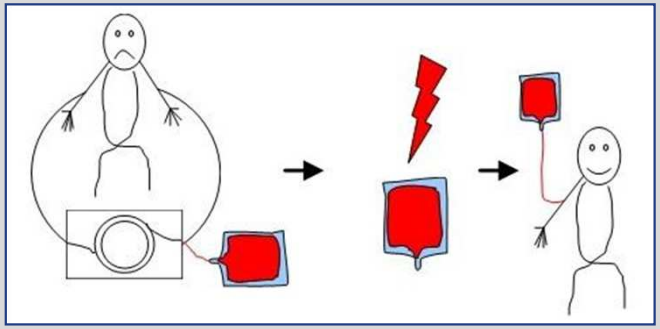
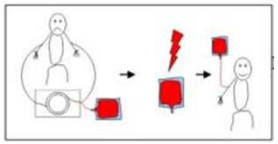
CRYO - Extracorporeal Photochemotherapy

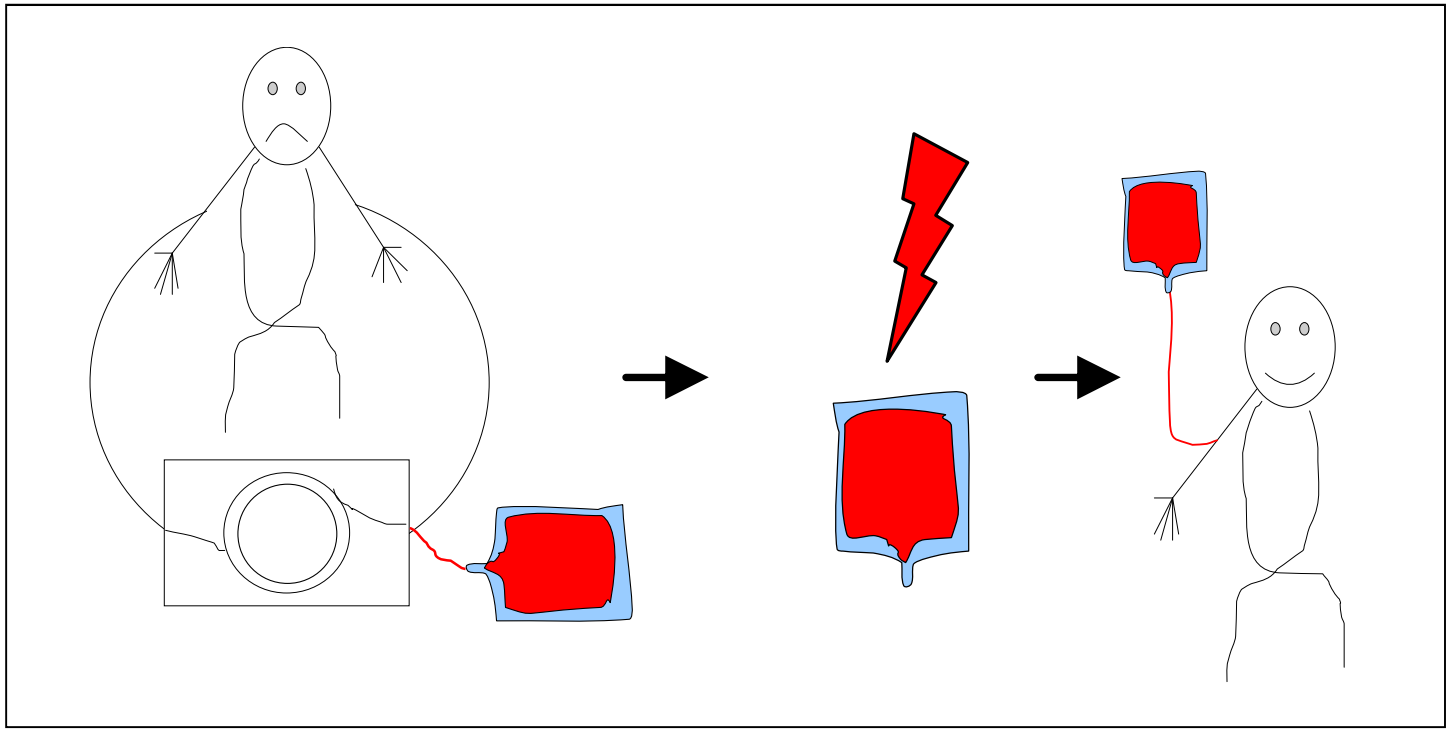
Justyna Kanold

Sérvice d'hemato-oncologie pédiatrique
CHU
Unité CRECHE INSERM CIC1405
Clermont Ferrand, France

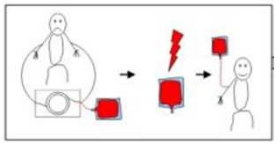




Extracorporeal Photochemotherapy



Collection des CMN ➔ **Photosensibilisation (psoralène)➔ Irradiation (UVA:2 J/cm^2)** ➔Re-injection/«transfusion»



Why ECP (in paediatric practice) is difficult?

- Thin (damaged) veins

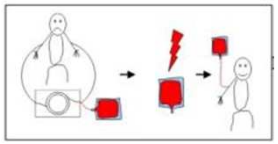
- Small body weight and small whole blood volume
- Relatively large extracorporeal volume of cell separators

↓

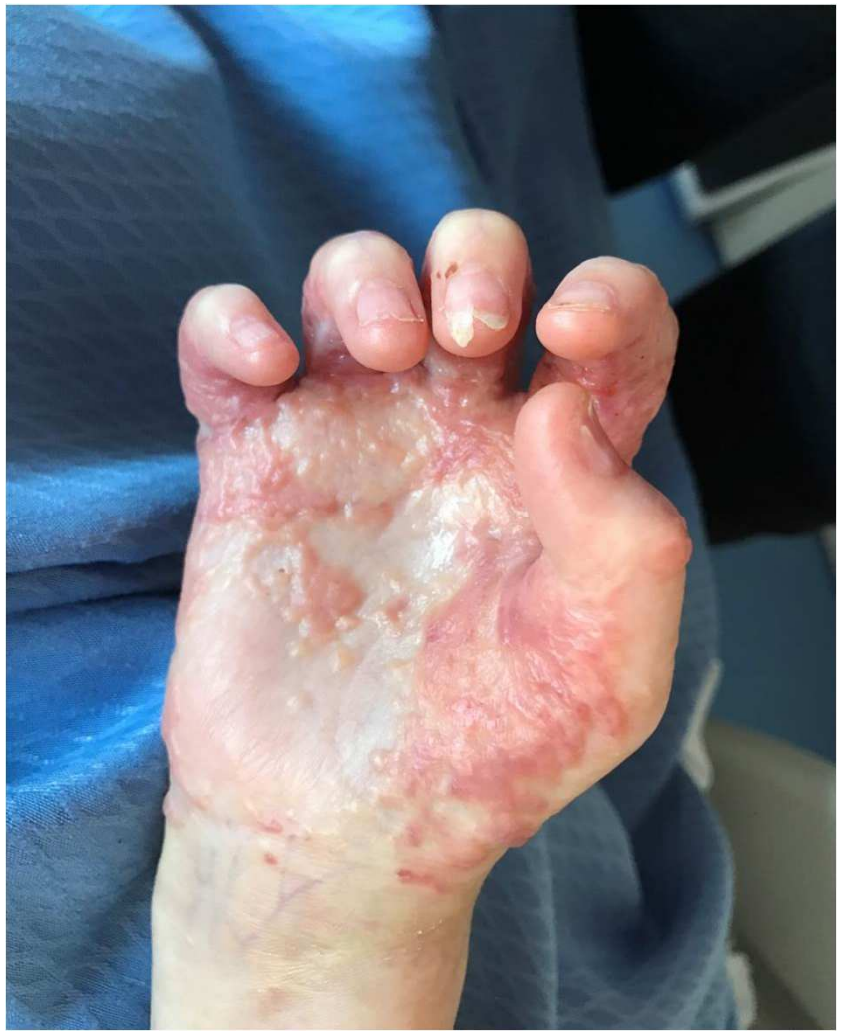
- Metabolic and hematologic problems

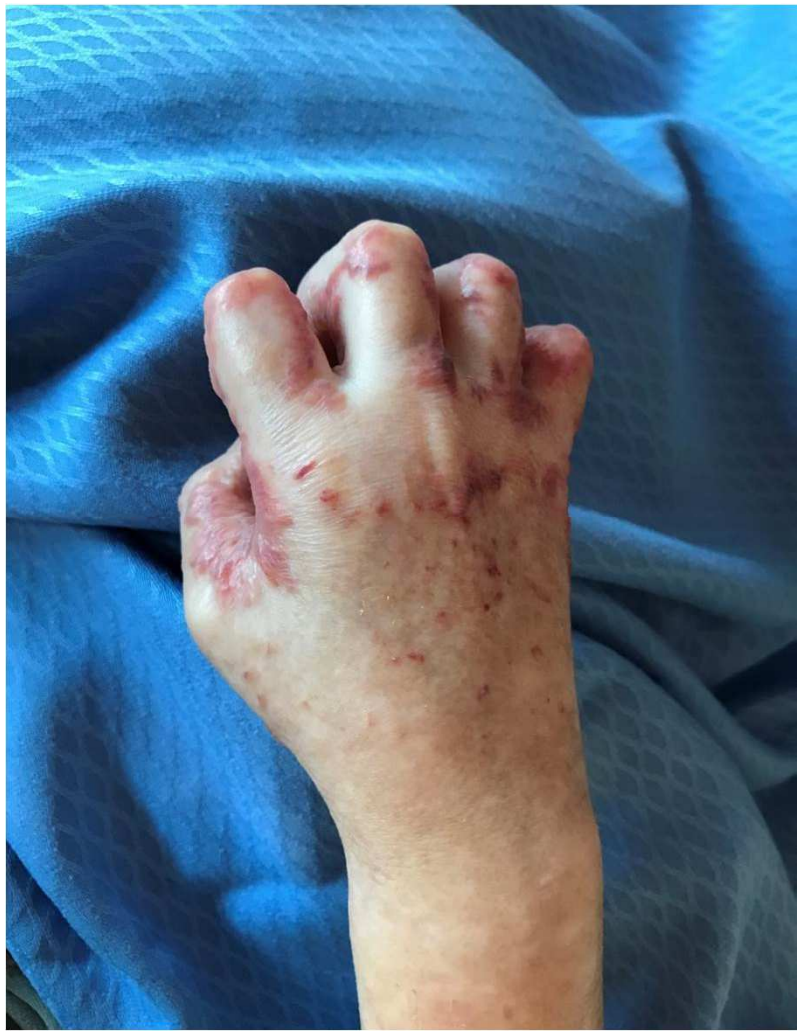
- Psychological tolerance

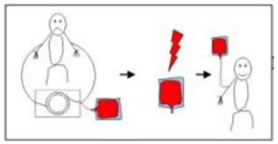
Needs of a sophisticated training in (paediatric) apheresis

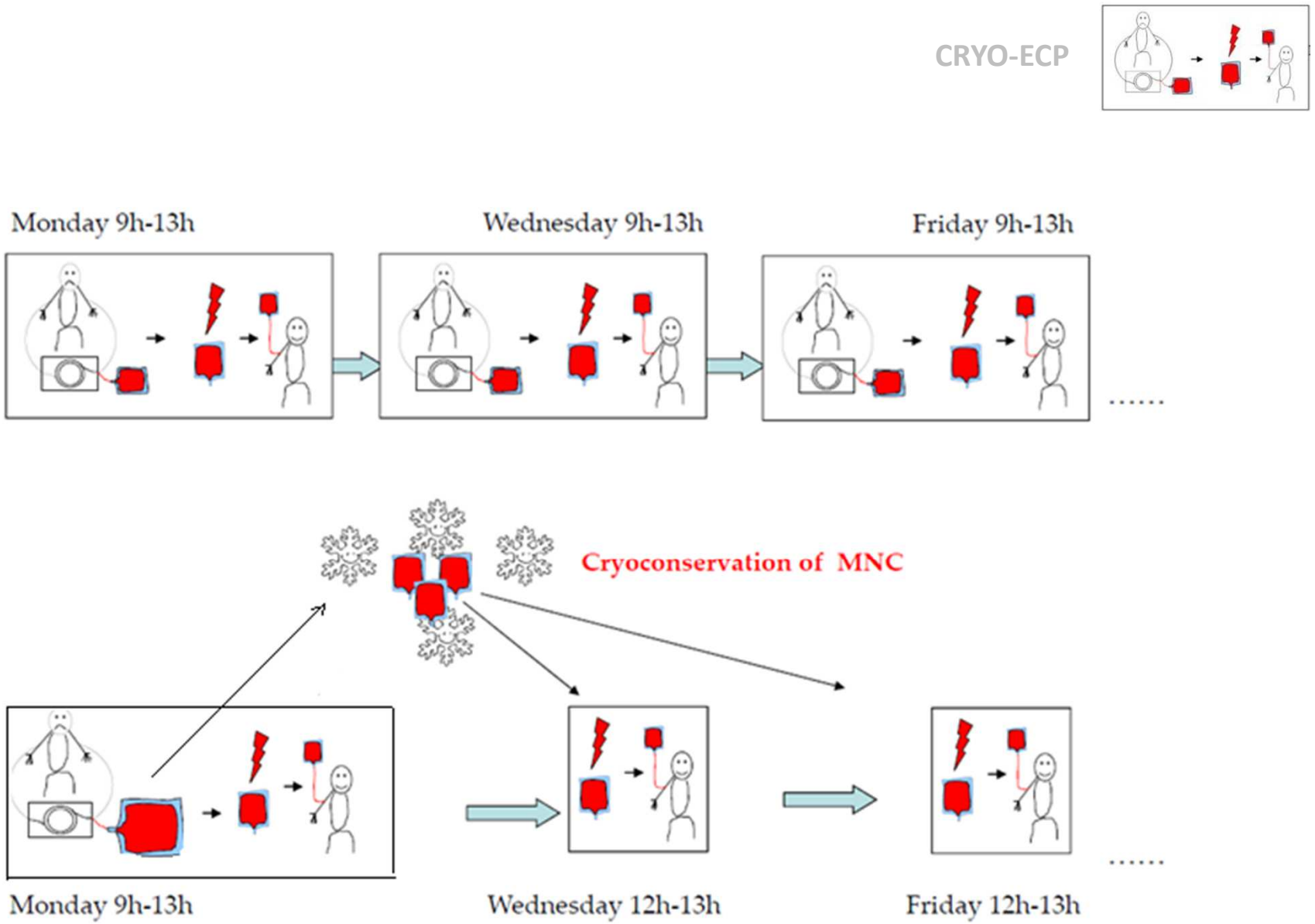


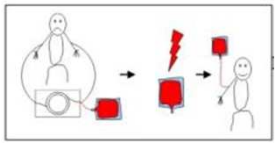
Why ECP (in paediatric practice) is difficult?







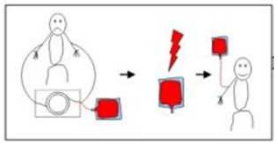

Monday 9h-13h
Wednesday 9h-13h
Friday 9h-13h
.....
Cryoconservation of MNC
Monday 9h-13h
Wednesday 12h-13h
Friday 12h-13h
.....



What will be the advantages of CRYO ECP ?

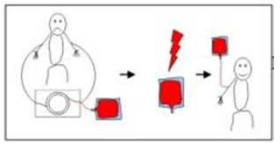
Reduced the number of apheresis while maintaining the rate of reinjections

- Improve treatment conditions
- Expand ECP indications
- Treat patients in centers not equipped for ECP
- Standardize cell product



CRYO ECP - results

Avant 2009 : 3 enfants (Clermont)
2009 – 2015 : 20 pts (Nancy, Clermont)
2016 – 2017: ?
2018 – 2019 : 11 pts (Clermont)



CRYO ECP - results

TRANSPLANTATION AND CELLULAR ENGINEERING

Use of cryopreserved autologous cells for extracorporeal photochemotherapy: clinical applications

Etienne Merlin, Florence Jacomet, Michel D'Incan, Pascale Halle, Marc Berger, Virginie Gandemer, Chirstophe Piguet, Pierre Souteyrand, François Deméocq, and Justyna Kanold

TRANSFUSION Volume 51, June 2011

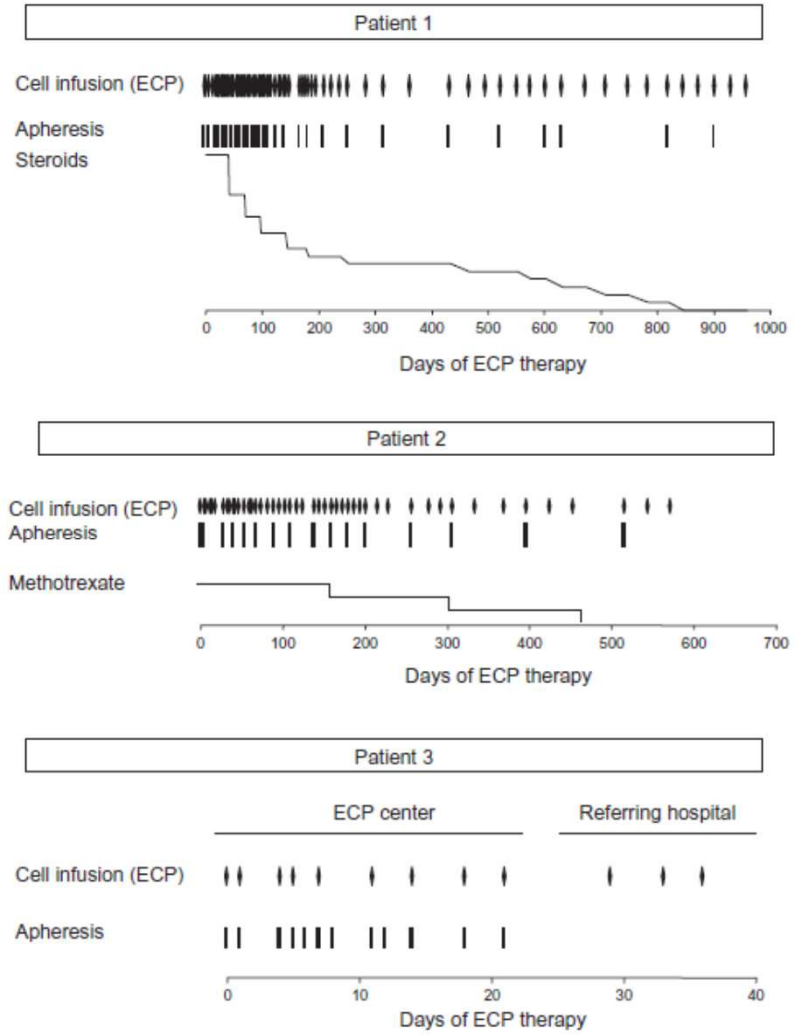
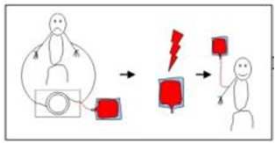


Fig. 1. Scheme illustrating cryo-ECP.



CRYO ECP - results

Bone Marrow Transplantation (2017) 52, 167–170

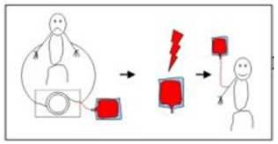
www.nature.com/bmt

LETTER TO THE EDITOR

Cryopreservation as a way to maintain extracorporeal photopheresis regimen for GvHD treatment while circumventing patient temporary inability to undergo apheresis

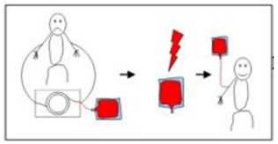
C Pochon[1], L Reppel[2], P Halle[3], A Zang[4], L Clément[1], D Michel[1], A Perrot[1], G Roth-Guépin[1], M Detrait[1], J Kanold[3,5], N Rouel[5], B Donzé[6], V Décot[2], S Mathieu-Nafissi[6], E Merlin[5] and D Bensoussan[2]

From 2009 to 2015, 231 'cryo-ECP' (including 83 in Nancy Hospital and 148 in CF Hospital) were performed in 20 patients including 10 males. Thirteen patients (8 children) were treated for acute GvHD (Patients 1–13). Seven patients (5 children) were treated for chronic GvHD (patients 14–20, Table 1). Skin was involved in 15 patients.



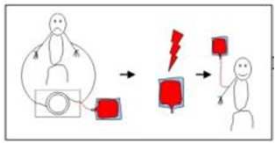
CRYO ECP - results

	Patients	Aphérèses	Reinjections CRYO
Rejet pulmonaire	3	27	28
GvH	3	23	32
Sezary	3	18	18
Rejet renal	1	4	4
Lichen plan	1	4	4
TOTAL	11 (3 enfants)	76	86



CRYO ECP - results

Duré de la congélation (jours)	13	(3-119)
CD3+ congelées (10^7/kg)		
par aphérèse	2.2	(0.1-28)
par fraction	**2.3**	(0.1-6.0)
Nb de fractions congelées/aphérèse	**1**	(1-**5**)
CD3+ reinjectées (10^7/kg)	2.1	(0.2-6.1)

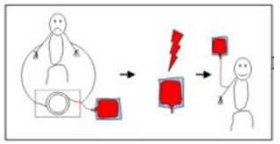


CRYO ECP - results

	Patients	CRYO ECP		
GvH	24*	266	NR 8/24	*Merlin 2012* *Pochon 2017*
Pulmonary rejection	3*	28	2/3 drugs-sparing effect	
Sezary	3	18	3/3 PR	
Renal rejection	1	4	?	
Lichen planus	1	4	?	
Juvenile dermatopolymyositis	1*	81	CR	*Merlin 2012*
Juvenile localized scleroderma	1*	52	CR	*Merlin 2012*
TOTAL	34	453		

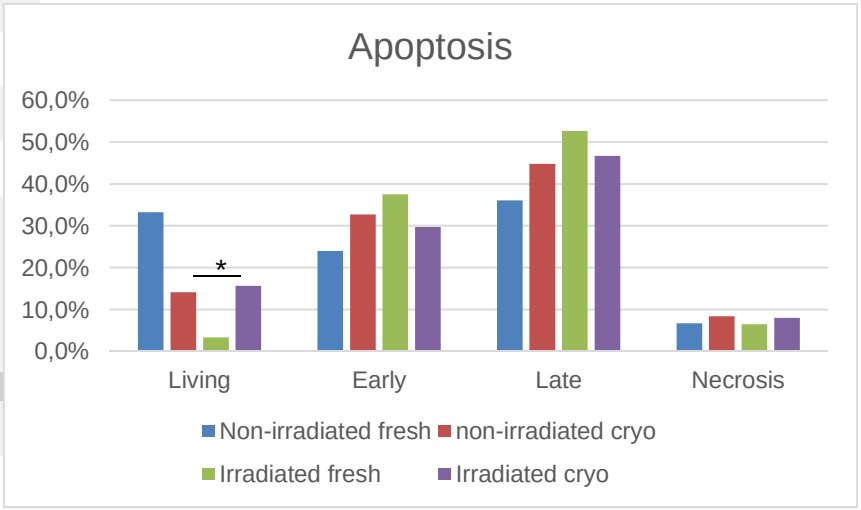
19 enfants*

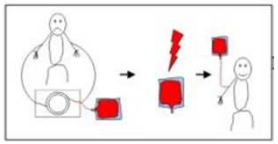
CRYO ECP - results



IMPACT OF CRYOPRESERVATION ON DIFFERENT LYMPHOCYTE POPULATIONS.

	FRESH (10^7/kg)	CRYO (10^7/kg)	P value
NO IRRADIATION			
TH1	0.62 [0.24 - 1.27]	0.27 [0.02 - 0.47]	NS
TH2	0.62 [0.45 - 0.86]	0.73 [0.42 - 1.02]	NS
TREG	0.20 [0.08 - 0.45]	0.15 [0.08 - 0.21]	NS
NAIVE LYMPHOCYTES	0.42 [0.12 - 0.61]	1.43 [0.43 - 2.66]	0.043
ALLOREACTIVE LYMPHOCYTES	1.39 [0.33 - 2.77]	0.63 [0.29 - 1.17]	NS
B CELL	1.85 [0.94 - 3.07]	1.47 [0.82 - 2.09]	NS
MONOCYTES – **CLASSICAL** – **INTERMEDIATED** – **UNCLASSICAL** – **DC**	0.07 [0 - 0.22] 0.36 [0.01 - 0.94] 0.33 [0.03 - 0.74] 0.24 [0.01 - 0.05]	0.08 [0.00 - 0.13] 0.45 [0.31 - 0.66] 0.14 [0.04 - 0.28] 0.32 [0.17 : 0.66]	NS
IRRADIATION			
TH1	0.72 [0.33 - 1.33]	0.21 [0.01 - 0.32]	0.043
TH2	0.41 [0.27 - 1.21]	0.48 [0.18 - 0.82]	NS
TREG	0.13 [0.03 - 0.28]	0.14 [0.05 - 0.21]	NS
NAIVE LYMPHOCYTES	0.51 [0.11 - 1.23]	1.50 [0.53 - 3.01]	0.043
ALLOREACTIVE LYMPHOCYTES	1.09 [0.27 - 2.03]	0.46 [0.36 - 0.54]	NS
B CELL	2.05 [1.06 - 3.88]	1.51 [0.79 - 2.21]	NS
MONOCYTES – **CLASSICAL** – **INTERMEDIATED** – **UNCLASSICAL** – **DC**	0.07 [0- 0.266] 0.53 [0.047 - 0.920] 0.03 [0.003 - 0.071] 0.37 [0.060 - 0.950]	0.08 [0.23 - 0.10] 0.047 [0.28 - 0.71] 0.16 [0.03 - 0.29] 0.29 [0.16 - 0.33]	NS

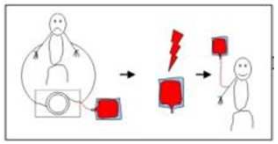




What are the advantages of CRYO ECP ?

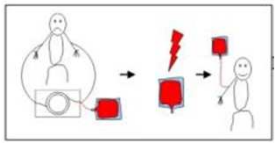
Reduced the number of apheresis while maintaining the rate of reinjections

- Improve treatment conditions **YES**
- Expand ECP indications **YES**
- Treat patients in centers not equipped for ECP **NO**
- Standardize cell product **NO**



What are the limitations of CRYO ECP ?

Est ce que ça marche vraiment ?

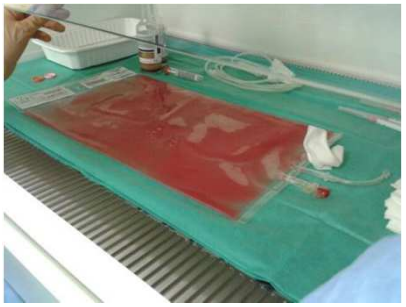


What are the limitations of CRYO ECP ?

Règlementaires et administratives :

•Autorisation ANSM / pathologie

•JACIE ?



Techniques et logistiques:

•Temps labo: (congélations/lavages/décongélations) x N

•Stockage des poches

•GHS aphérèse *vs* HDJ pour une réinjection simple et encore…….

Intellectuelles

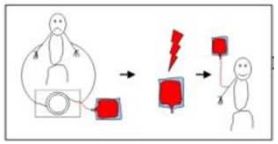
•Indications : patient ? pathologie ?

•Combien de cellules par fraction ?

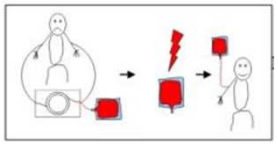
•Combien de fractions par aphérèse ?

•Quel délais de stockage max ? Réinjections de «vieux lymphocytes» ?

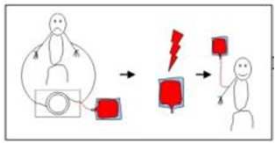
•Quel test ? (PHA est compliqué sur les cellules décongelées)



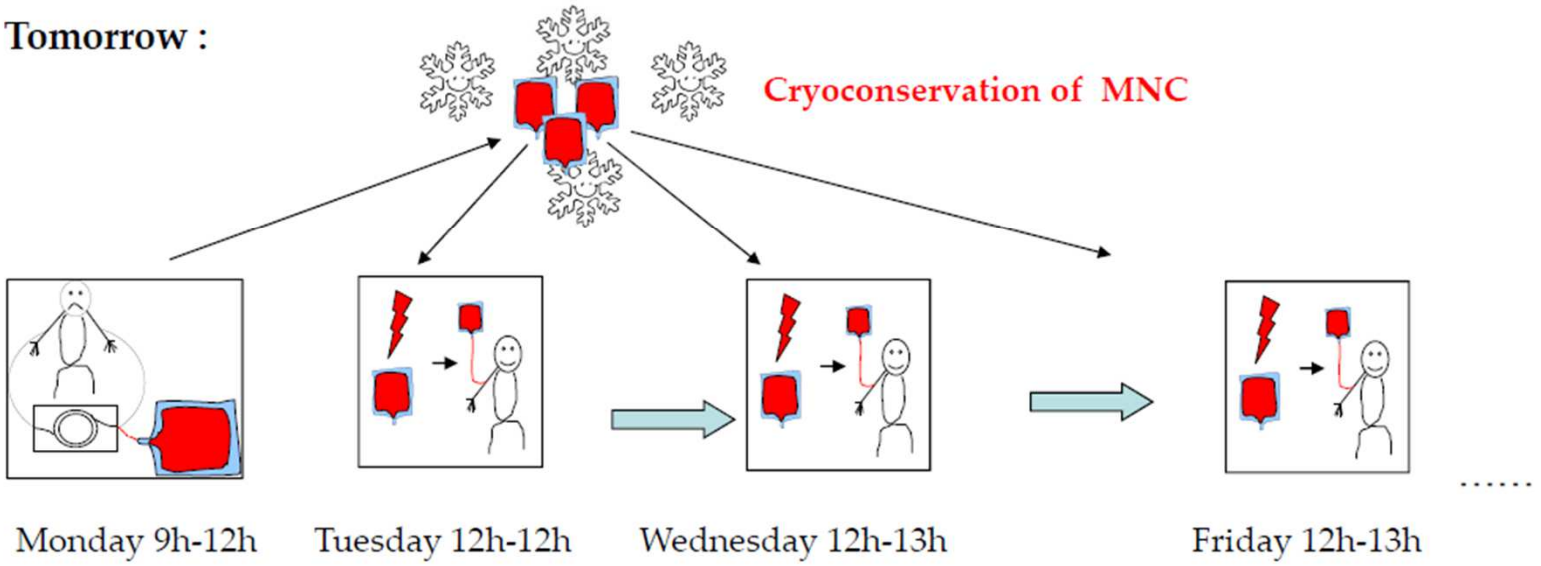
Conclusions/Perspectives:

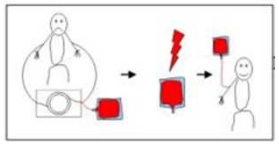


Guidelines !



How to set up future trials ?





Unité CRECHE

François Deméocq

Etienne Merlin

Victoria Grèze



Apheresis nursing staff

Valérie Hervé

Emmanuelle Lopez

Chantal Pic

Delphine Pages




Thank you !