Lysarc

THE LYMPHOMA ACADEMIC RESEARCH ORGANISATION

LYSARC, ACADEMIC PARTNER OF LYMPHOMA CLINICAL RESEARCH

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www.lysarc.org

THE LARGEST EUROPEAN ACADEMIC ORGANIZATION DEVOTED TO CLINICAL RESEARCH OPERATIONS IN THE LYMPHOMA FIELD

Lymphoma is the 6th most common cancer worldwide and the 1st blood cancer. **LYSARC, the Lymphoma Academic Research Organisation,** is a scientifically independent, non-profit organization focused on lymphoma clinical research.

It gathers around 140 engaged and qualified staff (MDs, PharmDs, PhDs, Engs, MBAs…) having for lot of them, beyond their knowledge of the public research sector, a work experience in pharma, biotech and/or service companies.

A STRONG INSERTION IN THE ACADEMIC ENVIRONMENT AND RESEARCH-DRIVEN TRIALS

LYSARC, created in 2000, is **the operational organization associated to the research activities of LYSA, the Lymphoma Study Association,** a cooperative group, international leader of lymphoma research.
This internationally renowned network of lymphoma experts closely collaborates with LYSARC at all stages of its studies.

Any project run by LYSARC must receive prior approval from LYSA's Board of Directors, following its assessment by LYSA's Scientific Board. Such selection process guarantees the scientific interest of those research programs performed by LYSA-LYSARC.

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

A LONG-STANDING EXPERIENCE OF INTERNATIONAL PARTNERSHIPS WITH ACADEMIA AND INDUSTRY

LYSARC clinical trials are mostly **multinational** and are conducted in collaboration with other cooperative groups or learning societies, hospitals, universities, local CROs, and healthcare companies throughout **4 continents.**

FROM FIRST-IN-MAN TO REGISTRATION TRIALS AND BEYOND…

LYSARC conducts clinical trials in the field of lymphoma, these studies having a sole academic purpose or also contributing to industrial developments:

- **Phase I trials, including first-in-man**
- **Phase IIa and IIb trials**
- **Phase III trials, including international pivotal studies aimed at registration**
- **Phase IV trials on marketed drugs, for safety surveillance**

NON-INTERVENTIONAL AND ANCILLARY STUDIES

LYSARC conducts non-interventional studies and supports numerous biological, histopathological, imaging, biostatistical and bioinformatics ancillary studies such as:

- **Specific long term, post-protocol, clinical follow-up studies (survival, late toxicities)**
- **Registers on public health topics**
- **Studies of clinical-biological correlations**
- **Meta-analyses**
- **Exploration of genetic data of sub-populations**

A FACILITATED ENROLMENT OF PATIENTS

Studies performed by LYSARC benefit from the large patient recruitment potential offered by the network of 120 LYSA centers in France, Belgium, Portugal and Israel and through its numerous collaborations with foreign academic groups, partners of LYSA (in Europe, Asia, North America and Australia), for studies requiring a greater enrolment or dealing with rare histological subtypes of lymphoma.

LYSARC has developed the smartphone application **ClinTrial Refer LYSA** to help study centers to increase lymphoma patient recruitment in LYSA protocols.

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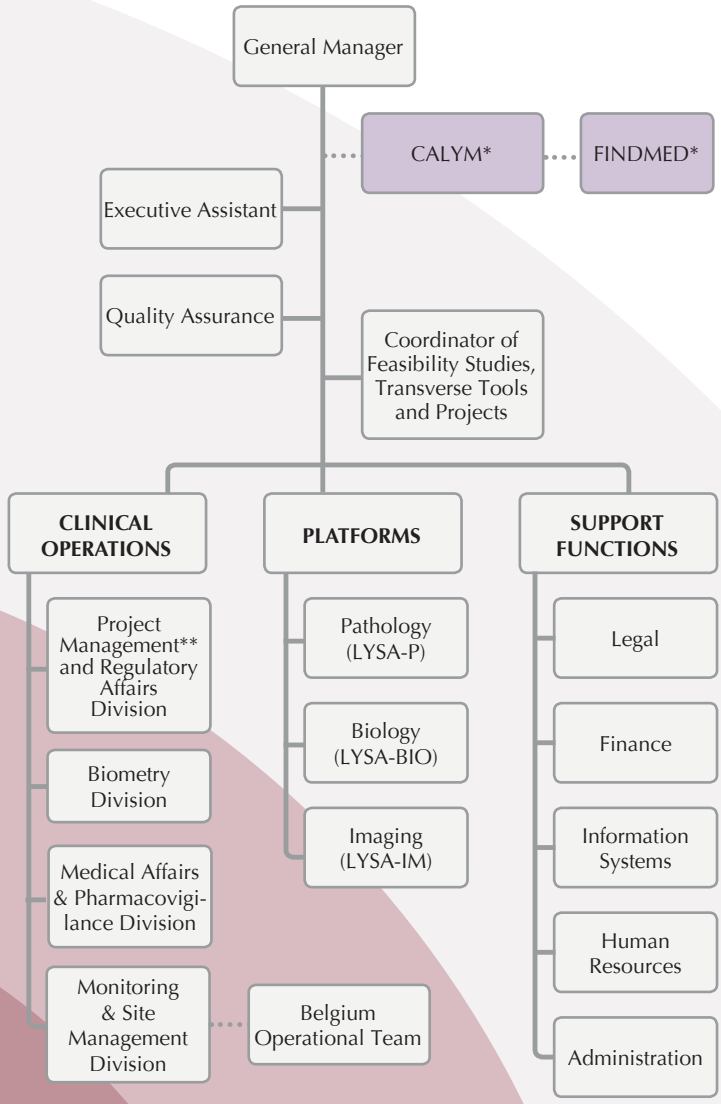
AN EFFICIENT CLINICAL RESEARCH ORGANIZATION

LYSARC is a **specialty, fully integrated clinical research organization**, usually sponsor of those trials it conducts. All clinical research functions are represented at LYSARC.: Professional support functions - finance and legal in particular - complete the skills of LYSARC which are very reactive, from the elaboration and signature of the first agreements (accelerated by the routine use of electronic signature) to the production of the final study report.

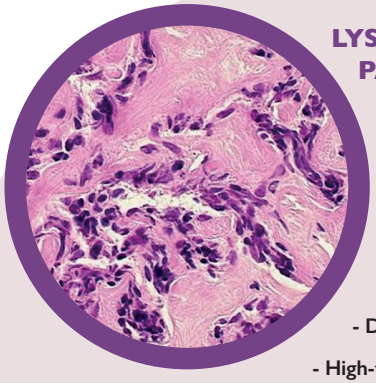


** Partnership research structures funded by the French National Research Agency for research under the "Investment for the Future" program*

*** Early phase clinical trials platform EARLY*

LYSA-LYSARC PLATFORMS

LYSARC brings its operational means and LYSA its scientific experts to several key platforms for the study of lymphoma therapies and biomarkers:



LYSA-P PATHOLOGY PLATFORM

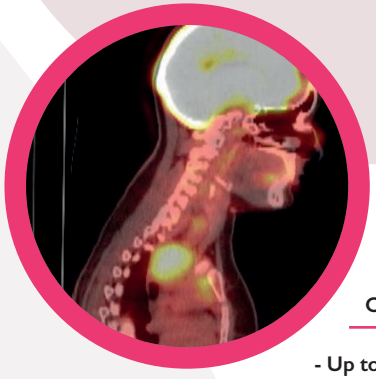
CENTRALIZED REVIEW OF PATIENT TUMOR SAMPLES

- More than 16,000 cases reviewed to date
- Dedicated laboratory
- High-tech equipment for digitalization, analysis and sharing of microscopic slides
- Automated high throughput analysis on large patient cohorts
- Large collection of annotated tumors: slides, paraffin blocks, frozen tissue, TMAs, DNA/RNA

EARLY EARLY PHASE CLINICAL TRIALS PLATFORM

PHASES I/IIA, FIRST-IN-MAN, FIRST-IN-LYMPHOMA OR FIRST COMBO STUDIES

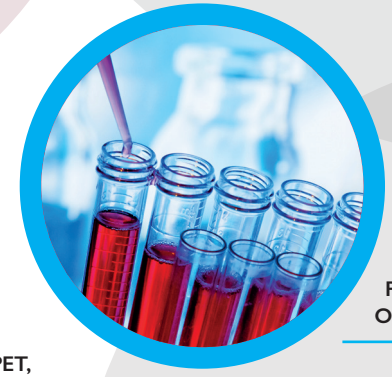
- Large experience in lymphoma early clinical development: more than 40 trials so far
- Structured and reactive clinical trial management
- Expanded access to patients through a network of selected expert LYSA sites, accredited early-phase centers ("CLIP^2" centers) by the French NCI
- Pharmacokinetics and pharmacodynamics tailored to study treatment



LYSA-IM IMAGING PLATFORM

CENTRAL REVIEW OF PATIENT IMAGES

- Up to 4,000 images reviewed per year (PET, TDM, MRI)
- Web exchange platform (Imagys® software) with a FDA approved viewer
- Real-time review (48 hours max) of images used for treatment decision-making
- Research on new evaluation parameters



LYSA-BIO BIOLOGY PLATFORM

PRE-ANALYTICAL MANAGEMENT OF BIOLOGICAL SAMPLES

- Collection, labeling, samples' management (plasma, DNA/RNA, fresh blood, live cells) in a controlled environment
- Personalized blood analyses
- Tailored immunological monitoring
- Specific genetic analyses

WHY LYSARC AS A RESEARCH PARTNER?

A unique expertise and experience in lymphoma

LYSARC puts its operational expertise and its long-standing experience of clinical research in the lymphoma field at the service of LYSA and its academic and industry (pharma, biotech, *in vitro* diagnosis, medical imaging) partners to help them answering at the shortest the unmet medical needs for this cancer.

A professional approach to clinical research

LYSARC is ISO 9001:2015 globally certified for the management and follow-up of its partnering activities. It pays specific attention to time, quality and budget objectives meeting.
Tools used by LYSARC for its activities are similar to those used by industry, with a focus on research data and material digitalization (eCRF, imaging software, digital pathology…).
All staff benefit from The Lymphoma Academy, an online training tool developed by LYSARC.

Unparalleled clinical databases and annotated biological collections

This very precious material, from more than 20,000 patients, is stored in optimal security conditions (data center, biobanks). It is the subject of scientific collaborations with academia and industry.

High quality and safety standards

LYSARC conducts its research in compliance with international quality standards: GCP, GLP, ICH. It has in-house regulatory affairs, pharmacovigilance and quality assurance departments. LYSARC is regularly audited by its partners and also audits study sites, its own services, its vendors, and validates the tools it uses for clinical research activities. All LYSARC staff receive training on quality assurance and internal standard operating procedures. All protocols and informed consent forms of trials performed by LYSARC undergo review by patients committees in the framework of a collaboration with the French Ligue 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.

SOME EXAMPLES OF CLINICAL TRIALS PROMOTED BY LYSARC AND CONDUCTED WITH LYSA AND ITS PARTNERS

SCOPE OF WORK

Project management
Legal and finance
Methodological advice
Trial design*
Study documents
Regulatory affairs
Blood and tumor banking
Pre-analytical and analytical histopathology*
Digital pathology*
Hemopathology central review*
Imaging central review*
IMP supply
IVRS/IWRS
Study monitoring
Study sites local support
Medical monitoring
Pharmacovigilance
Data management
Biostatistics
Medical writing (CSR)
Quality assurance
Training

** In collaboration with LYSA experts*

Ro-CHOP: a clinical program in the long run

In partnership with a leading biopharmaceutical company in onco-hematology, the addition of romidepsin to CHOP chemotherapy in first line for peripheral T-cell lymphoma patients has been the subject of a complete clinical evaluation by LYSA-LYSARC, from phase I to an international phase III registration trial.

PRIMA: a phase III clinical trial with many outputs

PRIMA phase III clinical trial, conducted in 25 countries in collaboration with a big pharmaceutical group, led to the registration of rituximab as a two-year maintenance therapy for follicular lymphoma patients responding to first-line immunochemotherapy. PRIMA also generated many ancillary biological studies leading to a significant number of results and publications (such as the new prognostic index, PRIMA PI. E. Bachy *et al.*, Blood 2018, 132:49-58). Long-term follow-up of this study showed that efficacy of rituximab maintenance persists after ten years of follow-up in follicular lymphoma (G. Salles *et al.* Blood 2017, 130:486).

GAINED: the role of imaging

This international multicenter phase III clinical trial aims at showing an improvement of two-year event-free survival of patients with diffuse large B-cell lymphoma following a treatment associating the monoclonal antibody obinutizumab GA-101 and a polychemotherapy such as CHOP-14 or ACVBP-14. Treatment adaptation was realized according to TEP real-time central reading: 688 patients, mean reading time 1.65 day, median 0.

GALEN: a multi-partner early phase study

Phases Ib and II clinical study of obinutuzumab combined with lenalidomide for the treatment of follicular lymphoma and refractory or relapsed aggressive B-cell lymphoma (large cell and mantle cell lymphomas). LYSARC conducts this trial in collaboration with LYSA and two pharmaceutical companies.

LYSARC IS A MEMBER OF

CALYM Carnot institute
Research consortium devoted to the acceleration of innovation and its transfer in the lymphoma field.

www.calym.org

CALYM is a member of FINDMED consortium
www.findmed.fr

ELI, The European Lymphoma Institute
Association of 13 European academic groups conducting joint research, communication and education actions on lymphoma.

www.eli.eu/fr/en

Groupes Coopérateurs en Oncologie
Network of French cooperative groups sponsoring cancer clinical research.

www.gco-cancer.org

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