

Tomorrow, Better Treating Patients with Lymphoma

LYSA-LYSARC ACTIVITY REPORT 2023



TOGETHER AGAINST LYMPHOMA



experts-recherche-lymphome.org



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01 2023 Editorial: A promising dynamic



Message from the LYSA and LYSARC President, Prof. Franck Morschhauser

We are pleased to present this new activity report of the LYSA-LYSARC intergroup, which provides a positive overview of 2023 and opens up promising prospects for the coming year.

The year 2023 once again confirmed the excellent scientific dynamism of the LYSA-LYSARC.

Our scientific production was substantial and of high quality. Our presence at congresses was particularly strong, with multiple recognitions in the form of posters and oral presentations. For example, the publication of the remarkable results of the ALCANTE trial testing a CAR-T treatment in early relapsed or refractory large B-cell lymphomas not eligible for autotransplantation in Nature Medicine, the first publications of work on ctDNA presented at congresses, and the growing and notable visibility of our DESCAR-T register...

We look forward to enriching our portfolio of randomized trials in 2024 with the launch of MORNINGLYTE in the first line of follicular lymphoma, OASIS 2 and CARMAN in mantle cell lymphoma, and MARSUN in relapsed marginal zone lymphoma.

We are also one of the few academic groups to offer an open randomized trial for peripheral T-cell lymphomas in the first line, the TRANSCRIPT study, whose recruitment is taking off.

We have many other original projects in the pipeline, whether they are clinical, translational studies, or new explorations of our large real-life cohorts DESCAR-T and REALYSA by integrating new technologies or statistical methodologies.

The year 2023 also highlighted the strong partnership dynamics of our group. We are strengthening our ecosystem and laying the foundations for new research projects based on diverse and innovative partnerships. I will mention two examples: the agreement signed with the prestigious MAYO CLINIC for the joint valorization of academic data and also the signing of the BIDIFY project (Biological and Imaging Data Integration for Follicular Lymphoma Research), a large-scale research program that we will launch in 2024 in partnership with the Institute for Follicular Lymphoma Innovation (IFLI).

In the same spirit, we have also worked to consolidate our links with many European academic groups: the GLA (German Lymphoma Alliance), the GELTAMO (Spanish Lymphomas and Bone Marrow Transplants Group), the FIL (Italian Lymphoma Foundation), the SAKK (Swiss Group for Clinical Cancer Research), and the DCLLSG (German CLL Study Group).

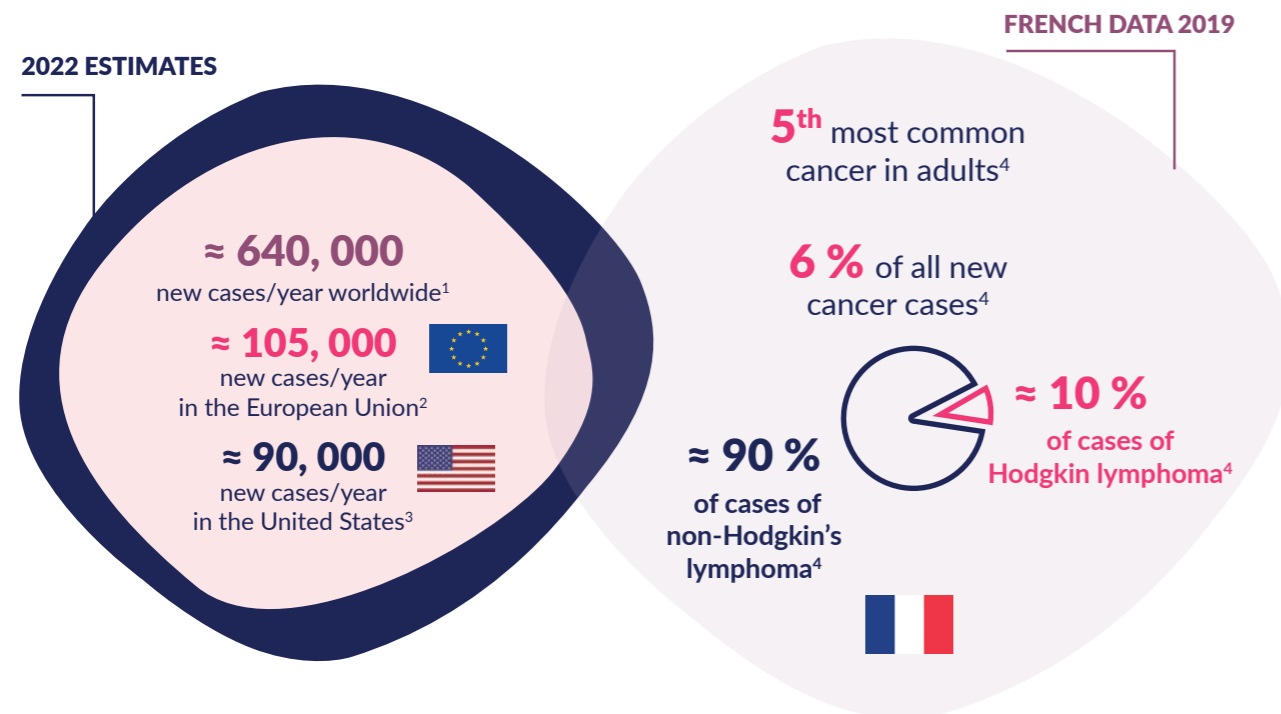
Finally, the year 2023 was also marked by the continuation of structuring and foundational projects for the future of our group. I am thinking in particular of the redeployment of the LYSA-P pathology platform, which will effectively move in 2024 to Henri Mondor Hospital in Créteil, and the work of the LYSA-LYSARC teams alongside the other members of the Carnot CALYM Institute to lay the foundations for CALYM-2.



02 Challenges in lymphoma research

01 KEY FIGURES FOR LYMPHOMA

Epidemiological data on lymphomas demonstrate the crucial global challenge represented by the fight against these cancers. The French scientific community is fully mobilized alongside researchers from all over the world to further advance knowledge and treatment.



02 PUBLIC HEALTH AND R&D CHALLENGES

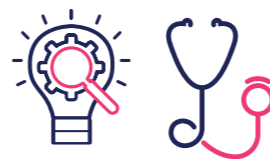
Although undeniable progress has been made in understanding and managing lymphomas, these cancers remain a major public health issue and a complex bioclinical field. Sustained efforts are necessary to overcome the many challenges in fundamental, translational, and clinical research.

PHYSIOPATHOLOGICAL CHALLENGES: Understanding the mechanisms involved in disease development and risk factors.

DIAGNOSTIC CHALLENGES: Diversity of lymphomas (over 80 types), delays, precision (interest in artificial intelligence).

PROGNOSTIC CHALLENGES: Identifying the right treatment for the right patient at the right time (search for biomarkers), reducing treatment toxicity for patients.

THERAPEUTIC CHALLENGES: New therapeutic targets, new treatments (immunotherapy, CAR-T cell treatment), new therapeutic combinations.



03 ECONOMIC CHALLENGES

Cancer research is associated with significant economic stakes for global pharmaceutical and biotechnology market players. Innovation is accompanied by a strong need for advanced expertise, which the academic research sector can meet.



ONCO-IMMUNOLOGY MARKET
Growth driver of the global pharmaceutical/biotechnology market
 Global market estimated at **about \$222 billion in 2023⁵**
 Dynamic market with a projection of **about \$521 billion in 2033⁵**
 Increasing role of **emerging biopharmas (SMEs)**
 Strong entry of a very competitive **Asian market**



GROWTH STRATEGIES
Extension to several indications
Strategic repositioning of candidates/medications
Rapid registration (niche strategies, from/to lymphoma)
Cost reduction (large phase III for registration purposes)
Decrease of the high failure rate of clinical trials (80-90%)



MARKET DEMAND
Integrated expertise in care/research network allowing:

- The biological rationalization of trial design
- The reconnection of discovery-innovation-transfer segments
- The interface of know-how of practices with the standards of academic and industrial spheres

1. Global Cancer Observatory - GLOBOCAN 2022
 2. European Cancer Information System - 2022
 3. American Cancer Society - 2022
 4. National Cancer Institute - 2019
 5. Market research report by Nova One Advisor - 2023



03 The LYSA-LYSARC'S Expertise in Lymphoma

01 THE LYSA-LYSARC INTERGROUP

The LYSA and LYSARC form a multidisciplinary ecosystem of professionals committed to lymphoma research. They are jointly labeled by the National Cancer Institute (INCa): "French cooperative intergroup of international dimension in the field of clinical cancer research."



Network of clinical research professionals on lymphomas



Operational structure for clinical research on lymphomas

FIELDS OF INTERVENTION

The LYSA-LYSARC intergroup specializes in clinical research on lymphomas, setting up interventional and non-interventional studies with a view to developing biological and/or medical knowledge. All phases of clinical trials can be carried out, from the first administration of new treatments to humans to the establishment of reference therapeutic strategies. Real-life registries are being set up in collaboration with other players in lymphoma research. Each year, the Intergroup also manages a vast portfolio of Data Reuse Studies (DRS).



A network of partner academic laboratories of excellence



A cooperative group of 'Key opinion leaders' clinicians



A professional operational structure dedicated to clinical research

OVERVIEW OF AVAILABLE RESOURCES

The LYSA-LYSARC intergroup is part of the **Carnot CALYM Institute**, alongside 18 public laboratories conducting cutting-edge research in the field of lymphomas. This academic research consortium allows capitalizing on numerous available resources and offering a unique R&D proposition.

> TECHNIQUES



- **CRISPR/Cas 9:** models, screen, barcoding
- **Single-cell:** single-cell RNA-seq, CITEseq, HYPERION, single-cell transcriptomics
- **-omics:** ATAC-seq, Chip-seq, WES, WGS, metabolomics
- **Proteomics:** Cytof, Multicolor FACS
- **ctDNA:** MRD, predictive

> EXPERIMENTAL MODELS



- **In vitro:** > 80 established cell lines, primary lines, modified lines
- **Ex vivo:** functional studies, PDX, co-culture, stroma, TME, 3D models, spheroids, organoids
- **In vivo:** syngeneic mice, KO/KI/Tg, xenografts, PDX, resistant models (R/G/RCHOP)
- **In ovo:** innovative chicken embryo PDX model

> COLLECTIONS & DATABASES



LYSARC Actions / Resources

- **TENOMIC / LYSATOMIC (T lymphomas):** > 900 patients
- **Bioclinical databases:** > 23,000 tumors, frozen, FFPE, TMA, blood, DNA/RNA, annotated, characterized, genotyped, phenotyped, immunotyped, WES, (sc)RNA-seq
- **Imaging database:** > 20,000 patients

External Actions / Resources

- **CeVi:** ISO 9001, annotated collection of viable cells, CRYOSTOR fragments, cryopreserved PBMCs and plasma from lymphoma patients. > 3,000 patients, > 3,800 samples, > 18,700 tubes
- **CeVi CAR-T:** ISO 9001, frozen PBMCs and plasma from lymphoma patients treated with CAR-T cells. 223 patients, > 1,200 samples, > 8,200 tubes
- **HEMSYS - Real-life data:** > 31,000 patients, 60,000 multidisciplinary consultation meetings (RCP)

> PLATFORMS



LYSARC Actions / Resources:

- **LYSA-IM:** imaging
- **LYSA-P:** pathology
- **LYSA-BIO:** biopathology
- **Bioinformatics:** pipelines, machine learning, artificial intelligence

External Actions / Resources:

- **Innovation Think Tank:** nurturing project ideas - CALYM action
- **French Connect:** harmonised ctDNA analysis (sequencing and bioinformatics analysis)
- **Lymphoma Data Hub:** cloud computing platform for the exploitation of massive data



ECOSYSTEM

The LYSA and LYSARC are prominent and active participants in both national and international lymphoma research ecosystems.

- They collaborate closely with a wide range of stakeholders worldwide, including hospitals, universities, research organizations, clinical research groups, Cooperative Oncology Groups (certified by INCa), scientific societies, health authorities, and patient associations.

A non-exhaustive list of our partners:

AMC Medical Research BV, Centre Henri Becquerel, CNRS-SCTD, FILO (French Innovative Leukemia Organization), FIL (Fondazione Italiana Linfomi), GELTAMO (Grupo Español de Linfomas y Transplantes de Médula Ósea), EORTC (European Organisation for Research and Treatment of Cancer), GLA (German Lymphoma Alliance), HOVON (Stichting Hemato-Oncologie voor Volwassenen Nederland), IELSG (The International Extranodal Lymphoma Study Group), IFLY (Institute for Follicular Lymphoma Innovation), IFM (Intergroupe Francophone du Myélome), INSERM (Institut National de la Santé et de la Recherche Médicale), INCa (Institut National du Cancer), Institut Necker, Klinikum der Universität München, MCL Network, Molecular Partners AG, Saarland University, Université de Bordeaux, Université Claude Bernard, Université de Montpellier.

- Founding members of ELI (The European Lymphoma Institute), which unites Europe's leading lymphoma specialists within an institute dedicated to research, training, and education on this disease.
- Members of the Carnot CALYM Institute, dedicated to advancing collaborative research in the field of lymphoma in France.



02 THE LYSA

The LYSA (The Lymphoma Study Association) is an academic cooperative group dedicated exclusively to clinical research on lymphoma. Formed in 2012 from the merger of groups active since the 1980s and 1990s, the LYSA is certified as a "Cooperative Oncology Group" along with the LYSARC by the Institut National du Cancer (INCa).



500 professionals
specializing in lymphoma in 2023

96 care centers
active in studies
between 2021 and 2023

3 countries
(France, Belgium, Portugal)

**International
collaborations**



MISSIONS

The LYSA aims to unite lymphoma specialists to promote clinical research on this type of cancer, improve patient care, and disseminate knowledge broadly.



Organizing a network of clinical research experts on lymphomas



Providing the means and resources necessary for research



Developing and conducting protocols at all stages of the disease



Supporting the activities of its member care centers



Promoting education and professional training



Evaluating new treatment approaches and therapies



Serving as a liaison with national and international agencies, regulatory bodies, and scientific societies



Facilitating translational research, linking experimental laboratories with clinical studies



Promoting research results through publications in peer-reviewed scientific journals and presentations at conferences



ENGAGEMENTS

Independence and transparency are fundamental to the LYSA's activities.

Independence: the LYSA is a non-profit research network (association under the French 1901 law), independent of any private or public entity. It has ratified the independence charter of Cooperative Oncology Groups.

Transparency: the LYSA is committed to transparency with all its stakeholders, particularly public institutions that fund its activities, patients participating in its trials, the broader scientific community, and its network members.

ORGANIZATIONAL STRUCTURE

The LYSA operates through its active members, its Board of Directors, its Scientific Council, and specialized scientific commissions.

Board Members, elected in October 2022

<p>President Franck Morschhauser</p>	<p>Treasurer Corinne Haioun</p>
<p>Executive board Members</p> <p>Marc André - Guillaume Cartron - Olivier Casasnovas - Marie-Hélène Delfau-Larue - Hervé Ghesquières - Corinne Haioun - Roch Houot - Fabrice Jardin - Camille Laurent - Steven Le Gouill - Franck Morschhauser - Catherine Thieblemont</p>	
<p>Board Members: Marc André - Caroline Besson - Françoise Bodere - Krimo Bouabdallah - Guillaume Cartron - Olivier Casasnovas - Sylvain Choquet - Gandhi Damaj - Marie-Hélène Delfau-Larue - Luc-Matthieu Fornecker - Thomas Gastinne - Philippe Gaulard - Hervé Ghesquières - Rémy Gressin - Corinne Haioun - Olivier Hermine - Roch Houot - Jean-Philippe Jais - Fabrice Jardin - Youlia Kirova - Camille Laurent - Steven Le Gouill - Thierry Molina - Franck Morschhauser - Vincent Ribrag - Karin Tarte - Catherine Thieblemont - Olivier Tournilhac - Alexandra Traverse-Glehen - Luc Xerri - Loïc Ysebaert</p>	

Members of the Scientific Advisory Board, appointed in October 2022 by the board members

<p>President Camille Laurent</p>	<p>Vice presidents Emmanuel Bachy - François LEMONNIER</p>
<p>Executive members of the LYSA's Scientific Advisory Board</p> <p>Emmanuel Bachy - Christophe Bonnet - Sylvain Carras - Anne-Ségolène Cottreau - Charles Herbaux - Camille Laurent - François LEMONNIER - Cédric Rossi - Clémentine Sarkozy - Benoît Tessoulin</p>	
<p>Members of the Scientific Advisory Board: Yassine Al Tabaa - Marion Alcantara - Sandy Amorim - Emmanuel Bachy - Marie-Christine Bene - Sophie Bernard - Côme Bommier - Christophe Bonnet - Antonin Bouroumeau - Julien Broseus - Julie Bruneau - Vincent Camus - Sylvain Carras - Morgane Cheminant - Anne-Ségolène Cottreau - Lucile Couronné - Gilles Crochet - Virginie de Wilde - Bénédicte Deau-Fischer - Roberta di Blasi - Eric Durot - Pierre Feugier - Marie Gomes da Silva - Romain Guieze - Charles Herbaux - Salim Kanoun - François LEMONNIER - Marie Maerevoet - Guillaume Manson - Laurent Martin - Charline Moulin - Marie-Christine Ngirabacu - Cédric Rossi - Mikhaël Roussel - Clémentine Sarkozy - David Sibon - Carole Soussain - Pierre Sujobert - Benoît Tessoulin - Eric Van Den Neste</p>	

Scientific Commissions and their leaders

Committee theme	Committee leaders
Large cell B lymphoma	Roch Houot, Fabrice Jardin
T-cell lymphoma	Gandhi Damaj, Laurence de Leval, Olivier Tournilhac
Follicular lymphoma and other indolent lymphomas	Guillaume Cartron, Franck Morschhauser, Catherine Thieblemont
Hodgkin's lymphoma	Marc André, Hervé Ghesquières
Mantle cell lymphoma	Morgane Cheminant, Olivier Hermine, Steven Le Gouill

LYSAGIVES PROMINENCE TO ITS YOUNG MEMBERS

The LYSA's dynamism relies significantly on the continuous renewal of its members. To fully integrate new talents, the cooperative group encourages young members to be actively involved in studies.



"The transgenerational integration of new investigators within the LYSA is well-designed, featuring a "duo" strategy that supports us in new missions. Developing the VERLEN study allowed me to understand the entire process of constructing a clinical trial, from the idea to the launch and follow-up. I appreciated the quality, commitment, and simplicity of exchanges with the LYSARC teams. Now, as the investigator of the VERLEN study and coordinator of the OASIS-II study with Professor Le Gouill, I am fully involved: handling requests from centers, responding to adverse events... The experience gained allows me to improve protocols in development. This role as a PI involves significant responsibility and is very rewarding on a personal, professional, and human level."

Dr Benoît Tessoulin, MD, PhD - CHU de Nantes



"The shift taken by LYSA-LYSARC towards the exploitation of its databases and the management of its biology/imaging collection is enabling ambitious studies to be set up, with a potential that is unique on an international scale. The BIDIFLY project, set up thanks to the group's collaborative capacity with researchers motivated by this common goal, will hopefully open up new avenues of translational research in follicular lymphoma. I am personally very proud to be part of this rewarding adventure. And it's just the beginning!"

Dr Clémentine Sarkozy, MD, PhD - Institut Curie



Video Presentation



"Lymphomas are diseases that have interested me since I was a student. They are rare and serious diseases, but they are also exciting in terms of research. My engagement with LYSA was natural. It enables us to carry out research projects and make advances in these rare diseases that would be impossible on the scale of an institution such as a university hospital, but which are essential for the development of our knowledge and patient care."

Dr Sylvain Carras, MD, PhD - CHU Grenoble Alpes



03 THE LYSARC

LYSARC (The Lymphoma Academic Research Organisation) is the operational arm of the LYSA and the largest academic structure in Europe dedicated to lymphoma research operations. It evolved in 2012 from GELARC (Adult Lymphoma Study Group - Clinical Research), which was established in 2000.

161 employees in 2023 (including temporary contracts, permanent contracts, and apprentices). Staff numbers are growing to support the group's dynamism.

1st academic structure dedicated to lymphoma research in Europe

- Clinical studies in phases 1, 2, 3, and 4
- Non-interventional studies / registries
- Data reuse studies (DRS)



MISSIONS

The LYSARC aims to produce high-quality data to enhance scientific understanding of the diagnosis, treatment, and care of lymphoma patients.



Conduct clinical, biopathological, epidemiological, and real-life studies on lymphomas.



Support other lymphoma research stakeholders by providing guidance, technical support, and training to investigational centers.



Contribute expertise to the strategic reflections and decisions of the LYSA's scientific decision-making bodies.

ENGAGEMENTS

Independence and transparency are foundational to the LYSARC's operations.

Independence: the LYSARC is a non-profit association (under the French 1901 law), independent of any private or public entity.

Transparency: the LYSARC is committed to transparency with all its stakeholders, including public institutions that fund its activities, patients participating in its trials, the broader scientific community, and its organization members.

VALUES

The LYSARC employees share strong values that are essential to research activities.



ENGAGEMENT

"Acting in the interest of patients for increasingly effective prevention and therapies against lymphomas."



COHESION

"Promoting mutual aid, team spirit, and maintaining good relationships with all stakeholders."



OPENNESS

"Being open to others and new practices, enriching ourselves through experiences and diversity by developing complementarity."

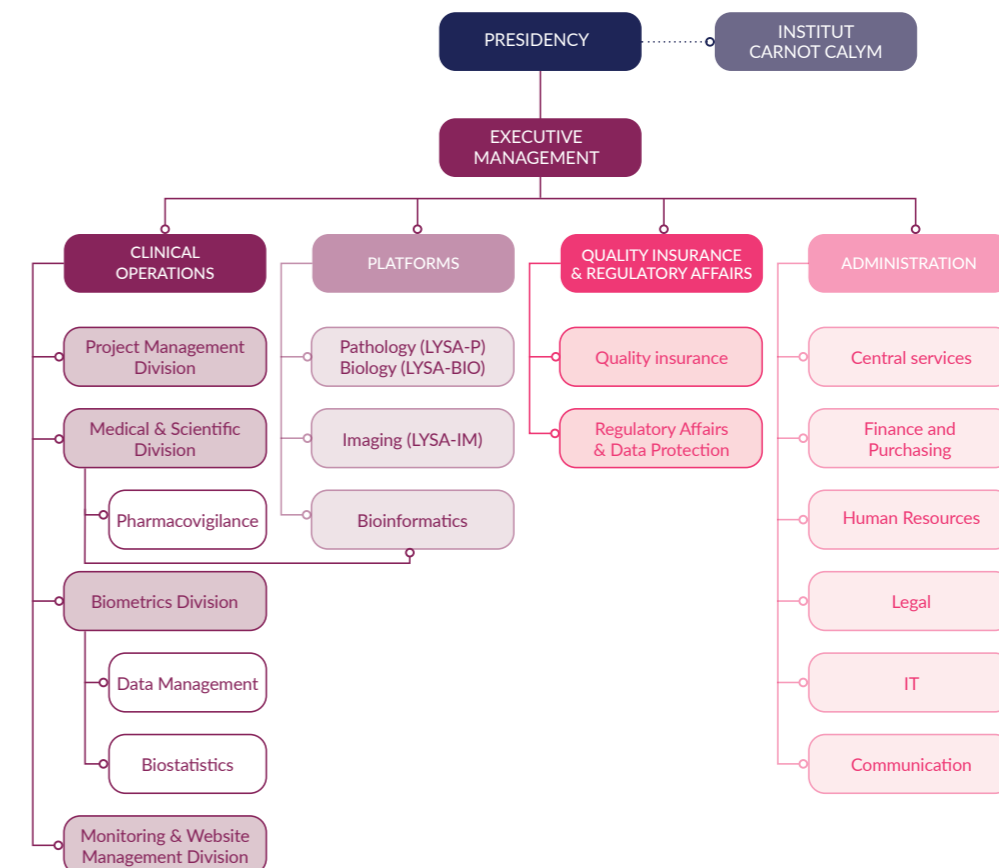


INTEGRITY

"Being authentic, honest, and fair with ourselves and others."

ORGANIZATIONAL STRUCTURE

The LYSARC brings together all the expertise necessary for conducting lymphoma research projects, including operational resources (clinical operations and platforms), transversal functions (General Services, Finance/Purchasing, Human Resources, Legal, Information Systems, Communication), and Quality Assurance & Regulatory Affairs. Governance is provided by its President, Professor Franck Morschhauser, and its General Director, supported by the Executive Committee (CODIR).



04 Looking back on 2023

Each year, the LYSA-LYSARC activity report highlights a selection of key moments for the intergroup. The year 2023 was marked by key advancements on a scientific standpoint: the culmination of the Ro-CHOP adventure in clinical research, the confirmed success by the figures of the REALYSA and DESCAR-T real-life registries, as well as quality scientific production highlighted in congresses and prestigious journals. It is also important to commend the intergroup's strong partnership dynamics, various media appearances, a successful team seminar, and remarkable initiatives to support the LYSA endowment fund.

01 THE CULMINATION OF THE Ro-CHOP ADVENTURE IN CLINICAL RESEARCH

The year 2023 marked the culmination of over a decade of clinical research around the Ro-CHOP combination (romidepsin + CHOP: cyclophosphamide, doxorubicin, vincristine, and prednisone) in patients with previously untreated peripheral T-cell lymphoma. A phase 1b/2 study was initiated in 2011, leading to a phase 3 study in 2013, with its latest update in 2023.



”

“The Ro-CHOP adventure demonstrates not only the expertise of the LYSA-LYSARC in managing clinical trials from early-phase to phase 3 but also the academic world’s ability to engage and mobilize key players in developing therapeutic strategies in France and internationally.”

Emmanuelle Robert-Eydoux,
Director of the Project Management Division

ROMIDEPSIN

Histone deacetylase inhibitor
Targeted therapy



CHOP

Cyclophosphamide, doxorubicin,
vincristine, and prednisone
Chemotherapy

➤ PREVIOUSLY UNTREATED
PERIPHERAL T-CELL LYMPHOMA



➤ PATIENTS AGED 18-80



RETROSPECTIVE OF THE Ro-CHOP ADVENTURE (2011-2023)

2011-2014* PHASE 1B/2 STUDY IN FRANCE

Objective: To evaluate the safety, tolerance, and activity of the Ro-CHOP combination in patients with previously untreated peripheral T-cell lymphoma

Phase 1b: Dose escalation management from 8 mg/m² to 12 mg/m² of romidepsin + CHOP and review of toxicities

Phase 2: Extension study with a dose of 12 mg/m² of romidepsin + CHOP

Conclusion: No deaths were attributed to toxicity in this Ro-CHOP combination study.

> **Results of the phase 1b/2 study** published in 2015 in The Lancet Hematology

> **Oral communication** at the 2014 American Society of Hematology (ASH) congress

2nd MILESTONE RO-CHOP: 2013-2023** INTERNATIONAL PHASE 3 RANDOMIZED MULTICENTER STUDY

Objective: To compare the efficacy and tolerance of the Ro-CHOP combination versus CHOP in patients with previously untreated peripheral T-cell lymphoma

Phase 3: Management of this international study centralized at LYSARC (project management, pharmacovigilance, data management...)

Conclusion: The results do not justify a change in first-line management for patients with peripheral T-cell lymphoma.

> **Results of the phase 3 study** published in 2011 in the Journal of Clinical Oncology

> **Final analysis publication** expected in 2024

> **Presentations** at several international congresses, including 2 editions of the ASH congress

PERSPECTIVES FOR DATA REUSE

1 STUDY PLANNED IN 2024: RO-CHOP ANALYSIS RADIOMICS

9 LYSA centers in France
37 patients included
18 patients treated in phase 1b
19 patients treated in phase 2

Access the study



”

“In this phase 1b/2 study, we highlight the responsiveness of the different teams involved in ensuring toxicity reviews. This collaborative work was done with great professionalism!”

Thomas Pleau-Pison,
Clinical Project Manager

9 countries
3 continents Europe, Asia, and Australia
98 centers
421 patients included

Access the study



”

“This international phase 3 study highlighted the adaptability of the LYSA-LYSARC teams to the constraints of different countries. A global supervision was set up with the involvement of all clinical research professions and cross-functional functions. The Ro-CHOP adventure was a great challenge!”

Fabienne Morand,
Clinical Project Management Manager



* Inclusions from January 2011 to May 2013, last update in 2014
Data extracted from the publication: Dupuis J, Morschhauser F, Ghesquières H, et al. Lancet Haematol. 2015 Apr;2(4)
** Inclusions between January 2013 and December 2017, last update in 2023
Data extracted from the publication: Bachy E, Camus V, Thieblemont C, et al. J Clin Oncol. 2022 Jan 20;40(3):242-251

02 SUCCESS OF THE REALYSA AND DESCAR-T REAL-LIFE REGISTRIES

The success of the REALYSA and DESCAR-T real-life registries, initiated in 2018 and 2019 respectively, can be seen both in terms of inclusions and of ongoing or already valued research projects (congresses and scientific publications). The figures speak for themselves...

FRENCH MULTICENTER REAL-LIFE COHORT OF ADULT PATIENTS WITH LYMPHOMA



INCLUSION OBJECTIVE ACHIEVED IN 2023
(end of inclusions)



6,015 patients included in total
(6,000 initially planned inclusions)
+ 1,000 patients included in 2023
35 recruiting centers in France

- **1st patient included** in November 2018
- **End of inclusions** in October 2023
- **Patient follow-up** until the end of 2028
(minimum 5 years of follow-up, 9 years for the first participants)

Detailed presentation and list of ongoing or already valued projects



MULTIPLE RESEARCH PROJECTS

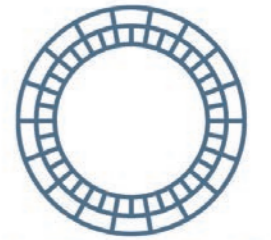
Over 10 projects launched in 2023
Over 20 projects ongoing in 2023
9 projects completed in 2023



INTERNATIONAL RECOGNITION

2 oral presentations
3 posters
1 scientific publication

FRENCH REGISTRY OF PATIENTS, ADULTS AND CHILDREN, SUFFERING FROM MALIGNANT HEMOPATHIES ELIGIBLE FOR CAR-T CELL THERAPY



NEW INCLUSION THRESHOLD REACHED IN 2023
(recruitment still ongoing)



3,000th patient included in August 2023
Over 2,400 patients diagnosed with lymphoma
+ 1,000 patients included during 2023
38 recruiting centers in France

- **1st patient included** in December 2019
- **End of inclusions** extended beyond 2024
(initial objective: end of 2024)
- **Patient follow-up over a 15-year period**

Detailed presentation and list of ongoing or already valued projects



MULTIPLE RESEARCH PROJECTS

Over 15 projects ongoing in 2023
5 projects completed



INTERNATIONAL RECOGNITION

10 oral presentations
5 posters
4 scientific publications

Collaboration of 4 academic partners

- > Hospices Civils de Lyon (HCL)
- > LYSA-LYSARC
- > Inserm
- > FRANCIM Cancer Registry Network

Support from 7 industrial partners

- > AbbVie
- > Amgen
- > AstraZeneca
- > Bristol Myers Squibb
- > Janssen
- > Roche
- > Takeda

Collaboration of 5 cooperative groups and scientific societies

- > GRAALL (Group for Research on Adult Acute Lymphoblastic Leukemia)
- > IFM (Intergroupe Francophone du Myélome)
- > LYSA-LYSARC
- > SFCE (Société Française de lutte contre les Cancers et les leucémies de l'Enfant et de l'adolescent)
- > FGM-TC (Société Francophone de Greffe de Moelle et de Thérapie Cellulaire)

Support from 3 industrial partners

- > Novartis
- > Gilead Sciences
- > Bristol Myers Squibb



03 PUBLICATIONS IN PRESTIGIOUS JOURNALS

The work of LYSA-LYSARC resulted in notable scientific production in 2023, including in reference scientific journals such as Nature Medicine, Journal of Clinical Oncology, Blood Advances, and Annals of Oncology. In total, the intergroup was responsible for over 71 publications in 2023.



EXCELLENT RESULTS OF THE PHASE 2 ALYCANTE TRIAL ON CAR-T CELL THERAPY

Phase 2 study evaluating the efficacy and tolerance of axicabtagene ciloleucel, an anti-CD19 CAR-T cell therapy, as a second-line treatment in patients with relapsed or refractory aggressive B-cell non-Hodgkin lymphoma and considered ineligible for hematopoietic stem cell transplantation.

“ALYCANTE is the first study evaluating axi-cel as a second-line treatment for R/R LBGC patients ineligible for transplantation. The results showed high response rates and durable remissions in this difficult-to-treat population. In France, these results have extended the early access program for axi-cel in the second line, regardless of transplant eligibility.”



Prof. Roch Houot, Head of the Hematology Department at Rennes University Hospital (France), Coordinator of the ALYCANTE study



FOCUS ON 6 MAJOR PUBLICATIONS



POSITIVE 7-YEAR RESULTS FROM THE LYMA PHASE 3 TRIAL IN MANTLE CELL LYMPHOMA

Long-term study on rituximab maintenance therapy in young patients with mantle cell lymphoma in the LYMA phase 3 trial.



ENCOURAGING RESULTS FROM THE PHASE 2 BREACH TRIAL IN HODGKIN'S LYMPHOMA

Phase 2 study evaluating brentuximab vedotin in combination with chemotherapy in patients with unfavorable stage I/II Hodgkin's lymphoma at diagnosis



REUTILIZATION OF DATA FROM THE RELEVANCE TRIAL IN FOLLICULAR LYMPHOMA

Analysis of the prognostic value of metabolic tumor volume in treatment-naive patients with follicular lymphoma in the phase 3 RELEVANCE trial.

“The imaging exams collected during our trials are exceptional data for LYSA-IM. They allow us to go further within our DRS framework, identifying new prognostic and/or predictive radiomics, ultimately improving the management of lymphoma patients.”



Romain Ricci, Director of the Imaging Department



PROOF OF CONCEPT FROM THE REALYSA COHORT

Analysis of a proof of concept on patients with diffuse large B-cell lymphoma in the first line, utilizing data from the REALYSA cohort.

“This publication underscores the quality of data collected in the REALYSA cohort, built on clinical trial standards and verified by a rigorous validation process. These data can be used to better understand treatment patterns and patient prognosis, as demonstrated by this article for first-line DLBCL patients. They also pave the way for studying the transferability of clinical trial results in real-life settings.”



Alice Pauc, Clinical Project Manager



NEW UTILIZATION OF DATA FROM THE DESCAR-T REGISTRY

Study of relapse-free mortality after CAR-T cell therapy in patients with large B-cell lymphoma, using data from the DESCAR-T registry.

“This new study could very practically assist healthcare professionals in patient selection and management. The DESCAR-T registry offers an exceptional database on CAR-T cell treatments. It enables the establishment of studies to better characterize the efficacy and tolerance profiles of these new drugs in real-life conditions.”



Karine Danno, Clinical Project Manager

04 LYSA-LYSARC VALORISATION AT CONGRESSES

Each year, LYSA-LYSARC's work is highlighted at various international congresses. The year 2023 was no exception, with significant involvement and recognition at the French Society of Hematology (SFH) congress, as well as a strong presence at the American Society of Hematology (ASH) congress for the third consecutive year. In total, the intergroup participated in 8 congresses and was responsible for over 75 valorisations in the form of posters or oral communications.



NOTABLE INVOLVEMENT AND VALORISATION AT THE FRENCH SOCIETY OF HEMATOLOGY (SFH) CONGRESS

LYSA organized **2 sessions with a total of 7 group speakers:** a cooperative group session with 6 presentations on follicular lymphomas and a topical session with 1 presentation on "Modeling and Analyses of Lymphomas".

LYSA-LYSARC's work was also featured in **11 valorisations in the form of oral communications and posters.**

Finally, LYSA and cooperative hematology groups (ALFA, FILO, GFM, GRAALL, IFM, LYSA, SFGMTC) **jointly developed the program for the ARC/TEC day at the SFH congress (March 30, 2023).**

ARC/TEC Day

CONTINUOUS COMMITMENT TO TRAINING

The LYSA was involved in developing the program for the **ARC/TEC day at the SFH congress in Paris on March 30, 2023.** It was also the same for the **ARTEC-GCO training organized in Paris on October 5-6, 2023, by the Cooperative Oncology Groups (GCO) network.** These training days were intended for ARCs/TECs/IRCs working on studies promoted by cooperative groups: ARCAGY-GINECO, CIGAL (ALFA, FILO, GRAALL, GFM, IFM), FFCO, GERCOR, GORTEC, IFCT, IFM, IGCNO-ANOCEF, LYSA-LYSARC. The goal was to strengthen knowledge on different types of cancers and expertise in data entry and transmission within the framework of a clinical research protocol.



REVIEW OF INTERGROUP PARTICIPATION/COMMUNICATIONS



STRONG PRESENCE AT THE AMERICAN SOCIETY OF HEMATOLOGY (ASH) CONGRESS

The year 2022 was already marked by a strong presence at the ASH congress with 15 abstracts valued. In 2023, this result was exceeded and almost doubled with **27 abstracts valued as oral communications and posters.**



"The valorisation of LYSA-LYSARC's work was exceptional at the 65th edition of the ASH congress in San Diego. Among all these notable highlights, we can especially note the interesting work on ctDNA and the remarkable visibility of the DESCAR-T registry."

Eve Gehlkopf,
Medical Officer



(from left to right):
Thomas Pleau-Pison,
Chloé Gourc-Berthod,
Laetitia Melgar, Eve Gehlkopf,
Emmanuelle Robert-Eydoux,
Jérôme Paget and Fanny Cherblanc

Valorisations



CELL THERAPY INNOVATION 360° (CTI 360°)

LYSA-LYSARC participation



SCIENTIFIC DAYS ON IMMUNITY AND CANCER (JSIC)

LYSA-LYSARC participation



FRENCH SOCIETY OF HEMATOLOGY (SFH) CONGRESS

1 LYSA cooperator group session
1 LYSA news session
8 oral communications
3 posters



AMERICAN SOCIETY OF CLINICAL ONCOLOGY (ASCO) CONGRESS

1 oral communication



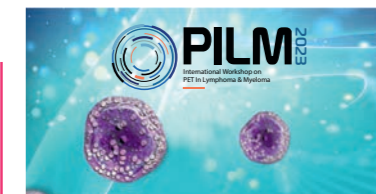
EUROPEAN HEMATOLOGY ASSOCIATION (EHA) CONGRESS

3 oral communications
3 posters



INTERNATIONAL CONFERENCE ON MALIGNANT LYMPHOMA (ICML)

11 oral communications
14 posters
1 abstract in the abstract book



INTERNATIONAL WORKSHOP ON PET IN LYMPHOMA AND MYELOMA (PILM)

4 oral communications
5 posters



AMERICAN SOCIETY OF HEMATOLOGY (ASH) CONGRESS

14 oral communications
13 posters

JANUARY 25-26, 2023
LYON, FRANCE

JANUARY 30-31, 2023
ISSY-LES-MOULINEAUX,
FRANCE

MARCH 29-31, 2023
PARIS, FRANCE

JUNE 2-6, 2023
CHICAGO, USA

JUNE 8-16, 2023
FRANKFURT, GERMANY

JUNE 13-17, 2023
LUGANO, SWITZERLAND

OCTOBER 6-7, 2023
MENTON, FRANCE

DECEMBER 9-12, 2023
SAN DIEGO, USA

+ REMOTE / VIRTUAL

+ REMOTE / VIRTUAL



05 THE SIGNING OF PARTNERSHIPS FOR GREATER IMPACT

With support from cross-functional teams enhancing our expertise, 2023 marked an expansion of partnership dynamics and facilitated the continuation of pivotal projects, significantly boosting the group's visibility. Notably, collaborative research projects will be initiated with two American entities: the Institute for Follicular Lymphoma Innovation (IFLI) and the Mayo Clinic. Additionally, joint endeavors will be undertaken with the French company PELyon (Pharmaco Epidemiology Lyon). Finally, a partnership with the French start-up Klineo will provide an innovative digital platform to streamline clinical trial recruitment and improve patient access.

ADVANCING KNOWLEDGE ON LYMPHOMAS

DATA SHARING / EXPERTISE

Research Partnership with the Mayo Clinic

The Mayo Clinic, a non-profit institution renowned for its education, research, and patient care, is actively involved in lymphoma studies.

> Partnership signed with the objective of facilitating collaborative research and data sharing between two leading lymphoma research entities.

- Agreement signed in July 2023 for a duration of five years.
- Pooling data to enhance research power through shared resources and mutual result validation
- Sharing of expertise between (US/Europe)
- Joint publications



"This partnership will propel lymphoma research to new heights. It overcomes data-sharing challenges while adhering to legal and regulatory landscapes, including GDPR"

Fanny Cherblanc,
Project Valorization Manager

REAL-LIFE DATA

Research Partnership with PELyon (Pharmaco Epidemiology Lyon)

PELyon is a French company that specializes in analyzing real-life health data, utilizing the French National Health Data System (SNDS) which aggregates key national health databases.

> Launch of joint research projects focused on lymphomas and collaboration on external projects with pharmaceutical industry players.



- Agreement signed in September 2023 for a duration of three years.
- First project in progress, aiming to enrich the REALYSA cohort data using SNDS information (comorbidities, healthcare utilization, long-term follow-up...)



ARTIFICIAL INTELLIGENCE

Research Partnership with the Institute for Follicular Lymphoma Innovation (IFLI)



IFLI, a California-based non-profit foundation, brings together multidisciplinary lymphoma expertise and is dedicated to accelerating the development of innovative treatments for follicular lymphoma patients.

"This inaugural IFLI/LYSA-LYSARC collaboration is poised to bring breakthroughs in follicular lymphoma research, significantly benefiting patients."

Pr Franck Morschhauser,
President of the LYSA-LYSARC

> Launch of the BIDIFLY (Biological and Imaging Data Integration for Follicular Lymphoma Research) program, using AI to enhance understanding of follicular lymphoma biology and accelerate innovative treatment development.

- Partnership announced in december 2023.
- Program Scope of €9 million over four years.
- Collaboration with globally recognized scientists and clinicians
- Leveraging advanced technologies to generate extensive multi-omic data analyzed through AI.



"We are thrilled to launch this partnership with internationally renowned scientific leaders in lymphoma clinical research. This collaboration marks a significant milestone for IFLI in our commitment to accelerate treatment development and ultimately cure follicular lymphoma."

Andy Peykoff,
President of the IFLI Board of Directors



FACILITATING ACCESS TO CLINICAL TRIALS

DIGITAL PLATFORM

Partnership with the Innovative Start-up Klineo

The French start-up Klineo has developed a digital platform enabling patients and doctors to swiftly find the most relevant ongoing clinical trials.

> Deployment of the digital clinical trial search platform developed by Klineo for all open lymphoma studies.

- First collaboration with an academic hematology research group
- Access to clinical trials via the platform: app.klineo.fr



"Through this partnership, we aim to enhance information dissemination and access to ongoing clinical trials. This platform is designed to be beneficial for both healthcare professionals and patients."

Valentin Moine,
Center Management Director



06 MEDIA COVERAGE OF THE LYSA-LYSARC'S ACTIVITIES IN THE PRESS

The dynamic scientific and partnership activities of the LYSA-LYSARC group in 2023 provided numerous opportunities for media engagement through press releases, followed by several appearances in specialized press outlets (e.g., Hospimedia and APMnews). The year also featured an article showcasing LYSA's activities on the front page of La gazette DIAG & SANTÉ, along with two podcast appearances by LYSA members: one on France Inter's "Le téléphone sonne" and another on the "Les voies de l'hématologie" podcast by the Association des Internes en Hématologie (AIH).



MEDIA COVERAGE



HOSPIMEDIA - APRIL 3, 2023

The League Against Cancer Collaborates with Oncology Cooperative Groups



APMNEWS - SEPTEMBER 18, 2023

CAR-Taxi-cel Potentially Useful as Second-Line Therapy for Large B-Cell Lymphomas Not Eligible for Autotransplant (French Study)



OUR PRESS STATEMENTS

MARCH 2023

Press Release by the Oncology Cooperative Groups Network (GCO*), including the LYSA-LYSARC
Partnership agreement signed between the League Against Cancer and the Oncology Cooperative Groups (GCO)

Access the press release



* The GCO network consists of 10 independent, non-profit academic cancer research groups, all certified by the National Cancer Institute (INCa).

SEPTEMBER 2023

LYSA-LYSARC Press Release
Announcement of the ALYCANTE study publication in Nature Medicine, demonstrating the clinical benefit of CAR-T cells (axicabtagene ciloleucel) as a second-line treatment for large B-cell lymphoma (LBGC) patients ineligible for autologous stem cell transplantation

Access the press release



LYSARC ON THE FRONT PAGE OF LA GAZETTE DIAG & SANTÉ

La gazette DIAG & SANTÉ highlighted the LYSA's activities through an interview with Fabienne Di Giambattista, LYSA's Medical Director in 2023:

1. Can you introduce the LYSA's main missions?
2. How does the LYSA operate?
3. Can you tell us about your research platforms?
4. What are the latest developments and innovations at the LYSA?



PODCAST APPEARANCES BY LYSA MEMBERS



"FOLLICULAR LYMPHOMA"

Podcast "Les voies de l'hématologie" by the Association des Internes en Hématologie (AIH) - October 1, 2023
Pr. Guillaume Cartron (CHU Montpellier), a member of the LYSA's Scientific Commission "Follicular Lymphoma and Other Indolent Lymphomas" and the LYSA Board of Directors, was featured in this podcast to share his expertise on follicular lymphoma, particularly low-tumor burden lymphoma. He responded to various questions posed by Charline Fuseau, AIH's Vice President.



"MOM HAS CANCER, BUT IT'S GOING TO BE OKAY"
FRANCE INTER'S "LE TÉLÉPHONE SONNE" OCTOBER 10, 2023



Pr. Steven Le Guill (Institut Curie), a member of the LYSA's Board of Directors, participated in a France Inter program discussing the process of cancer diagnosis disclosure by medical professionals and patients to their families. He was joined by Isabelle Huet, General Director of the patient association Rose Up. The guests responded to listener testimonies about their experiences during and after the cancer diagnosis announcement.



DECEMBER 2023

LYSA-LYSARC Press Release
Launch of BIDIFLY, a collaborative research program between LYSA-LYSARC and IFLI, with a €7.5 million budget using AI to better understand follicular lymphoma and develop new therapeutic tools.

Press conference scheduled for March 2024
More press coverage to follow...

Access the press release



07 LYSARC SEMINAR: SHARING AND CAMARADERIE

Discussing a variety of topics, getting to know each other better, and enjoying social moments outside the office... the LYSARC seminar in October 2023 lived up to expectations. All employees were invited to gather for various engaging activities.

- > Team building exercises
- > Lunch break in a beautiful park under the sun
- > Departmental photo sessions / group photo
- > Multi-themed plenary session (≈ 1.5 hours) covering topics such as the LYSA, the LYSA-P, partnerships, management and efficiency, employee development and retention
- > Dinner cocktail at an Italian restaurant in Lyon
- > Performance by artist **Caroline Le Flour**, who uses humor to openly discuss the fight against cancer and her personal battle with lymphoma



08 REMARKABLE INITIATIVES SUPPORTING THE LYSA ENDOWMENT FUND

LYSA extends its gratitude to all donors, individuals, and companies who contribute significantly to lymphoma research programs. This activity report is also an opportunity to highlight two remarkable initiatives benefiting the LYSA Endowment Fund: the "BRI'FIT EVENT" by the Kidisport association and Brigida Tolomeo's donation related to her "Raid des Amazones" project.

FOCUS ON 2 INITIATIVES

BRI'FIT EVENT BY THE KIDISPORT ASSOCIATION

For five years, Kidisport has been donating the proceeds from its "BRI'FIT EVENT" to the LYSA. This event is a day of fitness workshops open to all, where participants can join fitness classes led by renowned instructors. The LYSA warmly thanks Brigida Tolomeo, founder of Kidisport, and all its members.



THANK YOU TO THE DONORS!

RAID DES AMAZONES BY BRIGIDA TOLOMEO

Brigida Tolomeo, the driving force behind the previously mentioned BRI'FIT EVENT, also planned to participate in the Raid des Amazones in 2023. This is a 100% female and 100% charitable adventure race held in a different country each year. Although the project had to be canceled, Brigida Tolomeo decided to convert her initiative into a donation for the LYSA.



”

"We refunded sponsors who requested reimbursement and retained those willing to donate to the LYSA and 'Sport et Handicap'. I support the LYSA annually through another event, the BRI'FIT EVENT. My sister has lymphoma. This is my way of contributing."

Brigida Tolomeo,
Founder of Kidisport Association



05 2023 Scientific Report



Insights from Prof. Camille Laurent, President of the Scientific Council and Member of the LYSA Board of Directors

OUR INTERGROUP HAS REPEATED THE EXCELLENT SCIENTIFIC PERFORMANCE ACHIEVED IN 2022 AND EVEN IMPROVED CERTAIN RESULTS.

Our scientific output increased significantly compared to 2022, with a total of 71 articles published and more than 75 presentations at conferences in the form of posters or oral communications.

Beyond the volume, I want to especially highlight the quality of the work done, which was recognized multiple times throughout 2023. Notably, the highly anticipated results from the phase 2 clinical trials BREACH and ALYCANTE were published in The Journal of Clinical Oncology and Nature Medicine, respectively. Additionally, the quality of the data from our DESCAR-T and REALYSA registries was acknowledged through publications in the journal Blood Advances.

Continuing with the recognitions, 2023 saw a strong presence of the LYSA-LYSARC at the American Society of Hematology (ASH) conference. A total of 27 abstracts were featured at this conference, nearly double the number from the previous year. It is also important to mention our significant involvement in the annual conference of the French Society of Hematology (SFH): LYSA cooperative group sessions, LYSA update sessions, oral communications, posters, and more.

This scientific dynamism is made possible by the strong commitment of the LYSA-LYSARC members and collaborators. It is also reflected in the active work conducted in LYSA investigative centers and within the LYSA-LYSARC research platforms.

From 2021 to 2023, we had 96 active centers, which collectively enabled more than 9,000 inclusions across all studies in just three years. Specifically, 8,795 of these inclusions pertain to our REALYSA and DESCAR-T registries, which hold exceptional data exploitation potential! The LYSA-LYSARC biological/anatomic pathology and imaging platforms are fully engaged in expanding our scientific research using these cohorts, with several dozen projects in the pipeline.

2024 promises to be a radiant year for our group with a variety of ambitious and promising projects.

Several new clinical trials were initiated in 2023 or are set to begin in the coming months: CARMOD, GLOASIS, MORNINGLYTE, and FERTILE. We are also eager to continue the recently launched large-scale research program on follicular lymphoma: BIDIFLY (Biological and Imaging Data Integration for Follicular Lymphoma Research). This project, in collaboration with The Institute for Follicular Lymphoma Innovation (IFLI), aims to better characterize follicular lymphoma and identify early biomarkers for patients at high risk of relapse by leveraging LYSA databases through integrative artificial intelligence approaches.

In conclusion, we end 2023 with a positive outlook and exciting prospects for 2024. On behalf of the LYSA Scientific Council and the LYSARC, I extend our deepest gratitude to all researchers, clinicians, partners, institutions, and patients who contribute to our research. Together, we continue to advance the understanding and management of lymphomas!

Prof. Camille Laurent,
President of the LYSA Scientific Council

01 2023 SCIENTIFIC PROJECTS OVERVIEW



More than 45 projects in the pipeline

- 7 cohorts
- 8 phase I/II studies
- 21 phase II studies
- 13 phase III studies

Scientific Dynamism



- 6 projects in active preparation
- 12 projects open for recruitment
 - > 3 non-interventional studies
 - > 1 low-risk interventional study
 - > 8 interventional studies
- 11 projects with patients in treatment or post-treatment follow-up
- 16 projects in the finalization stage
- 128 statistical analysis reports



02 SPOTLIGHT ON 3 NON-INTERVENTIONAL STUDIES IN RECRUITMENT

DESCAR-T

National registry of patients with hematologic diseases eligible for CAR-T cell therapy.

> Ongoing Inclusions

- 3,497 patients included by December 2023
- Inclusions to continue in 2024
- Patient follow-up over a 15-year period

> Data Exploitation Ongoing, with multiple recognitions achieved

- Oral communications, posters, and publications (including a new publication in 2023 in Blood Advances)
- 15 + projects ongoing in 2023
- 5 projects completed

BIA-ALCL

Observational study of ALK-negative anaplastic large cell lymphomas associated with breast implants.

LYSATOMIC

Characterization of diagnostic, prognostic, and theranostic molecular biomarkers for clinical management of patients with T (and NK) lymphomas.



HAUTE AUTORITÉ DE SANTÉ

Recognized among "data sources mobilized to respond to the needs of the French National Authority for Health (HAS)."



03 SPOTLIGHT ON 1 LOW-RISK INTERVENTIONAL STUDY IN RECRUITMENT

REALYSA

National real-life study on lymphomas.

> End of Inclusions in October 2023

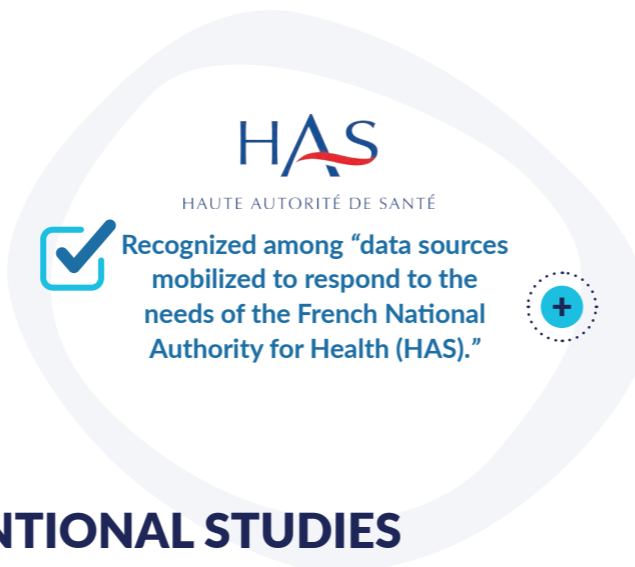
- 6,015 patients included since December 2018 (initial target met)
- Cohort now in follow-up phase until the end of 2028

> Data Exploitation ongoing, with multiple valorisations already achieved

- Oral communications, posters, and publications (including a new publication in 2023 in Blood Advances)
- Over 20 projects ongoing in 2023
- 9 projects completed in 2023

> Operational Advances in 2023

- Implementation of data quality control
- Launch of a review/confirmation of patient diagnoses through re-reading of pathology reports by pathologists
- Beginning of imaging exam centralization



04 SPOTLIGHT ON 8 INTERVENTIONAL STUDIES IN RECRUITMENT

BICAR

Study on the efficacy of glofitamab, a CD3xCD20 bispecific antibody, for patients relapsing after therapy with genetically modified T lymphocytes (CAR-T cells).

KILT

Study of lacutamab with GemOx versus GemOx alone in patients with relapsed or refractory peripheral T-cell lymphoma.

IELSG 47 - MALIBU

Study of the combination of ibrutinib and rituximab in untreated marginal zone lymphoma.

MARSUN

Study of mosunetuzumab-lenalidomide combination versus investigator's choice therapy in patients with relapsed or refractory marginal zone lymphoma.

NIVEAU

Study of nivolumab in elderly patients or those ineligible for high-dose chemotherapy with aggressive non-Hodgkin's lymphoma in first relapse or progression (treated with gemcitabine, oxaliplatin, and rituximab for DLBCL).

TRANSCRIPT

Study to verify if autologous transplantation reduces disease relapse compared to treatment without autologous transplantation in patients with T-cell lymphoma.

VALYM

Study of the efficacy and safety of valemestostat tosylate (DS-3201b) in patients with relapsed or refractory B-cell lymphoma.

VERLEN

Study evaluating lenalidomide combined with tafasitamab and rituximab as first-line treatment in patients aged 80 and over with diffuse large B-cell lymphoma.

05 SPOTLIGHT ON 128 STATISTICAL ANALYSES

The biostatistics activity shows a strong dynamic, as evidenced by the following figures: 100 reports in 2021, 115 in 2022, and 128 in 2023. This year was marked by an increase in reports on clinical projects: 48 in 2023, versus 36 in 2022. Projects using real-life data, such as those from the DESCAR-T registry, also represent a significant part of the production.



128 analysis reports in total



48 statistical reports on clinical projects

50 reports for data reuse studies (DRS)

30 database exports

06 SPOTLIGHT ON PROJECT IDEAS

The LYSA-LYSARC intergroup is fully committed to turning project ideas into scientific successes. 2023 once again illustrates this remarkable dedication with a high number of projects in the maturation/construction phase and a strong series of transformed projects.

Projects undergoing a Maturation/Construction phase in 2023:

eREVRI and GLOASIS Projects: scheduled for 2024

FERTILE Academic Project: scheduled for 2024

T-Cell Lymphoma Platform Project: several arms already under development with 2 industrial partners and a biotech

Participation in an international Project on Chronic Lymphocytic Leukemia* (CLL): anticipated solicitation for collaboration with the CLL and Waldenström's disease branch of FILO

* Initiative by the German DCLLSG Study Group - Deutsche CLL Studiengruppe

Transformed Projects:

CARMAN and MORNINGLYTE Projects: evidence of the LYSA-LYSARC's attractiveness for leading or participating in international clinical projects on innovative molecules such as CAR T and bispecifics

CARMOD Trial: proof of the virtuous contribution of the work of the LYSA-IM platform, as an imaging criterion from LYSA-IM analyses is included in the CARMOD clinical study criteria (total tumor metabolic volume > 80ml)



06 Activity of the LYSA Centers and LYSA-LYSARC Platforms

The dynamic nature of our intergroup is confirmed by the number of enrollments at LYSA investigator centers and the rich activity of the LYSA-LYSARC mixed research platforms. These platforms are crucial for conducting clinical studies and data reuse studies (DRS) in bioinformatics, pathology (LYSA-P), biopathology (LYSA-BIO), and imaging (LYSA-IM).

01 ACTIVITY OF THE LYSA INVESTIGATOR CENTERS

The network's activity continued at a strong pace in 2023, similar to the previous year. Inclusions were driven by the REALYSA and DESCAR-T real-life registries, each enrolling over 1,000 patients. REALYSA inclusions closed in October 2023, while DESCAR-T inclusions will continue into 2024.

96



Active* LYSA Centers between 2021 and 2022 (all studies combined**)

87



Active* LYSA Centers in 2023

83 in France
12 in Belgium
1 in Portugal

3,053 inclusions

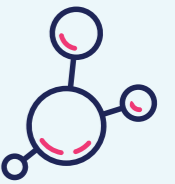
Interventional Studies in 2023
49 active centers*
154 inclusions

Observational Studies in 2023
79 active centers*
2,899 inclusions

* An active center is defined as one that has enrolled at least one patient
** All studies combined: interventional and observational

02 BIOINFORMATICS PLATFORM ACTIVITY

The bioinformatics platform maintained a comparable level of activity in 2023 as in 2022, contributing to conference presentations and publications. Growth is anticipated in 2024 with ongoing projects, the ramp-up of the BiDiFLY (Biological and Imaging Data Integration for Follicular Lymphoma Research) research program, and the launch of new projects.



2023 HIGHLIGHTS

- > **Participation in 9 DRS projects**
 - Primarily "Whole Exome Sequencing" and "RNA seq" analyses
 - Integration and analyses of multi-omic data
- > **Significant scientific recognition**
 - 6 abstracts
 - 2 published articles
- > **Completion of work relating to the BIO-RELEVANCE project**
 - Presentation of a new molecular classification of follicular lymphomas with theragnostic potential
 - Manuscript under review
- > **Launch of the BiDiFLY collaborative research program**
 - 1st actions to manage and plan the production of genomic data
 - Example: analysis of an initial test series of 24 samples
- > **Migration of storage and computing infrastructure to a new provider**

2024 PROSPECTS

- > **Continuation of ongoing projects**
 - Examples: Refractory Mantle Cell Lymphoma (MCL), CIT (tumor ID), TRANSCAN (TRANSLational CANcer research), BIO-RELEVANCE
- > **Ramp-up of the recent BiDiFLY collaborative research programme**
 - Forecasts: new collaborations, implementation of analysis tools in a cloud environment
- > **Launch of new projects**
 - Example: Epstein-Barr virus-positive diffuse large B cell lymphoma (EBV+ DLBCL)
- > **Engagement in structural activities**
 - Example: LYSARC 'Data warehouse' project
- > **Recruitment of a new team member to support activity growth**



03 THE LYSA-P / LYSA-BIO PLATFORM ACTIVITY (ANATOMOPATHOLOGY AND BIOPATHOLOGY)

The LYSA-P / LYSA-BIO platform had a busy year in 2023, managing a large project portfolio, data exports, and retrospective sample collections. Operational changes began in 2023, including preparing for the LYSA-P platform's relocation in 2024. The platform's activities in 2024 will be robust, with new studies, data exports, and the growth of the BIDIFLY (Biological and Imaging Data Integration for Follicular Lymphoma Research) collaborative research program.



"In 2023, LYSA-P and LYSA-BIO initiated the gradual implementation of a new structure. The first aspect of this evolution is the future integration of the LYSA-P platform into the pathology department of Henri Mondor Hospital in Créteil, led by Professor Emmanuelle Lechapt, planned for early 2024. The second structuring aspect is the establishment of a new organization that will result in new processes and professionalization. The goal is to gain operational efficiency and improve cross-functionality between LYSARC departments and partner platforms. The prospects for our new Biology and Pathology Department are promising!"



Emeline Mollaret,
Director of the Biology and Pathology Department

2023 HIGHLIGHTS

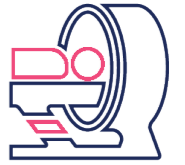
- > **A portfolio of over 65 projects**
 - 25 active clinical trials with samples
 - 6 feasibility studies (PLATFORM, E-REVRI, CARMOD, MORNINGLYTE, GLOASIS, MARSUN)
 - 1 registry
 - > 30 data re-use studies (DRS)
- > **Export of data to biometrics for analysis for 6 studies**
 - Studies involved: OASIS, ALYCANTE, TIRHOL, VALYM (DLBCL, FL and HL)
- > **Collection of retrospective samples for 34 centres and 11 studies**
 - 1,099 samples (448 plasmas and 651 sera) repatriated, centralised and processed
- > **Gradual implementation of a new structure**
 - Preparations for the relocation of the LYSA-P platform to the Henri Mondor hospital in Créteil
 - Transition phase, with team departures and arrivals
- > **Continuation of structuring projects to optimise activities in collaboration with the other departments**

2024 PROSPECTS

- > **Promising forecasts**
 - Studies launched, new data exports and new data re-use studies (particularly as part of the BIDIFLY program)
- > **Restructuring continuation**
 - Effective relocation of LYSA-P to the Henri Mondor Hospital in Créteil, scheduled for the end of February 2024
 - New recruitments planned
 - Organisational projects
- > **Continuous enhancement of tools**

04 LYSA-IM PLATFORM ACTIVITY (IMAGING)

LYSA-IM saw increased activity in 2023 compared to 2022, with a 40% rise in DRS studies. This growth was driven by the integration of imaging projects in REALYSA and DESCAR-T registries and research programs like French Connect and BIDIFLY. The focus in 2024 will include continuing these research programs, developing new prognostic scores based on imaging data, and launching new clinical trials.



HIGHLIGHTS 2023

- > **Dynamic clinical activity**
 - 17 studies with centralization and review of medical imaging exams
 - 9 clinical study analyses with data from LYSA-IM
 - 14 valorization activities (6 publications + 8 presentations at conferences)
- > **Increasing activity in data reuse studies (DRS)**
 - 19 statistical analyses conducted on ERD from LYSA-IM
 - 24 valorization activities completed (7 publications + 17 presentations at conferences), including 2 multi-omics valorizations (imaging + biology)
- > **Work on several structuring projects**
 - Development of 7 new platforms for image centralization and review
 - New version of the GaelO platform (web platform for image centralization and review) in collaboration with Pixilib: better tracking, easier data reuse, new image processing tools (e.g., semi-automatic segmentation)
 - Production deployment of PACS (Picture Archiving Communication System) to archive all imaging data
 - Implementation of a quarterly meeting between the Biometry team and LYSA-IM to deepen joint reflection on the research of new prognostic scores based on imaging data

2024 PROSPECTS

- > **New challenges for clinical activity with the launch of new platforms**
 - Example of the MORNINGLYTE study: capitalizing on acquired experience to optimize the workflow of imaging and clinical data review (main criterion)
 - Example of the CARMOD study: demonstrating the virtuous contribution of the LYSA-IM platform work, as an imaging criterion from LYSA-IM DRS is among the inclusion criteria of the CARMOD clinical study (total metabolic tumor volume > 80ml)
- > **Promising perspectives for data reuse studies (DRS)**
 - Continuation of collaboration between the Biometry team and the LYSA-IM on methodology and research of new prognostic scores based on imaging data
 - Execution of the group's research programs including BIDIFLY, TEP-CART, and French Connect
 - "Data Warehouse" structuring project by the LYSARC





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