclusion, we [7] strongly agree with Yin et al. [3] that a multimodal treatment for HCC with PVTT is necessary. However, we think the best choice is to consider Y90-RE in this multimodal setting, in order to improve patient survivals and patient quality of life, and finally with an intent to downstage these tumors to curative strategies like LT [7].

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S11-3

RFA for HCC

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Hepatocellular carcinoma (HCC) arises generally with advanced chronic liver diseases or cirrhosis, in which surgical resection is not often indicated. Loco-regional (ablative) therapy was developed more than 30 years ago in Japan as a form of percutaneous ethanol injection to treat unresectable small HCC. Today we have various options for loco-regional therapy such as microwave ablation, laser ablation, cryoablation and irreversible electroporation. Among them radiofrequency ablation (RFA) is the de-fact standard supported by cumulative evidence including randomized and non-randomized studies. We introduced RFA in 1999; the number of treated cases reached 10,000 in 2016. Because RFA showed higher potency in terms of local tumor control compared to ethanol injection, our interest and effort has been focused on the improvement of accuracy and safety. Artificial pleural effusion facilitates more effective treatment for HCC just under the hepatic dome; artificial ascites provides safe ablation to the lesion adjacent to other organs especially the intestine. Contrast ultrasonography using the second generation contrast media, Sonazoid®, facilitates accurate ablation in small HCCs in coarse liver parenchyma. For small tumors detected with CT or MRI and undetectable with ultrasonography, "fusion-imaging", a kind of real-time simulation using CT or MRI image as a reference is quite efficient. Although RFA is considered as minimally invasive compared to hepatic resection, patients sometimes encounter various complications including those potentially critical. We have shown that hemorrhagic complications can be reduced and controlled by careful planning prior to ablation and immediate procedure to stop bleeding when it occurs. Neoplastic seeding, a late complication that deteriorates long-term survival and has been considered as a major drawback compared to resection, can be reduced by avoiding percutaneous tumor biopsy prior to ablation and direct puncture to the tumor located on the surface of the liver. Biliary injury, another important late-complication, is still difficult to avoid when the tumor is adjacent to intrahepatic bile ducts. Recently developed irreversible electroporation can be an effective choice for such cases. Microwave ablation reappears as a second generation technology that enables larger ablation area with less susceptible to cooling effect. Because patients with HCC have chronic liver diseases with high risk of recurrence, to find recurrent tumor small in size and maintain liver function is a key to improve the long-term survival. With well-established surveillance system for post ablation and anti-viral treatment for hepatitis B and C, 10-year survival rate in HCC patients initially treated with RFA in our institution was 29%. The number would be further improved by recently introduced direct acting antiviral treatments for chronic hepatitis C.

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Session 12: Advances in Systemic Therapy – Cytotoxic and Molecular Targeted

S12-2

Beyond Sorafenib/Regorafenib – Is There a Role for Other Targeted Therapies in Advanced HCC?

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Hepatocellular carcinoma (HCC) has conventionally been labelled as an orphan disease due to a lack of effective drug treatment. This concept is no longer true in 2017. In addition to Sorafenib, there are a growing number of drug treatments for advanced HCC. In 2016, a phase III clinical trial (RESOURCE) established Regorafenib as the second-line treatment in patients who tolerated prior sorafenib treatment. In 2017, Lenvatinib was shown to be a non-inferior treatment to sorafenib in the first-line setting. Apart from those multi-targeted small molecules, a number of targeted agents with specific targets have been tested in advanced HCC. These agents typically demonstrated potentially selectivity of efficacy in biomarker enriched population of HCC. Examples include Rmucirumab in alpha-fetoprotein elevated HCC, C-met inhibitors in MET amplified HCC, Everolimus in TSC-2-loss HCC or FGFR4 inhibitors in FGF19 amplified population. In the lecture, these targeted agents are to be discussed with focus on the underlying enrichment approach and presentation of recent clinical trial data in the treatment of advanced HCC.

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Session 13: Advances in Systemic Therapy – Immunotherapy

S13-2

The Immune System is the Final Answer against HCC

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T-cells play a critical role in immune responses against cancer. Cytotoxic T-lymphocytes (CTL) are one class of effector T-cells that secrete cytokines and can specifically lyse target cells. However, on prolonged antigenic stimulation, T-cells may lose their effector functions even in the presence of antigens that they target. Such an "exhaustion" state renders T-cells incapable of clearing pathogens or eliminating neoplastic cells. Immune checkpoints provide a regulatory feedback mechanism to limit the effector phase of T cell differentiation. They play key parts in tolerance to self antigens, and provide the basis for fine-tuning of the T-cell response. PD1 is a transmembrane receptor. It binds to two ligands, programmed cell death protein 1 ligand 1 (PDL1), and PDL2, both of which are transmembrane proteins as well. PDL1 expression is a major mechanism by which tumor cells can evade immune attack.

Immune checkpoint modulators have recently emerged and offer encouraging results in cancer treatment. Nivolumab is a human IgG4 anti-PD-1 monoclonal antibody and it has been tested clinically in a series of CheckMate studies.

Interaction of hepatocellular carcinoma (HCC) with the immune system plays a major role in its progression. Inadequate co-stimulation, failure of antigen recognition and processing, along with suppression of effector cells are proposed mechanisms that result in weakened immune response in HCC patients. Notably, PD-L1 is over-activated in HCC, and its receptor is found to inhibit T-cell activation. In the presentation, we will discuss about the emerging data about the use of anti-PD 1 and its combination in advanced HCC population.

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Oral Abstracts

Translational Research, Pathology, Epidemiology

TRPE-10018

Correlation of Circulating Tumour Cells with Objective Response to SBRT for Inoperable Hepatocellular Carcinoma

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Introduction: Stereotactic body radiation therapy (SBRT) is one of the standard treatments for inoperable hepatocellular carcinoma (HCC). However imaging tool even with MRI may not be sensitive enough to evaluate tumour objective response after SBRT. Circulating tumour cells (CTC) may act as a surrogate biomarker of response evaluation. **Methods:** Ten consecutive patients with inoperable HCC received radical SBRT in 5 fractions (35-50 Gy) over 1–2 weeks. Peripheral blood was taken for CTC (7.5 ml collected in Cell-Free DNA tubes) and serum alfa-feto protein (AFP) before SBRT and then 3 months afterwards. Red cells were lysed before CTC isolation and enriched CTC outputs were labeled with DAPI, CK, EpCAM and CD45 antibodies. Nucleated CK/EpCAM+ CD45– CTCs were identified and enumerated using CellProfiler/CellProfiler Analyst software. Spearman's correlations were performed for correlation between (1) baseline CTC counts and gross tumor volumes (GTV) of all irradiated tumors and serum AFP and (2) change in CTC and objective response (CR, PR, SD and PD) based on modified RECIST with MRI scan with primovist, GTV and serum AFP at 3 months after SBRT. **Results:** The median baseline CTC, serum AFP and GTV were 18.5 counts per 7.5 ml blood (range 3–86 counts per 7.5 ml blood), 7 ng/ml (2–60521 ng/ml) and 28.3 cm^3 (1.98–221.2 cm^3) respectively. One, 8 and 1 patients achieved CR, PR and PD (metastasis to distant node outside SBRT field) after SBRT. Baseline CTC did not correlate well with baseline GTV ($r = -0.468$, $p = 0.172$), AFP ($r = 0.187$, $p = 0.606$) or log (AFP) ($r = 0.201$, $p = 0.577$). However, percentage change in CTC correlated very well with objective response at 3 months after SBRT ($r = 0.703$, $p = 0.023$) while percentage change in AFP ($r = 0.006$, $p = 0.987$) and percentage change in log (AFP) did not ($r = -0.328$, $p = 0.354$). **Conclusions:** CTC may be a better surrogate marker which correlated better than serum AFP with tumour response to SBRT for inoperable HCC.

TRPE-10032

Administration of Metformin Decreasing Number of Pre-Neoplastic Cells in Hepatocellular Carcinoma Rats Induced with Diethylnitrosamine

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Introduction: Anti-hyperglycemic agent, metformin, has been widely used for the treatment of type 2 diabetic; however its efficacy against transformation of pre-neoplastic hepatocytes in hepatocellular carcinoma with hyperglycemia is still largely debated. **Material and Methods:** Fifteen male Wistar rats, 200–220 gram at seven weeks of age were fed with high fat diet for 4 weeks and injected with Streptozotocin 45 mg/kg BW one or two times a week to develop hyperglycemia, then all rats were injected with diethyl nitrosamine 70 mg/kg BW weekly for 14 weeks. They were divided into three groups; group A (n = 5), as control, given only drinking water, group B (n = 5), given metformin 125 mg/kg BW, and group C (n = 5) given metformin 250 mg/kg BW. Fourteen weeks after DEN injections, all rat were sacrificed. Their blood were collected then tested for the level of Fasting Blood Glucose. Their livers were fixed and blocked in paraffin for histopathology observation. Immunohistochemistry staining with Ki67 antibody was performed to explore the proliferation of hepatic parenchymal cells. **Result:** The blood serum of rats treated with metformin showed decreasing level of FBG significantly ($p < 0.05$). Hepatic lobules architecture showed development of tumors consists of pre-neoplastic cells with prominent nucleoli, atypical mitosis and Ki67 proliferating cells. The decreasing number of prominent nucleoli in metformin treated groups demonstrated significant differences ($p <$

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0.05) compared to control group. **Conclusion:** We suggest that the efficacy of metformin in adequate dosage and given in a longer period may inhibit the progression of liver carcinogenesis. **Key words:** Hyperglycemia, Metformin, Hepatocellular carcinoma. All experiments were conducted in accordance with the National Institutes of Health Guidelines for the Care and Use of Laboratory Animals and were approved by the Mochtar Riady Institute of Nanotechnology Animal Care and Use Committee with number 01.1512034.

TRPE-10049

Postoperative Circulating Tumor Cells: A Useful Predictor of Extrahepatic Metastasis in Hepatocellular Carcinoma Undergoing Curative Resection

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Background: Postoperative extrahepatic metastases (EHM) contribute to a grim outcome in hepatocellular carcinoma (HCC). Currently, the detection of EHM mainly depends on imaging modalities. It is imperative to develop novel approaches for discriminating HCC patients at high-risk for postoperative EHM, facilitating identification of patients who might benefit from potential adjuvant therapies. This study investigated the clinical value of postoperative circulating tumor cells (CTCs) in predicting EHM as well as possible mechanisms. **Patients and Methods:** From March to June 2011, 103 HCC patients undergoing curative resection were recruited. CellSearch system was used to perform CTC detection one month after resection. Systemic inflammatory status was determined by neitrophil-lymphocyte ratio (NLR). **Results:** 29 of 103 patients had CTC 1 after operation. 10 of 103 patients developed EHM within one year after operation (9 lung metastasese and 1 abdominal cavity metastasis), which was positively correlated with tumor size and satellite lesion ($P < 0.001$). Patients with EHM had higher CTC level compared with those without EHM (mean: 5.1 vs. 0.58, $P = 0.025$). Patients with CTC 3 had higher incidence of EHM (45.5% vs. 5.4%) compared with those with CTC <3 ($P < 0.001$). Multivariate analysis showed that CTC 3 was an independent predictor for postoperative EHM ($P = 0.001$). A receiver operating characteristic curve analysis confirmed the capability of postoperative CTC 3 in prediction of EHM. The area under the curve of CTC 3 was 0.718 (95% confidence interval, 0.518–0.917, $P = 0.024$), with a sensitivity of 50% and specificity of 93.5%. In patients with postoperative CTC 3, further analysis showed those who developed EHM predisposed to higher NLR compared with those without EHM ($P = 0.011$), which indicated systemic inflammatory environment as an accelerator for metastatic colonization of CTCs. **Conclusion:** Postoperative CTC 3 is a surrogate marker for identifying HCC patients with a high-risk for EHM after operation. Systemic inflammatory response might orchestrate with CTC colonization in distant organ.

TRPE-10114

Deep Profiling and In Situ Mapping of Human HBV-Related Hepatocellular Carcinoma Immune Milieu: Where Are the CD103+ Resident Memory-Like T and NK Cells?

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HBV is the single most common cause of HCC that accounts for approximately 50% of all HCC cases worldwide, especially in developing countries. We are interested in understanding the liver-localized antigen-specific T cell mediated immune responses to both hepatitis B virus (HBV) and hepatocellular carcinoma (HCC). We combined two state-of-the-art technologies to study HBV-specific immune response across various patient cohorts; A) mass cytometry and highly multiplexed peptide-MHC tetramer staining for deep profiling of HBV-specific T cell populations and B) high-throughput multiplex Immunohistochemistry (mIF-IHC) for deep mapping of the distribution of such T cell populations and their interaction with other immune subsets as well as the structures in the liver microenvironment such as sinusoids, vessels, portal tracts, liver lobules and tumor islands. Following up on our previous study (Wong et al., Immunity 2016) that identified and profiled CD69+CD103+ resident T and NK cell populations in liver samples obtained from healthy donors, we compared the features of these and other resident lymphocyte populations derived from adjacent normal with tumor (near tumor) vs. tumor vs. normal liver far from tumor of HCC patients. We found that CD103+ cells can be subclassified into mainly CD8+ and CD8– subsets. Subsequently we also identified that the in situ geographical changes in the microenvironment and abundances of such subsets are associated with clinicopathological parameters and prognosis of the patients. Ongoing studies aim to compare the characteristics of HBV and HCC specific T cells derived from blood and liver tissues of HBV and HBV-related HCC patient samples to identify T cell based biomarkers for a variety of clinical outcomes.

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TRPE-10136

TrkC Is Essential for Tumorigenicity and Metastasis in Hepatocellular Carcinoma

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Introduction: TrkC induces tumor invasiveness and chemotaxis of malignant cells. TrkC is also important in the regulation of angiogenesis, induction of tumor growth, prevention of apoptosis and promotion of metastasis. Although TrkC plays an important role in the initiation and progression of many tumors, but, there are lack of evidences for the role of TrkC in Hepatocellular carcinoma (HCC). so, we investigated the role of TrkC in HCC development and progression. **Methods:** Clinical specimens from 33 individual HCC patients were analyzed for TrkC expression by immunohistochemical stain. The studies for metastasis and EMT program in HCC using TrkC knockdown cells (SNU387-shTrkC cells) and overexpression cells (PLC/PRF/5-TrkC cells) were compared with its control cells (SNU387 and PLC/PRF/5 cells) by immunoblotting, qRT-PCR analysis, and immunofluorescence staining. Also, the tumorigenicity and metastasis of HCC were compared using mouse xenograft model and the capacity for self-renewal and proliferation of HCC were evaluated. **Result:** TrkC was frequently overexpressed in HCC cell lines, and patients' HCC samples ($P < 0.0001$). TrkC expression was associated with poor survival and invasiveness ($P < 0.05$). Moreover, TrkC increased the ability to form mammospheres ($P < 0.001$), a property associated with cancer stem cells. Importantly, TrkC overexpression exhibits significant rapid tumor growth and metastasis in a mouse xenograft models, furthermore, TrkC enhanced metastatic potential and proliferation by aberrant gain of cancer stem cell markers. **Conclusion:** By using mouse models and molecular biology analyses, we demonstrate that TrkC acts as an activator in tumorigenicity and metastasis of HCC. TrkC can lead to deregulated cell growth, alters cellular behaviour and function, and enhanced metastasis of HCC. Our results propose TrkC as a novel indicator of prognosis in the patients with HCC and could serve as a novel therapeutic target for HCC.

Imaging and Diagnosis

IMDI-10028

Role of Dual Tracer PET-CT in Management of Hepatocellular Carcinoma

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Introduction: Dual-tracer PET-CT with 18F-fludeoxyglucose and 11C-acetate was reported to be sensitive to detect primary hepatocellular carcinoma (HCC) and its metastases. The pattern of tracer uptake by tumours was correlated with tumour cellular differentiation. Therefore, it is increasingly used as part of pre-resection and pre-transplant workup. However, the exact role of dual-tracer PET-CT in the workup of has yet to be defined. We aimed to clarify the usefulness of dual-tracer PET-CT in HCC work up and the candidates who might benefit from this costly investigation. **Methods:** The study included 198 patients who was referred for HCC work up at the Department of Surgery, Queen Mary Hospital between December 2012 and September 2015. All of them had pre-treatment triphasic CT/MRI and dual-tracer PET-CT. Patients (n = 46) with previous treatment and PET-CT as liver transplantation workup were excluded. Chi square test and binary logistic regression were performed for predictive factors of PET-detected metastases. **Results:** Total of 152 patients were included in the study. Hepatitis B carriers were predominant (113/152, 74%). Seventy nine (52%) patients had PET-CT for metabolic characterization as primary imaging showed indeterminate features of HCC. Surprisingly, all of them were confirmed to be HCC after PET-CT. Seventeen (11%) patients had PET-detected metastases. The metastatic group contained patients with poorer liver function, more advanced tumour status and higher alpha-fetoprotein. In multivariate analysis, AFP ≥400 (Relative risk 4.3, 95% confidence interval 1.41–13.15, p = 0.011) and bilobar involvement (Relative risk 4.21, 95% confidence interval 1.33–13.29, p = 0.014) were identified as independent predictive factors. If both of the two factors negative were combined to a surrogate, this can achieve a 96% of negative predictive value of PET-detected metastases. **Conclusion:** The main role of dual-tracer PET-CT in our group of patient was metastatic screening. AFP <400 along with unilobar disease can achieve good negative predictive value for PET-detected metastases.

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IMDI-10058

Predicting Early Recurrence of Hepatocellular Carcinoma with Texture Analysis of Pre-Operative Magnetic Resonance Imaging: A Radiomics Study

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Introduction: Post-operative recurrence of hepatocellular carcinoma (HCC) results in mortality and the time-to-recurrence is an independent prognostic factor of survival. The ability to identify these high-risk patients pre-operatively will guide surgical management, and post-operative monitoring and therapeutic interventions. This study aims to study the feasibility of using texture analysis in pre-operative magnetic resonance imaging (MRI) to predict early recurrence (ER) in hepatocellular carcinoma (HCC) post-curative surgery. **Method:** Institutional review board was obtained. A retrospective review of all patients who underwent hepatectomy between 1 Jan 2007 and 31 Dec 2015 was performed. Inclusion criteria: pre-operative MRI, tumor size ~1 cm, new cases of HCC. **Exclusion Criteria:** Loss-to-follow-up, ruptured HCCs, movement artifacts and previous hepatectomy or interval adjuvant therapy. Patients were divided into ER and late or no recurrence (LNR) groups. Early recurrence was defined as new foci of HCC within 730 days of curative surgery. T2, DWI, T1 arterial and T1 portovenous acquisitions were imported into MATLAB (Mathworks, Matick, MA, USA). Radiomics feature extraction was performed on the largest cross-sectional area of each tumor. The MaZda software was used to analyze 290 texture parameters and PRTools was used for feature selection. **Results:** Fifty-seven patients (49 male, mean age 66.5 years) were divided into ER (n = 21) and LNR (n = 36) groups. Alpha-fetoprotein level (p = 0.021), size (p = 0.011), restricted diffusion (p = 0.01) and vascular invasion (gross and/or microvascular, p = 0.047) were found to be statistically significant different between the 2 groups. There is 79% accuracy in classifying arterial images using 1-nearest neighbor using parameters S(1,0) Contrast or S(5,-5) Entropy. The parameter S(5,-5) Entropy has also resulted in 77% accuracy in classifying T2 images. **Conclusion:** Early recurrence of HCC can be predicted on pre-operative MRI with 79% accuracy using the appropriate texture analysis parameter.

Surgical Management of HCC

SMHC-10006

Long-Term Outcomes After Surgical Resection for Non B Non C Hepatocellular Carcinoma (NBNC HCC)

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Backgrounds: Although number of so-called NBNC HCC patients without infection of hepatitis C virus (HCV) and hepatitis B virus (HBV) has been increased, a little is known about biological behavior of NNBNC HCC. **Methods:** Among 648 patients undergoing initial surgical resection for HCC between 2002 and 2013, 12 patients with double positive HCV-Ab and HBsAg were excluded. The remaining 636 patients were included to this study, who were classified into 4 groups; HBV group defined by HBsAg+/HCVAb– (n = 126), HCVgroup by HBsAg–/HCVAb+ (n = 302), pastHBV group by HBsAg–/HBcAb+/HCVAb– (n = 61), and pureNBNC group by HBsAg–/HBcAb–/HCVAb– (n = 147). The distributions of alcohol abuse of the HBV, HVC, pastHBV, pureNBNC groups were 20%/17%/39%/40%, respectively. The incidences of diabetes mellitus of the 4 groups were 14%/24%/44%/46%, respectively. The median serum albumin per dL, indocyanine green retention rates at 15 minutes and maximum tumor sizes of the 4 groups were 3.9 g/3.7 g/3.8 g/3.8 g, 11%/17%/15%/14%, and 5.0 cm/3.9 cm6.0 cm/6.2 cm, respectively. **Results:** The recurrence-free survival rates of the 4 groups were 42%/37%/52%/33% at 3 years after surgery, and 28%/26%/47%/29% at 5 years, respectively. The overall survival rates of the 4 groups were 76%/64%/82%/74% at 5 years after surgery, and 69%/50%/53%/59% at 5 years, respectively. The prognosis of the pureNBNC group was the second worst. **Conclusions:** Although the liver function of the pure NBNC patients was preserved, postoperative long-term outcomes were not good may be due to the advanced tumor status suggested by the tumor size. Early detection would be important to improve the outcomes of NBNC HCC patients.

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SMHC-10016

RAM Score Is an Effective Predictor for Early Mortality and Recurrence After Hepatectomy for Hepatocellular Carcinoma

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Purpose: Liver resection is a standard treatment for hepatocellular carcinoma (HCC). However, early mortality and recurrence after surgery were still of major concern. RAM (Risk Assessment for early Mortality) scoring system is a newly developed tool for assessing early mortality after hepatectomy for HCC. In this study, we compared RAM scoring system with ALBI and MELD scores for their capability of predicting short-term outcome. **Materials and Methods:** We retrospectively reviewed patients with HCC who underwent hepatectomy at Chang Gung Memorial Hospital between 1983 and 2015. We applied RAM, albumin-bilirubin (ALBI), and model for end-stage liver disease (MELD) scoring systems to predict early mortality and recurrence after surgery. **Results:** A total of 1,935 patients (78% male) who underwent liver resection for HCC were included in this study. One hundred and forty-nine patients (7.7%) died within 6 months after hepatectomy. All the three scoring systems were effective predictor for early mortality, with higher score indicating higher risk of early mortality (AUC of RAM, ALBI, and MELD: 0.723, 0.682, and 0.590, respectively; p <0.001, <0.001, and 0.002, respectively). Cox regression multivariate analysis demonstrated that RAM class was the most significant independent predictor of early mortality after surgery. In addition to early mortality, RAM score was also predictive of early recurrence after surgery. **Conclusion:** This study demonstrated that RAM score is an effective and user-friendly bedside scoring system to predict early mortality and early recurrence after hepatectomy for HCC. In addition, the predictive capability of RAM score is superior to ALBI and MELD scores. Further study is warranted to validate our findings.

SMHC-10066

Predicting Survival After Surgical Resection for the Entire Spectrum of Anatomically Resectable HCC: A Metro Ticket Approach

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Background/Aims: Clinical outcomes after surgical resection in HCC is a continuum and is clearly related to tumor burden but needs better definition. We describe the use of the "metroticket" approach to analyze surgical outcomes over the whole spectrum of anatomically resectable HCC to define overall survival (OS) including intermediate stage tumors (BCLC B). The analysis we provide will enable clinicians to select the optimal surgical resection candidate based on robust long term survival data. **Methods:** Patients who underwent surgical resection for HCC from 6th January 2000 to 31st December 2011 by the joint hepato-pancreato-biliary surgery service at the Singapore Healthcare Group (Singapore General Hospital and National Cancer Centre Singapore) were retrospectively identified from a prospectively kept institutional database. The assessment of the size, number of nodules and vascular invasion of HCC were based on the pathological assessment of resected specimens. All resections were histologically confirmed as HCC. Patients with macrovascular invasion and extrahepatic invasion were excluded as were patients resected for other palliative intents (e.g. ruptured HCC). Cox regression analysis confirmed that number of nodules and size of nodules significantly impact OS. Number of nodules and size of nodules were then used to create isocurves adopting the metro-ticket approach which has been successfully used to prognosticate OS after liver transplantation. **Results:** The overall median follow-up was 45.5 months. Excluding those with macrovascular invasion and extra-hepatic metastases, 5-year OS was 56% and 5-year disease free survival (DFS) was 36%. Using the metroticket approach, isocurves effectively identify survival stratum on the basis of number and size of nodules into broad-band of 5-year OS of 20–40%, 40–60% and >60%. **Conclusion:** "Metroticket" approach to clinical estimation of survival outcomes with surgical resection allows better stratification of the impact of tumor burden and a more rational comparison with alternative modalities of treatment.

SMHC-10131

Role of Downstaging with Localized Concurrent Chemoradiotherapy in Hepatocellular Carcinoma with Portal Vein Tumor Thrombus

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Introduction: Locally advanced hepatocellular carcinoma (HCC) with portal vein tumor thrombosis (PVTT) has a poor oncological outcome. This study evaluated the oncological outcomes and prognostic factors of surgical resection after downstaging with localized concurrent chemoradiotherapy (CCRT) followed by hepatic arterial infusion chemotherapy (HAIC). **Methods:** From 2005 to 2014, 354

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patients with locally advanced HCC underwent CCRT followed by HAIC. Among them, 149 patients with PVTT were analyzed. Exclusion criteria included a total bilirubin ~2 mg/dL, platelet count <100,000/L, and indocyanine green retention test (ICG R15) >20%. During the same study period, 18 patients with PVTT underwent surgical resection as the first treatment modality. Clinicopathological characteristics and oncological outcomes between the groups were compared. **Results:** Among 98 patients in the CCRT group, 26 patients (26.5%) underwent subsequent curative resection. The median follow-up period was 13 months (range, 1–131 months). The clinicopathological characteristics showed more frequent tumor thrombosis in the first order and larger tumor sizes in the localized CCRT group. The overall survival differed significantly between the resection after localized CCRT and resection first groups (median 62 months [95% confidence interval (CI): 22.99–101.01] versus 15 months [95% CI: 10.84–19.16], respectively, p = 0.006). Multivariate analyses showed that resection as the first treatment was an independently poor prognostic factor for recurrence and overall survival. **Conclusions:** Downstaging with localized CCRT identified optimal surgical candidates in HCC with PVTT, known to be biologically aggressive. Patients showing a response to localized CCRT had a favorable oncological outcome after subsequent resection.

Loco-Regional Therapy

LRTH-10010

MicroRNA-146a-5p Attenuates the Effects of Irradiation and Lipopolysaccharide on Pro-Inflammatory Cytokine Production, Hepatic Stellate Cell Activation and Hepatocyte Apoptosis via Down-Regulation of TLR4 Signaling Pathway

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Introduction: Toll-like receptor 4 (TLR4)-dependent immune response promotes the development of radiation-induced liver diseases (RILDs) during liver cancer radiotherapy. MicroRNA (miR)-146a-5p is a key regulator of the innate immune response. Therefore, this study was conducted to identify the role of miR-146a-5p in the regulation of TLR4 triggered immune response in RILD. **Methods:** The human hepatic stellate cells LX2 were transfected with miR-146a-5p mimics for 24 hours, followed by treatment with lipopolysaccharide (LPS, 50 ng/mL) and or 8Gy X-ray irradiation. The proliferation and apoptosis of LX2 in 72 hours after treatment were measured by CCK8 and flow cytometry (FLC). qRT-PCR and Western blot were used to detect the expression level of TLR4 pathway molecules, pro-inflammatory cytokines and a-SMA. Moreover, human hepatocytes LO2 were irradiated with 8Gy and co-cultured with the culture medium from LX2 for 72 hours and then apoptosis of LO2 was measured using FLC. **Results:** miR-146a-5p mimics promoted apoptosis and attenuated pro-inflammatory cytokines production of LX2 after irradiation and LPS stimulation. Overexpression of miR-146a-5p significantly repressed the expression level of TLR-4, IL-1 receptor-associated kinase 1 (IRAK1), TNF receptor associated factor-6 (TRAF6) and phosphorylation of nuclear factor-kappa B (NF-B). In addition, miR-146a-5p mimics inhibited a-SMA production via reducing the TRAF6 dependent c-Jun N-terminal kinase (JNK) and Smad2 activation. When co-cultured with the medium from the irradiated and LPS stimulated LX2 pretreatment with miR-146a-5p mimics, the apoptosis of LO2 after irradiation was significantly decreased. **Conclusions:** miR-146a-5p down-regulates TLR4 pathway to alleviate irradiation and LPS-induced cytokine production and HSC activation as well as protect hepatocytes against radiation-induced injury, which provides novel insights for RILD study.

LRTH-10011

Central Hepatobiliary Tract Tolerance After Stereotactic Ablative Radiotherapy for Hepatocellular Carcinoma with Major Portal Vein Tumor Thrombosis: A Toxicity Analysis from a Phase II Study

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Purpose: To identify predictors of hepatobiliary (HB) toxicity in patients who received stereotactic ablative radiotherapy (SABR) for major portal vein tumor thrombosis (MPVTT) from hepatocellular carcinoma (HCC). **Methods:** A total of 28 patients received SABR for MPVTT in a prospective phase II trial. All patients had cirrhosis with Child-Pugh score <8. The prescribed dose was 40 Gy in four fractions. The central hepatobiliary tract (cHBT) was defined by a 10 or 15 mm expansion of the portal vein from the splenic confluence

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to the first bifurcation of left and right portal veins. We analyzed the clinical and dosimetric parameters, including multiple dose-volume histogram endpoints: Dmax (the maximum point dose), Dmean (the mean dose), V40Gy (volume of cHBT that received 40 Gy), V37Gy, V34Gy. HB toxicities were graded according to Common Terminology Criteria for Adverse Events version 4.0 and we defined grade 3+ HB toxicity as a severe HB toxicity. **Results:** Median follow-up duration was 9.9 months after SABR. Eight out of 28 patients (28.6%) experienced severe HB toxicity. Among clinical and dosimetric parameters, V40Gy of cHBT with 10 mm expansion were highly associated with severe HB toxicity: V40Gy >40 cm^3 (relative risk [RR]: 3.2, P<.011). However, clinical or other dosimetric factors, Dmax or Dmean of the bile duct and cHBT, did not have predictive value. The risk of severe HB toxicity for V40Gy >20 cm^3, > 20 cm^3, >30 cm^3, and >40 cm^3 are 8.3% (n = 1/12), 41.2% (n = 7/17), 46.2% (n = 6/13), and 54.5% (n = 6/11), respectively. **Conclusion:** SABR to the central liver lesions should be used with caution due to the risk of HB toxicity. Radiation doses to cHBT are associated with development of severe HB toxicity. We suggest that V40Gy <20 cm^3 as a potential dose constraint for cHBT when delivered in four fractions.

LRTH-10017

Is Switching Multiple-Electrode Better Than Single-Electrode in the Radiofrequency Ablation of 3–5 cm Hepatocellular Carcinomas? (Propensity Score Matching Study)

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Introduction: Radiofrequency ablation (RFA) with switching multiple-electrode (M-RFA) could treat large hepatocellular carcinoma (HCC) by inserting up to 3 electrodes into tumors. However, conventional RFA with single-electrode (S-RFA) has limitations to treat HCC larger than 3 cm. The purpose of the study is to compare the outcomes of 3–5 cm HCCs after treatment by M-RFA versus by S-RFA. **Methods:** Between 2008 and 2014, we retrospectively analyzed the patients with 3–5 cm HCCs received M-RFA or S-RFA by internally-cooled electrodes as primary treatment. Propensity score matching (PSM) was applied to select patients with comparable tumor size, number, and liver functions. M-RFA and S-RFA treated 74 patients (82 HCCs) and 54 patients (54 HCCs), respectively. M-RFA treated larger tumors (3.7 versus 3.4 cm, P = 0.002). **Results:** Both groups had comparable complete response rates (91.5% versus 85.2%, P = 0.253). After a mean of follow-up 35.1 months, a total of 9 (11.1%) tumors treated by M-RFA and 21 (41.2%) tumors treated by S-RFA had local tumor progression (P < 0.001). The rates of 1-, 3-, 5-year local tumor progression and overall survival for M-RFA versus S-RFA were 8.0%, 13.5%, and 13.5% versus 19.0%, 42.9%, and 54.6%, respectively (P < 0.001), and 94.5%, 83.8%, and 69.8% versus 83.3%, 61.7%, and 46.1%, respectively (P = 0.011). In the PSM model, M-RFA still had significantly lower local tumor progression rates (P = 0.002) and better overall survival rates (P = 0.025) than S-RFA. By Cox-regression for multivariate analyses, treatment with M-RFA independently associated with lower local tumor progression (HR = 0.264, 95% CI = 0.121–0.579, P = 0.001) and better overall survival (HR = 0.490, 95% CI = 0.250–0.963, P = 0.038). **Conclusions:** Switching multiple-electrode RFA is better for treating 3–5 cm HCCs with a lower risk of local tumor progression and improving overall survival.

LRTH-10097

Granulin-Epithelin Precursor and ATP-Dependent Binding Cassette (ABC) B5 Regulate Liver Cancer Cell Response to Transarterial Chemoembolisation (TACE) After Curative Hepatectomy

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Introduction: Transarterial chemoembolization (TACE) is the most commonly used adjuvant therapy for hepatocellular carcinoma (HCC) after curative resection. Responses to TACE are variable due to tumour and patient heterogeneity. We identified a novel growth factor, Granulin-epithelin precursor (GEP), which a functional molecule that regulated chemoresistance through a drug transporter, adenosine triphosphate-dependent binding cassette (ABC) B5. Expression of GEP and ABCB5 in liver cancer stem cells was associated with chemoresistance. The aim of this study is to evaluate the association between GEP/ABCB5 expression and response to adjuvant TACE after curative resection for HCC. **Methods:** Clinical samples from patients in an on-going randomized controlled study on adjuvant TACE after curative resection for HCC were identified. Clinical samples were retrieved for biomarker analysis. Patients were categorized into 3 risk groups according to their GEP and ABCB5 status for further analysis: low (GEP–/ABCB5-), intermediate (either GEP+/ABCB5– or GEP–/ABCB5+) and high (GEP+/ABCB5+). Early recurrence and disease-free survival were analyzed. **Results:** Clinical samples from 37 patients who had followed-up for more than 2 years were retrieved for further biomarker analysis. Among these 37 patients, 16 were randomized to adjuvant TACE arm and 21 were randomized to control (i.e. no adjuvant TACE) arm. Compared with the control arm, the recurrence rate at 2 years of the adjuvant TACE arm for low, intermediate and high risk groups were 0% vs. 22.2% (p >0.05), 14.3% vs. 83.3%, (p = 0.029) and 71.4% vs. 33.3% (p =

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0.286) respectively. The 2-year disease-free survivals of patients with and without adjuvant TACE in low, intermediate and high risk groups were 100% vs. 83.3% (p = 0.470), 85.7% vs. 28.6% (p = 0.008) and 28.6% vs. 68.6% (p = 0.367) respectively. **Conclusions:** Patients with different GEP/ABCB5 status demonstrated different response to TACE which was associated with significant difference in disease-free survival. A larger clinical study is warranted to confirm its role in patient selection.

LRTH-10099

Surgery versus Radiofrequency Ablation in the Treatment of Very Early or Early Stage Hepatocellular Carcinoma Patients with Portal Hypertension

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Intorduction: Surgical resection is not universally recommended in hepatocellular carcinoma (HCC) patients with established portal hypertension, even in single small cases. Radiofrequency ablation (RFA) is a formal alternative in treating such patients. A number of studies have concluded that portal hypertension should not be a contraindication for hepatic resection. We aimed to compare prognostic outcomes of surgical resection versus RFA in patients with solitary ablatable HCC and portal hypertension. **Methods:** This retrospective study included 189 resected or ablated patients who had a subclinical single HCC 3 cm and clinical signs of portal hypertension. All patients had well-preserved liver function with 105 (55.6%) and 84 (44.4%) primarily receiving surgery and RFA, respectively. Overall and recurrence-free survivals were compared between the two subsets, and clinical factors related to survival endpoints were identified in the entire set. **Results:** The number of patients belonging to BCLC 0 stage was 45 (42.9%) and 55 (65.5%), respectively in the resection and ablation groups (P < 0.05). The mean count of platelet before treatment was greater in the resection group (81.7 ± 13.8 K vs.71.7 ± 19.3 K; P < 0.05). During the median follow-up of 6.2 years, tumor recurrence and mortality from any cause were noted in 62 (59.0%) and 27 (25.7%) patients; and 50 (59.5%) and 26 (31.0%), respectively in the resection and ablation groups. The respective 5-year cumulative rates of recurrence-free and overall survivals were 40.6% and 82.9% versus 33.6% and 76.2% in the corresponding groups (Ps = NS). In multivariate Cox model adjusted for other confounders, resection and RFA was comparable in terms of risk of recurrence and death (Ps = NS). **Conclusions:** Our data indicate that guidelines-based RFA treatment can be justified as a primary option for compensated patients with single small HCC and portal hypertension, even though a tumor is resectable.

LRTH-10120

Radioembolization Induced Liver Disease (REILD) Complicating Patients with Hepatocellular Carcinoma (HCC) Who Underwent Y90 Selective Internal Radiation Therapy: A Retrospective Cohort Study

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Introduction: Selective internal radiation therapy is a form of treatment given to patients with hepatic malignancies like locally advanced HCC where microspheres of Yttrium-90 (y90) are embolized transarterially to tumours. REILD is defined as a condition of sinusoidal obstruction syndrome seen in patients who develop jaundice (bilirubin >51.3 umol/L), and ascites in the absence of cancer progression 1–2 months after receiving y90 treatment. Previous studies which include non-HCC patients and those who underwent chemotherapy put the incidence to be around 0–8%. AIM: To determine the incidence of REILD in patients who underwent y90 treatment for HCC. SECONDARY AIM: to grade the liver toxicity which developed in post-y90 patients. **Methods:** A retrospective single institution study of HCC patients who underwent y90 for HCC from 2008–2016 was done to determine the incidence of REILD based on their bilirubin and radiologic images. Relevant clinical data and the grade of liver toxicity as defined by NCI-CTCAE were collected. **Results:** Of 265 patients, REILD occurred in only 11 patients (4.15%). Of these, 4 patients were Child Pugh A and 7 were Child Pugh B at time of treatment. While most had progressive worsening bilirubin levels, 4 patients had improvement of their bilirubin levels after the bout of REILD. Pre-y90 treatment bilirubin levels ranged from 7 to 61. There were 4, 4 and 3 patients who develop grade 3, 4 and 5 toxicities respectively. One patient who had grade 3 REILD was subsequently given repeat y90 and developed a grade 5 REILD. Survival ranges from 105–358 with median of 151.5 days. **Conclusion:** REILD in HCC is rare condition but could lead to acceleration of hepatic decompensation independent of tumour progression. Previous history of REILD might predispose a patient to a more severe REILD on repeat y90. Diagnosis of REILD will likely require noninvasive or invasive medical treatment.

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Systemic Therapy

SYTH-10031

Safety of Ramucirumab in Combination with FOLFOX4 in Patients with Advanced Hepatocellular Carcinoma – A Phase 1b Study

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Introduction: Ramucirumab is a recombinant human monoclonal antibody that inhibits tumour angiogenesis by blocking vascular endothelial growth factor receptor-2. **Methods:** This phase 1b, multicenter, open-label, single-arm study (NCT02069041) investigated safety, tolerability, and preliminary efficacy of ramucirumab (8 mg/kg) plus FOLFOX4 as first-line treatment in patients with advanced hepatocellular carcinoma (HCC). **Results:** Of the 8 treated patients, 6 were male and 2 were female with a median age of 54.8 years. Seven patients had Barcelona Clinic Liver Cancer stage C and 1 had stage B. All patients had Child-Pugh score A, were viral hepatitis B positive, and had metastases to 1 or more sites. The median relative-dose intensity for ramucirumab was 93.9% (59.9–100.7%), oxaliplatin 83.3% (31.4–100%), folinic acid 89.5% (38.7–97.7%), 5-fluorouracil bolus 60.2% (7.7–93.3%), and 5-fluorouracil drip 84.1% (33.3–87.5%). Dose-limiting toxicities were observed in 3 patients (37.5%), including hepatic haemorrhage (grade 4), blood bilirubin increased (grade 3), and febrile neutropenia (grade 3). The most frequently reported grade 3–4 TEAE was neutrophil count decreased (n = 4). Two (25%) patients experienced AEs that led to discontinuation of study drug. Six (75%) patients experienced dose reduction or delay due to AEs. Six deaths occurred in this study, all due to study disease and none related to study drug. Of 8 patients, 2 achieved partial response, 3 stable disease, 1 progressive disease, and tumours were not evaluable in 2 patients. The disease control rate was 62.5% and overall response rate was 25%. **Conclusions:** The overall safety profile of ramucirumab (8 mg/kg) plus FOLFOX4 appears to be consistent with the toxicity profile of FOLFOX4 and the known safety profile of ramucirumab. The combination was not sufficiently tolerated in the patients with advanced HCC. Ramucirumab may enhance the efficacy of FOLFOX4 in patients with HCC. However, no efficacy conclusion can be drawn due to limited sample size.

SYTH-10091

Circulating Biomarkers of Nivolumab Treatment for Advanced Hepatocellular Carcinoma

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Introduction: Antibodies for programmed death 1 (PD-1) or programmed death ligand-1 (PD-L1) have progressed as a treatment for advanced cancers. We explore the potential of using circulating immune cells as biomarkers for the efficacy of such therapy. **Methods:** We enrolled patients who received nivolumab, an anti-PD-1 antibody, for advanced hepatocellular carcinoma (HCC) in clinical trials and who agreed to have their peripheral blood collected. We analyzed the lymphocyte subclasses and the positivity of PD-1 or PD-L1 positivity on immune cells through flow cytometry. These results were compared in patients with disease control (complete response, partial response, or stable disease) and for disease progression. **Results:** Sixteen patients were enrolled. The objective response rate was 19%, and the disease control rate was 75%. Hemogram distribution and the percentage of total $\pm^2$ T cells or CD4 T cells were not significantly changed after nivolumab treatment, nor were they associated with treatment outcomes. The number of CD8 T cells significantly increased after 4 weeks ($p = 0.016$), but this change was not associated with treatment outcomes. Patients with disease control exhibited significantly lower pretreatment PD-1 positivity on peripheral blood B cells than did patients with disease progression ($p = 0.042$). Patients with disease progression were more likely to exhibit increased PD-L1 positivity on monocytes after 28 ($p = 0.020$) or 42 ($p = 0.008$) days of treatment. **Conclusions:** Low pretreatment PD-1 positivity on peripheral blood B cells and stationary PD-L1 positivity on monocytes after treatment were associated with disease control after nivolumab treatment for advanced HCC.

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Poster Abstracts

Translational Research, Pathology, Epidemiology

TRPE-10002
Cyclophilin B as a Drug Target in Hepatocellular Carcinoma

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Cyclophilin B (CypB) performs diverse roles in living cells, but its role in hepatocellular carcinoma (HCC) is largely unclear. To reveal its role in HCC, we investigated the induction of CypB under hypoxia and its functions in tumor cells in vitro and in vivo. Here, we demonstrated that hypoxia-inducible factor 1± (HIF-1±) induces CypB under hypoxia. Interestingly, CypB protected tumor cells, even p53-defective HCC cells, against hypoxia- and cisplatin-induced apoptosis. Furthermore, it regulated the effects of HIF-1±, including those in angiogenesis and glucose metabolism, via a positive feedback loop with HIF-1±. The tumorigenic and chemoresistant effects of CypB were confirmed in vivo using a xenograft model. Finally, we showed that CypB is overexpressed in 78% and 91% of the human HCC and colon cancer tissues, respectively, and its overexpression in these cancers reduced patient survival. **Conclusion:** These results indicate that CypB induced by hypoxia stimulates the survival of HCC via a positive feedback loop with HIF-1±, indicating that CypB is a novel candidate target for developing chemotherapeutic agents against HCC and colon cancer.

TRPE-10012
Incidence of Primary Liver Cancer in Subjects with Chronic Hepatitis B in Korean National Liver Cancer Screening Program

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Introduction: To optimize efficacy of National Liver Cancer Screening Program (NLCSP) for subjects with chronic hepatitis B (CHB), it is needed to know the incidence of liver cancer and its predisposing factors in the program. **Methods:** From January 2010 to December 2014, all the HBsAg positive participants who received at least two or more abdominal ultrasonography under NLCSP were retrospectively enrolled in a single tertiary hospital. Annual incidence of primary liver cancer was calculated and related clinical factors were investigated. **Results:** During 5 years, 541 subjects were enrolled. Mean age was 53 years old and 292 subjects (54%) were receiving antiviral agents. Liver cirrhosis (LC) was diagnosed in 212 (39.2%). Mean follow-up time was 2.36 years and 15 hepatocellular carcinoma and 1 intrahepatic cholangiocarcinoma were diagnosed. Annual incidence of primary liver cancer was 9.8 per 1,000 patient year. Cumulative incidence at 1, 3, and 5 year was 0.6%, 2.6%, and 6.4%, respectively. In multivariate analyses, LC (hazard ratio [HR] 8.74, 95% confidence interval [C.I.] 1.97–38.71, P = 0.024), age (HR 1.08, 95% C.I. 1.01–1.15, P = 0.024) were significantly associated with cancer development. **Conclusions:** Despite of high rate of oral antiviral therapy, incidence of primary liver cancer is not low in CHB patients in Korea. Old age and presence of LC are independently associated with higher risk of cancer development during surveillance. This study could be used as baseline data for quality control of NLCSP.

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TRPE-10014

Delayed Viral Suppression During Antiviral Therapy Increases Hepatocellular Carcinoma in HBeAg-Positive Chronic Hepatitis B

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Background/Aims: The treatment option in chronic hepatitis B (CHB) patients with persistent low-level of viremia despite of entecavir or tenofovir monotherapy is not clear yet. This study investigated the development of hepatocellular carcinoma (HCC) or cirrhosis in hepatitis B envelope antigen (HBeAg) positive CHB patients, according to the time needed to achieve complete viral suppression. **Methods:** A total of 350 HBeAg-positive CHB patients who were recently started on antiviral therapy with entecavir or tenofovir were included. The enrolled patients were categorized into 2 groups with 4 separated criteria based on the time needed to achieve complete viral suppression: within 1, 2, 3, or 4 years of therapy initiation. The measured outcomes were development of HCC and cirrhosis. **Results:** Cumulative incidence of HCC was significantly higher in patients failing complete viral suppression within 1 year (hazard ratio (HR), 5.42; 95% confidence interval, 1.25–23.46; P = 0.024) or 2 years (HR, 4.47; 95% CI, 1.70–11.73; P = 0.020), than patients who achieved complete viral suppression within 1 or 2 years, respectively. Cumulative incidence of cirrhosis was also significantly higher in patients failing suppression within 1 year (HR, 2.09; 95% CI, 1.12–3.89; P = 0.021) or 2 years (HR, 2.70; 95% CI, 1.59–4.59; P < 0.001). When the time for achieving viral suppression exceeded 2 years, the cumulative incidence of HCC or cirrhosis was not different regardless of viral suppression. **Conclusions:** Complete hepatitis B virus suppression should be achieved within 2 years of antiviral therapy initiation to reduce the risk of cirrhosis or HCC development.

TRPE-10023

The Clinicopathologic and Prognostic Significance of Cancer Stem Cells in Hepatocellular Carcinoma

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Background: Cancer stem cells (CSCs) have been associated with aggressive behavior in several cancers. However, their role has not yet fully elucidated. This study aimed to explore the clinical and prognostic significance of cancer stem cells (CSCs) in hepatocellular carcinoma (HCC). **Materials and Methods:** In 248 HCC surgically resected in Kyungpook National University between 2005 and 2010, immunohistochemistry for CD133, CD44 and Aldehyde dehydrogenase 1 (ALDH1) was performed using tissue microarray containing two representative cores per each case. **Result:** The positivity of CD133, CD44 and ALDH1 was 8.5%, 4% and 98%, respectively. CD133 negativity correlated with high grade of Edmondson and Steiner grade (p = 0.009) and recurrence (p = 0.005). On the other hand, ALDH1 negativity was associated with lower T category (p = 0.035). However, CD44 status has no association with any clinicopathologic parameters. In univariate analysis, CD44 positivity was related to poor overall survival (OS) (p = 0.014), but not CD133 and ALDH1. Multivariate analysis demonstrated that CD44 positivity was and independent worse prognostic factor for OS (HR = 3.364, 95% CI = 1.533 to 7.379, p = 0.002). **Conclusion:** These findings suggest that targeting CSCs could be an attractive therapeutic approach to HCC patients.

TRPE-10037

Metformin Inhibits Growth and Metastasis with Enhancement of Radiation Response in Hepatocellulcar Carcinoma Xenograft Model

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Introduction: Metformin, one of the most widely prescribed drug for type 2 diabetes mellitus, has been shown to be clinically associated with antitumor effect. Preclinical studies also support an antitumor effect of metformin in

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various types of cancer. This study aimed to investigate the pntential of metformin to inhibits the growth and metastasis with enhancement of radiation response in hepatocellular carcinoma (HCC) xenograft mice model. **Methods:** Huh-7 HCC cells were injected to the right thigh in Balb/c nude mice. Huh-7 bearing mice were treated with local tumor irradiation with a single 15 Gy of X-ray (RT), intraperitoneal administration of metformin with 150 mg/kg/day until the day of sacrifice (MET), or combination of both (administration of metformin 6 hours prior irradiation) (RT-MET). Tumor response to treatment was determined by a tumor growth delay assay. Metastatic potential was evaluated by gross qualitative observation of spontaneous pulmonary metastasis in a lung metastasis model on day 45 and 60. **Results:** RT or MET resulted in a significant reduction of tumor growth and RT-MET enhanced it further than each treatment alone (55% reduction compared with RT and 67% reduction compared with MET). More importantly, RT or MET inhibited in the growth of metastatic nodules in lung and RT-MET enhanced it further than each treatment alone (93% reduction compared with RT and 76% reduction compared with MET). RT-MET decreased the expression of vascular endothelial growth factor and matrix metallopeptidase 9 by immunohistochemistry. **Conclusions:** Metformin inhibits the growth and metastasis of HCC with enhancement of radiation response in vivo. Our data suggest that metformin can be a clinically useful adjunct to radiotherapy in HCC.

TRPE-10059

In Vivo Cirrhotic Mouse Model to Predict Hepatocellular Carcinoma Biological Behavior

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Hepatocarcinogenesis takes place in the cirrhotic microenvironment with complex interactions between tumor and stroma. Existing patient derived xenograft models are non-cirrhotic and do not recreate this interface. We aim to create a mouse cirrhotic model of xenotransplant to better simulate Hepatocellular Carcinoma (HCC) biological behavior. To create a cirrhotic microenvironment, we treated NOD Scid gamma (NSG) mice with thioacetamide (TA) for 4 months to induce full-fledged cirrhosis. 11 primary human HCC were characterized based on degree of differentiation and epithelial to mesenchymal transition (EMT) markers. After dissociation, 1,000,000 cells from each human HCC were transplanted into NSG cirrhotic mice. To compare the effect of cirrhosis on tumor engraftment, a poorly differentiated human HCC was transplanted into 3 NSG TA cirrhotic mice and 3 NSG non cirrhotic mice. Of the 11 human HCC samples transplanted into cirrhotic mice, 3 HCCs (28%) engrafted into the mice livers. 3 out of 4 human HCCs (75%) with poorly differentiated histology engrafted into the cirrhotic mouse livers. None of the moderate or well differentiated tumors engrafted. HCC nodules were confirmed to be of human origin by human MHC1 immunolabeling. There was an average of 20 colonies per slide for the human derived xenograft transplanted into NSG-TA cirrhotic mice, compared with 3.7 colonies per slide for the xenograft transplanted into non-cirrhotic mice. The cirrhotic mouse model allows preferential engraftment of the poorly differentiated subtype with EMT compared to the more differentiated subtypes. It also allows for increased growth of the human HCC compared to the non cirrhotic model. The ability to predict the natural biology of HCC in a clinically relevant cirrhotic model holds tremendous implications for treatment of HCC.

TRPE-10062

RIsk Factors of Development of Hepatocellular Carcinoma After Direct-Acting Antiviral Therapy in Patients with HCV Infection

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Introduction: An incidence of HCC in HCV patients achieved SVR by direct-acting antiviral therapy (DAA) was not rare. The aim of this study was to evaluate the risk factors for HCC in patients after SVR by DAA. **Methods:** From September 2014, 572 patients with HCV treated by interferon-free DAA, with at least 12 weeks follow-up after the end of treatment, were enrolled (DCV+ASV 175, SOF/LDV 192, PTV/r/OMV 37, SOF+RBV 168). The cumulative HCC incidence rate (HIR) was calculated. The correlation between HCC incidence and the factors (age, gender, platelet count, FIB-4, cirrhosis +/–, history of curative therapy for HCC +/–, AFP, M2BPGi, achievement of SVR12 +/–) were also evaluated. **Results:** Median age was 67 (23–87), 321 (56%) were male, 207 (36%) had cirrhosis, 79 (14%) cases were with HCC history. SVR was achieved in 519 (91%). HIR in HCC history group (2-year, 37%) was significantly higher than that in HCC naïve group (4%) ($P < 0.01$). HIR was no difference between SVR and non-SVR group regardless of HCC history in this follow-up period. In all cases, HCC history positive ($P < 0.01$) and M2BPGi >2.3 at 12 week after DAA ($P = 0.02$) were significant risk factors for HCC incidence with multivariate analysis. In 455 cases with HCC naïve and SVR, AFP >4 ng/dl ($P = 0.04$) and M2BPGi >2.3 ($P < 0.01$) were significant risk factors. When

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AFP and M2BPGi were scored as 1 point for each, the 2-year HIR in 0, 1 and 2 points were 3%, 9% and 22%, respectively (P < 0.01), and the risk was well stratified. **Conclusions:** The recurrence of HCC was observed frequently despite achieving SVR in patients with history of curative therapy for HCC. AFP >4 and M2BPGi >2.3 were independent risk factors of development of HCC after SVR. The patients satisfied these conditions need more careful observation for incidence of HCC.

TRPE-10074

Treatment Outcomes of the National Cancer Centre Singapore Consensus Guidelines for Hepatocellular Carcinoma

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Introduction: The Comprehensive Liver Cancer Clinic (CLCC) at the National Cancer Centre Singapore (NCCS) has implemented consensus guidelines for hepatocellular carcinoma (HCC) since 26th September 2014. Since its' establishment, the guidelines have been used to guide clinical decisions, but the implications of it on treatment outcomes is yet to be assessed. AIM: To determine the treatment outcomes of patients who adhered to the NCCS consensus guidelines for HCC and assess its' effects on patients' disease control and survival. **Methods:** A cohort of 262 patients with HCC who were treated at CLCC in NCCS from the period of 1st June 2014 to 31st December 2016 was retrospectively analysed. Information on the staging as defined in the guidelines, the subsequent treatment implemented, and each patient's treatment outcomes – namely the time to recurrence/ progression of disease, and overall survival in the follow up period – were reviewed. These outcomes were compared between the patients that adhered to the guidelines vs. those that failed to adhere to the guidelines. **Results:** The overall rate of adherence to the NCCS consensus guidelines for HCC was 69.8%. When the patients who adhered to the guidelines vs. those who failed to adhere were compared, there was a statistically significant difference in both time to recurrence/ progression of disease (p-value 0.001) and overall survival (p-value 0.006). **Conclusion:** The NCCS consensus guidelines for HCC stratify the treatment protocol for patients based on their tumour burden and liver function. However, the final treatment recommendation is made following a multidisciplinary team discussion. This allows for personalised treatment plans and benefits the patient, as each treatment plan is made after considering the patient's final clinical assessment. This is reflected in the superior treatment outcomes of the cohort of patients that adhered to the guidelines.

TRPE-10080

Genetic Disruption of GATA4-Mediated Transactivation in Liver Cancer Impedes Precursor to Hepatocyte Transition

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The most frequent chromosomal structural loss in hepatocellular carcinoma (HCC) is of the short arm of chromosome 8 (8p). Genes on the remaining homologous chromosome are not recurrently mutated, however, and the identity of key 8p tumor suppressor genes (TSG) is unknown. Analysis of minimal commonly deleted 8p segments to identify candidate TSG implicated GATA4, a master transcription factor driver of hepatocyte epithelial lineage-fate. Liver-conditional deletion of one Gata4 allele, to model the haploinsufficiency seen in HCC, produced enlarged livers with a gene expression profile of persistent precursor proliferation and failed hepatocyte epithelial-differentiation. HCC mimicked this gene expression profile, even cases morphologically classified as 'well-differentiated'. HCC without chromosome 8p deletion also featured GATA4 loss-of-function via GATA4 germline mutation that abrogated GATA4 interactions with a coactivator MED12, or by inactivating mutations directly in GATA4 coactivators (e.g., ARID1A). GATA4 re-introduction into GATA4-haploinsufficient, or ARID1A re-introduction into ARID1A-mutant/ GATA4-intact HCC cells, activated hundreds of hepatocyte genes and quenched the proliferative precursor program. Thus, deficiency of GATA4-transactivating function in HCC suppresses hepatocyte epithelial-differentiation and sustains replicative precursor phenotype.

TRPE-10082

Decreased Expression of BRCA1-Associated Protein 1 Increased Tumor Cell Invasion and Indicated Poor Prognosis in Hepatocellular Carcinoma

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Introduction: BRCA1-associated protein 1 (BAP1) has been identified as a broad-spectrum tumor suppressor, yet its role in hepatocellular carcinoma (HCC) remains unknown. This study aimed to investigate the biological function and clinical significance of BAP1 in HCC. **Methods:** BAP1 expression was measured in stepwise metastatic HCC cell lines, tumor and peritumoral tissues by quantitative real-time PCR and Western blot. The function role of BAP1 in HCC was investigated by overexpression and knock-down of BAP1 in

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HCCLM3 and HepG2 cell lines, respectively. Tumor tissue microarrays of 396 HCC treated with curative resection was used to detect the expression of BAP1. The prognostic significance was assessed using Kaplan-Meier survival estimates and log-rank tests. The clinical relevance of BAP1 was also analyzed. **Results:** The mRNA and protein levels of BAP1 were significantly decreased in HCC cell lines with highly metastatic potential, and were downregulated in cancerous tissues from HCC patients. The depletion of BAP1 promoted tumor cell proliferation, G1/S cell cycle progression, cell migration and invasion in vitro, whereas BAP1 overexpression suppressed proliferation, cell cycle progression, migration and invasion. Notably, BAP1-regulated HCC invasiveness is accompanied by typical changes of epithelial-mesenchymal transition. Immunohistochemical analysis showed that decreased BAP1 expression was positively correlated with aggressive tumor characteristics, such as tumor size (P = 0.007), tumor number (P = 0.044), vascular invasion (P = 0.012) and TNM stage (P = 0.002). Patients with low BAP1 expression showed significantly shorter overall survival (OS) and recurrence-free survival (RFS) compared with those with high BAP1 expression (P < 0.001 and P < 0.001, respectively). Importantly, on multivariate analysis, decreased expression of BAP1 was demonstrated as an independent prognostic factor for OS (hazard ratio [HR] = 1.739, P < 0.001) and RFS (HR = 1.590, P = 0.002). **Conclusions:** Decreased expression of BAP1 was associated with HCC invasiveness and indicated poor prognosis of HCC after surgery. BAP1 may serve as a valuable prognostic biomarker and potential therapeutic target for.

TRPE-10095

HCC Surveillance in Patients with Advanced Fibrosis – Christchurch Experience

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Introduction: The incidence of Hepatocellular Carcinoma (HCC) in New Zealand has risen steadily over the last four decades and is projected to be 23% higher in 2016 compared to 2006. While HCC surveillance is recommended in patients with cirrhosis, international guidelines are inconsistent regarding HCC surveillance in patients with advanced fibrosis (F3). We retrospectively analysed the incidence of HCC in patients with cirrhosis and advanced fibrosis followed-up at Christchurch Hospital. **Method:** Out of 365 patients registered in the HCC-surveillance registry during 2012–2016, 332 consecutive patients with cirrhosis or advanced fibrosis were selected. Data was obtained from electronic health records. Cumulative incidence of HCC was evaluated using Kaplan-Meier analysis and compared using Log-rank test. **Results:** The mean-age was 56.6 years (20–82 years) with 67% male, 80.4% European and 13.5% Maori/Pacific Islanders. The most common aetiology was hepatitis C virus (HCV) (66.9%) followed by Alcohol liver disease (8.7%) and Non-alcoholic fatty liver disease (7.2%). 62.2% patients with HCV were cured and 15 of 19 patients with hepatitis B virus were under viral suppression treatment. During the cumulative surveillance period of 941.7 person-years (average 2.8 person-years) 21 HCCs were diagnosed (2.2% per 1 person-year). The cumulative 1-year and 5-year incidence rates in patients with cirrhosis (2.3% and 8.5% respectively) were similar to patients with advanced fibrosis (1.2% and 13.5% respectively) (P = 0.60). Most of the HCC diagnosed in advanced fibrosis (3 out of 4) were very early stage compared to only 3 of 17 patients with cirrhosis. Surveillance was discontinued in 18.35% patients commonly due to non-adherence (9.04%) and death (3.6%). **Conclusion:** Surveillance in patients with advanced fibrosis appears useful for early detection and curative treatment of HCC. Long-term studies are needed to ascertain whether successful therapy mitigates HCC risk sufficiently to discontinue surveillance in selected patients.

TRPE-10111

Comparison of Clinical Characteristics and Prognoses Between Child-Pugh Groups in Indonesian Hepatocellular Carcinoma Patients

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Introduction: Hepatocellular carcinoma (HCC) is the third highest cause of cancer death worldwide. Child-Pugh scoring system in HCC patients plays an important role in determining liver function. There is limited studies evaluating HCC survival related to Child-Pugh scoring system. The aim of this study is to compare the clinical characteristics and survival between Child-Pugh groups in HCC patients in Indonesia. **Methods:** This retrospective cohort study took place in a secondary referral hospital located in Tangerang, Indonesia. HCC data was taken from medical records of years 2013–2017. Prognosis was assessed using Chinese University Prognostic Index (CUPI) and overall survival rate. Analysis to find mean difference between Child-Pugh groups was done using One-way ANOVA or Kruskal-Wallis. Cumulative overall survival rates were estimated using Kaplan-Meier and tested by log-rank test. **Results:** A total of 52 patients were included, out of which 27 (51.9%) were male. Median age was 61 (34–73) years. There were 35 (67.3%) patients in Child-Pugh group B and 5 (9.6%) patients in Child-Pugh group C. Hepatitis B and C was the cause of HCC in 21 (40.4%) and 2 (3.8%) patients respectively. Mean overall survival was 3.9 (±2.3) months. Mean tumor size in Child-Pugh group A, B and C were 12.9 (±4.5), 11.8 (±6.4) and 4.1 (±2.6) centimeters respec-

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tively (P = 0.028). There was significant difference in mean platelet values between Child-Pugh groups (P = 0.045). There was significant association between TNM staging (P = 0.023) and CUPI (P < 0.001) with the Child-Pugh groups. Patients with Child-Pugh group A had significantly higher overall survival rate when compared with Child-Pugh groups B and C (P = 0.037). **Conclusion:** Higher platelet values, smaller tumor size, higher CUPI, and higher TNM stage had significant association with Child-Pugh groups B and C. Patients with higher Child-Pugh score had significantly lower overall survival.

TRPE-10121

Comparison of Selective Internal Radiation Therapy (SIRT) versus Sorafenib in Patients with Locally Advanced Hepatocellular Carcinoma in Mongolia: A Subgroup Analysis of SIRveNIB Study

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Background: Mongolia has one the highest hepatocellular carcinoma incidence in the world due to widespread hepatitis B and C endemic along with high alcohol consumption rate. The objective of this study is to evaluate the efficacy of Selective Internal Radiation Therapy using SIR-Spheres yttrium-90 microspheres versus sorafenib in Mongolian patients with locally advanced HCC patients at Barcelona Clinic Liver Cancer stage B and C patients without extrahepatic metastasis. **Methods:** SIRveNIB was a multi-center, randomized trial in which eligible patients with locally advanced inoperable HCC was randomized (1:1) to either single injection of SIRT or Sorafenib (oral 400 mg BD) and patients were followed up till progressive disease or unacceptable toxicity. Key endpoints were overall survival, tumor response rate, time-to-tumor progression, progression-free survival and toxicity. **Results:** 39 patients (20 SIRT, 19 Sorafenib) were enrolled from Mongolia. BCLC C patients without extra-hepatic metastasis comprised 62% of patients, 18% had portal vein thrombosis, 85% were Child-Pugh A, 45% were hepatitis B and 30% were hepatitis C. Altogether 4 of 20 patients (20%) in the SIRT arm failed to receive the study therapy. Intention-to-treat analysis was carried out with the OS in the SIRT and Sorafenib arms being 9.2 and 15.6 months, respectively, (HR 0.95, p = 0.889). Tumour response rate (TRR) was 10% and 0% (p = 0.487) respectively. Time-to-tumor progression (TTP) was 6.2 vs. 8.5 months (HR 1.01, p = 0.971) and PFS 5.9 vs. 8.5 months (HR 1.07, p = 0.842 for SIRT and Sorafenib, respectively. At least one severe adverse event (-3 grade) was found in 56% and 47% of patients in the SIRT and Sorafenib arms, respectively. **Conclusions:** In this subgroup analysis of a single center which is part of a larger multi-center, randomized controlled trial, 20% of the patients assigned to the SIRT arm failed to receive SIRT. On intention-to-treat analysis, there was no significant difference in OS, TRR, TTP and PFS between the SIRT and sorafenib arms.

TRPE-10124

Correlation between Tumor Engraftment in Patient-Derived Xenograft Models and the Expression of Cancer Stem Cell Markers in Hepatocellular Carcinoma Patients

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Introduction: The patient-derived xenograft (PDX) model is useful for studying carcinogenesis and for developing personalized medicine. However, PDX model could not be made from all patients with hepatocellular carcinoma (HCC); more aggressive tumors seem to be more suitable for making PDX models. The high expression of cancer stem cell (CSC) markers is related to poor prognosis in HCC patients. We investigated the relationship between tumor expression of CSC markers and success of PDX model establishment. **Methods:** The surgical tissues of the HCC patients were subcutaneously transplanted into the NOD/SCID mice and tumor tissue was serially transplanted for establishing a PDX model. RNA was extracted from the patient tissue used in the PDX model and cDNA was synthesized. The mRNA expression levels of EpCAM, CK8, CD133, CD44, CD18, SALL4, CD24, CD90, CD13, ALDH1A1, ALB, AFP and Glypican-3 were evaluated using the real-time qPCR. The relative fold change was analyzed. **Results:** All 40 HCC patients (median age 57 years, 95% male, 75% HBsAg positive) were involved in the PDX model development, and 26 patient tissues (success cases 8 vs. fail cases 18) were available for this study. The incidence of CD 133 expression was significantly higher in the PDX model success group (100%) than in the failing group (27.8%) (p < 0.001). CD 13 expression rate was lower in the success group (12.5%) than in the failing group (66.7%) (p < 0.05). Other CSC and tumor markers did not show significant difference. **Conclusions:** Expression of CD133 and suppression of CD13 might be related with success of tumor engraftment in HCC PDX model establishment.

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TRPE-10126

Non-Cirrhotic Hepatocellular Carcinoma: Etiology and Occult Hepatitis B Virus (HBV) Infection in an HBV-Endemic Area

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Objectives: Although hepatocellular carcinoma (HCC) usually develops in cirrhotic livers, a minority of cases occur in non-cirrhotic livers (NCLs). We investigated etiology, clinicopathological features, and occult hepatitis B virus (HBV) infection (OBI) in patients with NCL HCC in an HBV-endemic area. **Methods:** Seven hundred ten patients who underwent resection or transplantation for HCC at National Cancer Center, Korea, were enrolled. HCC and fibrosis stage were diagnosed pathologically. **Results:** One hundred seventy-eight patients (25%) did not have cirrhosis (NCL group). The main cause of HCC was HBV infection (77.2%), followed by cryptogenic disease (11.0%). The prevalence of NCL was 19.2%, 32.5%, 50.0%, and 48.7% among patients with HBV, HCV, alcoholic, and cryptogenic disease, respectively ($p < 0.05$); corresponding non-fibrosis rates were 8.1%, 0%, 19.0%, and 24.3%, respectively. The NCL group was significantly older, with a larger tumor size, smaller tumor number, lower tumor stage, and more frequent non-HBV etiology. Among non-HBV HCC cases, 130 (80.2%) had antibodies against HBV core and 55 (38.5%) had OBI. OBI-positive rates of 0%, 31.8%, and 52.6% were detected among HCV, alcoholic, and cryptogenic HCC cases, respectively. OBI did not correlate with advanced fibrosis. The NCL and LC groups did not differ in median overall survival. **Conclusion:** Regardless of etiology, a significant number of HCC patients, including half of non-viral cases, did not have cirrhosis. Half of cryptogenic HCC cases had OBI. This study promotes an understanding of fibrosis and OBI among patients with HCC in an HBV-endemic area. **Key Words:** Hepatocellular carcinoma, Non-cirrhotic liver, Occult hepatitis B virus infection

TRPE-10135

Rescuing GATA4-Deficiency Phenotypes by HNF4A Introduction in Hepatocellular Carcinoma

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Hepatocellular carcinoma (HCC) is the 3rd leading global cause of cancer death worldwide. Recently, we have discovered previously undescribed deletion and germline mutation of GATA4 and showed that GATA4 is a key differentiation driver and metabolic regulator in HCC. However, as GATA4 is mostly deleted in HCC, targeting GATA4-downstream molecules would be ideal. In this study, we intent to perform proof-of-concept experiments to show that introduction of HNF4A, which is a GATA4-regulated downstream target, could (partially) rescue the impaired phenotypes in GATA4-deficient HCC cell line. Correlation analysis using gene expression microarray of human HCC samples was conducted to identify genes that are positively correlated with GATA4. A transgenic mouse model with liver-specific conditional GATA4 knockout was designed to identify liver morphology and gene expression changes correlated with the loss of GATA4 in the mouse liver. CRISPR-mediated knockout of GATA4 and lentiviral HNF4A overexpression was carried out in GATA4-deficient HCC cell line, PLC/PRF/5, followed by functional assays. WST-1 proliferation assay, annexinV/7-AAD assay, cell cycle analysis by MUSE analyser, and senescence Î²-galactosidase staining were performed. Pearson correlation analysis from human HCC samples showed that expression of HNF4A is positively correlated with GATA4. Conditional GATA4 knockout mice livers had lower HNF4a expression when compared to age-matched control mice. Loss-of-function analysis by CRISPR-mediated GATA4 knockout further showed downregulation of HNF4A in GATA4-deficient PLC/PRF/5 cell line. Lentiviral HNF4A overexpression demonstrated reduced proliferation, increased apoptosis, and cell cycle arrest at G2/M phase when compared to control. However, no senescence induction has been detected from the HNF4A-overexpressing cells. HNF4A expression is positively correlated with GATA4 expression in HCC samples. Transgenic mouse data and CRISPR-mediated knockout showed that HNF4A is one of GATA4-downstream targets. HNF4A overexpression decreases proliferation.

TRPE-10137

Comprehensive Analysis of the Newly Established Drug-Resistant Cell Lines Reveals the Acquired Resistance Mechanisms and Potential Combination Therapies in Hepatocellular Carcinoma

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Hepatocellular Carcinoma (HCC) is one of the most prevalent cancers with a typically poor prognosis. Sorafenib is the only FDA approved standard treatment for advanced HCC since a decade ago. However, clinical and preclinical observations indicate uthat sorafenib treatment may have limited efficacy due to tumour progression from the rapid development of acquired resistance. In order to study the acquired resistance mechanisms, we have established several sorafenib-resistant HCC cell lines including Huh7 and Hep3B, by gradual

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increment of sorafenib over a period of time in culture. Transcriptome microarray, phospho-protein array, and Seahorse analyser were used to analyse the established cell lines. Several EMT and stemness-related markers have been measured in HCC parental and sorafenib-resistant cell lines by qPCR. According to GO enrichment analysis and gene set enrichment analysis (GSEA), epithelial-to-mesenchymal transition (EMT), EGFR pathway, purine metabolism, pyrimidine metabolism, glycolysis, and oxidative phosphorylation are activated in the resistant cells, whereas drug metabolism by cytochrome P450, fatty acid metabolism, and cholesterol biosynthesis are suppressed. Seahorse analysis further supported that there were elevated glycolytic and OXPHOS rates in the resistant cells. Both canonical and non-canonical NFB pathways are found to be activated and enhanced expression of CD44 and CD133 was detected in the resistant cells. Taken together, the data suggests that HCC cells would gain of EMT/stemness properties, modulate metabolic activities, and activate NFB pathway to become sorafenib-resistance. We believe that targeting such altered pathways and activities could sensitise the resistance cells to sorafenib treatment and possibly improve the outcome in combinations. Some combinations are being tested in in vitro and in vivo models with the established resistant cell lines.

TRPE-10139

Genomic Profiling Reveals the Mechanism of Sorafenib Resistance in Liver Cancer Patient-Derived Xenografts

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Introduction: Sorafenib is effective treatments for hepatocellular carcinoma (HCC). However, acquired evasive resistance is a major limitation of treatment with sorafenib. Our objective was to investigate mechanisms of sorafenib acquired resistance in HCC. **Method:** Two sorafenib-acquired PDX models (LV037 and LV068) were established using oral administration of sorafenib after 4~6 passages. Whole-genome sequencing was performed on PDX tissue pre- and post-sorafenib resistance and whole genomics variation were compared, and the normal liver tissue from the same patient was used as control, for eliminating the germline mutation. **Results:** LV037 and LV068 showed significant difference in mutation burden from pre- and final-passages. LV068 showed more SNV/Indel compared to LV037. Variant allele fraction of each somatic mutation was used to assess tumor heterogeneity and track clonal evolution. As expected, the variant allele fraction of TP53 was increased to 90% from 50% or 75%, which indicated that lose TP53 tumor-suppressor activity and acquire oncogenic gain-of-functions were come up during the acquiring sorafenib resistance. KIT, one target of sorafenib, was also showed contain clonal-expansion mutation in LV068. Interesting, the common mutation clonal expansions were only occurred in TP53 and USP17L1P. It indicated that the resistance of sorafenib might not depend on only one or certain common genes, but decide by cumulative effect of mutation. Protein-protein interaction network showed the topological properties of the genes between the two models were similar and independent. The interactions between the genes from two models are few, and TTN and RPSA were the most important genes in the PPI network, they might carry the driver mutations for sorafenib resistance. **Conclusion:** PDX model is very useful to picture the drug-resistance mechanism. The cumulative effect of genome variation might be the reason of sorafenib resistance. Moreover, there are many ways to gain the functions. Sorafenib resistance is complicated and more models.

Imaging and Diagnosis

IMDI-10021

Comparison of Acoustic Radiation Force Impulse Elastography and Transient Elastography for the Prediction of Hepatocellular Carcinoma Recurrence After Radiofrequency Ablation

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Introduction: To compare the clinical value of acoustic radiation force impulse (ARFI) elastography and transient elastography (TE) for the prediction of recurrence after radiofrequency ablation (RFA) of hepatocellular carcinoma (HCC) and to investigate other predictors for recurrence of HCC. **Methods:** A total of 130 patients with HCC who underwent ARFI elastography and TE within 6 months before curative RFA were enrolled prospectively, from 2011 to 2016. Independent predictors for recurrence of HCC were analyzed separately by using ARFI elastography and TE. The accuracy of ARFI elastography and TE to predict HCC recurrence was compared by receiver operating characteristic (ROC) curve analysis. **Results:** The mean age of HCC patients (98 men and 32 women) was 63.7 (range, 43–84) years. During the follow-up period (median 21.4 months), 61 (46.9%) patients had experienced recurrence of HCC. Patients with recurrence had significantly more frequent liver cirrhosis, lower serum albumin, higher prothrombin time, lower platelet counts,

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larger spleen size, higher alpha-fetoprotein, higher ARFI velocity, and higher TE value compared to patients without recurrence. In multivariate analysis using ARFI velocity, serum albumin and ARFI velocity (HR 2.639; 95% confidence interval [CI] 1.719–4.052, P < 0.001) were selected as independent predictors of recurrence and in multivariate analysis using TE value, serum albumin, total bilirubin, and TE value (HR 1.023; 95% CI 1.008–1.038, P = 0.002) were selected as independent predictors of recurrence. The area under the ROC curve of ARFI elastography (0.816, 95% CI 0.745–0.888) was not statistically different to that of TE (0.800, 95% CI 0.726–0.875) for predicting recurrence of HCC (P = 0.627). The optimal cutoff value of ARFI velocity and TE value were 1.6 m/s and 13 kPa, respectively. **Conclusions:** ARFI elastography and TE provide comparable assessment in predicting the recurrence after RFA of HCC.

IMDI-10042

Recurrent Spontaneous Rupture of Hepatic Epithelioid Hemangioendothelioma

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Hepatic epithelioid hemangioendothelioma (HEH) is a rare tumor of vascular origin with low to intermediate malignancy potential. Spontaneous rupture of HEH is rare and life-threatening. Here we report a case of HEH with recurrent spontaneous rupture. A 70-year-old man presented with severe pain on the right upper abdomen for 2 days. Abdominal computer tomography (CT) scan revealed a 9 cm-sized hypervascular hepatic mass with spontaneous rupture. Emergent transcatheter arterial embolization was performed. After 6 months later, he again presented with abdominal pain. Abdominal CT scan showed a 18 cm-sized heterogenous enhancing mass with intratumoral hemorrhage. Transcatheter arterial embolization was done. Magnetic resonance imaging showed a hyperintense rim on T1-weighted and hypointense rim on T2-weighted images with intratumoral hemorrhage. Liver transplantation was performed due to rapid tumor growing and progression of liver failure. Immunohistochemical examination showed features of HEH.

IMDI-10075

Improved Sensitivity of The 2010 AASLD Guidelines for Non-Invasive Diagnosis of HCC in a Surgical Cohort from a Hepatitis B Endemic Region

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Introduction: Diagnosis of hepatocellular carcinoma (HCC) is mainly by dynamic imaging techniques based on guidelines such as of the American Association for Study of Liver Disease (AASLD). No biopsy is required if criteria are met. The 2005 AASLD guidelines mandate that there be cirrhosis before an imaging diagnosis of HCC can be made. However, updates to the guidelines in 2010 have been expanded to chronic Hepatitis B carriers. **Aim:** To compare the sensitivity and positive predictive values of the 2005 and 2010 guidelines in a Hepatitis-B endemic region. **Secondary Aim:** To evaluate proportion of patients who avoided unnecessary biopsies. **Methods:** A retrospective study of 176 patients from 2006–2010 from a joint cancer service who had undergone surgical resection for presumptive diagnoses of HCC, were analysed. Their hepatitis status and imaging were also evaluated. Multiphasic CT-Liver images were re-examined by 2 oncologic radiologists and the diagnosis of HCC and cirrhosis was only made when there was concordance in opinion. **Results:** Of all cases, 86.9% of patients were histologically confirmed HCCs. Sensitivity of detecting cirrhosis on CT was 83.2% with an accuracy of 79.2%. Sensitivity of diagnosis based on the 2010 and 2005 guidelines were 58.1% and 7.85% respectively. When the two guidelines were compared using McNemar's Test, the revised criteria showed a 38.4% increase in sensitivity, p-value <0.000001. There was also an 85.9% reduction in the number of patients undergoing unnecessary biopsies. **Conclusion:** Diagnosis of HCC was based on the pre-operative diagnosis of cirrhosis which in this centre, was of high sensitivity and accuracy. The difference in sensitivities between the 2005 and revised 2010 AASLD guidelines for diagnosing HCC reduces the need for invasive biopsy and likelihood for tumour seeding.

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IMDI-10116

The Management of Safe and Reliable New Technology Using Simulation Software and Fusion System for RFA

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Abdominal ultrasound (US) is particularly operator-dependent and less objective compared with computed tomography (CT) or magnetic resonance imaging (MRI). To overcome these disadvantages, US fusion system was developed. Fusion systems are able to increase operator comprehension of the 3D relationship between the liver vasculature and tumors and allow the practitioner to easily comprehend spatial and positional relationships because the reference screen image reconstructed using DICOM data of CT and/or MRI is synchronized with the actual movements of the US probe. This fusion imaging is attracting the attention of operators who perform radiofrequency ablation (RFA) for the treatment of HCC. Fusion imaging can be a very useful tool in the management of HCCs that have poor ultrasound conspicuity, and the combination of fusion imaging and contrast enhanced US guidance in RFA therapy can sometimes be a more effective treatment for HCC with poor conspicuity on B-mode US and CEUS/fusion imaging. On the other hand, the volume analyzer SYNAPSE VINCENT® called Synapse 3D® internationally (Fujifilm Medical Co.) and Advantage Workstation® (GE Healthcare, Chalfont St. Giles, UK) are 3D image analysis systems that enables quick and easy access to high-definition 3D images of organs and vessels using previously captured CT or MRI, while also providing highly practical analysis functions at the workstation. Before RFA, we extracted DICOM data using the 3D volume analyzer system and integrated these DICOM data onto US platform. Using this method, we can make colorized fusion images and this new technology can also use contrast enhanced US mode. This new technology is useful and safe and reliable for RFA. In this presentation I will talk about the simulation software and fusion system for RFA.

Surgical Management of HCC

SMHC-10050

Can We Use ALBI Grade to Predict Post-Hepatectomy Mortality for Hepatocellular Carcinoma?

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Introduction: ALBI grade, a simple formula using albumin and bilirubin to reflect liver dysfunction of patients, was shown to have prognostic significance in long-term survival as well as post-hepatectomy liver failure for hepatocellular carcinoma after curative treatment. The aim of this study was to evaluate the relationship between ALBI grade and post-hepatectomy mortality after curative resection. **Methods:** We performed a retrospective study using a prospectively collected surgical outcome monitoring database from July 2009 to June 2015 to evaluate the use of ALBI grade in predicting various post-hepatectomy outcome for hepatocellular carcinoma. The primary outcome was 90-day mortality. Liver failure, massive blood loss, post-operative sepsis and surgical site infection were used as secondary outcome. Other potential predictive factors of post-hepatectomy outcome were also analysed with univariate and multivariate analysis. **Results:** 179 patients were recruited into this study, with 121 patients classified as ALBI grade 1 and 58 patients classified as ALBI grade 2 and 3. There was no significant difference in ASA class, type of hepatectomy, operation time, rates of massive blood loss, post-operative sepsis and surgical site infection between the two groups. There was no post-hepatectomy liver failure. Two patients (1.1%) developed 90-day mortality, all in ALBI 1 group, with no significant difference between groups. Type of hepatectomy, platelet count and bilirubin level were independent prognostic factors of post-op sepsis. ASA class was independent factor for massive blood loss and surgical site infection. **Conclusions:** We observed no association between ALBI grade and early post-operative outcome after hepatectomy for HCC in our series. The result might be limited by the small sample size in a well selected group of HCC patients with low 90-day mortality rate. Further evaluation with larger sample is needed before we can understand how to apply ALBI grade in addition to the current standard of pre-hepatectomy assessment.

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SMHC-10072

Role of Hepatic Trisectionectomy in Advanced Hepatocellular Carcinoma

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Introduction: Advanced hepatocellular carcinoma (HCC) with underlying cirrhosis poses a major operative challenge. Patients have a dismal prognosis without curative resection. The role of hepatic trisectionectomy in these patients is not established. The aim of this study was to analyze and compare the perioperative outcome and prognosis of patients undergoing trisectionectomy with hepatic resection of a lesser extent. **Methods:** From 2000 to 2014, 48 patients underwent hepatic trisectionectomy for HCC with background cirrhosis or chronic hepatitis (Group A). Another (Group B) 520 patients underwent liver resection of a lesser extent. Patient demographics, clinicopathological data, perioperative outcome and long-term survival were compared between the 2 groups. **Results:** Intraoperative bloodloss, operating time and total hospital stay were significantly higher in trisectionectomy patients. Tumors were larger and more advanced in group A. The morbidity rate was 43.8% in group A compared to 27.5% in group B, p = 0.027. In-hospital mortality was 6.3% for group A. Group A had a significantly shorter time to recurrence (4.5 months vs. 6.2 months, p = 0.036), as well as a poorer disease-free survival (DFS) than group B (6.3 months vs. 15.7 months, p = 0.02). Overall survival was comparable. Tumor number, size, albumin, INR, microvascular invasions and positive resection margins were predictors of disease-free survival. **Conclusion:** Hepatic trisectionectomy may be associated with a higher morbidity and lower DFS. However, these patients would not be suitable candidates for ablative therapy or liver transplantation. With careful patient selection and meticulous surgical technique, trisectionectomy is feasible and gives these patients the only hope of cure.

SMHC-10087

Novel Use of Percutaneous Thrombosuction for Hepatic Vein Thrombosis of the Liver Graft After Liver Transplantation

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Introduction: Early thrombosis of hepatic vein graft of liver graft after living related donor liver transplantation (LDLT) is a challenging problem and poses a high potential of graft failure or/and patient failure. Re-exploration faces the risk of repeated general anesthesia, adhesion and anatomical difficulty, family's attitude, and the potential of rethrombosis. **Methods:** A 54-year-old woman with hepatitis B viral infection related liver cirrhosis with two hepatocellular carcinoma (cT2N0M0) received LDLT with right hepatic lobe donated by her daughter. The outflow reconstruction using an artificial vascular conduit included the V5 and V8 with end-to-side anastomosis each. Anastomosis of the conduit with right hepatic vein orifice on IVC of the recipient was performed with 4-0 prolene suture. The liver enzyme, total bilirubin and lactate elevated since the 7th day postoperation. CT study showed thrombosis of V5 and V8 with hypoenhancement of the corresponding liver parenchyma. The hepatic artery and the portal vein were patent. **Results:** Heparin 5000U was given intravenously. After local anesthesia, we inserted a 7-French (Fr) sheath through right femoral vein, then 7-Fr Judkins guide catheter to approach hepatic vein, wiring to distal V5 branch with 0.014" HydroST wire (COOK medical). Thrombosuction with 7-Fr Pronto V4 (Vascular Solution) to extract thrombus was repeated smoothly. Balloon catheter angiography showed good flow from V5 to IVC. The function of the graft recovered and she discharged at the end of 3rd week after transplantation. She remained well for 6 months up to now. **Conclusion:** Thrombosuction had been used in the treatment of deep vein thrombosis of lower limbs, pulmonary embolism, thrombosis of hemodialysis fistula or of coronary vessels. We applied it for liver graft to avoid repeated major surgery and general anesthesia. To follow up imaging studies and appropriate anticoagulant therapy are necessary for those who had an episode of graft.

SMHC-10094

Laparoscopic Hepatectomy (With or Without Robot Assistance) versus Radiofrequency Ablation as Minimally Invasive Treatment for Very Early/Early Stage of Hepatocellular Carcinoma

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Introduction: Whether the liver resection or radiofrequency ablation (RFA) should be the first-line treatment for very early/early hepatocellular carcinoma (HCC) in patients who are candidates for both remains a hot debate. Recently, minimally invasive surgery has been introduced in liver surgery. The outcome of minimally invasive hepatectomy (MH) and RFA need reassessment and this is the aim of the present study. **Methods:** This is a retrospective analysis of patients who received MH and RFA for primary HCC from January 2005 to January 2015. Only patients with Barcelona Clinic Liver Cancer (BCLC) stage 0/A disease and only operations performed with the minimally invasive approach (percutaneous, laparoscopic and robot-assisted) were included. Baseline clinical and laboratory parameters were retrieved and reviewed from the hospital database. Perioperative outcomes, overall and disease-free survivals were compared.

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Propensity score matching analysis was performed to minimize the potential bias in clinicopathological factors. **Results:** A total of 225 patients underwent MH and RFA for primary HCC during the study period. Among them, 216 patients (59 patients received MH and 155 patients received RFA) were stage BCLC 0/A and eligible for the study. The median duration of follow-up was 47.2 (IQR = 27.0–72.3) months. Propensity score matching analysis performed and resulted in 59 pairs of patients/group. All patient, tumour and liver function factors were well balanced between two groups. There was no statistical difference in the complication rates and operative blood loss between two groups. However, MH provided significantly better overall and disease-free survival than RFA. **Conclusions:** MH provides better long-term overall and disease-free survival compared with RFA in patients with BCLC very early/early-stage HCC without an increase in the complication rate. If the minimally invasive approach is feasible, MH should be considered as the first-line treatment for these patients.

SMHC-10100

Possible Role of Surgery in the Treatment of Patients with Intermediate-Stage Hepatocellular Carcinoma and Preserved Hepatic Function

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Introduction: Based on scientific evidence, transarterial chemoembolization (TACE) is a current standard therapy for patients with intermediate-stage hepatocellular carcinoma (HCC). However, a large proportion of these patients cannot be cured by TACE alone, and repeated TACE can increase the risk of liver deterioration. Moreover, multiplicity of lesions is not a contraindication for radical hepatectomy, although it is a potential risk factor of recurrence. Based on these backgrounds, we aimed to identify the survival benefits of surgical resection compared with TACE, the standard-of-care, for patients with intermediate-stage HCC. **Methods:** A total of 548 patients with Barcelona clinic liver cancer (BCLC) stage B HCC and Child-Pugh A hepatic function underwent surgical resection (n = 163) or TACE (n = 385) as the primary therapy between 2007 and 2011 at our hospital. Their median age was 57 years (range, 51–65), and most were male (85.9%) and were infected by hepatitis B virus (73.7%). The all-cause and cancer-specific mortalities were compared between the surgery and TACE groups. **Results:** The mean number of tumors (2.3 ± 0.8 vs. 3.4 ± 1.5) and the proportion of portal hypertension (8.6% vs. 26.0%) were greater in the TACE group than in the surgery group (P < 0.05 for both). During a median follow-up of 3.6 years, resection provided a survival benefit over TACE at 5 years (63.2% vs. 32.2%; P < 0.05). The cancer-specific mortality rate at 5 years was also significantly lower in the surgery group (9.6% vs. 36.0%; P < 0.05). In the adjusted Cox model, resection was identified as an independent predictor of favorable all-cause and cancer-specific mortality outcomes (adjusted hazard ratio [95% confidence interval]: 0.46 [0.36–0.58] and 0.38 [0.28–0.51], respectively; P < 0.05 for both). **Conclusions:** Our data indicate that patients with resectable BCLC stage B HCC and good liver function may benefit more from surgical resection as the first-line therapy than from TACE.

SMHC-10101

Surgery or Chemoembolization for Rescuing Patients with Non-Ablatable and Non-Transplantable Multiple Hepatocellular Carcinomas at BCLC Stage A

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Introduction: Transarterial chemoembolization (TACE) is usually considered as second-line therapy for patients with non-ablatable and non-transplantable multifocal hepatocellular carcinomas (HCCs) who meet the Milan criteria. However, previous data suggest that patients with multiple tumors may be suitable for resection despite the higher risks of postoperative recurrence. Given the non-curability of TACE, this study aimed to evaluate the therapeutic performance of surgery compared with TACE in such cases. **Methods:** Subclinical patients with multiple HCC nodules 3 cm in diameter and Child-Pugh class A liver function, who met the Milan criteria, were included (n = 300). The patients were treated with surgical resection (n = 81) or TACE (n = 219) as the initial treatment. The median age of the patients was 57 years; 80.7% were male and 79.3% were infected by hepatitis B virus. **Results:** Patients with three nodules or clinical signs of portal hypertension were more frequently observed in the TACE group than in the surgery group (32.4% vs. 6.2% and 47.0% vs. 22.2%, respectively; P < 0.05 for both). During a median observation period of 5.6 years, overall and cancer-specific deaths occurred more frequently in the TACE group (57.5% vs. 19.8% and 37.4% vs. 12.3%, respectively; P < 0.05 for both). The median overall survival times in the TACE and surgery groups were 5.2 and 6.6 years, respectively, with 5-year overall survival rates of 52.5% and 85.2%, respectively (P < 0.05). Similar trends were observed for cancer-specific mortality (P < 0.05). Multivariate analyses revealed that surgical resection provided better overall and cancer-specific survivals independent of other clinical predictors, including tumor factors (hazard ratio [95% confidence interval]: 0.28 [0.16–0.48] and 0.24 [0.12–0.48], respectively; P < 0.05 for

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both). **Conclusions:** Considering our findings and the non-curability of TACE, surgical resectability should be assessed before TACE rescue in patients with multifocal HCCs meeting the Milan criteria and who are not eligible for local ablation or liver transplantation.

SMHC-10130

Prognosis and Treatment of Locally Advanced HCC Without Main Portal Vein Involvement

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Introduction: Patients with advanced hepatocellular carcinoma (HCC) were expected to have median survival duration of only 6 months. However, it is also obvious that the prognosis is different according to variables including liver function status and vascular invasion degree. This study was performed to retrieve the prognostic factors and appropriate therapy in locally advanced HCC patients without main portal vein invasion (MPVI), who expected to have a relatively better prognosis. **Methods:** Total 207 advanced HCC patients without MPVI at initial diagnosis from June 2004 to June 2015 were included. **Results:** Mean age of patients was 60.1 ± 12.5 years and men were predominant (80.7%). The median follow-up period was 7.8 (0.17–44.6) months, and 184 (88.9%) of these patients died. In univariate analysis, high Child-Pugh class, more than 4 liver tumors, more than 10 cm sized largest tumor, poor performance status, and initial treatment modality showed significant association with poor prognosis. ($p < 0.001$, < 0.001, 0.009, 0.001 and < 0.001, respectively). In multivariate analysis, High Child-Pugh class (hazard ratio [HR], 1.50; $p = 0.016$), more than 4 liver tumors (HR, 2.08; $p < 0.001$), more than 10 cm sized largest tumor (HR, 1.88; $p < 0.001$) and initial treatment modality ($p < 0.001$) were significantly independent factors for survival. In Child-Pugh class A, surgery showed significant survival benefit than other therapies. (median survival time, MST, 52.0 months; $p = 0.012$) In Child-Pugh class B, Locoregional treatment (MST, 4.1 months; $p = 0.003$) alone and Combination of LRT and radiation therapy (MST 15.2 months; $p < 0.001$) resulted in significantly improved survival time compared with best supportive care (MST 2.1 months). **Conclusion:** In locally advanced HCC patients without MPVI, the prognosis was affected by number and size of tumor, and liver function status. In addition, surgery could be recommended as first treatment in Child-Pugh class A of liver function.

Loco-Regional Therapy

LRTH-10001

Compensatory Increase in Future Liver Remnant Volume After External Beam Radiotherapy to Liver Tumors

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Introduction: Radiation to the focal liver can induce compensatory hypertrophy, which has been reported in radioembolization. In this study, we investigated whether external beam radiotherapy (EBRT) could induce compensatory hypertrophy of the liver. **Methods:** A total of 82 consecutive patients were recruited who received EBRT for hepatocellular carcinoma (n = 77) or cholangiocarcinoma (n = 5) from April 2012 to June 2014. The patients were divided into two subgroups according to whether their tumors were located in the right or left lobe. The left lateral and right lobes were considered to be unirradiated volumes in each respective group. Total liver volume (TLV), normal liver volume (NLV), left and right whole liver volume (LLWV and RLWV, respectively), volume of liver irradiated <30Gy (V30), Child-Pugh score, future liver remnant ratio (FLR) and percentage of FLR hypertrophy from baseline (%FLR hypertrophy) were assessed. **Results:** In the right lobe group, %FLR hypertrophy and LLWV increased significantly at all follow-up time points ($p < 0.001$). Clinical factors associated with %FLR hypertrophy were tumor volume, tumor location, and treatment method. Post-radiotherapy treatment affected Child-Pugh scores, which were significantly lower than baseline scores at the second, third, and fourth follow-ups. V30 and %FLR hypertrophy showed significant correlations at the first and second follow-up periods. In the left lobe group, %FLR hypertrophy and RLWV showed no significant changes during follow-up. **Conclusions:** Significant compensatory hypertrophy was observed after EBRT for liver cancers in the right lobe.%FLR hypertrophy values increased until the fourth follow-up (median: 396 days).

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LRTH-10019

Two-Week Schedule of Hypofractionated Radiotherapy as a Salvage Therapy for Recurrent Hepatocellular Carcinoma

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Purpose: Stereotactic body radiation therapy (SBRT) has emerged as an alternative, non-invasive local treatment option for patients with HCC when established curative treatment modalities cannot be applied. However, short-course SBRT may not be safe if the tumor is located around a critical normal organ. Therefore, we applied hypofractionated radiotherapy for these tumors and evaluated the long-term clinical outcomes of this treatment. **Methods and Materials:** A total of 77 patients (84 lesions) with HCC who were treated with hypofractionated radiotherapy were registered between December 2008 and July 2013 at our institution. A dose of 3.5-5 Gy per fraction was given over 2 weeks, resulting in a total dose of 35-50 Gy. Local failure was defined as the recurrence of the treated lesion; intrahepatic recurrence was defined as recurrence within the liver outside the treated lesion. Overall and recurrence-free survivals were estimated from the date of the start of SBRT to the date of death, the last follow-up examination, or to the date of tumor recurrence, respectively. **Results:** The median follow-up period of all patients was 33.6 months (range, 4.8–78.3 months). All patients had received various courses (range, 1–19 courses) of previous therapies. Overall survival rates at 3 and 5 years were 56.4% and 40.9%, respectively. Local control rate at 3 and 5 years were 86.7% and 76.7% in all treated lesions, respectively. The alpha-fetoprotein level before radiotherapy was a significant parameter for predicting overall survival by multivariate analysis. Grade E 3 hepatic toxicity was observed in two patients. **Conclusions:** This two-week schedule of hypofractionated radiotherapy for recurrent HCC was feasible with relatively good local control as a salvage treatment. This fractionation schedule can be used as an alternative treatment option for HCC located to a critical normal organ if shout-course, high-dose SBRT is not feasible.

LRTH-10026

Early Recurrence of Hepatocellular After Successful Therapy with Direct Acting Antiviral Agents for Chronic Hepatitis C: An Observational Study

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Background: Chronic HCV infection is the leading risk factor for HCC in the United States, and the second leading risk factor worldwide. Sofosbuvir is a nucleotide hepatitis C NS5B polymerase inhibitor with a pangenotypic antiviral activity and a high genetic barrier to resistance. Some recent studies have shown an unexpected high rate and pattern of tumor recurrence coinciding with HCV clearance and it was suggested that disruption of immune surveillance may facilitate the emergence of metastatic clones. Aim of the work: To assess recurrence of HCC after successful therapy in a cohort of Egyptian patients with chronic hepatitis C genotype 4 treated with a Sofosbuvir-containing Regimen. **Methods:** Patients were followed by a multislice triphasic CT and AFP every 4 weeks throughout therapy and for 12 weeks after the end of treatment. **Results:** Thirty nine patients (78%) were males, the mean age was 57.9 ± 6.3. Twenty patients (40%) were treated by Sofosbuvir/Ribavirin for 24 weeks, 14 patients (28%) were treated by Sofosbuvir/Daclatasvir, and 16 patients (32%) by Sofosbuvir/Simeprevir for 12 weeks. Twenty seven patients (54%) underwent RFA, 15 patients (30%) underwent TACE, 3 patients (6%) underwent combined RFA and TACE, and 5 patients (1%) were treated by Liver resection. Forty one patients (82%) had undetectable HCV RNA at the end of treatment. Twenty five patients (50%) developed HCC recurrence during follow up. The majority of cases (19 out of 25, 76%) developed a new lesion, whereas 6 patients (24%) developed a local recurrence. **Conclusions:** Treatment with a Sofosbuvir-based regimen was associated with a high recurrence of HCC in a cohort of Egyptian patients with HCC associated with chronic hepatitis C genotype 4. This high recurrence rate might be attributed to improper patient selection rather than a direct drug effect. Patients with HCC should be properly evaluated prior to antiviral.

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LRTH-10027

Can Hepatoma Arterial Embolization (HAP) Score Predict Survival in Egyptian Patients With Hepatcellular Carcinoma?

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Introduction: Hepatocellular carcinoma is the fifth most common cancer in men and seventh among women, worldwide. TACE is the standard of care for treatment of patients with an intermediate stage HCC. HAP score is a new score validated on HCC patients who underwent TACE to assess survival depending on 4 parameters: Bilirubin, serum albumin, AFP, and the size of the largest tumor. Aim: Evaluation of validity and utility of Hepatoma Arterial Embolization Prognostic score (HAP score) in a cohort of Egyptian patients with an intermediate stage HCC who are amenable for TACE. **Methods:** Data of HCC patients who underwent TACE at the National Liver Institute from Jan 2007 till May 2015 was collected retrospectively, 416 patients were included, HAP score was evaluated in all patients and overall survival was assessed w ith a minimum follow up period of 12 months. **Results:** The majority of patients were males (83.7% males versus 16.3% females), with a mean age of 58 ± 8.1 years. Out of 416 patients, 267 (64.9%) had Child class A cirrhosis, 143 (34.7%) had Child class B cirrhosis, and only one (0.2%) patient had Child class C cirrhosis at presentation. Out of 416 patients, 51 (12.3%) had HAP score of 0, 129 (31%) had score of 1, 164 (39.4%) had HAP score of 2, 72 (17.3%) had HAP score of >2. The median survival of patients with HAP 0, HAP 1, HAP 2 and HAP >2 was 53, 23, 22, 14 months respectively, showing a significantly shorter survival with advanced score, as shown in Fig. 1 Survival probability 18.6%, 13.1%, 9.2%, 7.3% for patients with HAP score 0, 1, 2, >2 respectively, with a P value <0.01. **Conclusion:** HAP score is a useful tool for prediction of survival after in a cohort of Egyptian patients with HCC.

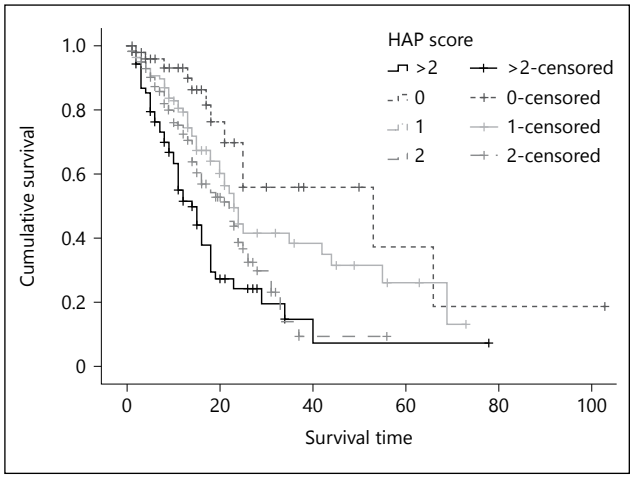

Fig. 1. (for Abstract no LRTH-10027).

LRTH-10046

Effectiveness of Drug-Eluting Bead-Transarterial Chemo-Embolization in Intermediate Stage of Hepatocellular Carcinoma

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AIM: According to the Barcelona Clinic Liver Cancer (BCLC) staging system, intermediate stage contains very heterogeneous hepatocellular carcinoma (HCC) patients. Recently, subclassification of intermediate stage on the basis of Milano criteria and up to 7 criteria is proposed. In this study, the effectiveness of drug-eluting bead-transarterial chemo-embolization (DEB-TACE) in intermediate stage was investigated. **Method:** 120 patients (M: F = 90:30; median age = 76; Child A: B: C = 72:44:4; BCLC stage A: B: C: D = 6:85:23:6) with unresectable HCC who received DEB TACE in our hospital were studied. The objective radiological response was classified according to the modified Response Evaluation Criteria in Solid Tumors (mRECIST) v.1.1 by using dynamic CT at one or two months after therapy. According to Bolondi's subclassification, the patients of BCLC B stage were divided into four groups (B1: 24, B2: 31, B3: 19, B4: 10). The response rate and tumor factor associated response in these patients group were examined. **Results:** The overall response rate and disease control rate in intermediate stage were 36% and 89%, respectively. Considering the subclassification, the response rate in B1 group (61%) was significantly higher than that of B2+B3 group (29%). Although B2+B3 group was constituted by the patients who did not satisfy the up to 7 criteria, to examine the response of only in the patients with less than 7 tumors, the response rate (60%) was similar to that of B1 group. Tumor factors associated response and found to be significant on univariate analysis were simple gross classification (simple nodular type) and number of tumor. Tumor diameter was not associated with the response. **Conclusion:** For the treatment of intermediate stage of HCC, although DEB-TACE is considered to be most effective in B1 group, it is suggested that DEB-TACE is also effective in the patients with less than.

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Predictors of Progressive Disease in Patients with Hepatocellular Carcinoma Who Undergo First Trans Arterial Chemoembolization

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Background: Hepatocellular Carcinoma (HCC) is a primary liver malignancy that frequently occurs in patients with chronic liver disease or cirrhosis. One of the therapeutic modalities for HCC is Trans arterial Chemoembolization (TACE), an infusion and embolization of cytotoxic agent at the site of malignancy. Some studies have found that non-responder (failure of TACE by mRECIST criteria: stable disease or progressive disease) is still quite high at around 30%. In fact, there have been studies in Indonesia which found that non-responders after undergoing TACE was 60%. Objective Determining predictors of progressive disease in HCC patients who undergo TACE. **Methods:** This study evaluates 75 patients that undergo TACE in 2012 until 2016. We collected patient's data from their medical record. We performed bivariate analysis using cross tab (for nominal data) and variables which p value <0.25, continued by performing multivariate analysis using logistic regression. **Results:** Patients mean age is 50.99 ± 12.83 years old, with 80% male and 41.3% are progressive disease. Child Pugh Score A is 57.3% and B is 47.2% and the etiology is mostly Hepatitis B (76%). Mean AST, ALT, AFP level, tumor size and amount of lesion are 141.77 ± 128.83 IU/L; 74.67 ± 53.19 IU/L; 688.59 ± 537.73 ng/L; 11.58 ± 3.89 cm; 1.38 ± 0.56 respectively. Bivariate analysis shows that AST level >40 IU/L and AFP level >600 IU/L, tumor size >5 cm and Child Pugh Score B are significant. From multivariate analysis, variables that significant as predictors for progressive disease are AFP level >600 IU/L with OR {5.467 (CI 1.482–20.170)}; Child Pugh Score B {OR 6.008 (CI 1.754–20.579)}. **Conclusion:** In this single center study, predictors for progressive disease are AFP level >600 and Child Pugh Score B (OR 5.467 and 6.008 respectively). Study with higher sample is still needed.

LRTH-10052

Evaluation of Liver Function and Tumor Characteristics After First Trans Arterial Chemoembolization in Hepatocellular Carcinoma

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Background: Trans arterial chemoembolization (TACE) is usually performed on unresectable HCC and is considered to be palliative. After TACE the prognosis of HCC can be assessed with tumor characteristics and liver function into account in the staging system; this may determine who will be stable, progressive and also decompensate after TACE. Objective Evaluate liver functions and tumor characteristics in HCC patients who undergo first TACE. **Methods:** This study evaluates 70 patients that undergo TACE in 2012 until 2016. We collected patient's data from their medical record, including age, gender, etiologies, tumor size, number of lesion, and AFP level. Laboratory examination such as complete blood count (Hemoglobin, Leukocyte, Thrombocytes), liver function test (AST, ALT, Bilirubin, Albumin, INR), AFP level, and CT-Scan performed before TACE and 1 month after TACE. Data was analyzed by paired t-test. **Results:** Patients mean age is 50.99 ± 12.78 years old, with 80% male. Child Pugh Score A is 57.3% and B is 47.2% and the etiology is mostly Hepatitis B (76%). Mean AST, ALT, AFP level, tumor size and amount of lesion are 137.20 ± 118.199 IU/L; 71.59 ± 48.698 IU/L; 688.9 ± 551.2 ng/L; 11.5 ± 3.9 cm; 1.37 ± 0.56 respectively. There were significant alteration in increased mean AST level 33.2 IU/L (p = 0.0006), CTP score 1.36 (p = 0.0001), size 1.32 cm (p = 0.020) and number of lesion 0.34 (p = 0.001) after 1 month post TACE. **Conclusion:** In 1 month post TACE evaluation; AST, CTP score, tumor size, and number of lesion are increased significantly.

LRTH-10053

Predictors of One Year Mortality in Patients with Hepatocellular Carcinoma Who Undergo Trans Arterial Chemoembolization

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Background: Hepatocellular Carcinoma (HCC) is the seventh major causes of morbidity in terms of cancer worldwide, and also the third most common cause of cancer-related death. A study showed overall median survival after the first Trans Arterial Chemoembolization (TACE) procedure

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was 17.1 ± 3.4 months, 2% patients underwent urgent liver transplantation, and 4% patients died within 6 weeks of TACE. Objective Determining predictors of one year mortality in HCC patients who undergo TACE. **Methods:** This study evaluates 50 patients that undergo TACE in 2012 until 2016. We collected patient's data from their medical record. We performed bivariate analysis using cross tab (for nominal data) and variables which p value <0.25, continued by performing multivariate analysis using logistic regression. **Results:** The mean age of the 50 patients was 52.24 ± 11.107 years old, 78% were male, and 66%had chronic HBC infection. Mean AST were 105.80 ± 62.174 IU/L, ALT 77.06 ± 57.261 IU/L, AFP level 631.36 ± 429.47 ng/L, tumor size 11.74 ± 4.12 cm and number of lesion were 1.42 ± 0.64. Six patients died after 1 month TACE procedure, and mean survival from this study was 6.2 ± 0.652 month. Bivariate analysis shows that high AFP levels >600 ng/L and multiple tumor lesion was significant. From multivariate analysis, variable that significant as predictor for mortality was multiple tumor lesion {OR 4.372 (CI 1.203–15.888)}. **Conclusion:** In this single center study, predictors for mortality was multiple tumor lesion with OR 4.372. Study with higher sample is still needed. **Key Words:** Hepatocellular carcinoma, Transarterial chemoembolization, One year mortality.

LRTH-10056

High Serum Alpha-Fetoprotein Levels and Previous Radiofrequency Ablation Predict Y90-Radioembolization Ineligibility in Hepatocellular Carcinoma Patients

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Introduction: Y90-radioembolization allows for targeted delivery of radioactive microspheres to treat hepatocellular carcinoma (HCC). A pre-treatment assessment including mapping angiography, lung shunt fraction (LSF) and tumor/liver microsphere uptake simulation determines treatment eligibility. Factors associated with assessment failure are largely unknown. We aimed to evaluate predictors of Y90-radioembolization eligibility and treatment outcomes in HCC. **Methods:** All consecutive HCC cases that underwent Y90-radioembolization assessment at our institution from 2009 to 2016 were evaluated. Baseline demographics, tumor parameters, Y90-radioembolization assessment/treatment and long-term outcomes were recorded. Categorical and continuous data were analyzed by Fisher's exact and Mann-Whitney U test, respectively. Survival was estimated with Kaplan-Meier analysis. **Results:** A total of 100 HCC cases underwent Y90-radioembolization eligibility assessment during the study period. Mean (SD) age of patients was 65.0 (±8.9) years with 82% male. Top 3 etiologies were: HBV 41%, fatty liver/cryptogenic 17% and alcohol 13%. Most cases were Child-Pugh A (73%), followed by B (22%). HCC was multi-nodular in 71.3% and alpha-fetoprotein was >400 ug/nl in 23.8% of cases. Barcelona Clinic Liver Cancer (BCLC) stages were: A (28%); B (48%); C (14%). Forty-six cases had prior transarterial chemoembolization (TACE) or radiofrequency ablation (RFA). Thirty-six cases (36%) failed assessment due to: excessive LSF 15 cases (41.7%); abnormal arterio-venous shunting 9 cases (25%); unfavorable tumor/liver microsphere uptake simulation 9 cases (25%). AFP level was higher in assessment failure group (mean 24707 versus 1256 ug/nl, p = 0.023). Prior RFA (OR 10.2; 95% CI 1.1–90.9; p = 0.038) was significantly associated with assessment failure whereas etiology, Child-Pugh stage, multi-nodularity and prior TACE were not. **Conclusion:** One-third of HCC patients intended for Y90-radioembolization therapy were deemed ineligible during assessment due to excessive LSF, prohibitive arterio-venous shunting and unfavorable tumor/liver microspheres uptake simulation. High serum AFP levels and previous RFA significantly correlated with Y90-radioembolization ineligibility and could be potential predictive factors to aid physicians in better selection of HCC patients for Y90-radioembolization treatment.

LRTH-10064

Utility of a New Function in 3D Sim-Navigator: Electric Field, Which Indicates the Predicted Ablative Area

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Background: 3D Sim-Navigator (HITACHI) is a navigation system that can be used in real-time virtual sonography (RVS) by simulating and navigating the 3D positions of electrodes. As an addition, 3D Sim-Navigator is now equipped with a new system that shows the predicted ablative area. This function indicates the electric field that occurs around the electrodes as the predicted ablative area on MPR images. The Electric-field Simulator (E-field) can manage various electrodes, such as monopolar and bipolar RF systems. We therefore examined the accuracy of E-field. **Methods:** We evaluated 10 nodules treated using bipolar electrodes (Celon-POWER; Olympus Medical Systems) and 72 nodules treated using monopolar electrodes (VIVARF System; STARmed) between April 2016 and March 2017 prospectively. We compared the major and minor axes of maximum axial ablative area for 72 nodules ablated by monopolar electrodes on both

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E-field and post-RFA computed tomography (CT). We then compared ablative volumes of 10 nodules ablated by bipolar electrodes on E-field and on post-RFA CT. Finally, we compared treatment efficacy using a grading system (J Gastroenterol. 2013;48(8):951–65.) on E-field and on post-RFA CT. **Results:** On evaluation of maximum axial ablative area by monopolar electrodes, major and minor axes were smaller on E-field than on CT, but these differences were not significant. On evaluation of ablative volume by bipolar electrodes, the correlation coefficient for ablative volumes on E-field and CT was greater than 0.96. On comparing treatment efficacy using the grading system, the degree of agreement between E-field and CT was 0.691 and the weighted kappa coefficient was 0.929. **Conclusion:** Ablative volume on E-field correlated well with that on post-RFA CT. Furthermore, good agreement was observed between the treatment efficacy based on E-field and post-RFA CT. The present results suggest that contrast-enhanced CT may become unnecessary for confirming therapeutic effects in the future.

LRTH-10077

Preoperative Transarterial Chemoembolization(TACE) for Resectable Hepatocellular Carcinoma(HCC): A Retrospective Comparative Analysis

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Objective: The disease-free survival was compared to evaluate the effect of preoperative TACE on surgical outcome after hepatic resection for HCC between the preoperative TACE group and no preoperative TACE group (control group). **Methods:** From April 2009 to June 2015, 122 patients who underwent liver resection due to HCC was included in this retrospective study. Among them, 21 patients were included the preoperative TACE group and the remained (n = 101) were included no preoperative TACE group. The clinicopathologic background and disease-free survival rates was compared after hepatic resection between two groups. Further survival analyses were done by subgroup analysis according to alpha-feto protein (AFP, ~200 ng/mL or <200 ng/mL), protein induced by vitamin K absence or antagonist-II (PIVKA-II, ~200 mAU/mL or <200 mAU/mL) and tumor size (~5 cm or <5 cm). **Results:** Eighteen patients in the preoperative TACE group (85.7%) received TACE only once and three patients twice. The mean interval between last TACE and hepatic resection was 51 days. The 2-year disease-free survival rates were 76.2% for the preoperative TACE group and 56.4% for the control group. In the preoperative TACE group, there's no recurrence in only high AFP level group and in patients with large size tumor and high PIVKA II level. **Conclusion:** Preoperative TACE improved surgical outcome. In addition, subgroup analysis showed an enhanced survival in TACE patients with high AFP level and in patients with large size tumor and high PIVKA II level. However, further studies with adequate follow-up must be needed to clarify the observed differences, potentially suggesting treatment guideline in this patient group.

LRTH-10079

Outcomes of Surgical Resection and Radiofrequency Ablation for Hepatocellular Carcinoma Down-Staged with Selective Internal Radiation Therapy

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Background: Locally advanced HCC may be defined as exceeding Milan Criteria, but without extrahepatic spread. Down-staging therapy may render patients better candidates for potentially curative treatment including surgical resection and radiofrequency ablation (RFA). This study aims to compare our institution's outcomes of surgical resection and RFA of locally advanced HCC down-staged with SIRT, to that of historical series. **Methods:** All HCC patients who were successfully down-staged with SIRT to within Milan Criteria and underwent surgical resection or RFA at the Singapore General Hospital and National Cancer Centre Singapore between January 2008 and January 2017 were included in this study. Patients who received potentially curative treatment before SIRT, or other forms of treatment in between SIRT and subsequent definitive treatment were excluded. Overall survival and recurrence were analyzed using the Kaplan-Meier estimator. Potentially predictive variables were determined using the log-rank test and cox regression. **Results:** The study sample comprises 20 patients who were predominantly male, Chinese and had chronic hepatitis. The median age is 60.5 years old. 9 patients underwent resection and 11 underwent RFA. The median time to definitive treatment after SIRT was 7.83 months. At median follow-up of 15.7 months, the overall 1-year and 5-year survival were 88% and 68.4% respectively. Median survival was not reached after maximum follow-up of 81.2 months. Recurrence at 1 and 5 years were 23.4% and 75.5% respectively. The median time to recurrence was 19.18 months. There were no significant differences in outcome between surgical resection and RFA, solitary and multifocal disease, and across BCLC stages. **Conclusion:** Patients with locally advanced HCC may benefit from down-staging with SIRT and experience outcomes comparable to that of patients with early HCC. Nonetheless, the role for down-staging with SIRT before definitive treatment in HCC can only be established by a prospective study.

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LRTH-10081

Catheter Directed Computed Tomography Hepatic Angiography for Yttrium-90 Selective Internal Radiotherapy of Hepatocellular Carcinoma: Correlation with SPECT-CT and Its Impact on Coiling Rates, Safety and Efficacy

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Objectives: To evaluate the use of catheter directed intra-arterial computed tomography hepatic angiography (CD-CTHA) in reducing the rate of prophylactic embolization of extrahepatic vessels in patients undergoing Yttrium-90 selective internal radiotherapy (Y-90 SIRT) of hepatocellular carcinoma (HCC). **Materials and Methods:** Between May 2010 to June 2015, 186 patients undergoing Y-90 SIRT with resin microspheres for HCC were analyzed. All the procedures were performed in a hybrid CT and digital subtraction angiography unit. CD-CTHA was performed for these patients during either the first procedure of exploratory hepatic angiography with technetium-99m macroaggregated albumin simulation or the time of Y-90 treatment delivery. Selective embolization of extrahepatic vessels was performed if extrahepatic enhancement was seen on CD-CTHA. Analysis of the rate of prophylactic embolization of extrahepatic vessels, technical success and the rate of complications was performed. Technical success of Y-90 SIRT was confirmed by imaging the biodistribution of Y-90 microspheres using bremsstrahlung SPECT/CT. **Results:** Thirty-five patients (18.8%) required selective embolization of extrahepatic vessels, which was lower than rates reported in literature that performed Y-90 SIRT without CD-CTHA (36.8–80%, $p < 0.001$). Technical success of Y-90 SIRT, as defined by tumor uptake assessed by bremsstrahlung SPECT/CT, was 99.5%. Extrahepatic uptake of Y-90 microspheres on bremsstrahlung SPECT/CT was 1.1% (n = 2, gastric and gallbladder). These two patients were monitored closely and were discharged without any complications. Two separate patients (1.1%) developed radiation gastritis, and one separate patient (0.5%) developed radiation pneumonitis. These rates were below the threshold suggested by the Society of Interventional Radiologists' Quality Improvement Guidelines (3.0%, and 1.0% respectively). **Conclusion:** The use of CD-CTHA in Y-90 SIRT of HCC reduces the rate of prophylactic embolization of extrahepatic vessels while maintaining a high technical success rate of treatment and a favorable side effect profile.

LRTH-10083

The Clinical Significances of Soluble PD-L1 Level in the Hepatocellular Carcinoma Patients Treated with Radiotherapy

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Purpose: This study was performed to investigate the clinical implications of soluble PD-L1 (sPD-L1) level in hepatocellular carcinoma (HCC) patients treated with radiotherapy (RT). **Materials/Methods:** HCC patients treated with RT between June 2011 and March 2015 were prospectively recruited and sPD-L1 levels were analyzed. RT was performed using either stereotactic body radiotherapy (SBRT) or conventional fractionated RT. Blood samples were obtained at the each day of RT start, RT end and 1 month follow-up, respectively. sPD-L1 was measured using an enzyme-linked immunosorbent assay (ELISA) in plasma. The association between the amount of sPD-L1 and both of the clinical features and treatment outcome was analyzed. **Results:** Fifty-three patients with HCC were included. Thirty-four patients received a conventional fractionated RT with a median dose of 45 Gy, while 19 patients received SBRT with 60 Gy in 4 fractions. Median follow-up period was 21.3 months. Initial sPD-L1 level increased as the BCLC stage increased ($P = 0.047$), which was also same in the mUICC stage ($P = 0.015$). Moreover, initial sPD-L1 level was significantly associated with portal vein tumor thrombosis ($P = 0.001$), vein invasion ($P = 0.006$), and tumor size ($r = 0.279$, $P = 0.043$). The overall-survival was significantly poor in patients with higher sPD-L1 (~1.315 pg/ml). Furthermore, the higher level of sPD-L1 at 1 month follow-up (~12.9 pg/ml) was significantly related to early lung metastasis within 4 months after RT ($P = 0.015$). Regarding the association with RT, sPD-L1 levels were significantly increased after RT. It continued to increase until 1 month follow-up in SBRT group, while it decreased at 1 month in conventional group compared to immediately after RT. **Conclusions:** The level of sPD-L1 was associated with tumor aggressiveness and increased after RT in HCC patients. This result implicates the clinical significances of sPD-L1 in HCC patients and suggests that combination treatment with RT and immune checkpoint inhibitors.

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LRTH-10088

A Prospective Phase II Study for the Efficacy of Radiotherapy in Combination with Zoledronic Acid on Painful Bone Metastases from Gastrointestinal Cancers Involving Liver Cancer

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Introduction: We investigated the efficacy of combined RT and zoledronic acid in treating painful bone metastases from gastrointestinal cancers. **Methods:** A total of 60 patients were enrolled between November 2014 and July 2016. The most common primary cancer type was hepatocellular carcinoma (HCC, n = 31) followed by pancreas (n = 9). Patients were treated with external beam RT of 30-54 Gy in 10–17 fractions or 20 Gy in 5 fractions for symptomatic bone metastases. On the first day of RT, patients received 4 mg of zoledronic acid intravenously, which was repeated monthly for a total of 6 cycles. **Results:** The mean pain score was 6.73. After combined treatment, this decreased to 2.75 at 1 month and 2.11 at 3 months ($p < 0.001$). Among the 24 patients who underwent a Magnetic Resonance Imaging at 3 months, 71% of patients were responders with a complete response in one and partial in 16 patients. There were significant changes in the expression of osteoclastogenic or tumor metastatic factor including MIP-1, MMP-2, and MMP-3 1 month after RT compared to baseline ($p < 0.05$). Additional changes in the expression of IL-6 and MMP-9 were observed in patients with HCC ($p < 0.05$). The mean quality of life (QOL) score, measured by EORTC QLQ-C30, also improved from 65.54 to 56.45 at 1 month ($p < 0.001$) and 55.37 at 3 months ($p = 0.016$). **Conclusions:** RT combined with zoledronic acid provided high rates of bone pain relief and QOL improvement for painful bone metastases. The objective methods including radiographic study and serum biomarkers offered close correlations with therapeutic response.

LRTH-10090

Prognostic Factors of Transarterial Chemoembolization for Initial Treatment in HCC

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Background: Transarterial chemoembolization (TACE) is a common intervention performed for hepatocelluar carcinoma (HCC). The aim of this study is to evaluate prognostic factor of the initial complete response during first TACE for HCC. **Methods:** We retrospectively reviewed a total of 130 patients who diagnosed as HCC and performed the first TACE in our institution. Tumor response was estimated based on the result of computed tomography after TACE. **Results:** Fourty-nine patients (37.6%) patients have no need for repeat TACE in 6 months. Mean number and size of HCC was 2.5 and 2.1 cm of complete response patients. Mean AFP level was 170 ng/dl. Complete response rate was 52.6% in HCC size <2 cm. More than 3 cm, 4 cm, and 5 cm HCC has 25%, 12.5%, and 0% complete response rate. Complete response was 46.1% (30/65), 32.1% (9/28), 33.3% (3/10) for the patients with one, two, and three HCCs, respectively. Patient with complete response as initial response have small HCC and small number of HCC. Measures of liver function and TACE approach were not predictive of complete response. **Conclusion:** TACE would be a curative treatment option for small size and small number of HCC.

LRTH-10093

Targeting Accuracy of Image-Guided Stereotactic Body Radiotherapy for Hepatocellular Carcinoma in Real-Life Practice: In Vivo Dosimetry Using Hepatic Parenchymal Changes on Gd-EOB-DTPA-Enhanced Magnetic Resonance Images

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Introduction: Stereotactic body radiotherapy (SBRT) has emerged as an alternative, non-invasive local treatment option for patients with hepatocellular carcinoma (HCC) when established curative treatment modalities cannot be applied. However, the targeting accuracy of SBRT in real-life practice had not been properly evaluated to date. We investigated in vivo dosimetry to evaluate the accuracy of image-guided SBRT with or without fiducial markers using hepatic parenchymal changes on Gd-EOB-DTPA-enhanced magnetic resonance (MR) images. **Methods:** We selected 29 patients with available data of follow-up MR images that were acquired 2–4 months after completion of SBRT. All patients were treated with doses of 45 Gy in three fractions. HCCs and hepatic parenchymal changes area in the hepatobiliary phase of MR images were delineated. We evaluated the discrepancies between the center of HCC and that of hepatic parenchymal change area (inter-center discrepancy [ICD]). We also analyzed the difference of ICD between those with or without intrahepatic markers. **Results:** The median ICD in three-dimensional direction was 6.81 mm (interquartile range [IQR], 4.27–9.61 mm). Those for the craniocaudal, left-right, and anteroposterior components were 2.70 mm (IQR, 1.83–4.06 mm), 1.63 mm (IQR, 0.76–3.49), and 4.12 mm (IQR, 1.20–6.96 mm), respectively. The median ICD for the patients with or without markers were 7.90 mm (IQR, 6.16–10.97 mm), and 4.84 mm (IQR, 3.63–6.81 mm), respectively. There was no significant statistical difference of ICD between those with

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markers and without markers (p = 0.060). **Conclusions:** We observed that the median ICD in three-dimensional direction was 6.81 mm. Image-guided SBRT without markers had comparable targeting accuracy to those with markers. Further research focused on reducing targeting error is needed.

LRTH-10103

A Multicenter Planning Study of Stereotactic Body Radiotherapy for Hepatocellular Carcinoma with Major Portal Vein Tumor Thrombosis

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Introduction: We investigated the current practice of stereotactic body radiotherapy (SBRT) for hepatocellular carcinoma with major portal vein tumor thrombosis (PVTT), which indicated PVTT of the main trunk or the first branch. **Methods:** Ten institutions affiliated with the Korean Stereotactic Radiosurgery Group were provided the contours of 4 cases: the first case was the first branch PVTT with sufficient normal liver volume, combined with extrahepatic metastases; the second case was the first branch PVTT with insufficient normal liver volume; the third case was the main trunk PVTT at confluence level; the fourth case was the main trunk PVTT with entire length. They were asked to make SBRT plan following the current treatment protocol at each institution. **Results:** For the first case, 9 institutions made SBRT plans with 32-60 Gy in 3–5 fractions. One institution declined SBRT because poor prognosis by PVTT. For the second case, 8 institutions made SBRT plan with 32-50 Gy in 3–5 fractions. Two institutions declined SBRT duo to insufficient normal liver volume (1 institution) or kidney toxicity by close location (1 institution). For the third case, 7 institutions made SBRT plan with 35-60 Gy in 3–5 fractions. Three institutions declined SBRT duo to the risk of gastrointestinal toxicity. For the fourth case, 4 institutions selected SBRT with 35-42 Gy in 4–5 fractions. Six institutions declined SBRT duo to the risk of gastrointestinal toxicity (5 institutions) or insufficient normal liver volume (1 institution). Although institution selected various SBRT dose, the preferred dose scheme was 40 Gy in 4 fractions for all cases. **Conclusions:** There was diversity in the practice and criteria of application for SBRT to HCC with major PVTT among institutions in Korea. Based on this study, further studies will be needed to keep a balance between efficacy and toxicity of SBRT to major PVTT.

LRTH-10105

A Clinical Scoring System for Predicting Overall Survival of HCC Patients with BCLC Stage C Undergoing Stereotactic Body Radiotherapy

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Introduction: The study aimed to identify prognostic factors of overall survival (OS) among hepatocellular carcinoma (HCC) patients with BCLC stage C treated with stereotactic body radiotherapy (SBRT). An easy-to-use scoring system was also derived to predict patients' prognosis based on the individualized profiles. **Methods:** Clinical data from the multicenter study consisted of 139 HCC patients with BCLC stage C. All of the patients underwent SBRT with a median dose of 43 Gy (range: 25-60 Gy) in 2–6 fractions. The model included age, gender, etiology, ECOG status, sorafinib use, number of tumor, tumor size, AFP value, presence of macrovascular invasion, Child-Pugh class, N stage, M stage, and biologically effective dose. Cox's proportional hazards models were utilized to estimate regression coefficients of death risk predictors and derive risk scores. The area under receiver operating curve (AUROC) was used to evaluate the performance of the risk models. **Results:** The median survival was 11.0 months, with 1-year and 2-year OS rates of 46.6% and 27.8%, respectively. There showed no significant differences in OS of each study site (p = 0.470). Multiple regression showed age (<75 vs. >75, HR = 2.65, p = 0.004), ECOG (1 vs. 0, HR = 2.06, p = 0.002; 2 vs. 0, HR = 2.87, p = 0.002), number of tumors (>3 vs. <3, HR = 2.10, p = 0.006), AFP (>20 vs. <20, HR = 2.03, p = 0.048), Child-Pugh class (B vs. A, HR = 2.55, p = 0.001), and M stage (1 vs. 0, HR = 2.33, p = 0.002) are statistically significant predictors for OS. All of these significant predictors were included in the risk prediction model. The

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total risk score of the prediction model ranged from 0 to 39. Each score had its corresponding risk of OS. The AUROC for predicting 6-month OS was 0.846. **Conclusions:** The scoring system had discrimination satisfactory predictability for OS. It can be used to stratify high-risk patients and select appropriate patients for future clinical trials.

LRTH-10107

Treatment and Prognosis of Advanced HCC with Metastasis

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Introduction: As hepatocellular carcinoma (HCC) progresses, it is accompanied by deterioration of liver function, which makes treatment difficult. In particular, advanced HCC involves not only impairment in liver function and general condition but also vascular invasion and other organ metastasis. It is very heterogeneous stage and needs to be further subdivided. In the present study, we investigated treatment outcomes and the factors associated with prognosis in HCC patients with distant metastasis. **Methods:** We analyzed data of 103 patients with advanced HCC with distant metastasis at initial diagnosis from June 2004 to June 2015. The patients received the first treatment for HCC in our hospital. **Results:** Mean age of patients was 57.3 ± 11.6 years and men were predominant (80.6%). The median observation period was 3.2 (0.3–39.1) months, and 99 (96.1%) of these patients died. There were no significant association with survival in sex, age, etiology and the number of liver tumors ($p = 0.274$, 0.094, 0.854 and 0.280, respectively). In multivariate analysis, Child-Pugh class ($p < 0.001$) and initial treatment modality ($p = 0.001$) were significantly independent factors for survival. In Kaplan-Meier curve, systemic chemotherapy-alone or combination of locoregional treatment (LRT) and cytotoxic chemotherapy has no significant difference on survival compared with best supportive care as initial treatment. (median survival time, MST, 2.3 vs. 1.6 months) However, LRT alone (MST 4.8 months) or combination of sorafenib and LRT (MST 4.3 months) showed significant survival benefit. ($p = 0.001$, 0.002). **Conclusion:** Child-Pugh score and treatment modality in HCC patients with metastasis showed significant prognostic relevance. We also found that locoregional control for primary liver mass therapy is important in the treatment of sorafenib.

LRTH-10109

8Gy Single Fraction (8Gy/1Fr) Palliative Radiotherapy (RT) for Hepatocellular Carcinoma (HCC): Safety and Efficacy

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8Gy/1Fr palliative RT has shown promising evidence on symptom palliation in advanced HCC, however, its efficacy in disease control and safety has not been reported. Herein we reported our experience on 8Gy/1Fr palliative RT. From year 2013–2015, 37 consecutive HCC patients received 8Gy/1Fr palliative RT were analysed; Patients were followed up regularly, radiation related side effects, symptom, serum alpha-fetoprotein level (AFP) and liver function were monitored. The primary endpoint was AFP response. Secondary endpoints were physician reported symptom response and safety in terms of Child Purge (CP) progression. At the time of analysis 1 patient was alive and median follow-up time was 5.6 months. Patients' and tumour characteristics were as follows: median age 61 (41–88), male: female (n = 31/6). ECOG0/1/2/ (n:1/23/ 13); Baseline CP score: A/B (n:26/11) BCLC stage B/C (n: 1/36). Cause of cirrhosis: chronic alcoholism/Hepatitis C/Hepatitis B, (n = 8/1/28); Median diameter of tumour 13 cm (6–19.4 cm); main portal vein thrombosis (PVT)/ branch PVT (n: 8/8). Presence of extrahepatic disease: n = 14 (37.8%); ≥3 liver lesions: n = 21 (56.8%). Previous treatment received before RT: TACE/SBRT/hepatectomy (n:13/2/2). Treatment after RT: Sorafenib /hepatectomy/ TACE/SBRT/ RFA/immunotherapy (n:16/1/3/5/1/1) Concerning safety,1 patient with heavy disease burden (18 cm tumour, CP 8) died within 1 week of treatment. 7 (18.9%) patients had CP progression within 1 month of RT. Only 1 (2.7%) patient reported Grade 3 toxicity (fatigue). The most common side effect was nausea: Grade1/2 (n = 5/1). 10 (27%) patients had physician reported symptom response. Median survival from diagnosis and start of RT was 5.6 and 4.2 months respectively. 14 patients (37.8%) had significant AFP drop after RT, Median days to reach AFP nidar was 41 days. In our early experience, 8Gy/1Fr palliative RT achieves promising median survival and AFP response in advanced HCC patients. It is a safe and effective means for symptom palliation and disease control which allowed many patients to receive subsequent liver directed treatment.

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Stratified Survival Outcomes for Patients with Advanced BCLC-C Hepatocellular Carcinoma (HCC) Invading Portal Vein after Yttrium-90 Selective Internal Radiation Therapy (Y90 SIRT)

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Introduction: The presence of macroscopic portal vein tumour thrombosis (PVTT) in patients with HCC is a significant factor for poor prognosis, with a median OS of <3 months without treatment. Such patients fall under BCLC-C where the current recommendation is that of a palliative approach. There have been diverse efforts to improve the management of BCLC-C HCC but they require further validation. We aimed to assess the stratified survival outcomes of HCC patients treated with Y90 SIRT. **Methods:** HCC patients with macroscopic PVTT who underwent Y90 SIRT from 2008 to 2016 were retrospectively identified. Extrahepatic metastases and a follow-up period of <3 months were excluded. Patients were stratified according to Child-Pugh status, bilirubin levels and extent of PVTT. **Results:** 60 patients were identified. The median OS was 11.2 months (95% CI, 9.5–12.8). Specifically for Child-Pugh A patients (n = 47, 78.3%), median OS was 11.5 months (95% CI, 0.9–22.0). For Child-Pugh B patients (n = 13, 21.7%), median OS was 6.3 months (95% CI, 1.2–11.4). (p-value = 0.07) Majority had bilirubin levels <34.2 umol/L (n = 55, 91.7%) where the median OS was 11.4 months (95% CI, 2.36–20.5). For bilirubin levels ≥34.2 umol/L (n = 5, 8.3%), median OS was 6.2 months (95% CI, 0.0–12.5). (p-value = 0.001) Number of patients with branch vs. main PVTT was 50 (83.3%) and 10 (16.7%) respectively and corresponding median OS were 11.2 (95% CI, 9.7–12.7) and 9.4 months (95% CI, 4.0–14.8). (p-value = 0.843) **Conclusion:** Y90 SIRT is an effective treatment for BCLC-C HCC patients with PVTT. The outcome of BCLC-C HCC is not homogeneously grim. The analysis provided better stratification of the survival outcomes in order to allow for more rational comparison with alternative modalities.

LRTH-10119

Post-TACE Ischemic Cholecystitis that Microscopic Images Showed Particles of DC Bead in the Wall of the Gallbladder

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Transarterial chemoembolization (TACE) is reportedly a useful palliative treatment in patients with unresectable or recurred hepatocellular carcinoma. Drug-eluting bead (DC Bead, Biocompatibles, UK) technology has provided the option of performing chemoembolization with less systemic exposure to anticancer drugs and a more standardized delivery. Major complication of DC Bead are hepatic insufficiency or infarction, hepatic abscess, tumor rupture, bile duct injury, ischemic cholecystitis, upper gastrointestinal bleeding, pulmonary embolism, splenic infarction or spinal embolization. We report a case of Post-TACE ischemic cholecystitis that microscopic images showed particles of DC Bead in the wall of the gallbladder. A 77-year old woman, with 1.5 cm sized hepatocellular carcinoma in segment V, was treated by DC Bead-TACE. 7 days after the DC Bead-TACE, she complained of severe epigastric pain with a positive Murphy's sign. The laboratory examination showed leukocytosis (WBC 5640/mm^3, seg 77.2%) and mild AST/ALT elevation (61/91 IU/ml). Computed tomography (CT) showed perforated acute cholecystitis. Antibiotics and percutaneous gallbladder drainage (PTGBD) were used until the patient stabilized. After 8 days, she was performed laparoscopic cholecystectomy. Microscopic findings showed particles of DC Bead in the gallbladder wall.

LRTH-10123

Changes in Immunologic Function after Transarterial Chemoembolization in Patients with Hepatocellular Carcinoma

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Background/Aim: Transarterial chemoembolization (TACE) is widely used as a treatment modality for intermediate stage of hepatocellular carcinoma (HCC). Although several studies showed enhanced natural killer (NK) cell response after local treatment for HCC have been reported, knowledge of impact on NK cell after TACE is still unrevealed. The aim of this research was to investigate immunologic changes after TACE in HCC patients. **Methods:** Total 23 patients undergoing TACE for hepatocellular carcinoma were enrolled. Absolute counts of peripheral blood lymphocytes followed by phenotypic and functional characterization of NK cell population were carried out the day before, 1 and 4 weeks

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after TACE. **Results:** Peripheral blood lymphocytes kinetics revealed decrease of NK cell population at 1 week after TACE from the baseline (4.18% at 1 week vs. 9.54% at baseline, P = 0.047), and restoration of NK cell population at 4 week after TACE from 1 week after TACE (12.24% at 4 week vs. 4.18% at baseline, P = 0.040). This was along with significantly increased level of inhibitory NK receptor, NKG2A, at both time points of 1 week and 4 week after TACE from the baseline (20.24% at 1 week from 4.26% at baseline, P < 0.001; 23.92% at 4 week from 4.26% at baseline, P < 0.001), while there were no significant changes in activating NK receptors. Anti-K562 cell cytotoxicity appeared consistently decreased in terms of absolute activity at 1 week after TACE as compared to baseline, and showed a tendency to restore at 4 weeks after TACE. **Conclusions:** Unlike previously reported immunologic changes in patients with local treatment for HCC, immunologic function seems to be compromised shortly after TACE. This result suggests that various therapeutic strategies can have different effects on body immune function, and better understanding of the changes in the immune system in HCC patients will promise better tumor control.

LRTH-10127

Preliminary Results of Hypofractionated Carbon Ion Radiotherapy for Cholangiocarcinoma

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Introduction: The aim of this study is to report initial results of hypofractionated carbon ion radiotherapy (C-ion RT) for cholangiocarcinoma. **Patients and Methods:** Key eligibility criteria were: i) cholangiocarcinoma confirmed by histology or clinical examination without metastasis; ii) medical inoperability due to comorbidity, or inoperability due to wide tumor extension; iii) no direct infiltration of the gastro-intestinal (GI) tract; iv) Performance status ≤2 in Eastern Cooperative Oncology Group classification; and v) Child-Pugh classification A or B. Prescribed doses were 52.8 Gy [relative biological effectiveness (RBE)] or 60.0 Gy (RBE) in four fractions for intrahepatic cases or 12 fractions for hilar hepatic/close to gastro-intestinal tract cases. Adjuvant and neoadjuvant chemotherapy were allowed in this study. Local control, progression-free survival and overall survival were calculated with the Kaplan-Meier estimate, and toxicity was graded according to the Common Terminology Criteria for Adverse Events, version 4.0. **Results:** Nine patients were enrolled in this study. There were two patients with stage I cancer, two with stage II, two with stage III, and three with stage IVA. The median follow-up period was 16.3 months. Local control was achieved in seven out of nine patients (71%). Median overall and progression-free survival time was 19.0 (95% CI: 14.4–23.6) months and 12.9 (95% CI: 5.3–20.5) months. There were no occurrences of acute or late toxicity of grade 3 or higher. **Conclusion:** Initial results show that hypofractionated C-ion RT appears to be tolerated and effective for cholangiocarcinoma.

LRTH-10132

Initial Experience of No-Touch Switching Monopolar Laparoscopic Radiofrequency Ablation Using a Separable Cluster Electrode in Patient with Hepatocellular Carcinoma

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Objective: Percutaneous radiofrequency ablation (RFA) in the treatment of hepatocellular carcinoma (HCC) located on the liver surface is challenging because of overlapping ribs or lung. The aim of this study was to evaluate the technical outcomes and safety of no-touch switching monopolar laparoscopic RFA using a separable cluster electrode in patient with HCC located on the liver surface. **Methods:** From November 2015 to December 2016, 7 patients with 8 HCCs located on the liver surface were enrolled and treated with no-touch switching monopolar laparoscopic RFA using a separable cluster electrode. Tumor characteristics, technical success, primary technical effectiveness, and the frequency of major complication rates were evaluated. **Results:** The mean diameter of the 8 HCCs was 26.9 mm (20–45 mm). 6 HCCs were located at liver dome. 1 HCC was located at surface of medial aspect of segment 6 and 1 HCC located at caudate lobe. No-touch switching monopolar laparoscopic RF ablation was performed successfully in all patients. When evaluated by enhanced CT after RFA, the primary technical effectiveness rate was 100%. No patients had a major complication after the RFA. **Conclusion:** No-touch switching monopolar laparoscopic RFA using a separable cluster electrode is a feasible and safe technique for the treatment of HCCs located on the liver surface.

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Management of HCC in a Resource Limited Situation; Real Life Experience of 39 Cases of TACE in Myanmar

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Introduction: Viral hepatitis and its complications are one of the major health problems in Myanmar, especially primary liver cancer. Viral hepatitis B and C account for about 70% of the etiology of HCC in Myanmar. Most of the cases presented in late stages and treatments modalities are limited in Myanmar. Basically surgical resection and TACE are the only two therapeutic options in Myanmar. More than 90% of cases are unresectable at the time of presentation. Therefore we are left with TACE only. TACE is usually performed in cases of well-defined tumors without portal vein thrombosis and CTP-A patients. **Method:** The data of HCC treated with TACE at Yangon GI & Liver Center Form November 2016 to March 2017, 39 patients with unresectable HCC were treated with TACE using Doxorubicin, cisplatin or mitomycin were retrospectively analyzed. **Results:** Among 39 cases of HCC treated with TACE occurs in both Hepatitis B & C and about 10% occurs in non-A, non-B hepatitis cases. Majority of cases occurred among Males. Involvement of Liver is more in the Right Lobe. Out of 39 cases, about 30.7% were multiple nodules. 69.3% were singles and most were larger than 5 cm. 66% had AFP level below 1000 ng/dl. 15% of the cases developed HCC after TACE treatment. **Conclusion:** In Myanmar, TACE has to be done in suitable patients with HCC patients. This paper try to describe the very limited treatments options in a developing country like Myanmar. According to our experiences TACE is a safe procedure with a good selection of patients. The efficacy, prolongation of survival data is not yet available. However HCC patients, families and relatives in Myanmar are highly expect to have treatment procedure when they come to a tertiary center. Therefore, we recommend TACE in unresectable cases of HCC with the compensated.

Systemic Therapy

SYTH-10055

The Prognosis and Treatment Modalities in the Patients with Hepatocellular Carcinoma with Portal Vein Tumor Thrombosis

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Background/Aims: Various treatment modalities exist in the patients with hepatocellular carcinoma (HCC) with portal vein tumor thrombosis (PVTT). The aim of this study is to evaluate factors related to survival in the HCC patients with PVTT to suggest better therapeutic options. **Methods:** Patients with newly diagnosed HCC at three tertiary hospitals between January 2004 and December 2012, were reviewed by medical record retrospectively. Barcelona Clinic of Liver Cancer stage C patients with PVTT were enrolled. Factors related to overall survival (OS) were analyzed and efficacies of the treatment modalities were compared. **Results:** Four hundreds sixty five patients with HCC and PVTT were included. Liver function (Child-Pugh score), tumor burden (sum of tumor diameter), presence of extrahepatic metastasis, alfa fetoprotein level, and treatment modalities were significant factors related to OS. The OS of the patients who received hepatic resection, radiofrequency ablation (RFA), transarterial chemoembolization (TACE), hepatic arterial infusion chemotherapy (HAIC), sorafenib, systemic cytotoxic chemotherapy, radiation therapy (without combination), and supportive care were 27.8, 7.1, 6.7, 5.3, 2.5, 3.0, 1.8, and 0.9 months, respectively ($P < 0.001$). Curative-intent treatments such as hepatic resection or RFA were superior to noncurative-intent treatments ($P < 0.001$). TACE or HAIC was superior to sorafenib or systemic chemotherapy ($P < 0.001$). Combining radiotherapy to TACE or HAIC did not provide additional benefit on OS ($P = 0.096$). **Conclusions:** Treatment modalities, baseline liver function and tumor factors significantly influenced on OS of HCC patients with PVTT. If possible, curative intent treatments should be preferentially considered. If unable, locoregional therapy would be a better choice than systemic therapy for first treatment modality in HCC patients with PVTT.

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SYTH-10067

Similar Efficacy of Sorafenib in Treatment-Naïve and Chemoembolization-Refractory Patients with Advanced Stage Hepatocellular Carcinoma

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Introduction: Although sorafenib monotherapy is a standard-of-care for advanced stage hepatocellular carcinoma (HCC), there are insufficient evidences regarding the practical role of sorafenib as a rescue option. We investigated the therapeutic efficacy and safety of sorafenib in transarterial chemoembolization (TACE)-refractory HCC patients compared with treatment-naïve patients. **Methods:** This study included 227 patients with advanced stage HCC and Child-Pugh class A or B. Among these, 124 (54.6%) patients underwent TACE before sorafenib (the rescue group) and 103 (45.4%) did not (the first-line group). The differences in tumor response, as measured every 6–8 weeks according to the modified Response Evaluation Criteria in Solid Tumors (mRECIST), overall survival (OS), and the treatment-related toxicity were compared between the two groups. **Results:** Most of patients were male (85.9%, n = 195), with a median age of 54 years. Gross vascular invasion and extrahepatic metastasis were observed in 80 (64.5%) and 82 (79.6%) patients; and 114 (91.9%) and 65 (63.1%) patients in the rescue and first-line groups, respectively (Ps < 0.05). Child-Pugh A liver function was more common in the rescue group (72.6% vs. 59.2%; P < 0.05). Over a median follow-up of 3.9 months, the objective response (5.6% vs. 1.0%) and disease control rates (43.5% vs. 43.7%) did not differ between both groups (Ps = NS). Although the median OS was significantly longer in the rescue group (5.1 vs. 3.6 months; P < 0.05), prior treatment with TACE was not independently associated with improved survival in the entire population after adjustment for demographic and tumor factors (hazard ratio 0.87; 95% confidence interval 0.60–1;27 P = NS). The frequency of grades 3 or 4 toxicities was similar between the two groups (16.9% vs. 10.7%; P = NS). **Conclusions:** Our data indicate that sorafenib therapy for patients with HCC refractory to TACE has similar efficacy and safety profiles to treatment-naïve patients. Sorafenib could be a reasonable option for the treatment of TACE-resistant HCC.

Other

OTR-10034

Hepatocellular Carcinoma in Jakarta

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Introduction: Hepatocellular carcinoma (HCC) is the fifth most common cancer in the world and regions with the highest incidence of HCC in the world were Eastern Asia and South-Eastern Asia. However, data on HCC patients in Indonesia, as the largest country in South-Eastern Asia is still lacking. **Methods:** Data of HCC patients from Medistra Hospital, Cipto Mangunkusumo Hospital, and Dharmais National Cancer Center Hospital, from January 2015 to December 2016, was retrospectively reviewed. **Results:** We identified a total of 349 HCC patients (median age 57, 77.7% male). Cirrhosis was present in 189 patients (54.2%) and alpha feto-protein level was below 200 ng/ml (the diagnostic level) in 37.8% of patients. The proportion of Child-Pugh A, B, C, and missing data were 168 (48.1%), 120 (34.4%), 32 (9.2%), and 29 (8.3%), respectively. The three most common etiologies of HCC were hepatitis B (58.2%), non-B non-C (16.9%), and hepatitis C (10.6%), respectively. Patients with BCLC A, B, C, and D stages, were 26 (7.4%), 126 (36.1%), 118 (33.8%), and 40 (11.5%), respectively. We could not determine the BCLC stage in 39 patients. Transarterial chemoembolization (TACE), liver resection, radiofrequency ablation (RFA), sorafenib, and external radiation were given as main treatment modalities in 72 (20.6%), 11 (3,2%), 17 (4,9%), 27 (7,7%), and 2 (0.6%) patients, respectively, while the rest were given only supportive therapies. **Conclusion:** Most patients diagnosed with HCC in Jakarta present at late tumor stages when curative treatment was no longer applicable and the prognosis is usually bad. A nationwide regular surveillance program in high-risk patients is needed to improve early detection.

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OTR-10038

Kahweol Induces Apoptosis of Human Hepatocellular Carcinoma Cell Lines Through Down-Regulation of Akt and STAT3 Phosphorylation and Activation of ERK and JNK

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Introduction: Coffee is among the most frequently consumed beverages and there is evidence that coffee intake is related with the risk of hepatocellular carcinoma. Khaweol, a coffee-specific diterpene, has been reported to induce apoptosis in several type of human cancer cells. However, it has not yet been reported whether kahweol induces apoptosis in human hepatocellular carcinoma cells. Here, we investigated whether kahweol induced human hepatocellular carcimoma cell apoptosis. **Methods:** We cultured human hepatocellular carcinoma (HCC) cell lines (HepG2, Hep3B, SUN182, SK-Hep1). The effect of kahweol on HCC cell apoptosis using CCK-8 and FACS analysis was examined. The expression of cleaved caspase-3, pAkt, pSTAT3, pERK and pJNK were determined by western blot analysis. **Results:** Kahweol significantly decrease cell viability, and increased the cell population on the G0/G1 phase by FACS analysis. Kahweol also increased expression of cleaved caspase-3. In addition, kahweol inhibited phosphorylation of Akt and STAT3 and increased phosphorylation of ERK and JNK. **Conclusion:** This study shows that kahweol increase HCC cells apoptosis through down-regulation of Akt and STAT3 phosphorylation and activation of ERK and JNK. The present study suggests that kahweol has anti-tumor effect in HCC cells.

OTR-10039

HCC-Risk Evaluating Score in Chronic Hepatitis B Patients Under Entecavir Treatment: HCC-RESCUE

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Background and Aim: The aim of this study was to develop and validate the risk prediction model for the development of hepatocellular carcinoma (HCC) in patients receiving antiviral treatment for chronic hepatitis B (CHB). **Methods:** We investigated 2,061 Korean patients with CHB and no HCC at baseline who treated with entecavir as an initial therapy. A risk score model for HCC development was developed based on multivariable Cox proportional hazards model in the single center (n = 990) and we validated the risk score model using the time-dependent area under receiver operating characteristic curve (AUROC) in other three centers (n = 1,071). We named it as HCC-RESCUE (HCC-Risk Evaluating Score in CHB patients Under Entecavir). Also, we investigated the difference of HCC development among risk groups (low, intermediate, and high) which are categorized by the risk score. **Results:** The cumulative incidence rates of HCC at 5 years were 11.2% and 8.9% in the testing and validation cohort, respectively. The risk score is formulated as [age + 15 x gender (women = 0 / men = 1) + 23 x cirrhosis (absence = 0 / presence = 1)]. The time-dependent AUROCs at 1 year, 3 years, and 5 years were 0.82, 0.81, and 0.81 in the validation cohort. There was a significant difference of HCC development in the validation cohort according to each risk groups which were defined by the 5-year HCC risk score (low risk group, 2.1%; intermediate risk group, 9.3%; high risk group, 41.2%, $p < 0.001$). **Conclusion:** The risk score model on HCC development for CHB patients receiving entecavir is based on age, gender and liver cirrhosis. It is useful to predict HCC development in CHB patients receiving oral antiviral treatment.

OTR-10054

To Assess the Utility of HCC-ART Score (HCC-Alphafetoprotein-Routine Test) for Early Diagnosis of Hepatocellular Carcinoma in a Tertiary Care Hospital in Southern India

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Introduction: Hepatocellular carcinoma (HCC), a terminal and fatal complication of liver cirrhosis, has an annual incidence of 2.0–6.6%. Use of AFP and ultrasonography (USG) as a screening test for early HCC is limited due to poor sensitivity (39–64% and35–37% respectively). Therefore AFP in combination with USG is a poor predictive model for detecting early HCC in cirrhotics. Thus, there is a need to develop better predictive models which can diagnose HCC in the early stages. As per a multicentre study in Egypt (2013), conducted by Attallah et al, a new score (HCC-ART) was derived for cirrhosis due to chronic HCV infection. This study suggested a cut-off score of 280 for suspecting HCC. In keeping with the same, we assessed the utility of HCC-ART score for diagnosing HCC in comparison with AFP alone. **Methods:** A retrospective analysis of data was conducted. This study compared two groups. First group included cirrhotic patients (irrespective of etiology) who were diag-

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nosed with HCC or those with a clinical suspicion of HCC. The second (control group) included patients who had cirrhosis (irrespective of etiology) without HCC, who were under regular surveillance with biannual USG and AFP monitoring. HCC-ART score was calculated as follows:(log AFP x AST/ALT ratio x Age x ALP)/s.albumin. **Results:** A total of 322 patients were analysed.203 patients (Males = 171, females = 32) comprised the first group, who were diagnosed with HCC on triple phase CT. Control group consisted of 119 patients (Males = 81, females = 38). Two cut-off values of AFP (16 ng/ml and 200 ng/ml) for suspecting HCC were used. Maximum sensitivity and specificity (81.3% and 96.6%, respectively) was observed at 9.75 ng/ml. With a cut-off of 16 ng/ml for AFP, sensitivity and specificity was 75.4% and 97.5% respectively. For a cut-off of 200 ng/ml the sensitivity decreased to 75.4% but with 100% specificity. As the level of AFP increased, sensitivity decreased and specificity increased.

OTR-10057

Treatment Response and Prognosis in Combined Hepatocellular Carcinoma and Cholangiocarcinoma

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Background: Combined hepatocellular carcinoma and cholangiocarcinoma (cHCC-CC) is an uncommon type of primary liver cancer that has rarely been reported in Korea. This study was performed in order to evaluate the clinicopathological characteristics and prognostic factors of cHCC-CC in single center. **Methods:** The clinicopathological features of patients diagnosed by biopsy or operated with cHCC-CC at Korea University Ansan and Guro Hospital between January 2012 and December 2016 were retrospectively studied by comparing them with patients with hepatocellular carcinoma (HCC) during the same period. **Results:** 26 of 366 patients (7.1%) were diagnosed with cHCC-CC and thus included in this study (Male 81%, median age: 64 years). According to the parameters of modified UICC stage, there were 4 (23.5%), 2 (11.7%), 3 (17.6%), and 8 (47.1%) patients with stages I, II, III, and IV, respectively. The overall survival period was longer in the HCC only group (median 22 months) than in the combined cHCC-CC group (median 10 months) (±0.001). The 5-year survival rate was 17.6% in the cHCC-CC group and 78.4% in the HCC group (±0.001). The disease free survival for patients with cHCC-HCC and HCC were median 4 and 17 months, respectively (~0.001). TACE or chemotherapy was not effective at cHCC-CCC patients. **Conclusions:** cHCC-CCC is uncommon tumor and shows early tumor recurrence and poor response to TACE or chemotherapy except resection compared to the usual HCC.

OTR-10061

Sarcomatoid Differentiation Arising in Early Stage Hepatocellular Carcinoma Without Anticancer Therapies

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Introduction: Finding sarcomatoid differentiation in hepatocellular carcinoma (HCC) is a rare event of the liver. The prognosis of this rare form of cancer is quite unfavorable. The precise pathogenesis of sarcomatoid transformation has not yet been fully clarified however, repeated non-surgical therapies for HCC such as transcatheter arterial chemoembolization and radiofrequency ablation therapy are presumed to promote this change. Sarcomatoid HCC without previous therapies is extremely rare. Herein, we described a case of sarcomatoid differentiation arising in early stage HCC without any previous therapies. **Case Report:** A 64-year-old man presented to our hospital diagnosed as having liver cancer originating from cirrhosis associated with hepatitis B and C coinfection without any previous treatment for HCC. The patient underwent the right hepatectomy. The resected liver revealed an expanding nodular mass of 2.4–1.5 cm. Histologically, the tumor consisted of a mixture of spindle-shaped, pleomorphic and rhabdoid sarcomatoid cells and typical well to moderately differentiated HCC cells. The tumor was partially encapsulated and microvascular invasion was not identified. Conclusions. Sarcomatoid differentiation of HCC is highly aggressive prognostic factor. Early detection through regular clinical follow-up and aggressive treatment with radical resection may improve the outcome of such patients.

OTR-10071

Serum Alanine Aminotransferase Level and Mortality from Hepatocellular Carcionoma in Patients with Chronic Hepatitis B

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Introduction: In patients with chronic hepatitis B (CHB), serum alanine aminotransferase (ALT) is associated with higher risk of hepatocellular carcinoma (HCC) development.

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However, it is not known which ALT level is significantly associated with HCC-related mortality in those patients. **Methods:** We used a Health Examination Cohort of National Health Insurance Service (NHIS) in Korea. The cohort included approximately 0.5 million individuals (40 to 79 years old) who received biennial health examination between January 01, 2002, and December 31, 2007. During the period, individuals with CHB were selected using specific disease diagnosis code. Other liver diseases such as chronic hepatitis C, alcoholic liver diseases, or liver cirrhosis were excluded. Mortality from HCC was investigated according to baseline serum ALT levels. **Results:** During 111,844 person-years (mean 9.0 years of follow-up), 213 out of 12,486 individuals with CHB were died from HCC. Elevated ALT level was positively correlated with mortality from HCC in both sexes. The mortality rate in men was 0.13%, 0.16%, 0.23%, 0.48%, 0.60%, and 0.60% in serum ALT <19, 20–29, 30–39, 40–49, 50–79, and â‰¥ 80 U/L, respectively. The mortality rate in women was 0.02%, 0.07%, 0.10%, 0.54%, 0.46%, and 0.27% in the same interval, respectively. In a multivariate Cox proportional hazards model adjusting age, body mass index, hypertension, serum triglyceride level, gamma-glutamyl transferase, and total cholesterol, serum ALT level was the independent predictor of death from HCC. The best cut-off level of serum ALT to predict HCC-related mortality was >34 IU/L in men and >29 IU/L in women. **Conclusions:** Among patients with CHB older than 40 years, HCC mortality rate is strongly associated with baseline ALT level. HCC mortality increases even in low range of serum ALT level. Careful monitoring or earlier antiviral therapy should be considered even in CHB patients with low ALT level.

OTR-10076

Substaging of Barcelona Clinic Liver Cancer Stage C Hepatocellular Carcinoma with a National-Wide Validation

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Introduction: Advanced hepatocellular carcinoma (HCC) [Barcelona Clinic Liver Cancer (BCLC) stage C], which encompasses wide range of diseases with various prognoses, needs subclassification for a more accurate prediction of survival. This study aimed to establish a substaging system of the BCLC stage C for predicting prognosis and proper management of advanced HCC patients. **Methods:** Data of 564 patients with newly diagnosed BCLC stage C HCC from three tertiary hospitals affiliated with the Korea University (training set) were analyzed retrospectively. The variables affecting overall survival (OS) were analyzed and the patients were substaged according to the number of prognostic factors. The substaging system was validated using a national-wide database from the Korean Liver Cancer Association (n = 742). **Results:** In the training set, tumor factors such as tumor burden 10 cm, major portal vein invasion, and distant metastasis, and underlying liver function were independently associated with OS. BCLC stage C was classified into four substages (C1–4) according to the number of risk factors in the training set. Substage C1 (no risk factors), C2 (one risk factors), C3 (two risk factors), and C4 (three or more risk factors) showed median OS times of 17.50 (95% confidence interval [CI], 8.57–26.43), 10.13 (95% CI, 8.17–12.09), 4.20 (95% CI, 3.42–4.98), and 2.90 months (95% CI, 2.34–3.46), respectively ($p < 0.050$). This substaging also had good discrimination ability in predicting survival in the validation set. In addition, different OS was observed by treatment modalities in each substage. Curative treatment such as surgery or RFA was most effective from substage C1 to C3. TACE showed better outcomes than sorafenib in substage C2. There was no significant OS difference between sorafenib and TACE in substage C3. **Conclusion:** Substaging of BCLC stage C is expected to help predicting patient prognosis and guiding treatment modalities more accurately.

OTR-10086

Prognostic Significance of Hemodynamic and Clinical Stages in the Prediction of Hepatocellular Carcinoma

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Background and Aims: Early identification of hepatocellular carcinoma (HCC) is associated with improved survival for patients with chronic liver disease (CLD). We evaluated the prognostic significance of hemodynamic stage (HS) and clinical stage (CS) in predicting HCC in CLD patients. **Methods:** Between January 2006 and May 2014, 801 patients with CLD who underwent hepatic venous pressure gradient (HVPG) measurement were prospectively enrolled. HS was classified by HVPG (mm Hg) as follows: HS-1 (HVPG-6), HS-2 (6CS was classified as follows: CS-0 (no cirrhosis), CS-1 (cirrhosis without varix), CS-2 (cirrhosis with varix), CS-3 (varix bleeding without other complications), CS-4 (first nonbleeding decompensating event), and CS-5 (any second decompensating event). The HCC development and risk factors for HCC were evaluated in all patients and patients with cirrhosis, respectively. **Results:** HCC developed in 53 patients (6.6%). The incidence densities of HCC according to HS-1~5 and CS-0~5 were 4, 16, 36, 45, and 49/1,000 person years and 0, 15, 25, 33, 36,

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and 53/1,000 person years of observation, respectively. Ascites aggravation (p = 0.008, OR [odd ratio] = 2.33), HVPG >12 mm Hg (p = 0.033, OR = 2.17), CS >2 (p = 0.039, OR = 2.36), and alpha-fetoprotein (AFP; p = 0.017, OR = 1.01) were significant predictors of HCC development in all patients. For patients with cirrhosis, ascites aggravation (OR = 2.51), HVPG >12 mm Hg (OR = 2.46), and CS >2 (OR = 2.62) were were correlated with HCC development. Areas under receiver operating characteristic curves of the prediction-model, CS, HVPG score, and AFP were 0.797, 0.707, 0.701, and 0.653, respectively. **Conclusions:** HCC development correlates with advancing liver fibrosis or disease as measured by HS and CS. In addition, ascites aggravation and elevated AFP appears to be associated with increased incidence of HCC.

OTR-10089

Up-Stage Treatment Migration Improved Overall Survival of Selected BCLC B and C Hepatocellular Carcinoma Patients

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Background: In real world practice, hepatocellular carcinoma (HCC) treatment deviates markedly from the widely endorsed BCLC staging system due to patient heterogeneity, availability of treatment modalities and local practices. Clinical impact of such treatment deviation has not been well elucidated, especially in Asia. We aimed to evaluate the impact of HCC treatment deviation in a large tertiary Singapore hospital. **Method:** We evaluated all consecutive adult HCC cases seen at our hospital from 2009 to 2014. Baseline demographics, clinical/tumor parameters and long-term outcomes were recorded. Categorical and continuous data were analyzed by Fisher-exact and Mann Whitney U test, respectively. Survival was estimated with Kaplan-Meier curve. **Results:** A total of 594 HCC cases were enrolled. BCLC recommended treatments were received by 244 (41.1%) patients. Up-stage treatments were received by 61 (20.1%) out of 303 cases, and down-stage treatments were received by 274 (48.2%) out of 568 cases. Median overall survival (OS) was 59.8, 25.6, 12.7 and 2.1 months (p < 0.001), respectively. Among BCLC B patients, up-stage treatment with ablation/resection had better OS than TACE (p = 0.029). In BCLC C group, median OS was 24.5 months for up-stage treated patients compared to 5.0 months for sorafenib (p = 0.054). Down-stage treated BCLC 0/A patients had worse median OS of 35.7 vs. 58.9 months for ablation/resection (p < 0.001). In BCLC B group, TACE and down-stage treatments were associated with median OS of 21.1 and 5.4 months, respectively (p = 0.005). Among BCLC C patients receiving only best supportive care, median OS (2.2 months) was worse than sorafenib (p = 0.006). **Conclusion:** BCLC stage appropriate recommended treatments were received by only 41.1% of HCC patients at our hospital. Up to 21% of well-selected BCLC B & C patients were eligible for up-stage treatment and had significantly improved OS. Down-stage treatments were received by up to 51.7% of cases across all BCLC stages and were associated with worse OS.

OTR-10096

Discriminative Ability of the Albumin-Bilirubin Grade in Asian-Pacific Hepatocellular Carcinoma Patients

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Background: Liver function influences the prognosis of patients with Hepatocellular Carcinoma (HCC). A recently developed Albumin-Bilirubin (ALBI) grade, serves to provide an objective assessment of liver function. We evaluated the discriminative ability of the ABLI grade for overall survival (OS) in non-resectable and resectable patients from two prospective randomized clinical trials (AHCC06 and AHCC03 respectively) conducted in the Asia-Pacific region. **Methods:** A total of 292 non-resectable patients who received Sorafenib (n = 162) or SIRT (n = 130), and 103 patients who received either 131I-Lipiodol (n = 55) as adjuvant therapy or no further treatment (n = 48) included in the study. ALBI grade (1-mild, 2-moderate, 3-severe) was calculated using baseline serum albumin and bilirubin based on thresholds outlined in the original published paper. OS was compared among ALBI grades using the Kaplan-Meier method and Cox regression analysis (unadjusted and adjusted for study treatment). **Results:** Among non-resectable patients, 35.6% (n = 104), 61.0% (n = 178), and 3.1% (n = 9) had ALBI grade 1, 2 and 3 respectively. The corresponding survival rate at 1-year was 54.6%, 43.3% and 33.3%. The hazard ratio for OS was 1.37 (p-value = 0.032) and 0.99 (p-value = 0.984) for comparison between ALBI grade 2 vs. 1 and 3 vs. 2, respectively. Among resectable patients, 46.6% (n = 48) and 53.4% (n = 55) had ALBI grade 1 and 2 respectively. The corresponding survival rate at 5-years was 56.0% and 53.0% respectively. The hazard ratio for OS was 1.01 (p-value = 0.908) for comparison between ALBI grade 2 vs. 1. Hazard ratios adjusted for study treatments were similar to unadjusted ones in both non-resectable and resectable patients. **Conclusion:** ALBI grade demonstrated potential discriminative ability in predicting OS in non-resectable HCC patients of mild and moderate severity. The study provides insufficient evidence for the discriminative ability of ALBI grade in prognosticating patients with resectable HCC patients.

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OTR-10098

Size Limit for a Single Nodule in the Criteria for Early-Stage Hepatocellular Carcinoma: Is It Really Necessary?

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Introduction: In the updated Barcelona clinic liver cancer (BCLC) guidelines, a cut-off point of 5 cm for classifying a single hepatocellular carcinoma (HCC) as BCLC stage A is no longer used. However, the need for size criteria for single stage A tumors remains controversial. Here, we aimed to assess whether such a size cutoff is necessary, based on the survival outcomes of patients receiving treatment according to the guideline recommendations. **Methods:** We included 301 patients with solitary BCLC-A HCC >5 cm in size and normal portal hypertension who initially underwent resection (n = 238; standard A group) or transarterial chemoembolization (TACE) (n = 63; non-standard A group) and 385 patients with BCLC-B HCC undergoing TACE (standard B group). All patients had Child-Pugh A liver function. Overall survival was compared between the treatment groups at different stages. We also examined the independent effect of each treatment on survival. **Results:** The mean tumor size was similar between the standard and non-standard A groups (8.8 ± 3.2 vs. 8.9 ± 3.4 cm). During a median follow-up of 5.5 years, the 5-year survival rates were 69.7% and 34.9% in the standard and non-standard A groups, respectively ($P < 0.05$). Compared with TACE, surgical resection had a multivariate hazard ratio (HR) of 0.34 for survival (95% confidence interval, 0.24–0.50; $P < 0.05$). The 5-year survival rate was significantly higher for standard A than for standard B group (69.7% vs. 32.6%; $P < 0.05$). This trend persisted after adjustment for confounding covariates, with an adjusted HR of 0.27 in the standard A group (95% confidence interval, 0.20–0.35; $P < 0.05$). However, there was no significant difference in the 5-year survival outcome between the non-standard A and standard B groups (34.9% vs. 32.2%). **Conclusions:** Our between-group comparison data on survival support the defining of all single HCCs of any size as stage A in the BCLC staging system, ultimately guiding the treatment decisions.

OTR-10106

Hospital-Volume and Outcome of Hepatectomy in Chronic Hepatitis Prevalent Area – Insight on Surgical Service for Hepatocellular Carcinoma

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Introduction: Hospital-volume has been known to be inversely associated with mortality rate in hepatectomy for hepatocellular carcinoma (HCC). In this study, we aim to devise a better strategy to optimize patient outcome after hepatectomy for HCC by evaluating the difference in mortality rate regarding hospital-volume and different pathology. **Methods:** The public hospitals provide more than 90% of service to the 7 million population of Hong Kong. We performed a retrospective review from the territory-wide surgical audit report on the outcome of major and minor hepatectomy to evaluate the relationship between hospital-volume and 30-day mortality rate. The 30-day mortality rate of different pathology relating to the hepatectomy was also reviewed in one of the centers serving 1.26 million population. **Results:** The mean annual caseloads of major and minor hepatectomy in public hospitals in Hong Kong were 327 and 482 respectively. 64% of these hospitals had a mean hospital-volume greater than 40 hepatectomy per year, of which at least 12 were major hepatectomy. The overall mortality rates for major hepatectomy and minor hepatectomy were 2.3% and 0.9% respectively. An inverse association between hospital-volume and 30-day mortality was demonstrated in major hepatectomy, but not in minor hepatectomy. The mortality rate of hepatectomy for gallbladder cancer (5.3%) and cholangiocarcinoma (8%) was higher than the mortality rate for HCC (0.3%). **Conclusion:** Minor hepatectomy for HCC could be performed safely in small-volume hospital. For high risk case requiring major hepatectomy, small-volume hospital should consider networking with high-volume hospital to optimize the surgical outcome. Standardization of case selection criteria and clinical pathway might also help to reduce mortality rate.

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Portal Vein Thrombosis as a Prognostic Factor for Survival Rate in Hepatocellular Carcinoma Patients

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Introduction: Portal Vein Thrombosis (PVT) is found in 10%-40% Hepatocellular carcinoma (HCC) patients. There is still limited data about PVT as prognostic factor of HCC in Indonesian population. The aim of this study is to see whether PVT plays a role as prognostic factor of HCC patients. **Methods:** A retrospective cohort study conducted in a General hospital Karawaci, Banten, Indonesia We evaluated HCC patients if they were still alive or not from the medical records database in period year 2013 to 2017. Diagnosis of HCC and PVT were made using three phase helical CT scan. Cumulative overall survival was estimated using Kaplan Meier method and P value was found using log-rank test. We evaluated if PVT was prognostic factor in HCC patients. **Results:** A total of 52 patients met fulfilled the criteria of HCC and PVT. There were 25 (48.1%) female patients. Median age of patients was 61 (34–73) year. There were 8 (15.4%) patients that had PVT. Hepatitis B and C was the etiology of HCC in 21 (40.4%) and 2 (3.8%) patients respectively. Mean INR of the patients was 1.14 (±0.15). Median estimated overall survival in all patients was 3.93 (±2.3) months. Median estimated overall survival in PVT and non-PVT groups were 2.28 (±1.53) and 4.25 (±2.25) months respectively. Patients with PVT had a lower overall survival when compared patients without PVT (HR: 6.9; P = 0.009). **Conclusion:** HCC patients with PVT had a significantly lower estimated overall survival rate when compared with they without PVT.

OTR-10112

Reviewed the Possible Factors Affecting 30-Days Mortality in Radiofrequency Ablation and Curative Surgery for Hepatocellular Carcinoma

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Introduction: The surgical resection and radiofrequency ablation (RFA) are common used as curative treatment for hepatocellular carcinoma (HCC). Although the incidence of 30-days mortality is very lower, to know the risk factors and to prevent the severe adverse event are critical issue in real world practice. We tried to review the possible factors that affecting 30-days mortality for HCC treatment. **Methods:** From May-2013 to Apr-2017, the patients with HCC received surgical resection or RFA were enrolled. Fourteen patients died within 30-days after procedure. Possible death associated factors were reviewed. **Results:** The 14 patients were 10 men and 4 women; surgical resection (7), liver transplantation (1), surgery and RFA combination (1), and RFA (5). The mean age was 64.7 ± 16 years old. Most of them had many co-morbidity disorders. 50% patients died within 48 hours. Mine patients had liver cirrhosis, 5 with Child-Pugh B. Tumor BCLC stage were A:4, B:8 and C:2 respectively. In surgical group, four patients had huge HCC (7.5 to 18 cm), two patients had multiple tumors or liver resection history. In RFA group, three deaths were related with bleeding and liver failure, and one patient was suspected pulmonary emboli. One died due to suicide. **Conclusions:** The possible causes of 30-days mortality were not unique. Old age, huge tumors and poor liver function are the possible risk factors for surgery. Expert's experience and history of surgery or trans-arterial embolization should be attended in RFA. Multiple treatment in short duration may not be a good strategy. Otherwise, psychological support is also important under aggressive treatment.

OTR-10129

Comparison of Hepatocellular Carcinoma Staging Systems for Predicting Survival Rate in Indonesian Patients

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Introduction: In Indonesia, the prognosis of Hepatocellolar Carcinoma (HCC) is very poor with less than 1 year survival range. HCC staging system played important role for predicting survival, yet the best HCC staging system for Indonesian patients is still unknown. Therefore, a research about HCC staging systems comparison in Indonesian patients was done. **Methods:** A retrospective cohort study on 52 HCC patients in Siloam General Hospital from 2013–2017 was conducted. This study compares Cancer of the Liver Italian Program (CLIP) score, Japan Integrated Staging (JIS) score, Hong Kong Liver Cancer (HKLC) staging system, and Barcelona Clinic Liver Cancer (BCLC) staging system. We took this information from medical records and called the patient's family for dead or alive status. Baseline characteristics related to HCC and liver status were presented. Comparison of staging systems for survival prognostic was analyzed using Kaplan-Meier and Cox-Regression method. **Results:** A total of 52 patients with median age 61 (34–73) years old and BMI 19.55

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(15.60–23.80) were enrolled to the study. The majority of patients were male (51.9%). The overall 1,3,5,7-months survival rate were respectively 84.61%, 53.85%, 23.07%, and 7.69% and the median survival rate was 4 months. All of the staging systems have significant value ($p < 0.05$) for predicting HCC survival rate. CLIP score had the best prognostic ability (HR = 1.345, p value <0.001) followed by JIS score (HR = 1.246, p value = 0.001). Next was HKLC staging system (HR = 0.913, p value = 0.010) and finally BCLC staging system (HR = 0.530, p value = 0.018) **Conclusion:** CLIP score is the best staging system for predicting survival rate of Indonesian HCC patients.

OTR-10133

Association Between Tumor Size and Number with Occurrence of Portal Vein Thrombosis in Indonesian Hepatocellular Carcinoma Patients

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Introduction: Portal Vein Thrombosis (PVT) is a lethal complication that can occur in patients with hepatocellular carcinoma (HCC) and have a negative influence on the prognosis. There is lack of information related to PVT and tumor characteristics of HCC. The aim of this study is to identify the association between tumor size and number with occurrence of PVT in Indonesian HCC patients. **Methods:** Data was collected by cross sectional method from medical records of 52 HCC patients in a teaching hospital located in Tangerang, Indonesia from years 2013 to 2017. PVT was diagnosed using abdominal Multi-slice helical CT Scan. Tumor size and number was estimated using ultrasonography or CT scan. Tumor size was categorized as single or multiple nodules. Categorical variables were analyzed using Chi-Square. Analysis to find difference in mean values between PVT and non-PVT group was done using T-test. **Results:** Majority of patients were male (51.9%). Median age was 61 (34–73) years. Mean BMI was 19.9 (±2.2) kg/m^2. Hepatitis B and C was the etiology of HCC in 21 (40.4%) and 2 (3.8%) patients respectively. Mean INR of the patients was 1.14 (±0.15). Most patients were categorized as TNM stage II (48.1%), followed by stage III (30.8%), stage I (11.5%) and stage IV (9.6%). Mean tumor size of the patients was 10.8 (±6.3) centimeters. There were 17 (32.7%) patients that had multinodular tumor. There were 8 (15.4%) patients that had PVT. Patients with and without PVT had a mean tumor size of 12.7 (±5.2) and 10.4 (±6.5) centimeters respectively (P = 0.386). Multinodular tumor did not have significant association with PVT (P = 0.893). **Conclusion:** Tumor size and number did not have significant association with occurrence of PVT. Patients with PVT had a larger mean tumor size compared with patients without PVT but not significant statistically.

OTR-10140

Comparison of Survival Outcomes According to Additional Therapies (Hepatic Arterial Infusional Chemotherapy versus Sorafenib) After Localized Concurrent Chemoradiotherapy for Advanced Hepatocellular Carcinoma

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Patients with advanced stage hepatocellular carcinoma (HCC) have a poor prognosis. Treatments such as hepatic arterial infusional chemotherapy (HAIC) or sorafenib have been tried to treat advanced stage HCC, but the median overall survival (OS) is reported to be less than 1 year. Localized concurrent chemoradiotherapy (CCRT) has shown favorable response for advanced stage HCC through initial reduction of tumor burden. However, beneficial effects of additional therapies after localized CCRT remain to be elucidated. Therefore, we aimed to compare survival outcomes according to additional modalities (HAIC vs. sorafenib) after localized CCRT for advanced stage HCC. We analyzed a total of 142 patients with Barcelona Clinic Liver Cancer C stage who were treated with localized CCRT between 2014 and 2016. In the course of radiotherapy for 5 weeks, hepatic arterial infusion of 5-fluorouracil (500 mg/day) via implanted port was applied during the first 5 and the last 5 days of radiotherapy. 4 weeks after localized CCRT, 95 patients received HAIC with 5-fluorouracil and cisplatin every 4 weeks (CCRT-HAIC group), whereas 46 received sorafenib (CCRT-SOR group). The primary endpoint was OS. Among the entire population, the mean age was 59.4 years old (124 male). 75 (52.8%) patients had the major portal vein invasion (tumor invasion at main trunk or the first order branch). All had well-preserved liver function. The median OS was 18.4 months. Between CCRT-HAIC and CCRT-SOR group, there was no difference in the mean age (p = 0.08) and the proportion of male gender (p = 0.608), and the major portal vein invasion (p = 0.515). There was no significant difference in the median OS between two groups (18.0 vs. 18.4 months, p = 0.631). Survival outcomes according to additional modalities (HAIC vs. sorafenib) after localized CCRT were similar. Both groups showed the median OS of 18.4 months, which is longer than that of a historical control. Further randomized trial is warranted.

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