Combined use of AFP and PIVKA-II as Surveillance Biomarkers for Hepatocellular Carcinoma: A Case Control Study

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I. Introduction and Significance of the Study

Hepatocellular carcinoma (HCC) is one of the most common and deadly cancer in the world. In adult men, it is the fifth most frequently diagnosed cancer, and in adult women, it is the ninth most commonly diagnosed cancer worldwide (1). There are marked geographic differences in its prevalence, reflecting the varied risk factors in different regions of the world. HCC incidence rates in the world are reported by registries in Asia and Africa. Approximately 85% of all liver cancers occur in these areas, with Chinese registries alone, reporting over 50%. In addition to registries in China, other Asian registries with rates greater than 20/100,000 persons include those of Seoul, Korea and Osaka, Japan. (2) In the Philippines, HCC ranks as the fourth most common cancer with an age-standardized rate of 6.7 per 100,000 persons in 2005. The incidence rates are about 2-3 times more in males than females. In the Philippines, HCC is the second and seventh leading cause of cancer deaths for men and women, with age-standardized mortality rates of 11 and 3.2 per 100,000 persons, respectively. (3)

Worldwide, the two most important risk factors for HCC are chronic HBV and HCV infection. This is true in Asia as well. HBV is the most common etiological agent related to pathogenesis of HCC in most Asian countries except in Japan where more than 80% HCC patients are infected with the HCV. In the past three decades, we have seen an increasing incidence of HCC in the developed countries probably related to the HCV infection epidemic from the 1970s to the 1990s as well as the observed increase in prevalence of obesity and its relation to the development of nonalcoholic steatohepatitis (NASH) and its sequelae of cirrhosis and HCC. (4)

Despite knowing the at-risk populations for HCC development, the lack of sensitive and specific means of surveillance hampers disease detection at curable stages. Both the American Association for the Study of Liver Diseases (AASLD), and the European Association for the Study of the Liver/European Organization for Research and Treatment of Cancer (EASL-EORTC) produced guidelines on the diagnosis, management and surveillance protocols for HCC. Both guidelines, agree on screening at-risk patients at least every six months with abdominal ultrasonography. There is no consensus on the use of serum biomarkers such as AFP and PIVKA-II.

Alpha-fetoprotein (AFP) is the most commonly used biomarker for diagnosis of hepatocellular carcinoma (HCC) in the Philippines and in the world. However, AFP is not tumor specific. AFP has limitations in detecting of HCC; thus, new biomarkers for detection of HCC are needed. (5-7) Protein induced by vitamin K absence or antagonist-II (PIVKA-II), is another biomarker for HCC. PIVKA-II and AFP are independently produced in the human body and are not strongly correlated with each other. Therefore, measurement of PIVKA-II together with AFP may offer improved diagnostic performances on HCC detection compared to either AFP or PIVKA-II alone. (8-13)

Data on the performance of PIVKA-II is lacking especially in the local setting. In line with this, this study aims to compare the diagnostic performance of AFP and PIVKA-II alone or in combination in detecting the overall and early HCC among high-risk patients.

II. Statement of the Problem

Among patients who are at risk for developing HCC, what is the clinical utility of AFP and PIVKA-II, either alone or in combination as a surveillance biomarker for HCC?

III. Objectives:

General Objective:

The objective of this study is to determine the clinical utility of AFP and PIVKA-II either alone, or in combination, in the overall and early detection or diagnosis of HCC among high-risk patients.

Specific Objectives:

A. To compare the levels of AFP and PIVKA-II in patients with HCC and in high risk patients without HCC.
B. To define the level of each tumor marker with the best sensitivity and specificity for HCC diagnosis.
C. To correlate the levels of these markers with respect to size and tumor burden.

IV. Study Design

This is a case-control study that will be conducted in Makati Medical Center, Makati City Philippines. All patients of Makati Medical Center, both from outpatient clinics and hospital admissions, who will be diagnosed with HCC from March 2018 to November 2018 will be considered as cases, while patients with cirrhosis, chronic Hepatitis B and Hepatitis C infection and those with F3 and above score on elastography or LiverFast without HCC will be considered as controls.

V. Methodology:

A. Study Population

- All patients aged 18 and above who will meet the following inclusion criteria will be enrolled in this study:

  - Case: HCC patients
    - The diagnosis of HCC will be made either histologically or by non-invasive criteria, based on the guidelines of The AASLD, EASL or APASL.
    - Radiologic hallmark of HCC :
      - Hypervascular in the arterial phase with washout in the portal venous or delayed phases observed on one of the following imaging techniques: 4- phase multidetector computed tomography or dynamic contrast-enhanced magnetic resonance imaging.
  - Exclusion criteria:
    - Those who have received prior treatment for HCC (Transplantation, Resection, Ablasion, TACE, SIRT).
    - Those with malignancy other than HCC.
    - Those patients taking warfarin or vitamin K within 1 month.

  - Control: At risk patients for HCC
    - All cirrhotic patients
      - Cirrhosis will be defined by histology or clinical criteria.
      - When the histology is not available, cirrhosis will be defined as follows:

      (1) Ultrasonographic findings suggestive of cirrhosis, including a blunted, nodular liver edge
      (2) Presence of portal hypertension (Varices, splenomegaly)
      (3) Overt complications of liver cirrhosis, such as ascites, variceal bleeding, and hepatic encephalopathy

    - Chronic Hepatitis B and Chronic Hepatitis C Patients
      - HBV infection will be confirmed with a positive hepatitis B surface antigen (HBsAg) for more than 6 months
      - HCV infection will be identified with both anti-HCV and HCV RNA positivity

    - F3 and above on liver elastography and LiverFast/Fibrotest

  - Exclusion criteria:
    - None of these patients should have radiologic evidence of HCC by ultrasound, MRI or CT scan.

- The Barcelona clinic liver cancer (BCLC) staging system will be used for HCC staging.
- A written consent from all patients according to the international ethics committee guidelines, and IRB approval will be obtained.

B. Sample Size

The sample size was computed using the equation $n = \frac{\left[Z_{\frac{\alpha}{2}}\sqrt{2\times\bar{P}(1-\bar{P})}+Z_{\beta}\sqrt{P_1(1-P_1)+P_2(1-P_2)}\right]^2}{(P_1-P_2)^2}$, intended for the computation of sample size when comparing two diagnostic tests. This equation uses either sensitivity or specificity. Based on literature, the sensitivity and specificity of PIVKA-II are 54.9% and 92.8%, respectively. On the other hand,

the AFP has sensitivity of 74.5% and specificity of 87.0%. For this research, the sample size computation was performed using sensitivity. The power used was 70% $(Z_{\beta} = 0.52)$. At 95% confidence interval $(Z_{\frac{\alpha}{2}} = 1.96)$, result showed that the sample size is 82 per group. To account for the non-responses, there should be additional 10%. The computation is as follows:

$$N_{final} = 73 + .10N_{final}$$
$$0.90N_{final} = 73$$
$$N_{final} = 81.11$$

The final sample size is 82 per group.

C. Description of Study Procedure

This is a case-control study that will be conducted in Makati Medical Center, Makati City Philippines. A total of 164 patients will be enrolled and will be divided into 2 groups: The Case and the control groups consisting of 82 subjects each. All patients who will seek consult at Makati Medical Center, both from outpatient clinics and hospital admissions, who will be diagnosed with HCC (Histologic or radiologic) from March 2018 to November 2018 will be considered as cases, while patients with cirrhosis, chronic Hepatitis B and Hepatitis C infection and those with F3 and above score on elastography or LiverFast without HCC will be considered as controls.

Blood samples for AFP and PIVKA-II assays from patients deemed at risk for HCC (controls) and patients suspecting to have HCC (cases), will be collected as part of routine screening test. As part of an introductory offer of Abbott Laboratories for the PIVKA-II assay, the first 180 patients who will avail of the said blood test will be free of charge. Likewise, if complications will be encountered during blood draw (e.g. bleeding, infection, pain), standard medical care will be provided by Abbott Laboratories.

All patients fulfilling the inclusion criteria will be given a laboratory request form (Appendix II). For HCC patients, samples will be collected at the time of diagnosis or prior to commencing treatment. For control patients without HCC, the samples will be obtained at the time of diagnosis or fulfillment of inclusion criteria. Blood samples will be collected through venipuncture by licensed phlebotomists at the Makati Medical Center Laboratory Department, Ground floor tower 2 or at bedside if the patient is admitted.

Concentrations of PIVKA-II and AFP in serum samples will be determined by chemiluminescent microparticle immunoassay (CMIA) on ARCHITECT i2000 (Abbott Diagnostics, Abbott, USA). The cutoff values for PIVKA-II and AFP will be defined at 40 mAU/mL and 20 ng/mL, respectively in accordance with previous studies.

The following clinical information will likewise be obtained at the time of consult.

Name
Age and Gender
Co-morbidities e.g. DM, Malignancy, Hypertension, Dyslipidemia
Medications
BMI
Diagnosis of HCC • Biopsy • Radiologic hallmarks
Cirrhosis • Child Pugh • MELD • Etiology of liver disease: NASH, HBV, HCV, Ethanol, Cryptogenic
Chronic Hepatitis B infection
Chronic Hepatitis C infection
F3 on elastography/LiverFast

Case-Control Study that will be conducted at Makati Medical Center from March 2018 to November 2018

All patients from outpatient clinics and hospital admissions, who will satisfy the inclusion and exclusion criteria will be included

A total of 164 patients will be enrolled and will be divided into 2 groups

CASE: 82 patients	CONTROL: 82 patients
• Diagnosed with HCC either histologically or radiologically • No prior treatment for HCC • No malignancy other than HCC • No intake warfarin or vitamin K within 1 month	• At risk for HCC o Patients with cirrhosis, chronic Hepatitis B and Hepatitis C infection and those with F3 and above score on elastography or LiverFast without HCC

Blood samples for AFP and PIVKA-II assays from patients deemed at risk for HCC (controls) and patients suspecting to have HCC (cases), will be collected as part of routine screening test

For HCC patients, samples will be collected at the time of diagnosis or prior to commencing treatment	For at risk patients for HCC, the samples will be obtained at the time of diagnosis or fulfillment of inclusion criteria

For outpatients, blood samples will be collected through venipuncture at the Makati Medical Center Laboratory Department, Ground floor tower 2

For inpatients, blood samples will be collected through venipuncture at bedside

Blood will only be collected once consent forms were signed

Procedure and possible complications will be thoroughly explained to the patient

As part of an introductory offer of Abbott Laboratories for the PIVKA-II assay, the first 180 patients who will avail of the said blood test will be free of charge

If complications will be encountered during blood draw (e.g. bleeding, infection, pain), medical care will be provided by Abbott Laboratories

Concentrations of PIVKA-II and AFP in serum samples will be determined by chemiluminescent microparticle immunoassay (CMIA) on ARCHITECT i2000 (Abbott Diagnostics, Abbott, USA)

Data processing

VI. Statistical Analysis

Descriptive statistics such as mean and standard deviation will be used to present data. Frequency distributions will be used to present categorical data. Sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) will be computed. Logistic regression will be conducted to screen for parameters that have impact on biomarkers. A p-value ≤ 0.050 will be considered significant. Youden's index will be employed for evaluation of the ideal cut-off levels of AFP and PIVKA-II for detection or diagnosis of HCC and will be calculated using the formula: Youden's index sensitivity specificity 1.

VII. Sample Tables

Table #. Baseline characteristics of patients (n=__)

Variables	Mean ± SD	
	With HCC (n=___)	At risk for HCC (n=____)
Age		
Gender		
...		

Table #. Result

PIVKA-II	With HCC (n=___)	At risk for HCC (n=____)	Total
Positive			
Negative			
Total			

AFP	With HCC (n=___)	At risk for HCC (n=____)	Total
Positive			
Negative			
Total			

Table #.

Parameter % (95% CI)	PIVKA-II	AFP	P – value
Sensitivity			
Specificity			
Positive Predictive value			
Negative predictive value			

VIII. Ethical Considerations

This study will adhere with the ethical principles set out in relevant guidelines (Declaration of Helsinki 2008, WHO Operational Guidelines, ICH-GCP and National Ethics Guidelines for Health Research) where all data will be collected prospectively using standard tests at Makati Medical Center. Written and informed consent will be obtained from all participants upon recruitment to ensure that they fully understood the objectives and methodology of the study. Patient's confidentiality will be a priority at all times. The PIVKA-II assay will be conducted free of charge and patients will be assured that the risk involve in participating in this study is minimal in which the probability and magnitude of harm or discomfort in the proposed research are not greater than those ordinarily encountered in daily like, or in the performance of routine physical or psychological exams or tests. The results of the tests will be given to the patients for follow up with their attending physicians. This study does not involve any intervention or treatment.

IX. Time Table

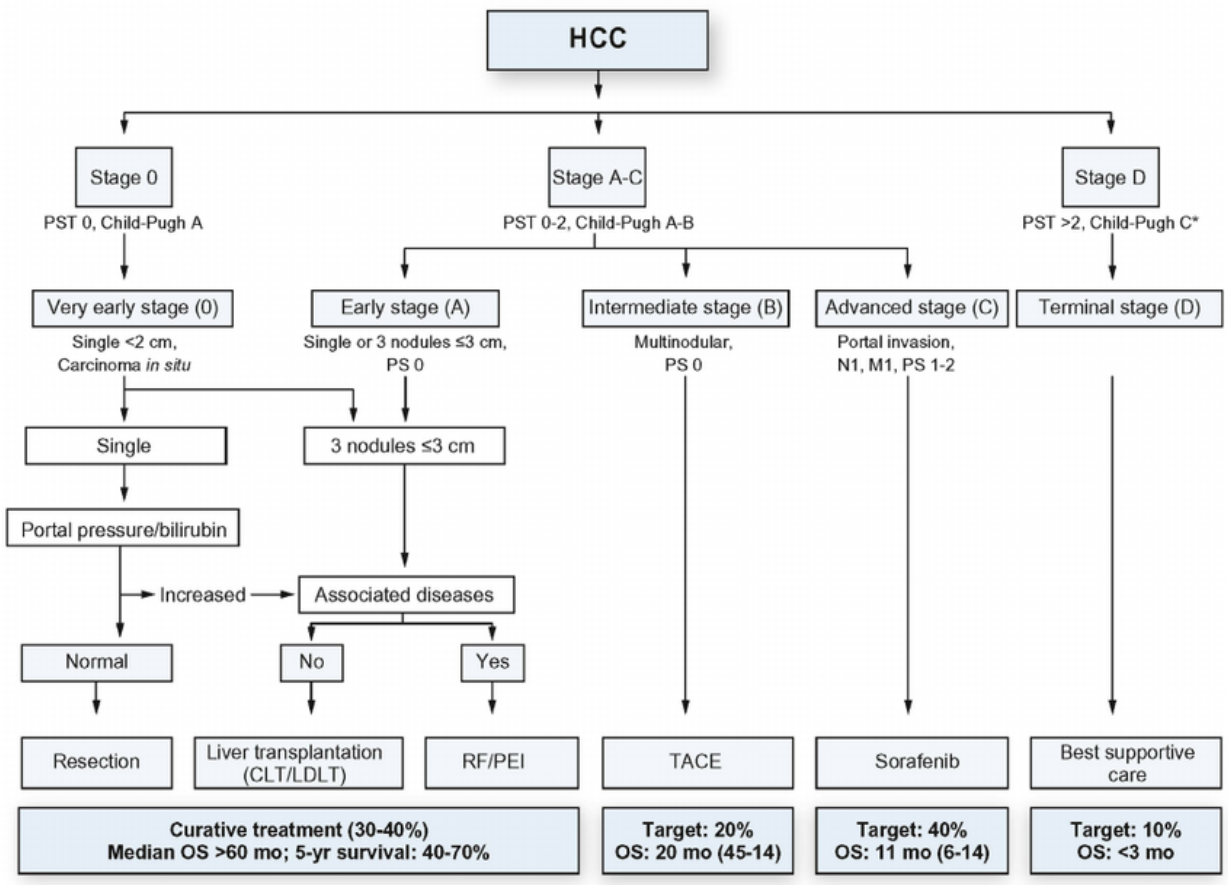
ACTIVITIES	MONTHS											
	Aug 2017	Sept 2017	Oct 2017	Jan 2018	Feb 2018	Mar 2018	Nov 2018	Jan 2019	Jan 2019	Feb 2019	Feb 2019	Mar 2019
Pre-work												
Determining the research question												
Literature search												
Approval from department												
Protocol preparation												
Protocol writing												
Consultation with statisticians												
Meeting with co-authors												
Submission to IRB												
Initial submission												
Re-submission for revisions												
Approval												
Data Collection												
Study Proper												
Data encoding												
Analysis												
Preparing the Results Section with the statistician												
Preparing the Discussion Section with co-authors												
Manuscript Preparation												
Initial draft for approval												
Final version												
Submission of Manuscript												
Oral Presentation of Research Paper												

X. Budget

Budget Items	Description	Quantity	Unit Price	Total Cash Cost
Printing/Photocopying services	Long Bond Paper	5 rims	170.00/rim	850.00
	Photocopy	1,400 pieces	0.50/copy	700.00
AFP	Assay	82	2500	-
PIVKA-II	Assay	82	3000	-
Professional services	Statistician			12,000.00
			TOTAL PHP	13, 550

XI. Appendix

Appendix I: The Barcelona clinic liver cancer (BCLC) staging system



Appendix II. Sample Questionnaires

COMBINED USE OF AFP AND PIVKA-II AS SURVEILLANCE BIOMARKERS FOR HEPATOCELLULAR CARCINOMA: A CASE CONTROL STUDY

PARTICIPANT DATA SHEET / LABORATORY REQUEST FORM

NAME OF CONSULTANT

☐ Alpha-feto Protein
☐ PIVKA-II

Control No. _____ Date_____
Name_____ Age_____ Sex_____
Contact No. _____
Past illness ___Diabetes mellitus ___Cancer ___Hypertension ___Others: _____
Medications_____
Height_____ Weight_____ BMI_____

☐ Hepatocellular Carcinoma
  - ☐ Biopsy
  - ☐ MRI
  - ☐ CT scan
  - ☐ Treatment naïve

☐ Cirrhotic
  - ☐ Hepatitis B
  - ☐ Hepatitis C
  - ☐ Ethanol
  - ☐ NASH
  - ☐ Cryptogenic
  - ☐ History of overt complications of liver cirrhosis, such as ascites, variceal bleeding, and hepatic encephalopathy

☐ Chronic Hepatitis B

☐ Chronic Hepatitis C

☐ F3 or F4 on Elastography/LiverFast

CONSENT TO PARTICIPATE IN COMBINED USE OF AFP AND PIVKA-II AS SURVEILLANCE BIOMARKERS FOR HEPATOCELLULAR CARCINOMA: A CASE CONTROL STUDY

TITLE: COMBINED USE OF AFP AND PIVKA-II AS SURVEILLANCE BIOMARKERS FOR HEPATOCELLULAR CARCINOMA: A CASE CONTROL STUDY

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What is the purpose of this Combined Use of AFP AND PIVKA-II as Surveillance Biomarkers For Hepatocellular Carcinoma: A Case Control Study*?*

Hepatocellular carcinoma (HCC) is one of the most prevalent causes of death in the world. In the Philippines, HCC ranks as the fourth most common cancer. Worldwide, the two most important risk factors for HCC are chronic HBV and HCV infection. This is true in Asia as well. Despite knowing the at-risk populations for HCC development, the lack of sensitive and specific means of surveillance hampers disease detection at curable stages.

Alpha-fetoprotein (AFP) is the most commonly used biomarker for diagnosis of hepatocellular carcinoma (HCC) in the Philippines and in the world. However, AFP is not tumor specific. Protein induced by vitamin K absence or antagonist-II (PIVKA-II), is another biomarker for HCC. PIVKA-II and AFP are independently produced in the human body. Therefore, measurement of PIVKA-II together with AFP may offer improved diagnostic performances on HCC detection compared to either AFP or PIVKA-II alone.

Data on the performance of PIVKA-II is lacking especially in our local setting. In line with this, this study aims to compare the diagnostic performance of AFP and PIVKA-II alone or in combination in detecting the overall and early HCC among high-risk patients.

Who is being asked to participate in this Combined Use of AFP AND PIVKA-II as Surveillance Biomarkers For Hepatocellular Carcinoma: A Case Control Study*?*

All newly diagnosed HCC patients who will satisfy the inclusion and exclusion criteria, as well as patients with cirrhosis, chronic Hepatitis B and Hepatitis C infection and those with F3 and above score on elastography/LiverFast without HCC.

What will my participation in this Combined Use of AFP AND PIVKA-II as Surveillance Biomarkers For Hepatocellular Carcinoma: A Case Control Study *involve?*

If you agree to participate in this study, we will be able to compare the diagnostic performance of AFP and PIVKA-II alone and in combination in the early detection of HCC.

What are the possible risks of my participation in the Combined Use of AFP AND PIVKA-II as Surveillance Biomarkers For Hepatocellular Carcinoma: A Case Control Study?

Blood samples for AFP and PIVKA-II assays from patients deemed at risk for HCC and patients suspecting to have HCC, will be collected as part of routine screening test. All patients fulfilling the inclusion criteria will be given a laboratory request form. Blood samples will be collected through venipuncture (blood draw) at the Makati Medical Center Laboratory Department, Ground floor tower 2 or at bedside if the patient is admitted. As part of an introductory offer of Abbott Laboratories for the PIVKA-II assay, the first 180 patients who will avail of the said blood test will be free of charge. The risk for physical injury is minimal, nonetheless, if complications will be encountered during blood draw (e.g. bleeding, infection, pain), medical care will be provided by Abbott Laboratories.

Participation in this research does involve the possible risk that information about your health status becomes known to researchers in Makati Medical Center. We will attempt to preserve your medical record confidentiality by assigning a special research code number to your medical record information stored in this study and by removing personal identifiers (for example, your name, medical record number) from information stored about you in this study. Information linking the research code number to your name and other personal identifiers will be stored in a separate secure location. Access to any identifiable information about you that is contained within this study will be limited to investigators associated with Makati Medical Center only.

What are the possible benefits of my participation in the Combined Use of AFP AND PIVKA-II as Surveillance Biomarkers For Hepatocellular Carcinoma: A Case Control Study?

The results of your tumor marker tests will be given to your attending physician. This will allow further evaluation and proper treatment by your attending physician.

In addition, medical record information contained within this study will be used for research studies directed at improving the early detection rate of Hepatocellular cancer especially in high risk patients.

Will I be charged for my participation in Combined Use of AFP AND PIVKA-II as Surveillance Biomarkers For Hepatocellular Carcinoma: A Case Control Study?

If you fulfill the inclusion criteria of this study, then AFP assay is part of your routine screening for HCC. PIVKA-II on the other hand is an additional blood test that will be extracted together with AFP and is free of charge. As part of an introductory offer of Abbott Laboratories for the PIVKA-II assay, the first 180 patients who will avail of the said blood test will be free of charge.

Will I be paid for my participation in the Combined Use of AFP AND PIVKA-II as Surveillance Biomarkers For Hepatocellular Carcinoma: A Case Control Study?

No, you will not receive any payment for participating in this study.

Who will know about my participation in this Combined Use of AFP AND PIVKA-II as Surveillance Biomarkers For Hepatocellular Carcinoma: A Case Control Study?

Any information obtained from your medical records will be kept confidential. In addition, you will not be identified by name in any publication that will arise from this research.

What is the nature of my medical record information that will be placed into the Combined Use of AFP AND PIVKA-II as Surveillance Biomarkers For Hepatocellular Carcinoma: A Case Control Study?

All of your past, current and future medical record information related to your condition and other co-morbids will be recorded in this study.

Who will have access to my identifiable medical record information contained in the Combined Use of AFP AND PIVKA-II as Surveillance Biomarkers For Hepatocellular Carcinoma: A Case Control Study?

Access to your medical information contained within this study will be limited to the study investigators.

For how long will my medical record information continue to be placed in the Combined Use of AFP AND PIVKA-II as Surveillance Biomarkers For Hepatocellular Carcinoma: A Case Control Study *and for how long will this information be used for research purposes?*

We will continue to use your medical record information this study until you withdraw your permission for participation in the said study.

Is my participation in the Combined Use of AFP AND PIVKA-II as Surveillance Biomarkers For Hepatocellular Carcinoma: A Case Control Study *voluntary?*

Your participation in the study is completely voluntary. Whether or not you provide your permission for participation in the said study will have no effect on your current or future medical care at Makati Medical Center. Whether or not you provide your permission for participation in this study will have no effect on your current or future relationship with Makati Medical Center.

May I withdraw, at a future date, my consent for participation in Combined Use of AFP AND PIVKA-II as Surveillance Biomarkers For Hepatocellular Carcinoma: A Case Control Study?

You may withdraw your consent at any time. However, any research use of your medical record information prior to date that you formally withdraw your permission will not be destroyed.

To formally withdraw your permission for participation in this study, you should provide a written and dated notice of this decision to the principal investigator of the said study at the address listed on the first page of this consent form.

The subjects' inclusion in this study is voluntary and would not include any monetary nor material compensation. Denial of inclusion would not result to denial of any medical service to the patient. The study is considered safe and no complications are expected to arise during the study period.

In case of an unfavorable incident, the subject will be given the standard medical care needed. This will include explanation of the abnormal results and its possible course, prescription of medications if needed and scheduling of follow up visits. Standard medications for the illness will be prescribed but no free medications will be given since the objectives of this study do not include the use of medication.

VOLUNTARY CONSENT

All of the above has been explained to me and all of my current questions have been answered. I understand that I am encouraged to ask questions about any aspect of my participation in this study at any time, and that such future questions will be answered by the principal investigators. I understand that a copy of this consent form will be given to me.

I understand that any questions which I may have about my participation in this study will be answered by answered by the principal investigators.

By signing below, I agree to participate in this study on Combined Use of AFP AND PIVKA-II as Surveillance Biomarkers For Hepatocellular Carcinoma: A Case Control Study.

_____ _____

Printed Name and signature of Participant Date

_____ _____

Printed name and signature of witness Date

CERTIFICATION OF INFORMED CONSENT

I certify that I have explained the nature and purpose of the Combined Use of AFP AND PIVKA-II as Surveillance Biomarkers For Hepatocellular Carcinoma: A Case Control Study to the above named individual, and I have discussed the possible risks and potential benefits of participation in this Combined Use of AFP AND PIVKA-II as Surveillance Biomarkers For Hepatocellular Carcinoma: A Case Control Study. Any questions the individual has about the said study have been answered, and the physicians associated with Makati Medical Center will be available to address future questions as they arise.

_____

Printed Name of Person Obtaining Consent

_____ _____

Signature of Person Obtaining Consent Date

PAHINTULOT PARA SA PAKIKILAHOK SA COMBINED USE OF AFP AND PIVKA-II AS SURVEILLANCE BIOMARKERS FOR HEPATOCELLULAR CARCINOMA: A CASE CONTROL STUDY

PAMAGAT: COMBINED USE OF AFP AND PIVKA-II AS SURVEILLANCE BIOMARKERS FOR HEPATOCELLULAR CARCINOMA: A CASE CONTROL STUDY

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Ano ang layunin ng pananaliksik at pag-aaral ng Combined Use of AFP and PIVKA-II as Surveillance Biomarkers for Hepatocellular Carcinoma: A Case Control Study?

Ang Hepatocellular Carcinoma (HCC) ay isa sa mga pangunahing sanhi ng pagkamatay ng mga tao sa mundo. Ang mga prognosis o babala nito ay nagkakaiba batay sa laki ng tumor at iba pang sakit sa atay. Kamakailan, natuklasan ang iba't ibang paraan sa pagbigay lunas, kasama dito ang transarterial chemoembolization at percutaneous ethanol injection,napabubuti nito ang short-term prognosis ng isang maliit na HCC. Naiulat na ang 5 taong survival rate ay umaabot sa 28% kung ang tumor ay may sukat na 3cm sa dayametro. Upang mapakinabangan ang pagusbong ng iba't ibang pagsulong na ito ay kinakailangan ng maagap na pagkakatuklas sa HCC lalong-lalo na sa mga pasyenteng may mas malaking tiyansang maka-kuha nito.

Ang Alpha-fetoprotein (AFP) ay isa sa madalas gamitin bilang biomarker sa pagsusuri ng HCC sa Pilipinas.Gayunman, ang AFP ay hindi tumor specific. Ang protein induced by vitamin K absence o antagonist-II (PIVKA-II), ay isa pang biomarker ng HCC. Ang PIVKA-II at AFP ay magkahiwalay na umuusbong sa katawang ng tao at hindi nakikiaayon sa isa't isa. Kung kaya't ang sukat ng PIVKA-II at AFP panel ay maaring may mas mainam na diagnostic performance sa HCC kumpara sa AFP o sa PIVKA-II lamang.
Kung gayon, ang layunin ng pag-araal na ito ay matuklasan o mapagpasiyahan ang gamit at bisa ng AFP at PIVKA-II ng nag-iisa o magkasama, sa pagtuklas ng kabuaan o maagap ng HCC sa mga pasyenteng may malaking tiyansang makakuha nito.

Sino-sino ang maaring makilahok sa Combined Use of AFP and PIVKA-II as Surveillance Biomarkers for Hepatocellular Carcinoma: A Case Control Study?

Ang lahat ng bagong pasyente na mapasaiilalim ng inclusion at exclusion criteria, mula Marso 2018 hanggang Nobyembere 2018 na may HCC ay ihahanay bilang cases, samantalang ang mga pasyenteng may cirrhosis, chronic Hepatitis B at Hepatitis C infection at ang mga pasyenteng may F3 at mataas ang nakuha sa elastography na walang HCC ay ihahanay bilang controls.

Ano ang kailangan kong gawin kung sasali ako sa Combined Use of AFP and PIVKA-II As Surveillance Biomarkers For Hepatocellular Carcinoma: A Case Control Study?

Kapag sumali ka sa pagsasaliksik na ito, ang iyong nakaraan, kasalukuyan at mga susunod pang impormasyong medikal ay ilalagay sa pag-aaral.

Ano ang mga posibleng panganib ng aking pagsali sa ng Combined Use of AFP and PIVKA-II as Surveillance Biomarkers for Hepatocellular Carcinoma: A Case Control Study*?*

Kung ikaw ay may panganib na magkaroon ng HCC, kasama sa mga blood test na hihingin ng iyong doctor and AFP and PIVKA-II. Ang pagkuha ng dugo para sa nasabing blood test ay gagawin sa Makati Medical Center Laboratory Department, Ground floor tower 2 or sa iyong kwarto kung ikaw ay nalalabi sa ospital. Halos walang panganib o pinsalang pisikal ang iyong pagsali sa pagsasaliksik. Kung meron mang pinsala kagaya ng pagdudugo or impection sa lugar kung saan kumuha ng dugo, and Abbott Laboratories ang sasagot sa pagpapagamot.

Kaakibat ng iyong pagsali sa pagsasaliksik na ito ang posibleng panganib na paglabas ng impormasyon tungkol sa iyong kalusugan mula sa Makati Medical Center.

Susubukan naming pangalagaan upang manatiling pribado ang iyong talang medikal sa pamamagitan ng pagtatalaga ng isang espesyal na bilang sa iyong impormasyong medikal na nakalakip sa pagaaral na ito, at sa pamamagitan ng pag-aalis ng personal na pagkakakilanlan (halimbawa, iyong pangalan,bilang ng talang medical) mula sa impormasyong tungkol sa iyo. Ang impormasyong naguugnay sa bilang palatandaan sa iyong pangalan at iba pang personal na pagkakakilanlan ay itatago sa isang hiwalay at ligtas na lugar.

Ano ang mga posibleng benepisyo ng aking pagsali sa ng Combined Use of AFP and PIVKA-II as Surveillance Biomarkers for Hepatocellular Carcinoma: A Case Control Study*?*

Ibibigay sa inyo ang resulta ng mga test na ginawa upang mabigyan kayo ng angkop na gamutan para sa inyong karamdaman o kundisyon.

Gayon man, ang impormasyong medikal na nasa loob ng pagaaral na ito ay gagamitin sa pag-aaral na nakatuon sa pagpapalawak ng ating kaalaman at gamutan sa mga pasyenteng lumahok sa pagaaral na ito.

Sisingilin ba ako sa aking pagsali sa ng Combined Use of AFP and PIVKA-II as Surveillance Biomarkers for Hepatocellular Carcinoma: A Case Control Study*?*

Kung ikaw ay may panganib na magkaroon ng HCC, kasama sa mga blood test na hihingin ng iyong doctor and AFP and PIVKA-II. Dahil bago lamang ang blood test na PIVKA-II assay sa aming ospital, magbibigay ng libreng test sa mga maaunang 180 na pasyente ang Abbott Laboratories.

Makatatanggap ba ako ng kabayaran sa pagsali sa ng Combined Use of AFP and PIVKA-II as Surveillance Biomarkers for Hepatocellular Carcinoma: A Case Control Study*?*

Hindi, wala kang matatanggap na anumang kabayaran sa pagsali sa pagaaral na ito.

Sino ang makakaalam tungkol sa aking pagsali sa ng Combined Use of AFP and PIVKA-II as Surveillance Biomarkers for Hepatocellular Carcinoma: A Case Control Study*?*

Anumang impormasyong mula sa iyong talang medical sa Combined Use of AFP AND PIVKA-II as Surveillance Biomarkers For Hepatocellular Carcinoma: A Case Control Study na ito ay pananatilihing konpidensyal hangga't maari. Gayundin, hindi ka ipakikilala sa pangalan sa anumang publikasyon ng mga resulta ng pag-aaral na gumamit ng iyong impormasyong medikal maliban na lamang kung may pinirmahan kang hiwalay na kasulatan ng pahintulot na nagbigay ng iyong permiso.

Ano ang katangian ng aking impormasyong medical na ilalagay sa Combined Use of AFP and PIVKA-II as Surveillance Biomarkers for Hepatocellular Carcinoma: A Case Control Study*?*

Lahat ng iyong nakaraan, kasalukuyan at susunod pang impormasyong medical na may kinalaman sa iyong nutrition ay itatala sa pagaaral na ito. Ang impormasyong ito ay kokolektahin mula sa iyong rekords sa Makati Medical Center at rekords sa ospital.

Combined Use of AFP and PIVKA-II as Surveillance Biomarkers for Hepatocellular Carcinoma: A Case Control Study*?*

Ang makakaalam sa impormasyong medical na tutukoy sa iyo sa ay limitado sa mga imbestigador ng Makati Medical Center at kanilang mga kawani. Isang bago at kumpletong listahan ng mga indibidwal na ito ay ibibigay sa iyo kung gagawa ka ng liham na humihiling nito.

Gaano katagal pananatilihing nasa Combined Use of AFP and PIVKA-II as Surveillance Biomarkers for Hepatocellular Carcinoma: A Case Control Study *ang aking impormasyon medical at gaano katagal gagamitin ang mga impormasyong ito sa pananaliksik?*

Patuloy naming ilalagay ang iyong impormasyong medical sa Combined Use of AFP AND PIVKA-II as Surveillance Biomarkers For Hepatocellular Carcinoma: A Case Control Study hanggang ito ay iyong pinahihintulutan.

Boluntaryo ba ang aking pagsali sa Combined Use of AFP and PIVKA-II as Surveillance Biomarkers for Hepatocellular Carcinoma: A Case Control Study*?*

Ang iyong pagsali sa pagaaral na ito, kasama na ang pagggamit ng iyong impormasyong medical para sa pananliksik na inilarawan sa itaas, at ganap na boluntaryo. Magbigay ka man o hindi ng iyong permiso sa pagsali dito, hindi nito maapektuhan ang

pangangalagang medical sa iyo sa kasalukuyan o sa darating na panahon sa Makati Medical Center, sa affiliated health care provider, o sa health care insurance provider sa kasalukuyan o sa darating na panahon.

Maari ko bang bawiin, sa darating na panahon, ang aking pahintulot na sumali sa Combined Use of AFP and PIVKA-II as Surveillance Biomarkers for Hepatocellular Carcinoma: A Case Control Study *na ito?*

Maari mong bawiin, sa anumang oras, ang iyong pahintulot na sumali sa pagaaral na ito, kasama na ang karagdagang koleksyon ng iyong impormasyong medical at ang karagdagang gamit para sa pananliksik na inilarawan sa itaas. Gayon man, aumang gamit pananaliksik ng iyong impormasyong medical bago ang araw ng iyong pormal na pagbawi ng iyong permiso ay hindi sisirain.

Ang pagsali sa research na ito ay boluntaryo at walang bayad na matatanggap. Ang hindi pagsali sa pag-aaral na ito ay hindi nangangahulugan na hindi pagbigay ng kaukulang pagaalagang medikal. Ang pagaaral na ito ay ligtas at walang komplikasyon na inaasahan sa panahon ng pananaliksik.

Sa pagkakataong may aksidenteng naganap, kayo ay makatatanggap ng sapat na pagaalagang medikal. Kasama dito ang pagpapaliwanag ng mga hindi normal na resulta, pagbibigay ng gamot kung kailangan at ang pag-balik sa doktor. Ang sapat ng pagaalagang medikal sa sakit ay ibibigay,ngunit walang libreng gamot na makukuha dahil hindi kasama ang pagbigay ng gamot sa pagaaral na ito.

Ang kalahok sa pagaaral na ito ay makatatanggap ng mga kaalaman tungkol sa diabetes at ang mga sapat sa impormasyon tungkol sa pagaaral na ito ay ibabahagi sa pasyente.

BOLUNTARYONG PAHINTULOT

Ang lahat ng nasa itaas ay naipaliwanag sa akin at lahat ng aking mga katanungan ay nasagot. Nauunawaan ko na ako ay hinihikayat na magtanong tungkol sa alin mang aspekto ng aking pagsali sa nasabing pagaaral sa anumang oras, at sa darating na panahon ay masasagot ang mga ito ng mga mangagamot ng Makati Medical Center.

Nauunawaan ko na anomang katanungang mayroon ako tungkol sa aking mga karapatan bilang kalahok ng nasabing pagaaral ay sasagutin ng Makati Medical Center.

Sa pagpirma sa ibaba, sumasang-ayon ako na sumali sa Combined Use of AFP and PIVKA-II as Surveillance Biomarkers for Hepatocellular Carcinoma: A Case Control Study.

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Nakaprint na Pangalan ng Kalahok

_____ _____
Lagda ng Kalahok Petsa

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Lagda ng Saksi Petsa

KATIBAYAN NG KASULATAN NG PAHINTULOT

Pinatutunayan ko na naipaliwanag ko ang mga katangian at layunin ng Combined Use of AFP AND PIVKA-II as Surveillance Biomarkers For Hepatocellular Carcinoma: A Case Control Study sa taong tinutukoy sa itaas, at naipaliwanag ko ang mga posibleng panganib at potensyal na benepisyo sa pagsali sa pagaaral na ito. Anumang katanungan mayroon ang kalahok tungkol sa nasabing pagaaral ay nasagot, at ang mga doctor at kawani ng Makati Medical Center ay handang sumagot sa maaring maging mga katanungan sa darating na panahon.

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Nakaprint na pangalan ng Taong kumukuha ng Pahintulot

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Lagda ng Taong kumukuha ng Pahintulot Petsa

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