Prevention of HEpatitis B related Liver CANcer
Epidemiology of Viral Hepatitis B

Viral Hepatitis B │ In brief

- 257 million people (3.5% of the population) with chronic HBV infection
- Chronic HBV infection results in > 1 million deaths/year from cirrhosis and liver cancer
- Prophylactic vaccine but no universal cover
- Antiviral therapies to slow down progression but no cure and not available for the majority of Chronic carriers
- 10 genotypes (A to J) based on genome sequence divergence (>8%) which determine disease progression
Le Carcinome Hépatocellulaire (CHC) :

5ème cancer le plus fréquent
626 000 nouveaux cas/an
3ème cause de mortalité suite à un cancer (poumon, estomac)
598 000 morts/an (Parkin et al, 2005)

Facteurs de risque :
- Infections chroniques par les virus des hépatites B et C (VHB, VHC)
- Consommation chronique d’alcool
- Syndromes du métabolisme
- Exposition alimentaire à l’Aflatoxine B1 (AFB1)

Hepatocellularcarcinoma - More than 50% due to HBV

HCC incidence in men per 100 000, 2008 (GLOBOCAN 2008, CIRC)
PHELICAN Partners

- Lyon 2 University – Lead? M Préau
- INSERM U1052, Lyon, France
- International Agency for Research on Cancer (?) Prevention section
- MRC Laboratories, Fajara, Gambia (?)
- Ministry of Health, Banjul, Gambia
- Le Dantec Hospital, Dakar, Senegal
- Pasteur Institute Morocco?
- European countries eligible as LMC?
- CHU Lyon, Limoges, France?
Efficient Identification of Patients with HCV

50 million “risk identified” or ~80 million 1945-1965 cohort who need to be tested for HCV in US

4 -5 million people with HCV in US

25% diagnosed with HCV

Treatment and Management

Improve Diagnosis

1Tomaszewski Am J Public Health 2012; 102 (11):e101
Research Agenda

• Two research Cohorts
  – Hepatocellular Carcinoma Case Control study (HC₃)
  – HEP B patient Cohort (HEPBC)

• SHS Approaches
  – Lyon 2, CRCL
  – Prevention service? – IARC
  – Virology - Inserm
HEPBC: Hepatitis B Chronic Carriers and clinical setting

- Primary Objective

Determine/Compare who and where are Chronic HBV carriers in Several countries
And Compare the clinical setting to promote improvements
HEPBC STUDY:

- Sample SIZE ? Different countries???
- To be evaluated
Hepatocellular Carcinoma Case-Control Study – HC$_3$

• Objectives
  – To develop a research platform for scientific studies of hepatitis B virus (HBV) viral genetics of HCC and promote treatment (Curative or Palliative)
HC₃ - Design

• Study design
  – Hospital-based case-control study of incident HCC patients and two sets of control participants matched on age and sex. One set of controls will be HBV infected without HCC and one set will be uninfected healthy controls.

• Study duration
  – Recruitment of study subjects will take place over a period of 2 years.
HC$_3$ Investigations

- Standardized structured interview to assess socio-demographic, lifestyle and dietary exposures
- Clinical examination & Nutritional assessment (skinfold thickness)
- HBV serology & HBV DNA
- HCV serology
- Voluntary counselling and testing (VCT) followed by HIV serology*
- Liver function tests (LFTs)
- Complete blood count (CBC)
- Clotting studies
- Alfa-fetoprotein (AFP)
- HbA1c
- Liver ultrasound (US)
- Serum / plasma sample for viral sequence and genotype analysis
- Serum / plasma and urine samples for biomarkers of cancer development (annually)
- Serum for aflatoxin adducts
- EDTA blood sample for human genetic analysis
PoC Testing Hospital testing?

- HBsAg positive
  - Clinical Assessment
    - EASL Criteria +
      - Data & Sample Collection
        - Treatment
    - EASL Criteria -
      - Data & Sample Collection
        - Observation

- HBsAg negative
  - Data & Sample Collection
  - HCC Cases
    - HCC Case Identification
Political / Public Health Agenda

• Programmatic development for HBV in Several countries
  – Feasibility analysis
  – Identification of patients
  – Modelling impact of treatment on burden of disease

• Integration of HBV with HIV services?

• Lobbying global fund / GAVI for reductions in drug costs
Training Agenda

• Research training of doctors in France
• Research training of French doctors in XXX?
• Clinical training of doctors in France

Is it good to include?
HEPBC STUDY - Endpoints

• **Primary:** Identify HBV patients in several countries/
  Hospitals to identify/improve clinical setting caveats

• **Secondary:**
  – Proportion of adult population with chronic HBV infection and the “targeted populations”
  – Incidence of Hepatocellular Carcinoma over the period of study in a treated cohort of patients with chronic HBV
  – Number of patients with chronic HBV infection who meet EASL treatment criteria and the proportion really treated
  – Proportion of patients with undetectable HBV DNA < 400 copies/ml at 1, 2, 3, 4 and 5 years of treatment.
  – Incidence of hepatocellular Carcinoma in patients who do not meet EASL treatment criteria.
  – Treatment adherence rate.
  – Average change in Fibroscan score after 3 years