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A French biobanking initiative intended to monitor CAR-T cells administration in the lymphoma field

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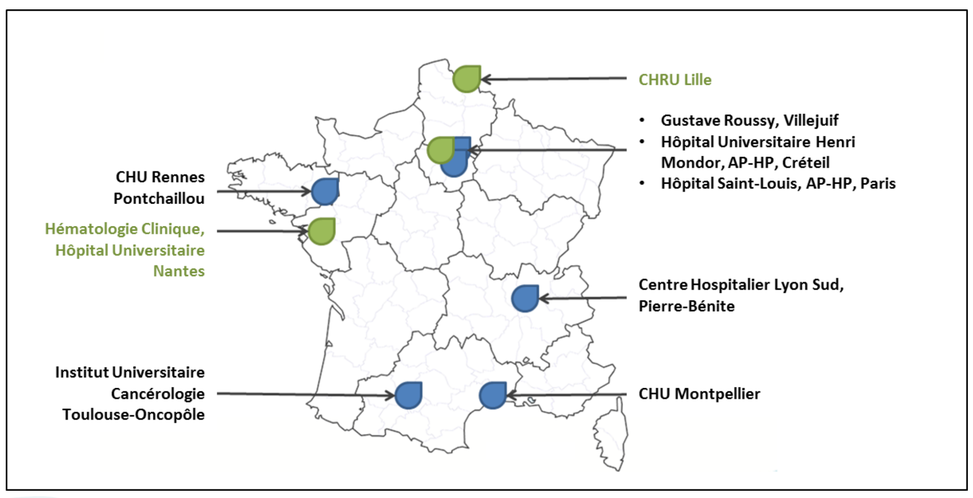
1 Introduction

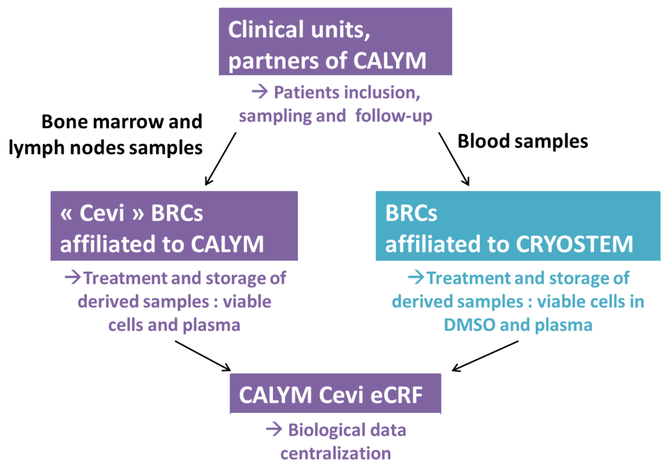
While **Chimeric Antigen Receptor (CAR) T cells therapies** are a promising way to treat relapsed/refractory hematologic cancers, authorities are facing concrete issues regarding not only economic aspects but also **efficiency and adverse effects evaluation** of these new therapeutic agents. Currently, 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.***

2 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. Currently, 9 centers have been identified : 6 centers have all the prerequisites available to be opened to the process ; 3 additional centers are ongoing qualification.



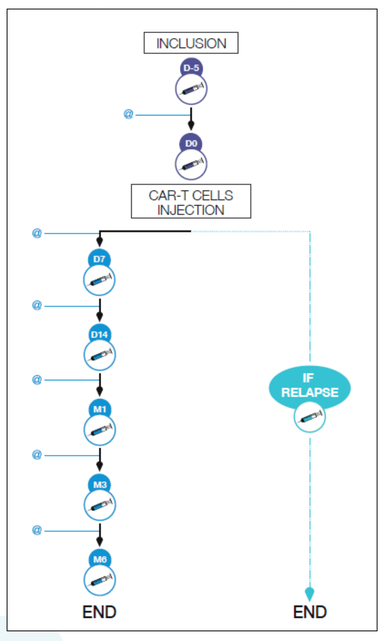


Any patient suffering from lymphoma, justifying a CAR-T cells treatment, is eligible to be included in the protocol. Several type of samples are derived pre- and post-CAR-T cells administration, in line with a specific schedule. **Dedicated and harmonized procedures and protocols** have been established 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).

3 First achievements of the CeVi_CAR-T collection

In less than one year, CRYOSTEM and CALYM have succeeded in designing all the specifications needed for the ancillary study : **practices harmonization and standardization**, establishment of the most suitable **sampling kinetics** integrated to patients' health care pathway, **estimation of the collecting rate** of each sampling point according the treatment failure and the mortality rate and finally **opening of 5 out of the 9 centers** identified.

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



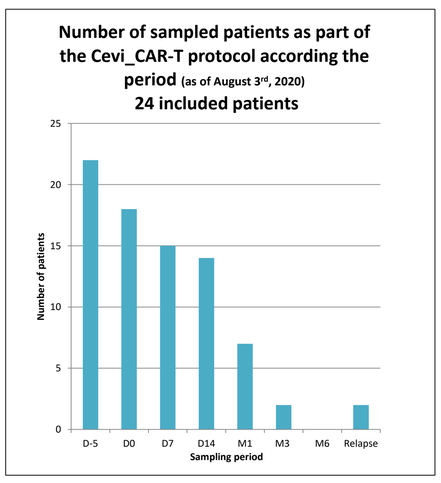
Blood sampling
D-5 : Start of conditioning chemo
D0 : CAR-T cells injection

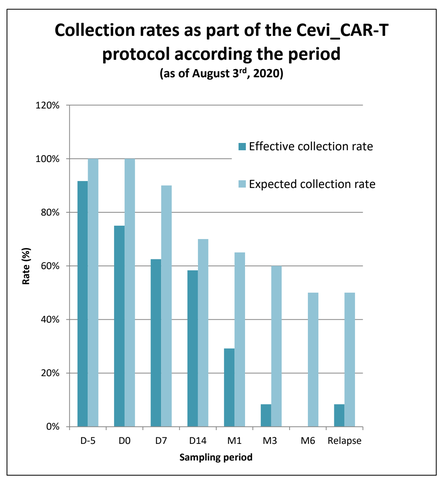
DX : X days post-injection of CAR-T cells
MX : X months post-injection of CAR-T cells
@ : Email alert

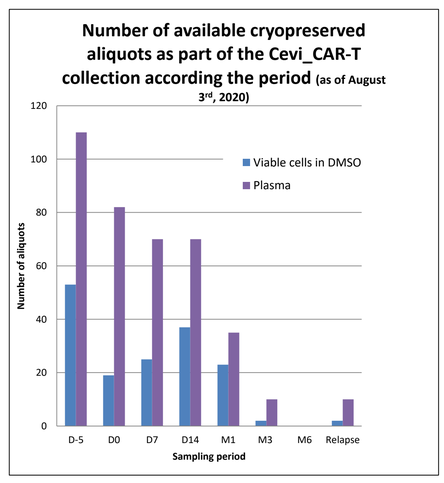
The collection started with a 4-month pilot phase launched in **CHU Rennes Pontchaillou**, including the **1st patient** on January 20th, 2020. To date, 4 additional centers are now opened to inclusions : IUC-Toulouse, CHU Montpellier, Centre Hospitalier Lyon Sud and Gustave Roussy.

In only six months, **24 patients** have been included in the CeVi_CAR-T protocol and sampled (as of August 3, 2020), corresponding to **80 blood samples**.
2 patients were sampled at the time of their relapse. Nearly **158** samples (plasma and viable cells in DMSO) have been generated and are available for research.

54% of the blood samples have ben treated **in less than 4 hours** with a **median delay of treatment** estimated at **3 h 50 minutes**, thus limiting the proteins damaging in plasma samples.







4 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. Some issues are still raised and 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 with stools and urines samples**, to answer other scientific approaches. However, this diversification needs a preliminary **standardization and harmonization phase** to address specific items regarding collection, treatment, aliquoting and storage technics, before implementing it for the CeVi_CAR-T collection.

This new biological collection CeVi_CAR-T is meeting with a **real success and full support** from **patients and physicians**, 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 .

CALYM and CRYOSTEM intend to make this project study **a proof of concept** for expanding ancillary studies in the field of CAR-T cells therapies, whatever the initial hematological disease treated.

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