Lysa
THE LYMPHOMA STUDY ASSOCIATION

Lysarc
THE LYMPHOMA ACADEMIC RESEARCH ORGANISATION

EARLY,
the LYSA-LYSARC Lymphoma Early Phase Clinical Research Dedicated Platform

An Extensive Experience in Designing and Conducting **Lymphoma Early Phase** Clinical Studies

First-in-man, First-in-lymphoma, First combo studies

www.lysa-lymphoma.org
www.lysarc.org

40 Lymphoma Phase I/IIa Trials Successfully Designed and Performed so far

First-in-man, First-in-lymphoma and First combo studies

Integrated Expertise for Better Outcomes

The EARLY platform benefits from the synergistic combination of:

the outstanding **scientific and therapeutic expertise** of internationally renowned **lymphoma specialists** from the **LYSA** cooperative group

&

the capacity and operational means of **LYSARC**, the **largest European academic organization** devoted to **clinical research operations** in the lymphoma field.

LYSARC, the operational arm of LYSA, has been created to implement and run all the projects that have been previously assessed by LYSA's Scientific Board and approved by its Board of Directors. This systematic selection process guarantees the scientific interest for the research program and efficient projects start-up.

Access to Extensive Scientific and Therapeutic Expertise

Our LYSA scientific leaders have a broad experience of scientific boards and are able, through their contacts, to bring together and work effectively with international networks of thought leaders.

- **LYSA is a network of 500+ lymphoma experts including** early phase clinical, translational and biological research investigators and **international KOL**:
  - more than **30 years of advancing lymphoma research**,
  - **120** clinical centers across **4** countries (France, Belgium, Portugal, Israel)

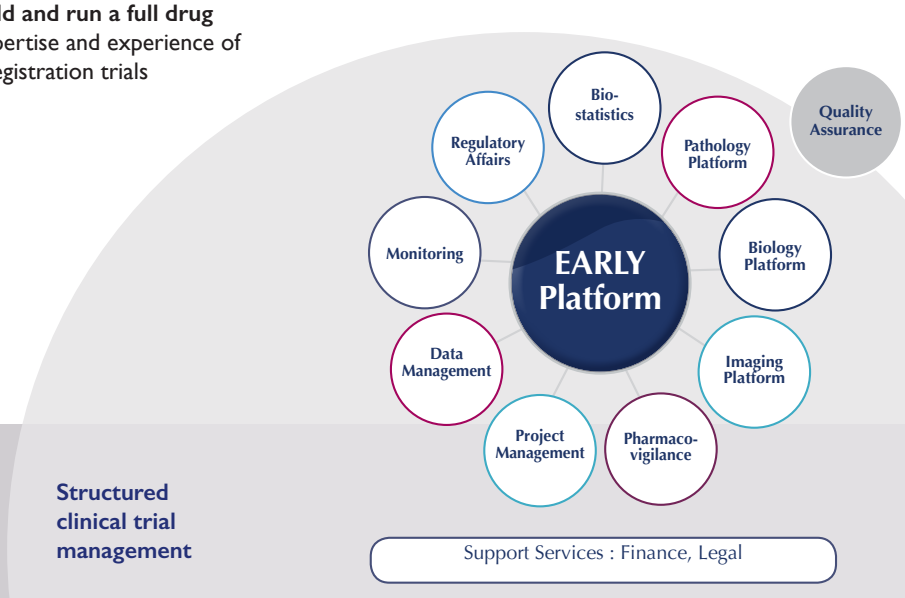
- **Unique, high level, scientific production**: **250+** publications in leading medical journals, with several landmark papers with **1000+** citations

- **The demonstrated capacity to build and run a full drug development** through additional expertise and experience of Phase II/III lymphoma international registration trials

Full Scope of Clinical Research Operations and Skills to Conduct Early Lymphoma Studies

EARLY phase clinical research operations are conducted in house by **LYSARC**, usually sponsor of the trials:

- **Devoted and trained staff**, all lymphoma specialists with a track record in early phase clinical research
- **Fast implementation of clinical trials**: usually less than 6 months between the collaboration agreement and first patient in (accelerated by the routine use of electronic signature)
- **High quality standards**: regular industry audits, low incidence of non-compliance, corrective and preventive actions plan respected
- **High ethical and safety standards**: compliance with patient safety rules and requirements of international regulatory guidelines
- **Safety committee** (standard operating procedure)



Faster Patient Enrollment

Network of selected LYSA sites (the EARLY network), accredited "early-phase clinical research centers (CLIP²)" by the French NCI

Clinical trial centers with a large panel of skills: devoted pharmacists, practitioners, CRAs, clinical trial nurses, 24/24 pharmacokinetics, imaging transfer software…

Free Download on iOS or Android Store

The ClinTrial Refer LYSA App: a tool to accelerate patient enrollment

ClinTrial Refer LYSA offers an interface between physician and patient, providing real-time information for each on-going LYSA trial. It allows physicians to actively participate in patient enrollment without the need to know the details of the clinical studies. This application, available on iOS or Android store, is completely anonymous and does not store confidential data.

Accelerating the Translation of Promising Lymphoma Drug Candidates to Treatments for the Patient

LYSA and LYSARC take part of a unique research consortium, the **CALYM Carnot Institute**. Its mission is to encourage and reinforce lymphoma translational research through the collaboration of basic researchers and clinicians. CALYM is composed of 13 basic research groups, plus LYSA and LYSARC, therefore bridging the bench to the bedside. This integrated research approach is a major asset to identify and advance new lymphoma treatments.

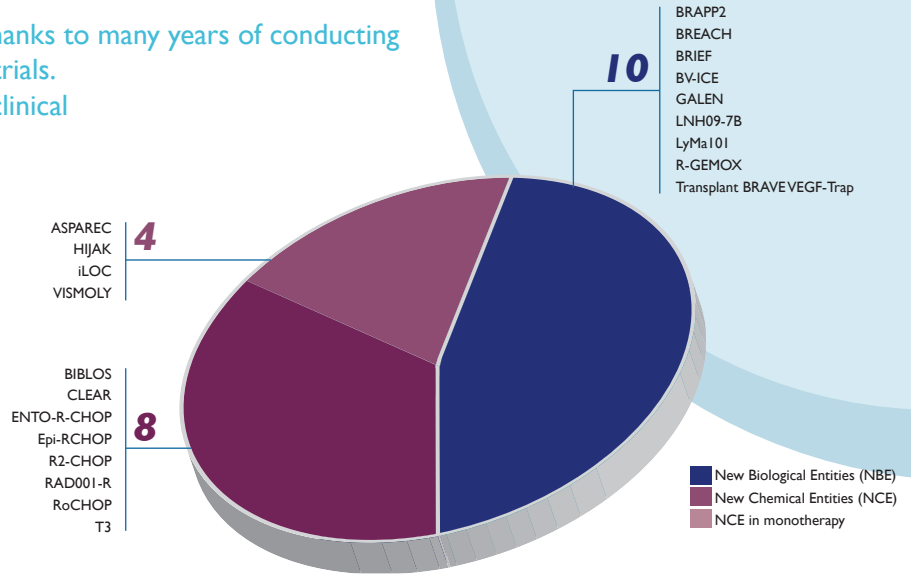
Our EARLY platform provides **tailor-made solutions**, including the **appropriate use of biomarkers** to stratify patients and **customized pharmacokinetics** and **pharmacodynamics studies**.

INSTITUT CARNOT CALYM

www.calym.org

Examples of EARLY Phase LYSA-LYSARC Trials

We have an extensive experience in early trials thanks to many years of conducting first-in-class therapies and first-in-human clinical trials. We have the capacity to perform preclinical and clinical evaluation of novel combinations of cancer treatments. Our current portfolio contains a diverse range of about **15** agents including naked or conjugated antibodies or targeted small molecules.



Categories of drugs tested in Phase I/IIa trials

First-in-Human First-in-Class Studies

ASPAREC

NCT01551524
(ClinicalTrials.gov identifier)

Phase I first-in-man dose-escalation study

Drug: mPEG-r-crisantaspase

Condition: relapsed or refractory hematological malignancies

Number of patients: 14 adults

Period: 2012 -2014

Novel Drug or Combination

VISMOLY

NCT01944943

Phase II trial

Drug: vismodegib

Condition: relapsed or refractory lymphoma and chronic lymphocytic leukemia

Number of patients: 31 adults

Period: 2013 - 2014

Publication: R. Houot *et al.* "Inhibition of Hedgehog signaling for the treatment of lymphoma and CLL: a phase II study from the LYSA".
Ann Oncol (2016) 27 (7): 1349-1350.

T3

NCT01389427

Phase Ib multicenter dose escalation study to evaluate safety, feasibility and efficacy

Drugs: Temsirolimus + CHOP - Rituximab / Temsirolimus + Fludarabine Cyclophosphamide - Rituximab / Temsirolimus + DHA - Rituximab

Condition: relapsed or refractory mantle cell lymphoma

Number of patients: 41 adults

Period: 2011 - 2015

Ro-CHOP

NCT01280526

Phase I escalation phase and expansion phase

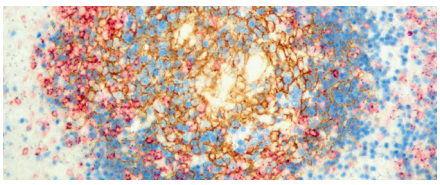
Drugs: combination of romidepsin with CHOP

Condition: relapsed or refractory peripheral T-cell lymphoma.

Number of patients: 37 adults

Period: 2011- 2013
Results are being confirmed in the Ro-CHOP study, a registration trial currently sponsored and conducted by LYSARC in 420 patients in 9 countries.

Publication: J. Dupuis et al. "*Combination of romidepsin with cyclophosphamide, doxorubicin, vincristine, and prednisone in previously untreated patients with peripheral T-cell lymphoma: a non-randomised, phase 1b/2 study.*" Lancet Haematol. (2015) Apr;2(4):e160-5



Imaging and Translational Research

GALEN

NCT01582776

Phase Ib to establish the maximal tolerated dose and Phase II expansion cohort

Drugs: combination of lenalidomide and obinutuzumab

Condition:

- Phase I: relapsed/refractory follicular lymphoma

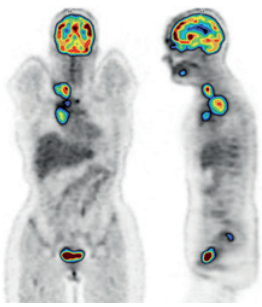
- Phase II: 3 separate populations of patients: relapsed/refractory follicular lymphoma, relapsed or refractory aggressive lymphoma (diffuse large B-cell lymphoma and mantle cell lymphoma and upfront follicular lymphoma)

Number of patients: 300 adults (target)

Period: 2014-2017 (in progress)

Imaging: some centers have been selected to perform **immuno-PET**, a new molecular innovative imaging approach

Ancillary biological studies: including analyses of the genetic susceptibility to toxicity and efficacy of lenalidomide, tumor gene expression profiles, and lymphocyte subpopulation alterations under treatment and their association with treatment response. Results from these analyses can potentially be used to improve comprehension of the disease, better define the prognostic criteria in lymphoma, and identify new factors that influence treatments results and outcome.



Why Partner With Us?

A Unique Expertise and Experience in Lymphoma

• **Long standing and extensive clinical research partnering** with the pharmaceutical and biotechnological sectors: more than 40 industry partners worldwide.

• **LYSARC and LYSA are together accredited by the French National Cancer Institute** "French Cooperative Intergroup of International Dimension in the Field of Cancer".

• **Access to an unparalleled network** of world renowned KOLs in the field of hematology.

A Professional Approach to Clinical Research

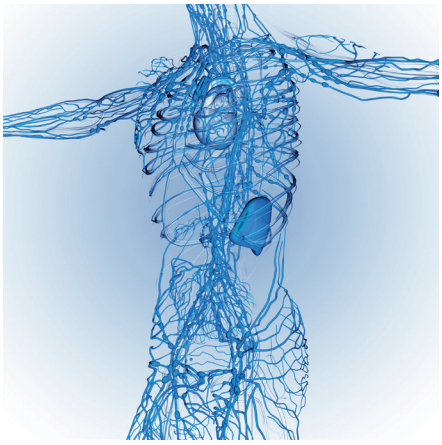
• **LYSA and LYSARC are ISO 9001:2008** certified for the management and follow-up of partnering research with industry. They pay specific attention to time, quality and budget objectives.

• **LYSARC conducts its research in compliance with international quality standards**: GCP, GLP, ICH. It is regularly audited by its partners and also audits study sites, its own services and its vendors and validates the tools it uses for clinical research activities.

• **All protocols and informed consent forms of trials performed by LYSARC** undergo review by cancer patient committees in the framework of a collaboration with the French League Against Cancer.

Research Tax Credit

LYSARC is accredited for the French research tax credit scheme. Eligible entities (must be subject to corporate tax in France) having collaborative R&D projects with LYSARC can save up to 30 % of audited R&D expenses.



Lysa
THE LYMPHOMA STUDY ASSOCIATION

Lysarc
THE LYMPHOMA ACADEMIC RESEARCH ORGANISATION

CONTACT

LYSARC
Centre Hospitalier Lyon-Sud
Secteur Sainte Eugénie
Pavillon 6D
69495 Pierre-Bénite Cedex FRANCE

www.lysarc.org
partnering@lysarc.org

www.lysa-lymphoma.org
www.lysarc.org