PARIS HEPATITIS CONFERENCE
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Research in viral hepatitis: the French ANRS experience

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- **Public Agency aimed at funding researches in all areas relevant to HIV/AIDS and hepatitis**
- **Annual budget of research: 44 Millions euros**
- **Supported by :**
  - **Ministry of Research (39 Millions euros)**
  - **Ministry of Health**
  - **Ministry of Foreign Affairs**
  - **Institutional partners : INSERM, CNRS, Pasteur Institute, IRD, Esther**

% Distribution of funds according to research area 2012 (42 M €)

- Basic Science HIV 14 %
- Vaccine HIV-HCV 12 %
- Clinical trials and cohorts (HIV) 28 %
- Epidemiology/socio-behavioral science 7 %
- Resources limited countries (HIV-Hepatitis) 20 %
- Hepatitis B and C 19 %

To be confirmed

PUBLICATIONS ANRS

	2003	2004	2005	2006	2007	2008	2009	2010	2011
Fondamental VIH	119	110	135	123	159	131	150	131	143
Vaccin	19	15	21	11	3	4	12	10	12
SHS	21	24	40	36	47	48	34	36	40
PED	57	52	44	53	56	110	100	105	100
Clinique VIH	72	64	79	118	84	111	145	118	106
Hépatites virales	18	28	34	89	77	76	147	148	131
TOTAL	306	293	353	430	426	480	588	548	532

ANRS STRENGTHS

- Good international visibility
- New generation of researchers
- Interaction with civil society : NGOs
- Multidisciplinary approach
- Research in resource-limited countries
- A coordinating and funding agency that has demonstrated the capability of incorporating an additional pathology (viral hepatitis)

ANRS 2012: Autonomous agency within INSERM

- Integration within Inserm as of 1 January 2012
- Scientific and budgetary autonomy
- Scientific organisation conserved
- Funding of the different laboratories: Inserm, CNRS, Institut Pasteur,IRD…
- An international Scientific Advisory Board
- An orientation committee
- Director nominated for 4 years
- ANRS-ANRS / H

aviesan
alliance nationale
pour les sciences de la vie et de la santé

Maladies infectieuses
Inserm
Institut national
de la santé et de la recherche médicale

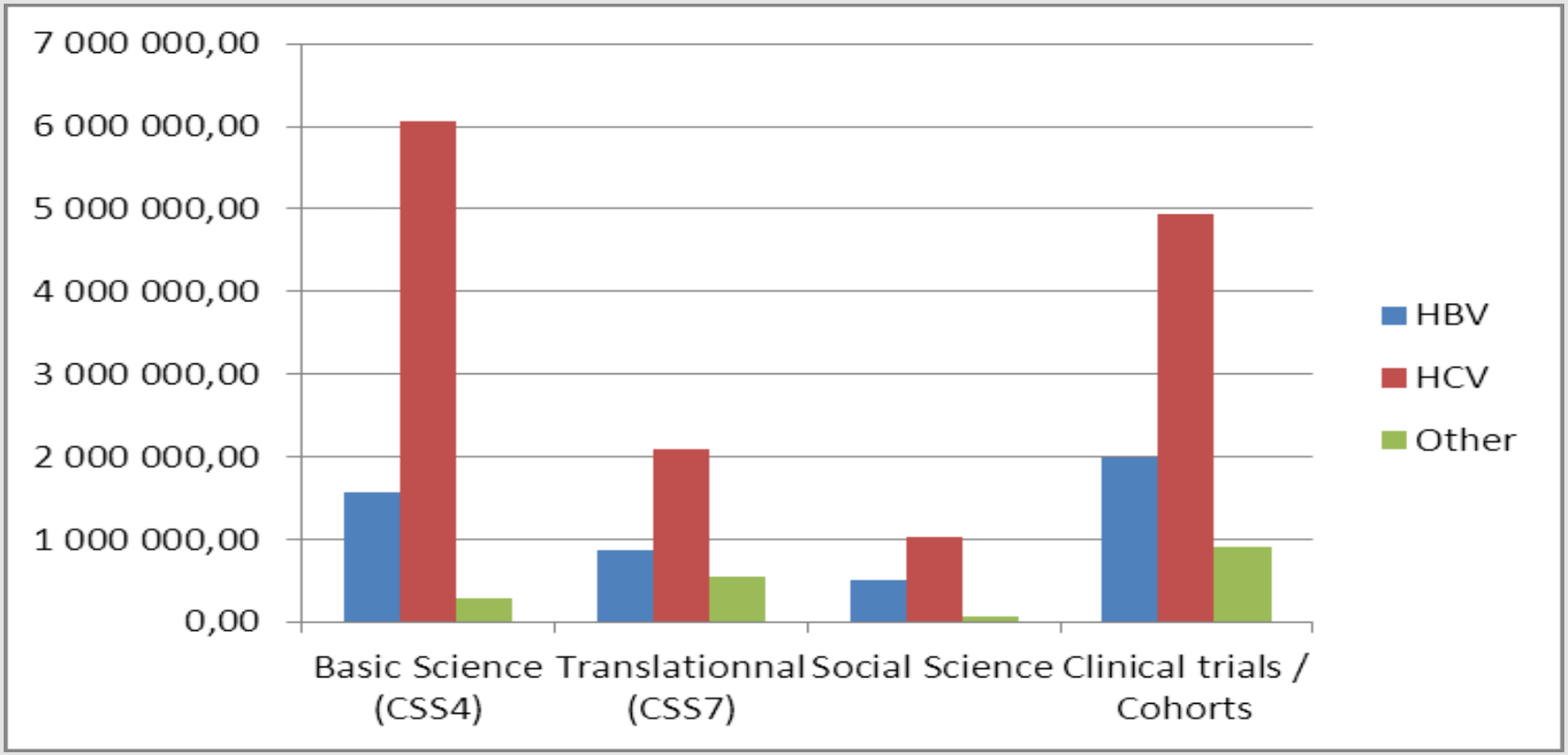
ANRS HEPATITIS FUNDING EVOLUTION IN THE HEPATITIS FIELD

- Before 1999: no specific funding
- 1999-2005: Basic Research and Science Social Research
- 2005-2012: Basic, Science Social Research and Clinical Research
- Late 2013: ANRS ⟶ ANRS/H

AGENDA of the ANRS : 4 main priorities for HEPATITIS

- Molecular mechanisms involved in cell-virus interactions
- Relationships between fibrosis, inflammation and viral replication
- Strategic evaluation of new molecules anti HVC (Cohorte, coinfections...)
- New tools for prevention

ANRS Funding 2008 - 2009 - 2010 -2011



The Coordinated Action (AC) in the field of viral hepatitis

Basic Research:

-AC 29: Entry and assembly mechanisms of hepatitis viruses in their target cells (Pres: J Dubuisson)

-AC 33: Medical virology in the hepatitis field

-AC 33: Resistance to antiretrovirals of Hepatitis B and C viruses (co Pres: JM Pawlotsky and F Zoulim)

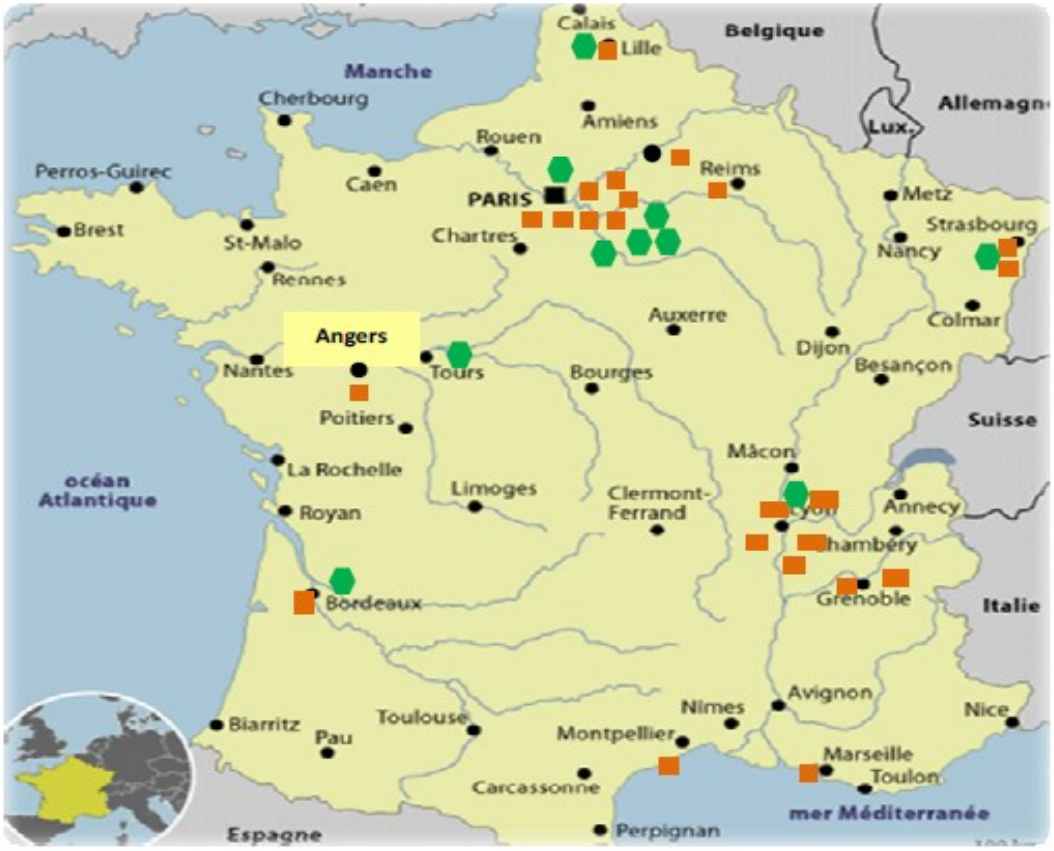
Clinical Research:

-AC 7: Cohorts (Pres: G Chêne)

-AC 24: Clinical trials in viral hepatitis infection (Pres: M Bourliere)

-AC 5/24: Clinical trials in HIV-Hepatitis co-infection (Co Pres: M Bourliere and JM Molina)

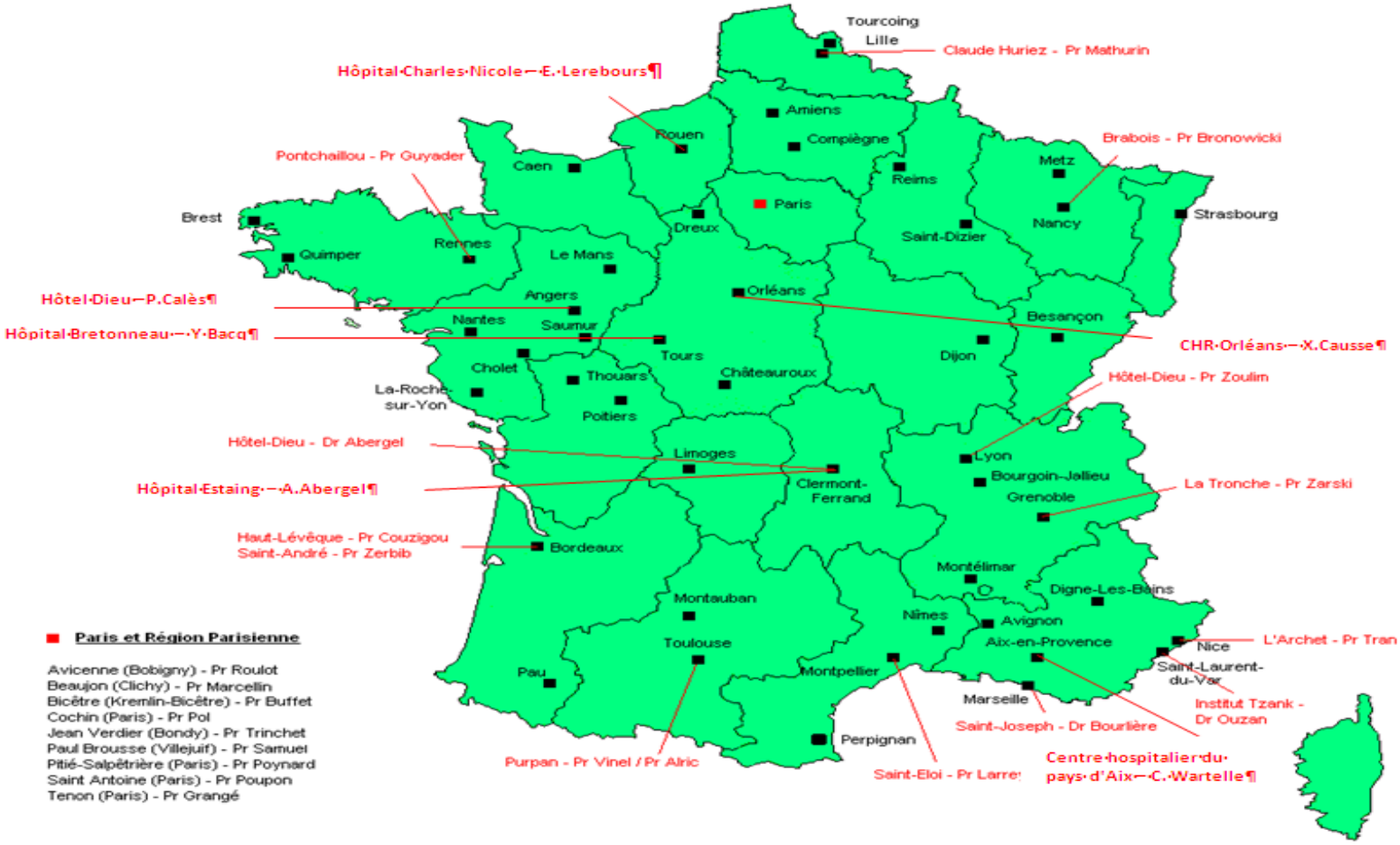
INSERM, CNRS, UNITS, INVESTIGATED IN HEPATITIS FIELD RESEARCH



CNRS, INSERM, UMR

INSERM

ANRS Staff support in hepatitis clinical sites



AC24, AC 5/24, AC7 - Clinical Trials, physiopathological studies and Cohorts (01.2013)

Number of completed trials since 2005 (n=17) (# 2000 patients)

Ongoing clinical studies (n = 22) (# 3500 patients)

- Clinical trials HBV or HCV with medicinal products / mono and co infection : 14
- Physiopathological studies: 8

Ongoing Cohorts (n= 4) (# 4500 patients)

- ANRS CO 12 CIRVIR,
- ANRS CO 13 HEPAVIH,
- ANRS CO 20 CUPIC,
- ANRS CO 22 HEPATHER

anRS
Agence nationale de recherches sur le sida et les hépatites virales
French National Agency for Research on AIDS and Viral Hepatitis
Agence autonome de l'Inserm
An autonomous agency at Inserm

SAFETY OF TELAPREVIR OR BOCEPREVIR IN COMBINATION WITH PEGINTERFERON ALFA/RIBAVIRIN, IN CIRRHOTIC NON RESPONDERS FIRST RESULTS OF THE FRENCH EARLY ACCESS PROGRAM (ANRS CO20-CUPIC)

C Hézode[1], C Dorival[2], F Zoulim[3], T Poynard[4], P Mathurin[5], S Pol[6], D Larrey[7], P Cacoub[4], V de Ledinghen[8], M Bourlière[9], PH Bernard[10], G Riachi[11], Y Barthe[2], H Fontaine[6], F Carrat[2], JP Bronowicki[12] for the CUPIC study group (ANRS CO 20)

Hôpital Henri Mondor, Créteil[1], UMR-S 707, Paris[2], INSERM U871, Lyon[3], Hôpital de la Pitié-Salpêtrière, Paris[4], Hôpital Claude Huriez, Lille[5], Hôpital Cochin, Paris[6], Hôpital Saint-Eloi, Montpellier[7], Hôpital Haut-Lévèque, Pessac[8], Fondation Hôpital Saint Joseph, Marseille[9], Hôpital Saint André, Bordeaux[10], Hôpital Charles Nicolle, Rouen[11], Hôpital de Brabois, Nancy[12], France

AFEF ASSOCIATION FRANÇAISE POUR L'ETUDE DU FOIE
CUPIC AnrS CO20
Instituts thématiques
UPMC PARISUNIVERSITAS
Inserm Institut national de la santé et de la recherche médicale

French Early Access Program

ATU

The Temporary Authorization for Use (ATU) is an early access program for medicinal products which have undergone full clinical development and are waiting for marketing authorization by the French Health Products Safety Agency (Afssaps)

CUPIC

Compassionate Use of Protease Inhibitors in viral C Cirrhosis

National multicenter observatory in the setting of the ATU

Promoter: ANRS

Aim: to prospectively collect clinical data and biological specimen

CUPIC: Preliminary conclusions

- In this large cohort of compensated cirrhotic patients, the safety profile of TVR or BOC in triple combination was poor as compared with phase III trials (Increased rates of SAEs and more difficult management of anemia) but associated with high rates of on-treatment virologic response

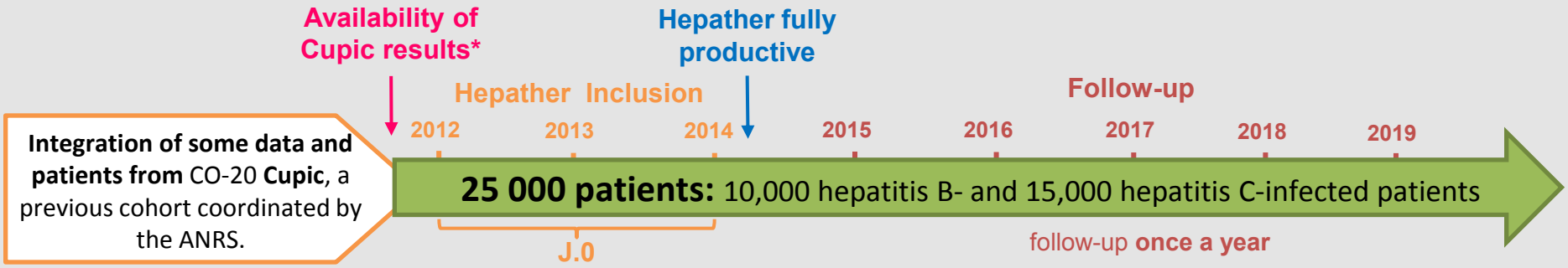
- Risk / benefit ratio should be assessed in cirrhotic experienced patients with platelets count <100,000/mm^3 and albumin level <35 g/L. These patients should be treated on a case by case basis due to high risk to develop severe complications

- However, cirrhotic experienced patients without predictors of severe complications should be treated but cautiously and carefully monitored

✓Main scientific objective of Hepather (ANRS CO 22)

To improve quality and effectiveness of medical cares in taking into account the new treatment options and host characteristics by integrating genetic, pharmacogenomics, clinical, environmental and behavioral data in a large number of patients.

✓Data collection and Hepather timeline:



• ***Database:*** **Clinical**, **biological**, **treatment**, **environmental** and **social** data integrated through **clinician and self-reporting** (80% of historical patient data would be imported from existing medical files)

• ***Biobank:*** **Blood, serum and urine sampling.**

• ***Database:*** **Combination of systematic follow-up visit by using the various different national administrative databases** and sources to ascertain death and other health-related information (RNIPP, CépiDc, SNIIR-AM, Plastico).

• ***Biobank:*** **Sampling follow-up is not systematic** but will be **motivated by a specific research project or a medical event** such as disease progression or the initiation of a new treatment.

*: HEP DART Dec. 2011, EASL Apr. 2012.

HIV/HCV HEPATITIS CO-INFECTION

- **ANRS HC26 « TELAPREVIH » : Pilot Study of PegInterferon-Ribavirin-Telaprevir Efficacy and Tolerability in HIV-HCV Coinfected Patients Who Had Previously Failed a PegInterferon-Ribavirin Regimen**

- **ANRS HC27 « BOCEPREVIH » : A pilot study to assess the efficacy and the safety of Boceprevir in combination with PegInterferon alfa and Ribavirin, in subjects with HCV/HIV coinfection, in failure to a previous therapy of Peginterferon/Ribavirin**

- **ANRS HC29 « BOCEPRETRANSPLANT » : Pilot Study on the Efficacy of Pegylated Interferon-Ribavirin-Boceprevir Triple Therapy in Patients Infected With Genotype 1 HCV With Cirrhosis and Awaiting Liver Transplantation**

- **ANRS HC30 « QUADRIH » : Pilot study to assess the efficacy and safety of a Quadruple therapy with Asunaprevir, Daclatasvir, Ribavirin and pegylated Interferon alpha2a, in HIV and HCV genotype 1 or 4 co-infected patients, previously null responders to a standard Pegylated interferon – Ribavirin regimen**

ANRS research programme on HCV in Egypt

HCV risk factors
-Iatrogenic
-Intra-familial

Factors associated with HCV clearance
-epidemiology
-lipids
-virology
-immunology

Treatment efficacy
- Acute phase
- Chronic infection

Mathematical modeling
-Prediction
-cost-effectiveness

END