



IACH

CeVi_CAR-T : a unique biological collection to support and accelerate research in the field of CAR-T cells therapy for lymphoma

Juliette Canard¹, Emilie Robert¹, Claire Fontenille¹, Régis Peffault de Latour¹, Jean-Hugues Dalle¹, Boris Calmels¹, Emeline Mollaret², Delphine Sondaz², Emmanuel Gomez², Bertrand Nadel², Thierry Fest³, Loïc Ysebaert⁴, Catherine Thieblemont⁵, Cristina Castilla-Llorente⁶, Franck Morschhauser⁷, Steven Legouill⁸, Corinne Haïoun⁹, Emmanuel Bachy¹⁰, Guillaume Cartron¹¹, Roch Houot¹²

¹Association CRYOSTEM, Marseille, France, ²Institut Carnot CALYM, Lyon, France, ³Department of Hematology, CHU Rennes, Rennes, France, ⁴Department of Hematology, Institut Universitaire Cancérologie Toulouse-Oncopôle, Toulouse, France, ⁵Hematology Department, Hospital Saint-Louis, Paris, France, ⁶Department of Hematology, Gustave Roussy, Villejuif, France, ⁷Department of Hematology, CHRU Lille, Lille, France, ⁸Clinical Hematology, Nantes University Hospital, Nantes, France, ⁹Lymphoid Malignancies Unit, Henri Mondor University Hospital, APHP, Créteil, France, ¹⁰Department of Hematology, Centre Hospitalier Lyon Sud, Hospices Civils de Lyon, Pierre Bénite, France, ¹¹Department of Hematology, CHU St. Eloi, Montpellier, France, ¹²Department of Hematology, CHU Rennes Pontchaillou, Rennes, France

INTRODUCTION

Chimeric Antigen Receptor (CAR) T cells drugs are revolutionizing therapeutic strategies for relapsed or refractory lymphomas. However, CAR-T cells efficacy and resistance mechanisms remain to be explored to optimize the line-up strategies of CAR-T therapies. This justifies the set-up of a dynamic and adaptive collection of well-annotated biological samples from patients treated with CAR-T cells with the objective of providing epidemiological, clinical and biological information for research programs.

In this context, the Carnot-labeled academic consortium CALYM (www.experts-recherche-lymphome.org), bringing together LYSA, LYSARC and 18 research entities, dedicated to research in the field of lymphoma which have set up the first collection of viable cells from lymphoma patients (CeVi_Collection) and the biobanking network CRYOSTEM (www.cryostem.org), which has implemented the first European biological resources collection dedicated to hematopoietic stem cell transplantation, have combined their expertise to create a biocollection of lymphoma patients receiving CAR-T cells, named the CeVi_CAR-T Collection.

RESULTS

1- CRYOSTEM / CALYM networks structuring and functioning

The collaboration between CRYOSTEM and CALYM translates into the superposition of both networks bringing together hematological clinical units and biological resources centers (BRCs) resulting in patients' inclusion, samples collection-process-and storage. 6 centers have all the prerequisites and are involved in the process.

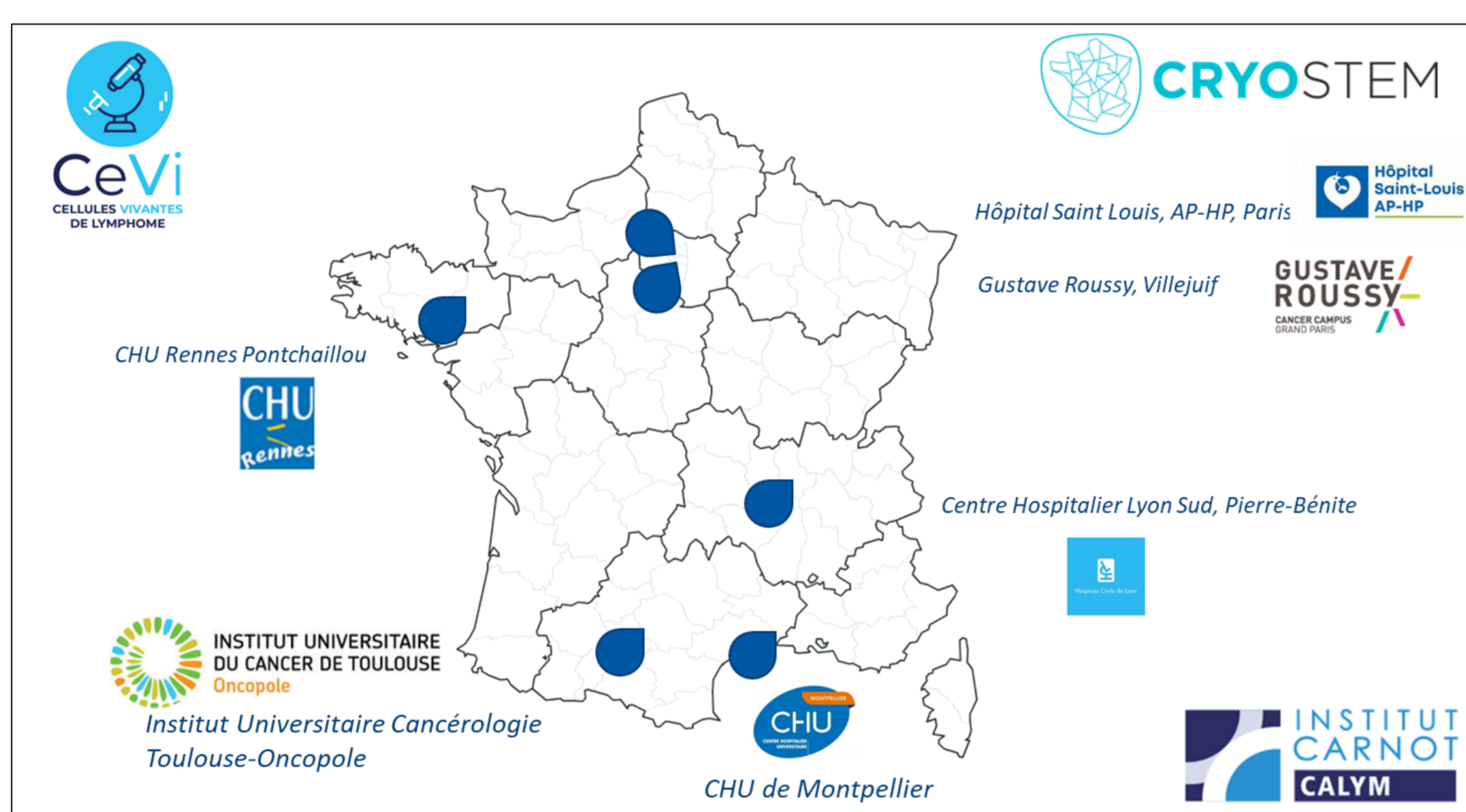


Fig. 1: CeVi_CAR-T network

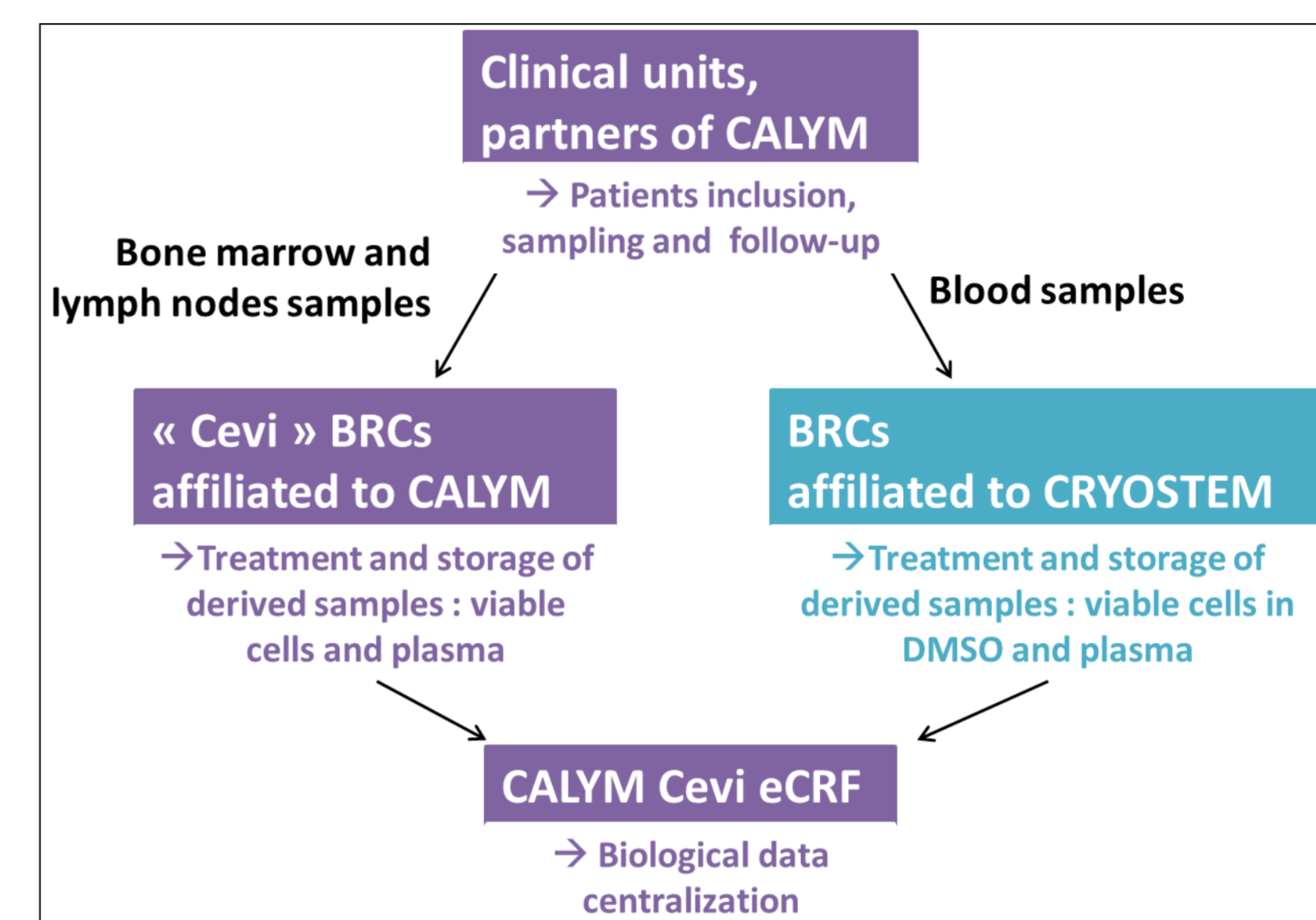
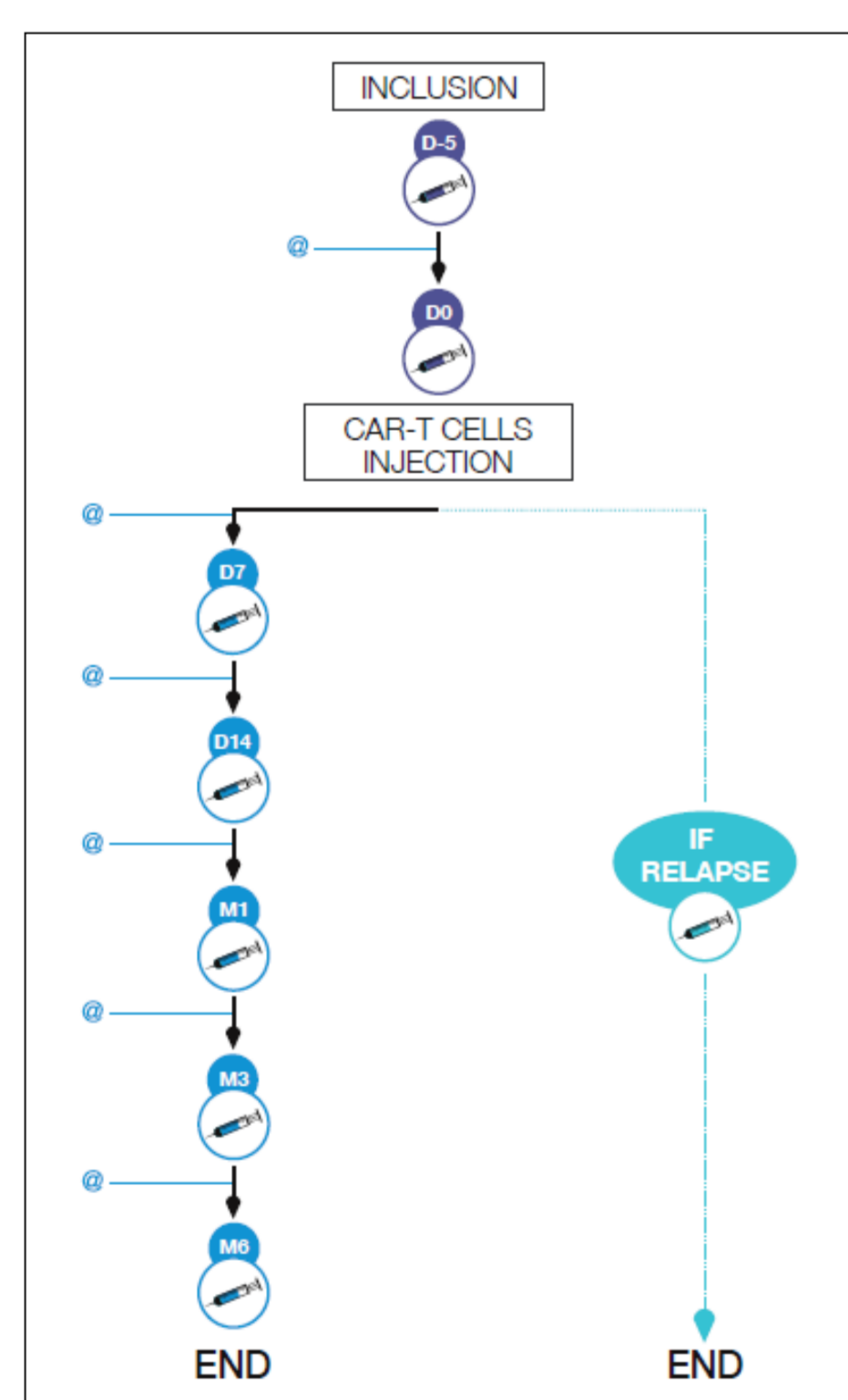


Fig. 2: Organization of the CeVi_CAR-T collection's sampling process

Any patient suffering from lymphoma, justifying a CAR-T cells treatment, is eligible to be included in the protocol. Several types of samples are derived pre- and post-CAR-T cells administration, in line with a specific schedule. Dedicated and harmonized procedures and protocols have been established as part of the collaboration between CRYOSTEM and CALYM regarding the blood sampling collection. The biological samples collection is centralized in the CALYM database. Associated clinical data are extracted from the LYSARC CAR-T registry (DESCAR-T) and correlated with the EBMT registry ID (ProMise).

2- CeVi_CAR-T collection achievements

Regarding the kinetics, 8 blood sampling points are scheduled, from the apheresis up to 6 months post-injection, including the relapse onset.



DX: X days post-injection of CAR-T cells
MX: X months post-injection of CAR-T cells
@: Email alert
D-5: Start of conditioning chemo
D0: CAR-T cells injection

Fig. 3: CeVi_CAR-T Collection blood sampling

To date, 6 centers are opened to inclusions: CHU Rennes Pontchaillou, CHU Montpellier, Centre Hospitalier Lyon Sud, IUC-Toulouse, Gustave Roussy and Hôpital Saint-Louis Paris.

The collection started with the inclusion of the 1st patient on March 11th, 2020. In less than 3 years, 184 patients were included in the CeVi_CAR-T protocol and sampled, corresponding to 950 blood samples (as of August 1st, 2022).

In total, 4 666 plasma and 1 712 viable cells in DMSO aliquots have been generated and are available for research.

84% of the blood samples have been treated in less than 4 hours with a median delay of treatment estimated at 2 h 20 minutes, thus limiting the proteins damaging in plasma samples.

Inclusion criteria are dynamically reviewed according to the authorizations in use for CAR-T therapies in French hospitals. Overall, 145 Diffuse Large B Cell Lymphoma, 30 Mantle Cell Lymphoma, and 9 Follicular Lymphoma were included. CeVi_CAR-T collection contains lymph nodes from 28 patients, associated with blood samples derived from viable cell aliquots and plasma, and bone marrow samples.

A first project using 184 plasma aliquots has highlighted an appropriate sample quality for metabolic analyses and a high synergy between CeVi and DESCAR-T registries.

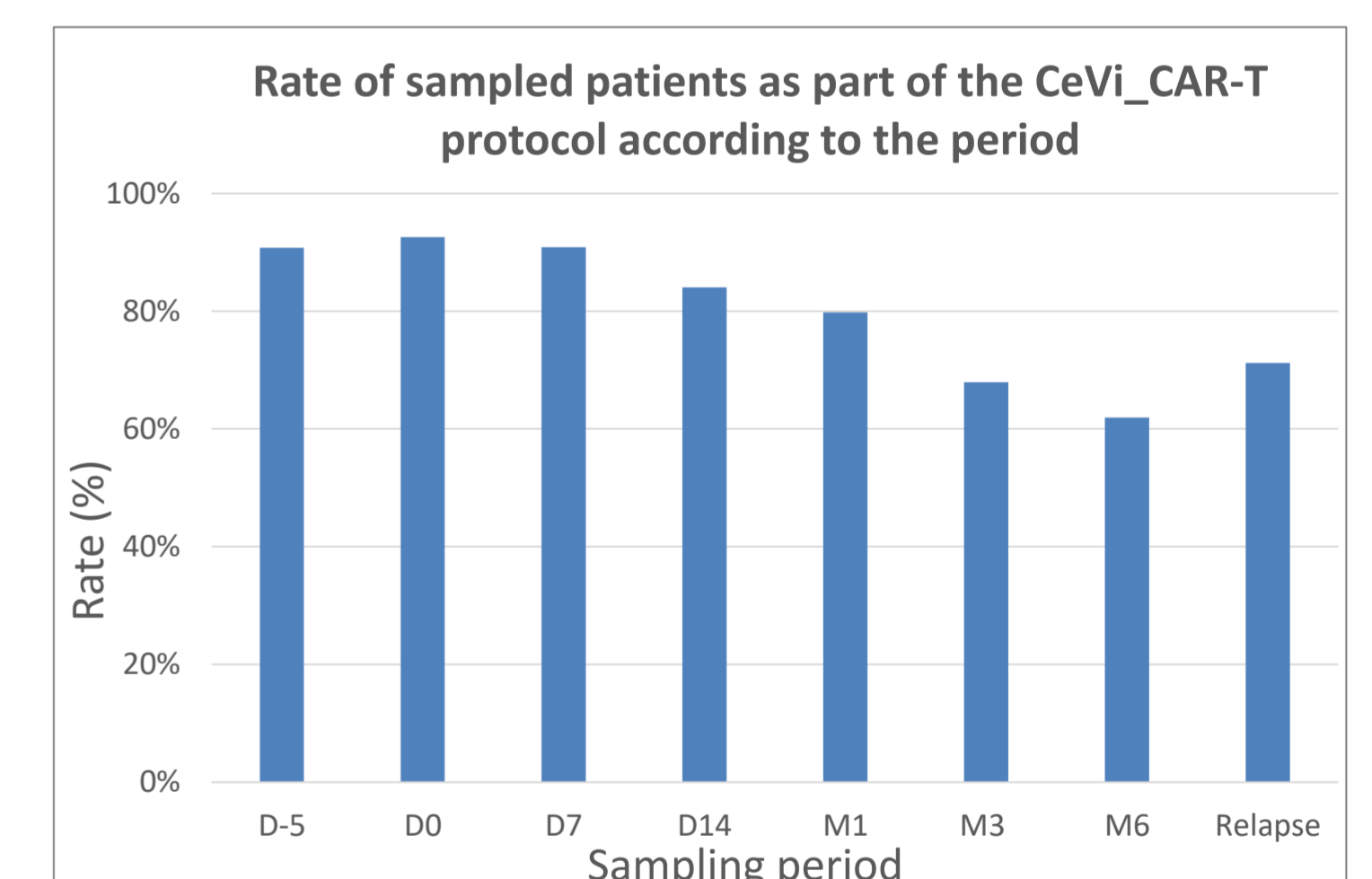


Fig. 4: Rate of sampled patients as part of the CeVi_CAR-T protocol according to the period (as of August 1st, 2022)

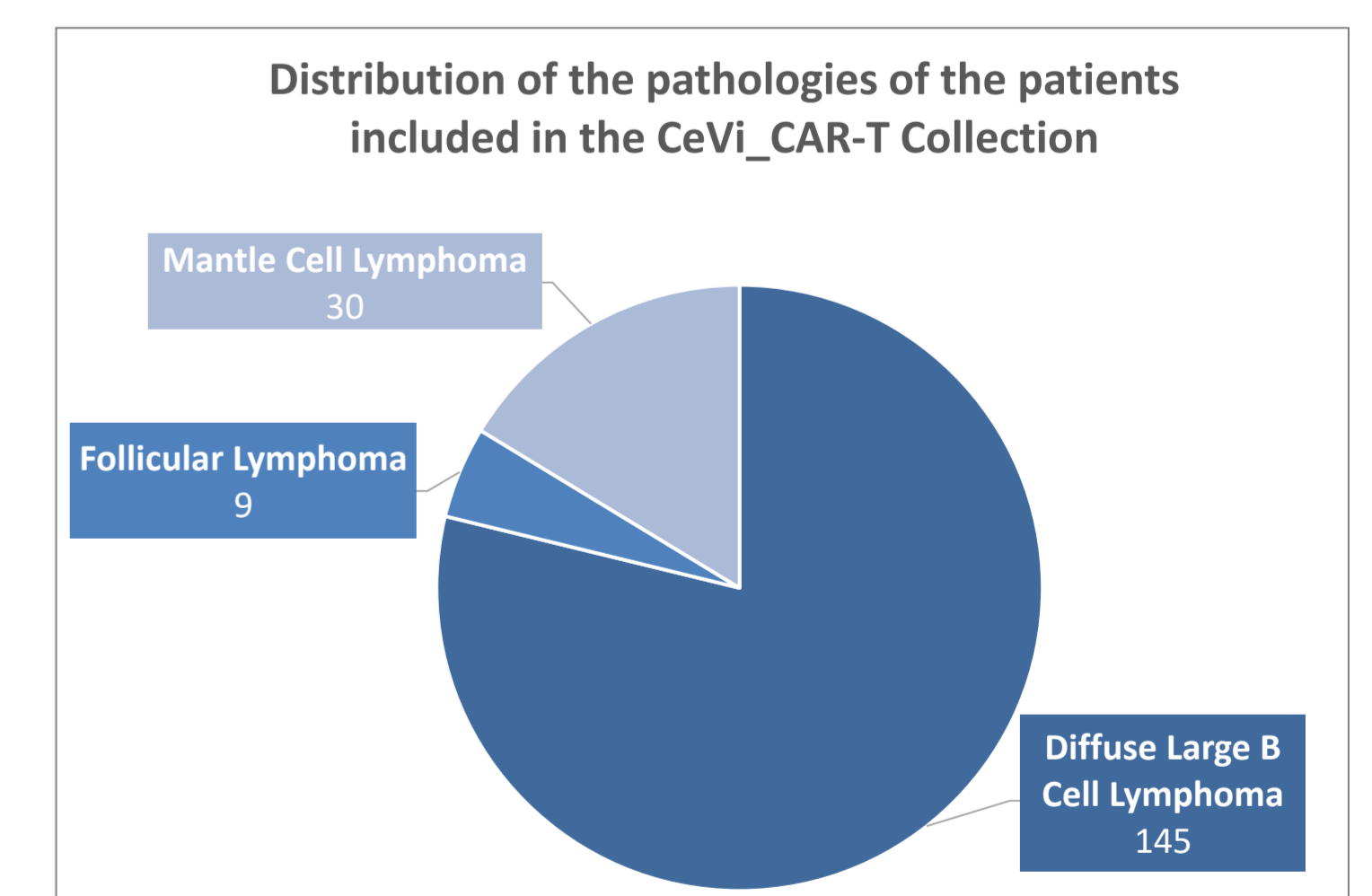


Fig. 5: Distribution of the pathologies of the patients included in the CeVi_CAR-T Collection (as of August 1st, 2022)

CONCLUSION

The processes are continuously improved to optimize the network functioning and the collection rates. With the creation of the first biobank focused on lymphoma patients treated with CAR-T cells, CALYM-CRYOSTEM collaboration allows the access to raw material and CAR-T cells treatments would be positively impacted by consolidating knowledge on the in vivo effects of this recent cell-based therapeutic approach. The next step aims at enriching the current collection including stool and urine samples of interest in the context of CAR-T cells to answer other scientific approaches. This collection CeVi_CAR-T is meeting with a real success and full support from patients and physicians.

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www.iachlive.cme-congresses.com

contact@cryostem.org
contact@calym.fr