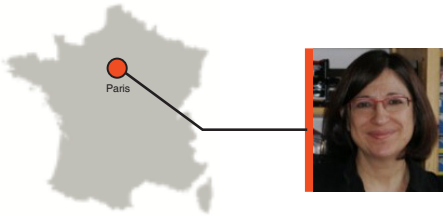
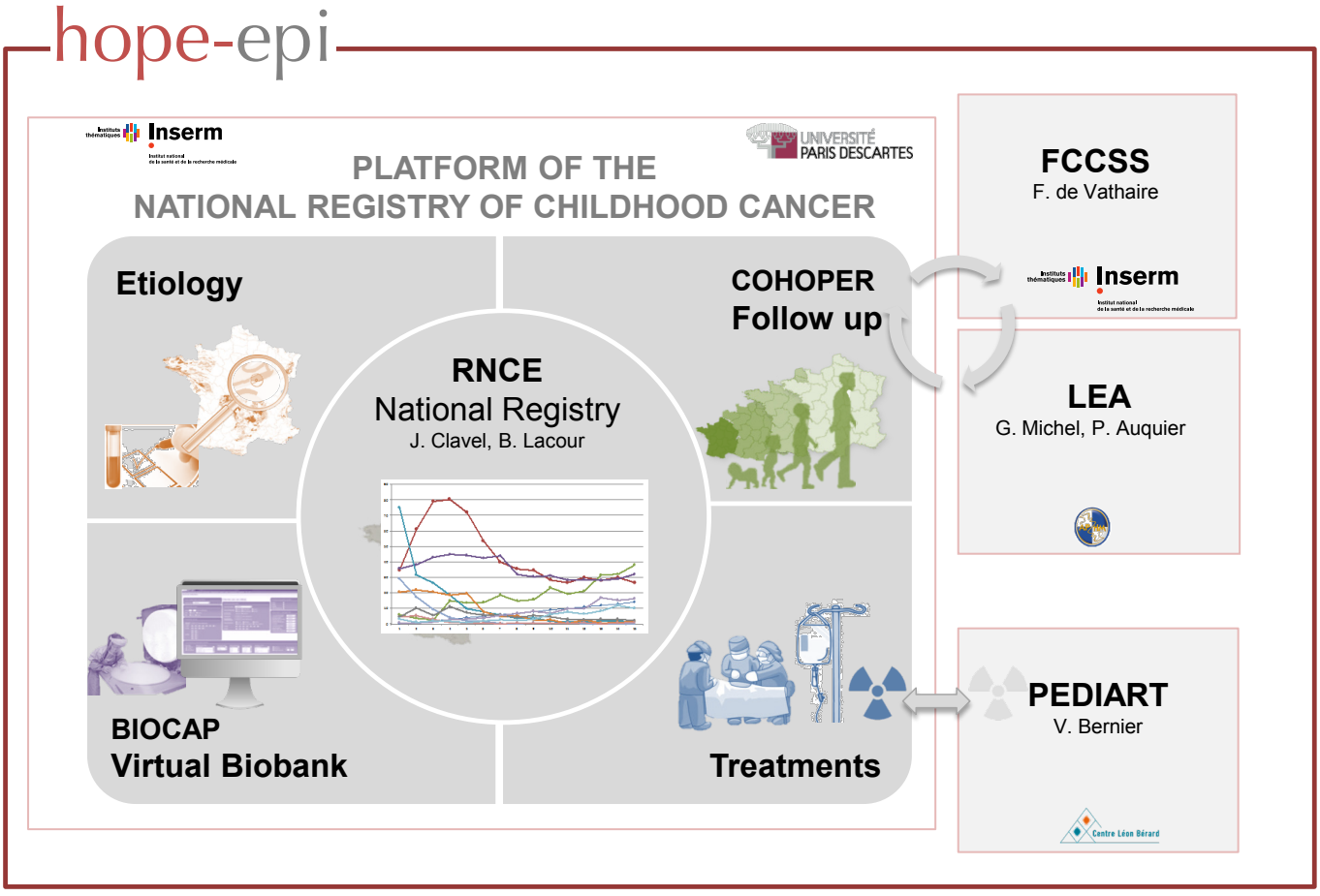
hope-epi



Dr. Jacqueline CLAVEL
M.D., Ph.D., Research Director at Inserm, Center of Research in Epidemiology and Statistics Sorbonne Paris Cité

jacqueline.clavel@inserm.fr

OVERVIEW



LEADERSHIP

HOPE-EPI's leadership team is set up with J. CLAVEL, F. de VATHAIRE, P. AUQUIER, and the representative of the National Network of Pediatric Oncologists (SFCE)

Coordination of the Platform of the national registry since 2000

J. CLAVEL, M.D., Ph.D., Research Director Inserm, Paris-Descartes University

- Head of the team Epidemiology of child and adolescent cancers, UMRS 1153, Inserm
- Creator and Head of the National Registry of Childhood Hematopoietic malignancies
- Creation and direction of the program of research on environmental and genetic risk factors of childhood cancer
- More than 70 articles on childhood cancer in international journals over the last 10 year

B. LACOUR, M.D., Ph.D., Research Director Inserm, Paris-Descartes University

- Member of the National Registry of Childhood Solid Tumors direction group
- 20 articles on childhood cancer in international journals over the last 10 years

Coordination of the FCCSS cohort of solid Tumors 1946-1999

F. de VATHAIRE, Ph.D., Research Director Inserm, Paris-Sud University

- Head of the Radiocarcinogenesis and IIatrogenic effects of Treatments team, UMRS 1018
- Creation a radiotherapy dosimetry team which has set up several programs for the evaluation of the radiation doses received by various organs
- Extensive experience in cohorts in national and international contexts
- Coordination of two European projects addressing constitution of international cohorts
- 30 articles on the fate of childhood cancers survivors over the last 10 years

Co-coordination of LEA cohort of Childhood Hematopoietic Malignancies since 1980

G. MICHEL, Pr. in Pediatrics, Timone (Marseille) Head of the Pediatric Hematology and Oncology Department

- Coordination of the inter-regional organization for recourse in pediatric oncology
- Chairs the SFCE Hematopoietic Stem Cell Transplant committee

P. AUQUIER, M.D., Ph.D., Pr. in Epidemiology , Healthcare Economics and Prevention, Marseille North University Hospitals

- Head of the Public Health and medical information department,
- Co-director of the emergent Research Institute of Public Health-Inserm-Public Health Branch, Quality of Life and Chronic Diseases team
- Coordination of over 40 projects on quality of life (100 referenced articles on the same topic)

SCIENTIFIC NETWORK & MANAGEMENT

Collaboration network with European or International cohorts:

> **French network of pediatric oncology SFCE** (the national network of pediatric oncologists): HOPE-EPI is being developed under the auspices of the SFCE in the work of the childhood cancer epidemiology

> Research network with **ENCCA** (European Network for Cancer Research in Children and Adolescents), a project of observational clinical research based on registries founded by the European Commission through the 7th Framework Program

> Collaboration with **European registries ACCIS** (Automated Childhood Cancer Information System), **ENCR** (European Network of Cancer Registries), **IACR** (International Association of Cancer Registries), **EuroCare** (Childhood Cancer Survival in Europe, a European survival data bank)

> **Research network with International studies on risk factors** (CLIC Childhood Leukemia International Consortium, I4C International Childhood Cancer Cohort Consortium)

Through its Scientific Committee, HOPE-EPI implicates experts in:

> **Pediatric oncology:** Jean Michon, President of SFCE (Scientific Committee President) and Dominique Valteau-Couanet, President of SFCE scientific board

> **Epidemiology of childhood cancer:** Jacqueline Clavel (HOPE-EPI coordinator - COHOPER and national registry) and Brigitte Lacour (COHOPER and national registry)

> **Epidemiology of radiation:** Florent de Vathaire (FCCSS)

> **Quality of life, epidemiology and public health:** Pascal Auquier (LEA)

> **Pediatric hemato-oncology:** Gérard Michel (LEA)

> **Radiotherapy:** Valérie Bernier (PEDIART)

> **Representative of Pancare** (a FP7 European project studying the impact of treatment regimes on the long-term health of childhood cancer survivors), of the European Network for Cancer Research in Children and Adolescents (ENCCA), associations of parents and CNAM (French national health insurance)

HOPE-EPI RESEARCH COLLABORATION OPPORTUNITIES

Phase IV Product approval Phase III Phase II Phase I Pre-clinical Proof of concept

Translational research

> **Identification of environmental risk factors** (exposures of the residence to radon, high-voltage power lines, road traffic, nuclear site, household waste incinerators, and other industrial sites)

> **Identification of genetic risk factors:** (Genetic polymorphisms, gene-environment interactions)

> **Contribution to basic research projects** by the **BIOCAP** virtual biobank

Clinical development

> **Observational clinical research**

> **Access to care and social inequalities:** identification of potential limitations in access to care after the initial diagnosis or during relapses, the differences in management and their social and territorial determinants

Outcomes research

> **Pharmaco-epidemiological studies:** drug safety, "real-world" use, effectiveness, practices patterns, acceptance, risk/benefit, risk management

> **Long-term effects, sequels:** data on the risk of second cancer and long-term effects (e.g. heart diseases) post-chemotherapy and radiotherapy

> **Quality of life studies:** state of health, psycho-behavioral and cognitive development, quality of life, management and access to care

BIBLIOGRAPHY

Translational research

> Sermage-Faure C, *et al.,* **Childhood leukaemia close to high-voltage power lines - the geocap study,** 2002-2007. *Br J Cancer* 2013; 108(9):1899-906

> Amigou A, *et al.,* **Folic acid supplementation, MTHFR and MTRR polymorphisms, and the risk of childhood leukemia: The ESCALE study (SFCE).** *Cancer Causes Control* 2012; 23(8):1265-77

> Orsi L, *et al.,* **Genetic polymorphisms and childhood acute lymphoblastic leukemia: GWAS of the ESCALE study (SFCE).** *Leukemia* 2012

Translational research

> Desandes E, *et al.,* **Pathways of care for adolescent patients with cancer in France from 2006 to 2007.** *Pediatr Blood Cancer* 2011

Outcomes research

> Alloin AL, *et al.,* **Prevalence and risk factors of cataract after chemotherapy with or without central nervous system irradiation for childhood acute lymphoblastic leukaemia: An LEA study.** *Br J Haematol* 2013

> Berbis J *et al.,* **A French cohort of childhood leukemia survivors: Impact of hematopoietic stem cell transplantation on health status and quality of life.** *Biol Blood Marrow Transplant* 2013; 19(7):1065-72

> Girard P, *et al.,* **Symptomatic osteonecrosis in childhood leukemia survivors: Prevalence, risk factors and impact on quality of life in adulthood.** *Haematologica* 2013; 98(7):1089-97

> de Vathaire F *et al.,* **Radiation dose to the pancreas and risk of diabetes mellitus in childhood cancer survivors: A retrospective cohort study.** *Lancet Oncol* 2012; 13(10):1002-10

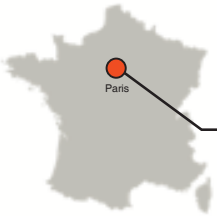
> Haddy N, *et al.,* **Relationship between the brain radiation dose for the treatment of childhood cancer and the risk of long-term cerebrovascular mortality.** *Brain* 2011; 134(Pt 5):1362-72

> Minaya P, *et al.,* **The caregiver oncology quality of life questionnaire (cargoqol): Development and validation of an instrument to measure the quality of life of the caregivers of patients with cancer.** *Eur J Cancer* 2012; 48(6):904-11

HOPE-EPI:

Focus on The Platform of the National Registry of Childhood Cancers (RNCE)

rnce
registre national
des cancers de l'enfant



Dr Jacqueline CLAVEL
M.D., Ph.D., Research Director at Inserm, Center of Research in Epidemiology and Statistics Sorbonne Paris Cité

jacqueline.clavel@inserm.fr

OVERVIEW

AT A GLANCE

> **All the cases of childhood cancers <18 years**
> **National registry of childhood cancers:** diagnosis, treatments, response to treatments
> **COHOPER cohort:** follow-up of cases since 2000
> **BIOCAP** virtual biobank since 2011
> Coordinated by **Jacqueline Clavel**
> Paris Descartes University sponsorship
> Funded by ANR and INCa
> Key words : **cancer registry, childhood,** risk factors, access to healthcare, **cancer survivor,** long term follow-up, quality of life

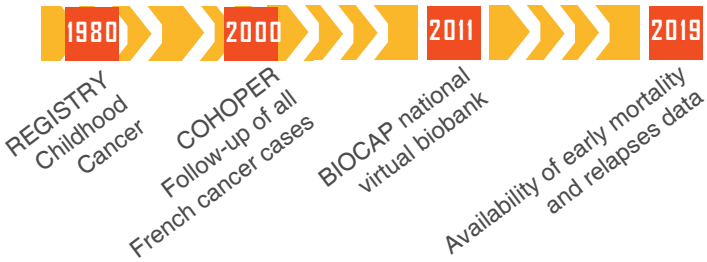
KEY FACTS & FIGURES

> National registry: **2,200 new cases per year**
> Cohort of survivors **COHOPER**:
>> **Inclusions and follow-up on-going in 40 centers**
>> **Retrospective and prospective data collection**
>> **35,000 cases** (all cases 2000-2019)
>> Medico administrative database linkage with SNIIRAM considered
> **Nationwide virtual biobanking BIOCAP:** tumoral and constitutional specimens **stored in hospital biobanks**

RNCE platform aims:

To make available high quality transdisciplinary data (diagnosis, biology, treatments and follow-up) for research in pediatric oncology

To **increase knowledge on environmental and genetic risk factors,** on iatrogenic effects of treatments and on short-, intermediate- and long-term state of **health of people having suffered from childhood cancer**



Positioning

> Collaboration with **European Network for Cancer** Research in children and adolescents as a work package leader/member dedicated to **the contribution of registries to clinical research in pediatric oncology**

> Similar cohorts aiming to make available a the long-term follow-up of childhood cancer cases have just started in Europe

PROJECT DESCRIPTION

SCIENTIFIC OBJECTIVES

Research on the risk factors for childhood cancer, the disparities in **cancer management** and their determinants, the iatrogenic effects of treatments, **the short-intermediate and long term state of health of childhood cancer survivors** and the determinants of their **quality of life**

In consequence, ability to contribute to:

> **Primary prevention:** prevention of exposure to environmental risk factors, genetic counseling and screening for genetic risk factors

> **Elucidation and prevention of potential inequalities** in healthcare access related to social or territorial characteristics

> **Reduction of the diseases induced by treatment:** screening for sequelae, and contribution to personalized follow-up of iatrogenic risks

> **Improvement in the management of cancer survivors**

> **Improvement in the quality of life** of cancer survivors

> **Improvement in treatments and post-marketing surveillance:** risk/benefit ratio of future treatments through enhanced anticipation of their long-term effects

INNOVATIVE SCIENTIFIC FEATURES

Data collected thanks to the **development and the enrichment of the high-performance tools held on a single platform**

Provides registry data, virtual biological collection and cohort data subject to **high quality requirements**

Promotes the exchange of knowledge between epidemiology, fundamental, biology, genetics, clinical research and human and social sciences

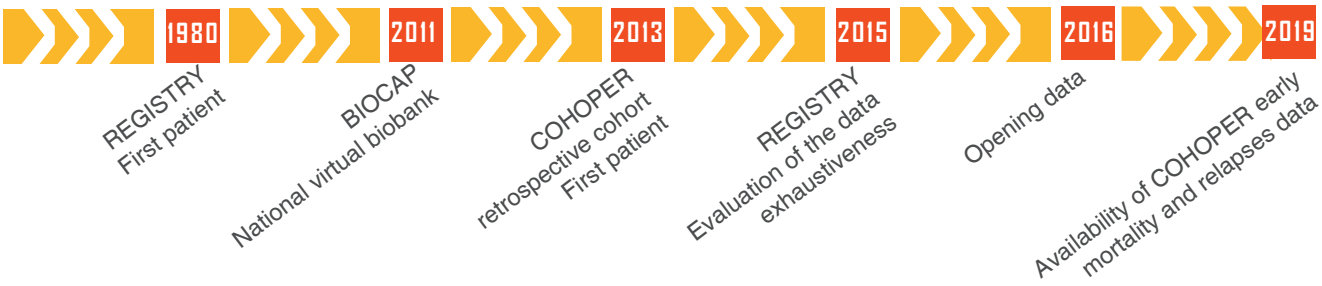
METHODOLOGY QUALITY

Control of completeness based on the registry, with multiple independent sources (health insurance, hospital files, biology and pathology departments, clinical trials...), SOPs for data collection and data management

International rules of cancer registration and coding, INCa rules of registration of biobanking items

Labelisation by the Registries Evaluation Committee (last 5-year renewal in 2014)

DESIGN, METHODOLOGY & TIMELINE



Recruitment objectives: 35,000 cancer cases expected in 2020

Sites: 40 centers widespread on the French territory
70 laboratories (BRCs and pathology labs)

Inclusion criteria: <18 years
All cancers in compliance with national and international criteria
France and overseas departments (Guyane, Réunion, Martinique, Guadeloupe)

INCLUSION COLLECTION

Database: socio-demographic, geolocation, diagnosis, treatment, responses to treatments, health care system

Virtual biobank: information related to tissues, cells, blood, serum, plasma, DNA and RNA, collected from patients and stored in the hospital biobanks

FOLLOW-UP:

COHOPER collects follow-up data from 3 years after the diagnosis.

BIOCAP is supplied once a year with all informations regarding the newly collected biospecimens

Database: events (relapses, second cancers, deaths), health (medical records, questionnaires and medico-administrative databases)

Virtual biobank: information related to tissues, cells, blood, serum, plasma, DNA, RNA collected from patients notably in case of relapses or second cancers, and stored in the hospital biobanks

DATABASE CONTENTS

TYPE	VARIABLE DESCRIPTION REGISTRY and COHOPER	VARIABLE DESCRIPTION BIOCAP (virtual biobank)
PATIENT	Patient identification number, Name, Forename, Date of birth, Sex, Vital status, Medical centers…	Patient identification number, Name, Forename, Date of birth, Sex, Vital status, + Consent status
BIOPSY		Hospital name, Hospital ID (National files of Social and Health Institutions), Hospital department, Biopsy ID, Biopsy date, Biopsy time, Date of biopsy receipt, Biopsy collection mode, Biopsy type
DIAGNOSIS	Date of diagnosis, Histology, Cytology, Cytogenetics, Immunophenotype, Molecular biology, Topography, Staging (/classification) Coding (ICD-O and ICCC) Healthcare pathway,	Disease ontology, Classification of International diseases (CIM) 0/Systematized NOmenclature of MEDicine (SNOMED) Organ category , CIM0/SNOMED Histopathological grading, Association of computerization development in Cytology and Anatomo-pathology (ADICAP) edition, ADICAP Organ category, ADICAP , Tumoral grade Histopathological grading, Tumoral stage, pTNM edition, pT, pN, pM, Disease Stage
TREATMENT	Risk classification, Date treatment started, Protocol arm, Chemotherapy (date, drugs, cumulative doses), Surgery (date, type and site), Radiotherapy (date, type, site and dose), Stem cell transplantation (date, type and source)	
RESPONSE TREATMENT	Resection adequacy, Necrosis extent/early MRD bone marrow, Date treatment completed	
FOLLOW-UP	Date of last contact, Date, Site of relapse, Date of blast transformation, Date, cause of death	
SAMPLE		Sample collection ID, Tumoral , Conservation mode, Biospecimen type, Processing method, Delay of freezing, Freeze date, Freeze time, Control tissue, Control precision, Number of aliquots, Tumor cell percentage, cDNA, DNA extraction protocol, cRNA, RNA extraction protocol, Derived proteins, Repository name, Repository ID (National files of Social and Health Institutions)
RELATED BIOLOGICAL MATERIAL		Serum, Plasma, Whole blood, Other liquid, Other liquid / type, Constitutionnal DNA, Repository name, Repository ID (National files of Social and Health Institutions)
ADDITIONAL	Clinical trials, PMSI, Death	Standard diagnostic pathology report available, Associated clinical data, Therapeutic protocol inclusion, Research protocol inclusion, Sample delivery, Number of required tubes, Delivery date, Destination assignment, Delivery purpose

BIOCAP – THE PLATFORM VIRTUAL BIOBANK

Originality

> **BIOCAP is a virtual biobank,** leaned on the National Registry of Childhood Cancers

> BIOCAP allows to get access **to the overall information regarding each biospecimens** collected from patients during their current cares and **hosted into a hospital biobank** of a BRCs or an anapath labs participating to the project

> **Strengths:** permanent, **sustainable collection, exhaustiveness** (all childhood cancers in France)

> **Quality:** clinical annotations and control procedures are set up

Scientific objective

> Facilitate project on rare tumors spread over the national territory (identification, documentation of the cases)

> Project on prognosis for different types of tumors with a common transcript

> Oncogenesis molecular mechanisms

> Prognostic value of molecular markers

> Environmental (road traffic, background radiation...) and genetic risk factors of childhood cancers

Samples

> Nature of the biospecimens : tissue, biopsies, cells, blood, serum, plasma, DNA and RNA

> First sampling-data in BIOCAP:

>> From January 1st 2009 (Paris area)

>> From January 1st 2011 (other regions)

> ≈ **3,5 samples per patient**

> Data on biospecimens stored are already collected for **2,600 patients (10,000 specimens in total)**

> **2,200 patients with specimens expected each year**

> BIOCAP **update: once a year,** with the data associated to the newly collected biospecimens

Associated resources

> The resources to exploit the biospecimens depend on the human resources and the know-how of each center that hosted the local biobank

BIOCAP - TECHNICAL MODALITIES & SPECIFICATIONS

BIOBANK SAMPLE ACCESS MODALITIES

- **BIOCAP Scientific responsible:** Dr. Jacqueline Clavel
- BIOCAP opening to the research community from June 2016
- To access to BIOCAP, industrials as academic teams are invited to apply to the scientific call of the Platform planned in June 2016 for the first and every 6 months thereafter. BIOCAP access modalities are specified in the charter written in the context of HOPE-EPI and available

BIOLOGICAL SAMPLE ANALYSES

- Each local biobank center is responsible for its biospecimens, follows specific procedures (SOPs) for their treatment process, ensuring their safe transport and uses its proper identification system
- Access to biospecimens for investigators, after successful access to BIOCAP database, requires specific agreements with the local biobank centers, with the support of the platform coordination

COST

- The financial estimation of the biospecimens is still under discussion, with reference to the BIOBANQUE program

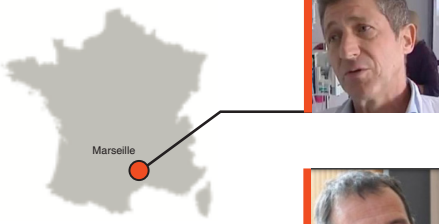
BIOCAP - BIOLOGICAL SPECIMENS IN THE VIRTUAL BIOBANK

ICCC diagnosis group		Patient with at least 1 specimen			Specimens by patient (mean)
		≥ 1 tumoral	≥ 1 non-tumoral	Any specimen	
1.	Leukemias	1,193	241	1,440	4,0
2.	Lymphoma	229	65	302	3,7
3.	Brain tumors	695	10	720	6,0
4.	Neuroblastomas	237	31	261	4,6
5.	Retinoblastomas	195	152	199	3,5
6.	Renal tumors	349	268	367	4,5
7.	Hepatic tumors	48	38	50	6,6
8.	Malignant bone tumors	148	23	169	4,6
9.	Soft tissue tumors	298	43	351	4,1
10.	Germ cell tumors, gonads	100	10	117	3,9
11.	Carcinomas	82	20	90	3,5
	TOTAL	3,574	901	4,066	4,4

HOPE-EPI:

Focus on the LEA cohort (Childhood and Adolescent Leukemia)

L.E.A.
Leucémies de l'Enfant et de l'Adolescent



Prof. Gérard MICHEL
Head of pediatric onco-hematology department – La Timone Hospital – Marseille

Prof. Pascal AUQUIER
Head of EA 3279, Public Health Department – Aix Marseille University

OVERVIEW

AT A GLANCE

> **Onco-hematology and quality of life**
> **Malignant haematological diseases, particularly Acute Leukaemia (AL)**
> Children treated for AL since January 1980, surviving at 24 months for myeloblastic AL and lymphoblastic AL grafted in first complete remission
> Coordinated by **Prof. P. Auquier, Prof. G. Michel**
> AP-HM (Assistance Publique-Hôpitaux de Marseille, Marseille University Hospitals)
> Funded by ANR
> **Key words: childhood leukemia,** quality of life, late effects, late outcomes

KEY FACTS & FIGURES

> Inclusion on going
> **More than 3,000** expected patients
> **More than 3,400 included patients** by now
> Follow-up is planned until included patients are 50 years-old
> **National multicentric cohort** (actually 16 paediatric onco-haematology units are involved in the project)
> No biobank until now

LEA aims at **studying the determinants** (medical, socioeconomic, behavioral and environmental) **of a medium and long-term outcomes of patients treated for AL.**

Positioning

> LEA is involved in a PanCare project
> Coordinators are implicated in others epidemiologic studies: MuSIQoL Cohort (Multiple Sclerosis International Quality Of Life Cohort), SQoL (Schizophrenia Quality Of Life questionnaire), PLH Study (PolyHandicap Study), UCSA (Un Chez Soi d'Abord - French Housing First Program)

LEA - DATABASE CONTENT

Clinical, medical, biological, socioeconomic, demographic, social insertion and environmental data

Quality of life of the patients and their parents (if patient under 18)

Imagery data

> **Thyroid Echography**
>> Global result normal/abnormal, thyroïdian nodule or not, date of discovery, cytologic analysis yes or no -> if yes result of the cytological analysis and type of therapeutic care
>> Available for 839 patients

> **Cardiac echography**
>> Global result normal /abnormal, date of discovery if abnormal, shortenning fraction and left ventricular ejection fraction, medical treatment or not and which one, cardiac graft or not and date
>> Available for 3,363 patients

> **Bone densitometry**
>> Global result normal /abnormal, date of discovery if abnormal, BM.D., T score, Z score, medical treatment or not and which one;
>> Available for 2,179 patients

> **Hepatic MRI**
>> Hepatic iron concentration
>> Available for 45 patients