



IACH

CeVi_CAR-T : a unique biological resource to speed-up research in the field of CAR-T cells therapy for lymphoma *CAR-T cells for leukemia, lymphoma and myeloma*

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INTRODUCTION

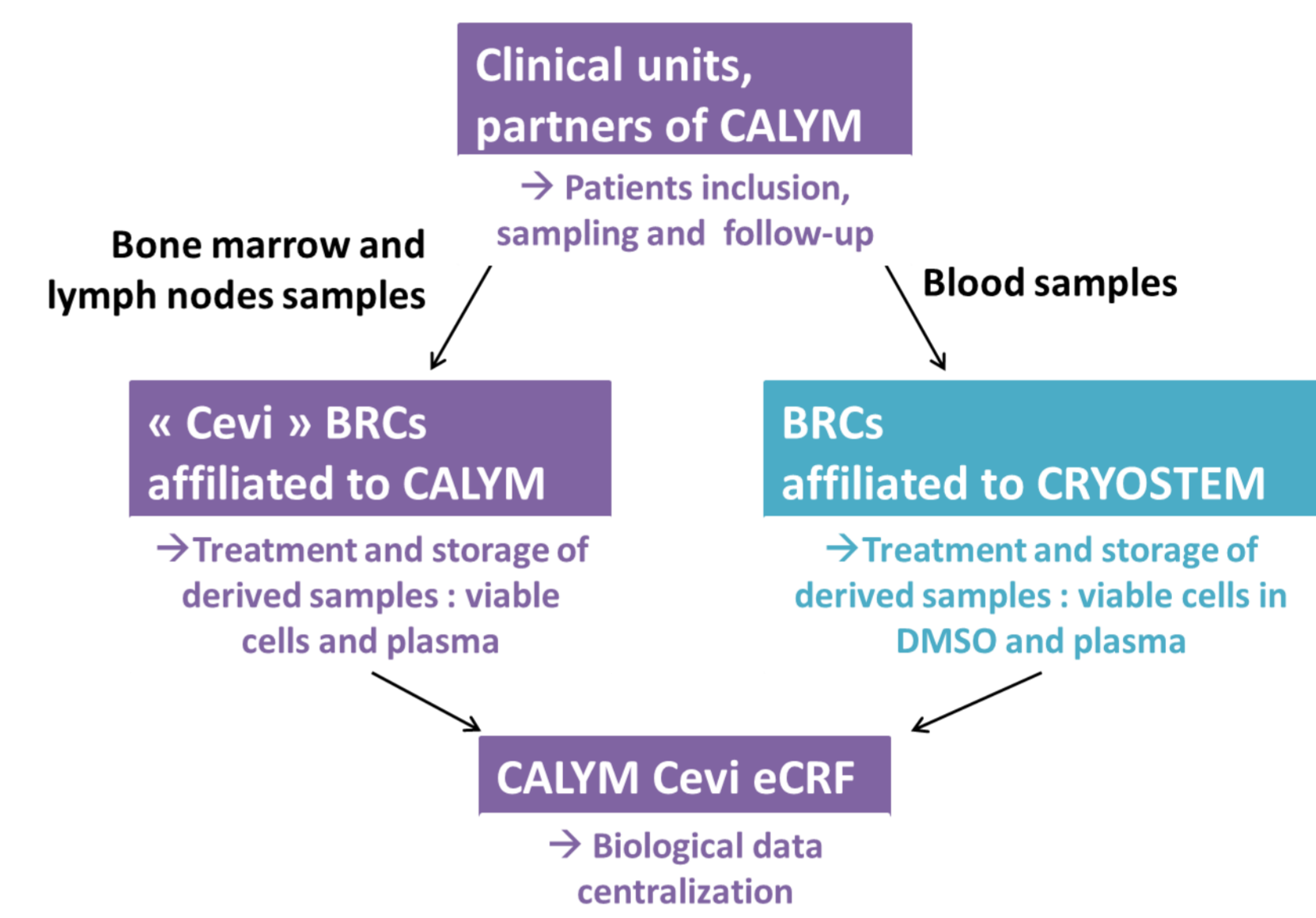
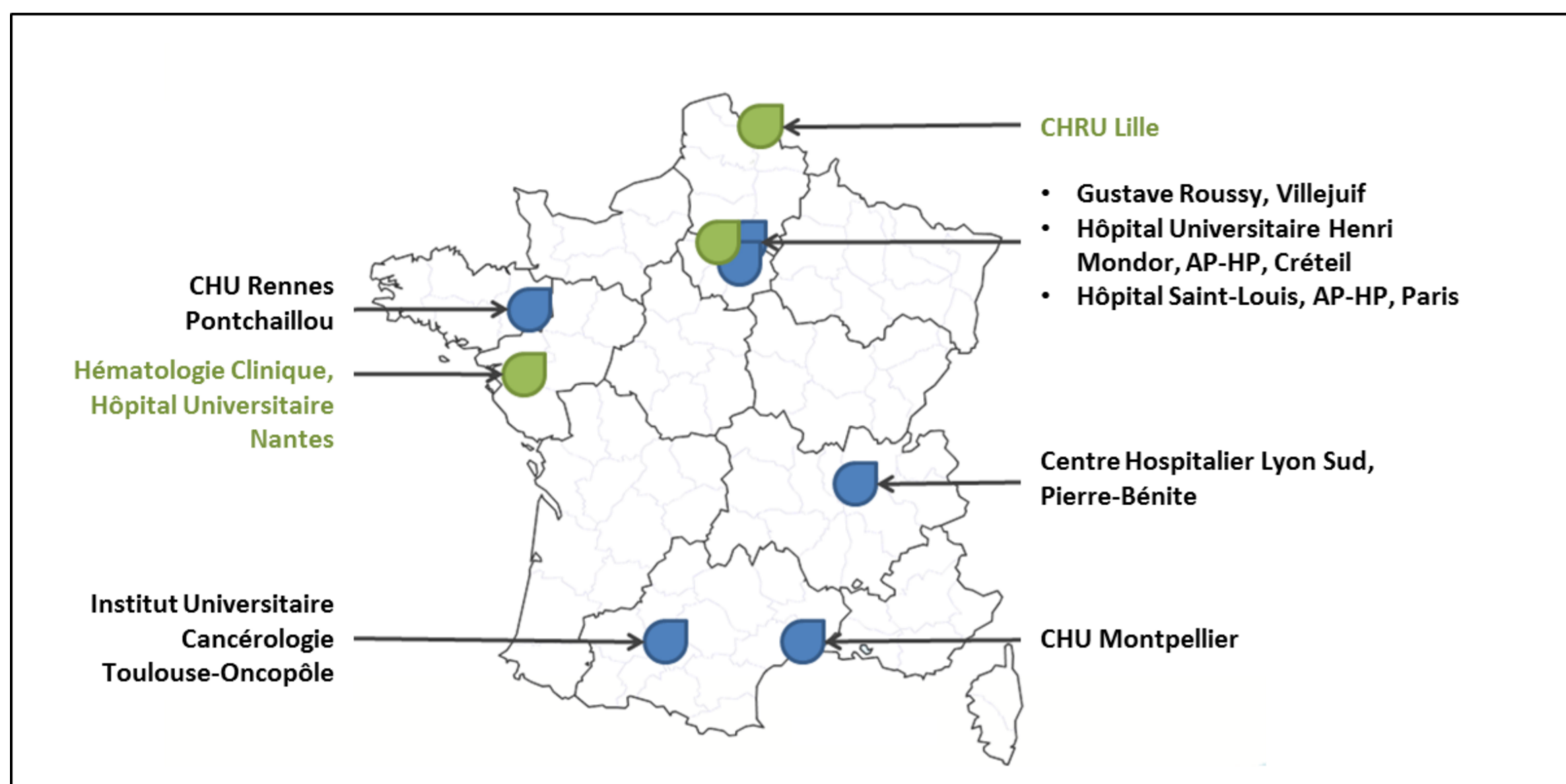
While **Chimeric Antigen Receptor (CAR) T cells therapies** are a promising way to treat relapsed/refractory hematologic cancers, authorities are facing concrete issues regarding not only economic aspects but also **efficiency and adverse effects evaluation** of these new therapeutic agents. Currently, the number of patients with a CAR-T cells indication is increasing, as well as the number of hematological cancers likely to be treated. Consequently, the constitution of **nationwide collections of biological resources** is warranted to **supply scientific projects** to monitor CAR-T cells treatments and to **improve the understanding of the underlying biological mechanisms**.

In this context, a biobanking initiative has resulted from the collaboration of two French consortia : **CALYM** (www.experts-recherche-lymphome.org), a Carnot labelled academic consortium, including LYSA, LYSARC and 18 research entities, devoted to research in the field of lymphoma and **CRYOSTEM** (www.cryostem.org), a collaborative biobanking network. After demonstrating their ability to set up the first collection of viable cells from lymphoma patients (CeVi_Collection) and the first European collection of biological resources dedicated to Hematopoietic Stem Cell Transplantation respectively, CRYOSTEM and CALYM joined their expertise to constitute a biocollection from lymphoma patients receiving CAR-T cells, named **CeVi_CAR-T Collection**.

RESULTS

1- CRYOSTEM / CALYM Networks Structuring and Functioning

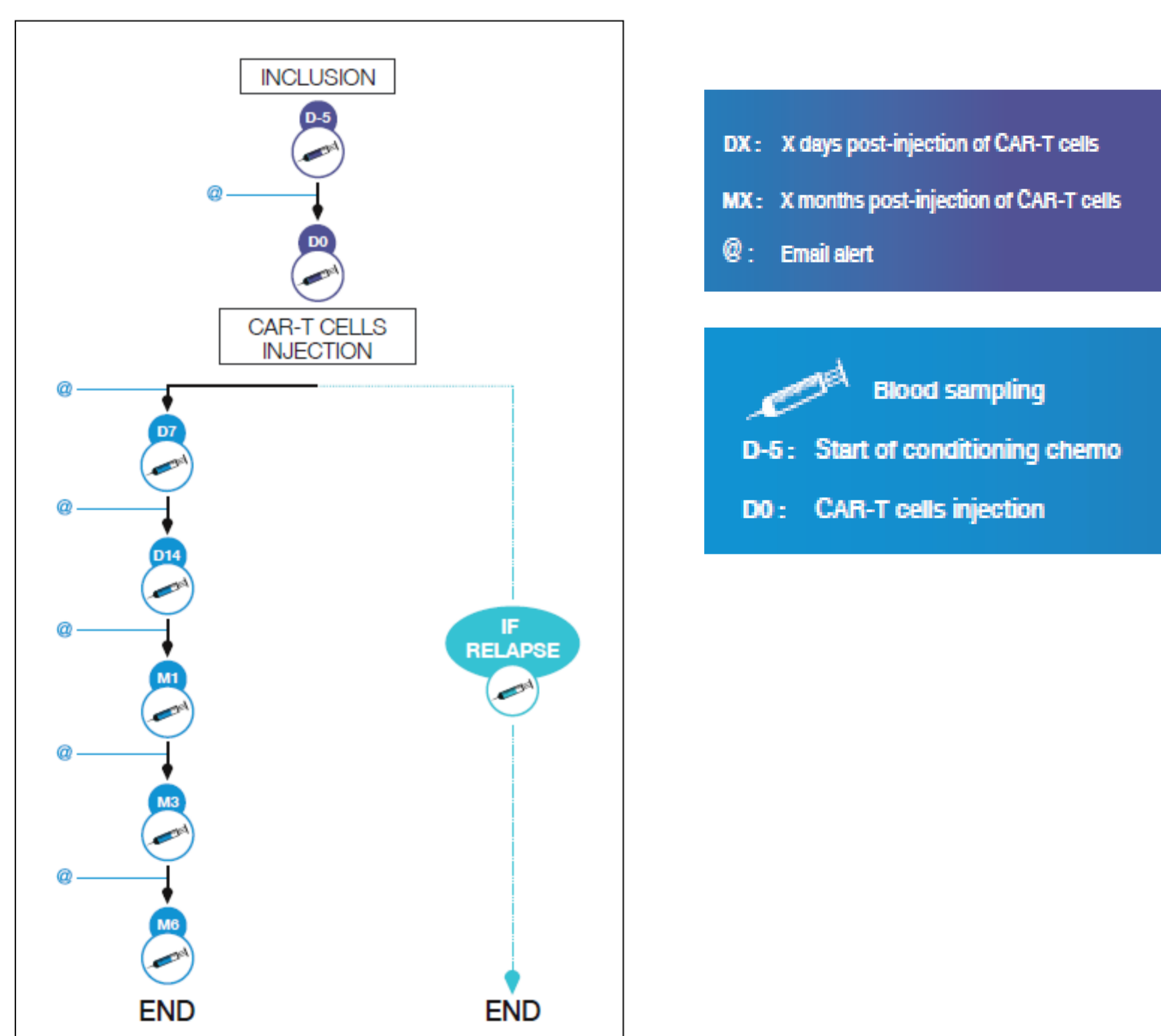
The collaboration between CRYOSTEM and CALYM translates into the **superposition of both networks bringing together hematological clinical units and biological resources centers (BRCs)** collaborating in including patients, collecting and processing samples. 9 centers have been identified : 6 centers have all the prerequisites available to be opened to the process ; 3 additional centers are ongoing qualification.



Any patient suffering from lymphoma, justifying a CAR-T cells treatment, is eligible to be included in the protocol. Several type 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 planned, from the apheresis up to 6 months post-injection, including the relapse onset.

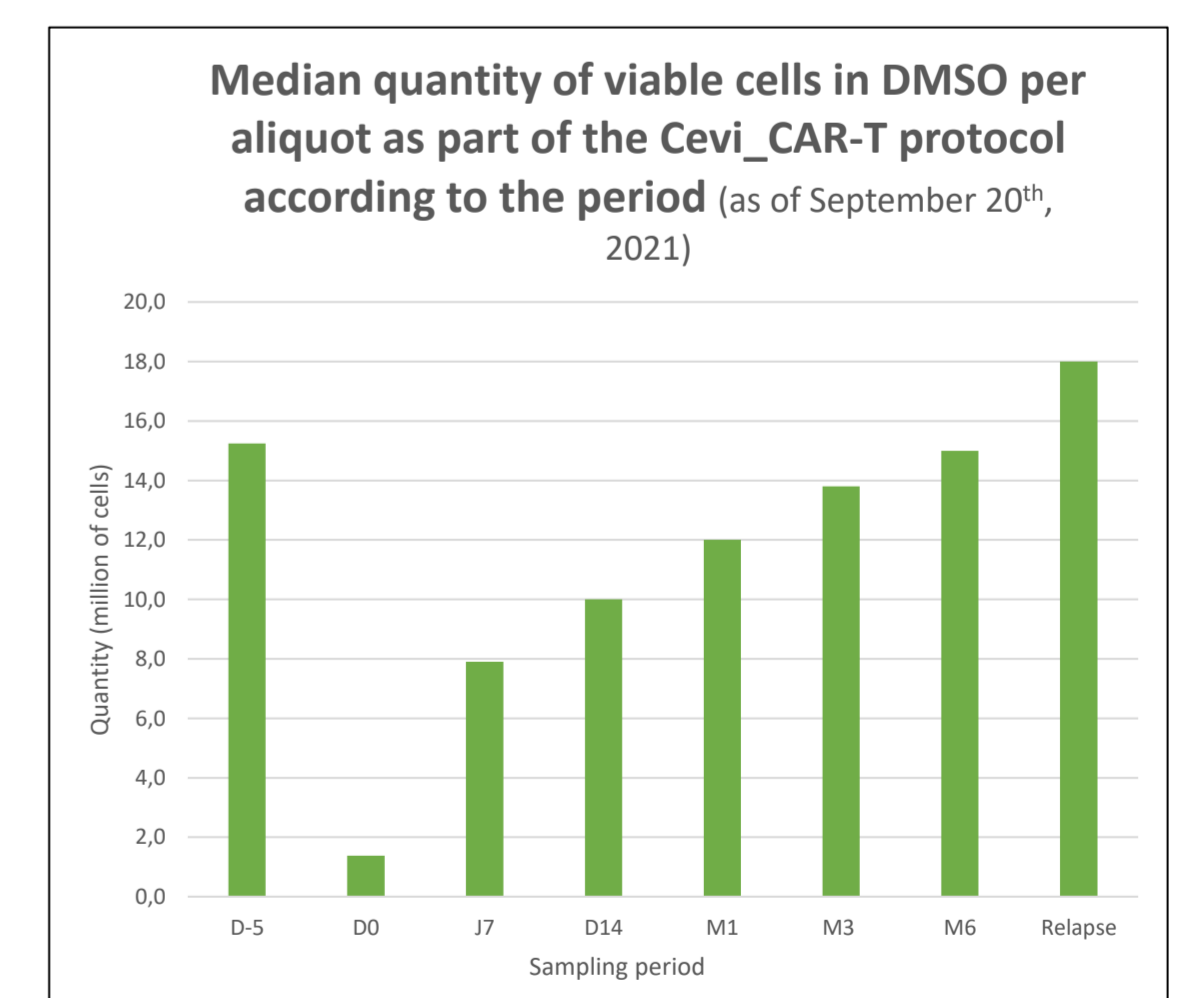
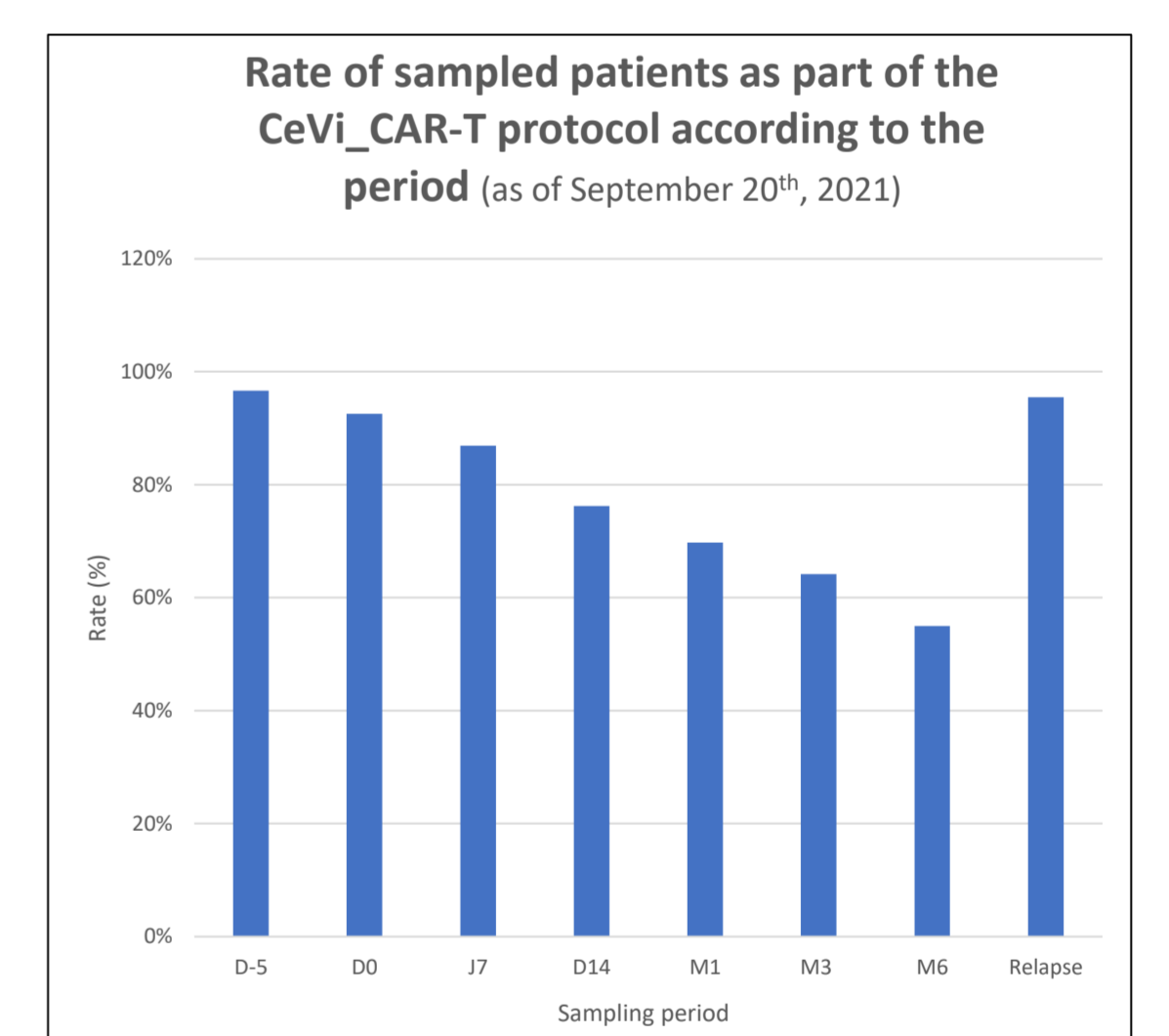


The collection started with a 4-month pilot phase launched in **CHU Rennes Pontchaillou**, including the **1st patient** on March 11th, 2020. To date, **4 additional centers** are now opened to inclusions : CHU Montpellier, Centre Hospitalier Lyon Sud, IUC-Toulouse, Institut Gustave Roussy.

In nearly 18 months, **148 patients** have been included in the CeVi_CAR-T protocol and sampled (as of September 20th, 2021), corresponding to **717 blood samples**.

21 patients were sampled at the time of their relapse. In total, **3 545 aliquots of plasma** and **1 296 aliquots of viable cells in DMSO** have been generated and are available for research.

85,5% of the blood samples have been treated in **less than 4 hours** with a **median delay of treatment** estimated at **3 h 03 minutes**, thus limiting the proteins damaging in plasma samples.



CONCLUSION

The pilot phase in Rennes has demonstrated the **efficiency of the logistics** implemented in terms of **inclusion, collecting rate and delay of treatment**, enabling to open the other centers from June 2020. The processes are continuously improved to increase the network functioning and to optimize the collection rates.

The next step aims at **enriching the current collection** 1) **pairing blood samples with lymph node samples**, considering their key role in the antitumor activity and resistance to CAR-T, 2) **including stool and urine samples** of interest in the context of CAR-T to answer other scientific approaches.

With the creation of the first biobank focused on CAR-T cells treated lymphoma patients, CALYM-CRYOSTEM collaboration opens new research perspectives by providing access to raw material with the objective to improve understanding of CAR-T cells treatments and to consolidate current knowledge on the **in vivo effects** of this recent cell-based therapeutic approach. This collection CeVi_CAR-T is meeting with **a real success and full support from patients and physicians**.