Official Study Title:
A Prospective, Interventional, Longitudinal APAC Study Evaluating Clinical Utility of the GAAD Score for Detection of Hepatocellular Carcinoma in a High-Risk APAC Patient Population

Study Acronym:
STOP HCC-GAAD-APAC-Thailand

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Brief Summary

Hepatocellular carcinoma (HCC) surveillance is frequently underutilized, and currently available biomarkers, such as alpha-fetoprotein (AFP), demonstrate suboptimal diagnostic performance. This prospective study aims to evaluate a simplified multivariate index, the GAAD score—comprising gender, age, alpha-fetoprotein (AFP), and protein induced by vitamin K absence or antagonist-II (PIVKA-II)—for its ability to improve the detection of hepatocellular carcinoma in patients with chronic liver disease.

The study hypothesizes that the addition of the GAAD score to standard surveillance strategies will improve diagnostic performance for HCC and may provide evidence to support its inclusion in future clinical practice guidelines.

Study Design

- **Study Type:** Interventional (Diagnostic Utility Study)
- **Study Phase:** Not Applicable
- **Primary Purpose:** Diagnostic
- **Study Model:** Single Group Assignment
- **Allocation:** Non-Randomized
- **Masking:** None (Open Label)
- **Study Start Date:** To be determined
- **Primary Completion Date:** 24 months (follow-up period)
- **Study Completion Date:** 36 months (enrollment plus follow-up)

Outcome Measures

Primary Outcome Measures

Measure: Relative true positive rate and relative false positive rate of surveillance modalities
Description:
To evaluate the diagnostic performance of ultrasound, serum AFP, and the GAAD score as standalone surveillance tests, as well as the combinations of ultrasound plus AFP and ultrasound plus GAAD. The GAAD score cut-off for this endpoint is 2.57.
Time Frame: Over 24 months of patient follow-up

Secondary (Exploratory) Outcome Measures

1. **Measure:** Comparative clinical performance of GAAD
   Description: To compare the clinical performance of the GAAD algorithm with ultrasound, AFP, PIVKA-II, and the combination of ultrasound plus AFP, including positive predictive value (PPV), negative predictive value (NPV), sensitivity, specificity, and area under the receiver operating characteristic curve (AUC), stratified by HCC stage and etiology.
   Time Frame: Over 24 months of patient follow-up

2. **Measure:** Biomarker kinetics
   Description: To assess longitudinal changes in Elecsys AFP, Elecsys PIVKA-II, and the GAAD score leading up to an HCC diagnosis in confirmed cases.
   Time Frame: Over 24 months of patient follow-up

3. **Measure:** Additional early-stage HCCs identified
   Description: To quantify the number of additional early-stage hepatocellular carcinoma cases identified through use of the GAAD score compared with standard surveillance methods.
   Time Frame: Over 24 months of patient follow-up

4. **Measure:** Additional imaging procedures triggered
   Description: To count the number of additional computed tomography (CT) or magnetic resonance imaging (MRI) procedures triggered by positive GAAD, AFP, or ultrasound results and to calculate the relative false positive rate.
   Time Frame: Over 24 months of patient follow-up

Arms and Interventions

Arm: High-Risk Cohort

Intervention: Diagnostic Test – GAAD Score

All enrolled participants will undergo standard hepatocellular carcinoma surveillance consisting of blood sampling and abdominal ultrasound every 6 months for 24 months. Blood samples will be analyzed for serum AFP and PIVKA-II to calculate the GAAD score.

A GAAD score of ≥ 2.57 will trigger a recall procedure, defined as further diagnostic evaluation using multiphasic contrast-enhanced CT or MRI. This is in addition to standard recall triggers, including detection of a suspicious hepatic lesion measuring ≥ 1 cm on ultrasound or elevated or rising serum AFP levels (≥ 20 ng/mL).

Eligibility Criteria

Ages Eligible for Study: ≥ 18 years
Sexes Eligible for Study: All
Accepts Healthy Volunteers: No

Inclusion Criteria:

- Signed informed consent form
- Age ≥ 18 years
- Chronic liver disease with an indication for HCC surveillance, including:
    - Liver cirrhosis of any etiology (e.g., chronic hepatitis B virus, hepatitis C virus, metabolic dysfunction–associated steatohepatitis, or alcohol-related liver disease)
    - Non-cirrhotic chronic liver disease with evidence of stage F3 fibrosis
    - Chronic hepatitis B virus infection with a clinical diagnosis of non-cirrhotic liver disease

Exclusion Criteria:

- Any active malignancy other than non-melanoma skin cancer
- History of prior malignancy, including hepatocellular carcinoma
- Life expectancy < 2 years
- Use of vitamin K antagonists within 1 week prior to enrollment
- Pregnancy or breastfeeding
- Estimated glomerular filtration rate < 60 mL/min/1.73 m^2

- Significant hepatic decompensation or Child–Pugh class C liver disease
- Unwillingness or inability to undergo CT or MRI
- Unwillingness or inability to participate in the study