



## CINEVAS Study

Comparison of ANCA and anti-GBM auto-antibodies removal kinetics between Plasma Exchanges and Immunoabsorption in patients with ANCA-associated vasculitis or anti-GBM disease



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# AAV and anti-GBM disease

- Apheresis : used since 1975 in AAV and anti-GBM disease, with IS therapies
- MEPEX study (2007): short-term benefit of PEx over IV MeP on renal recovery if creat > 500 uM
- PEXIVAS study awaited : PEx / no PEx in patients with less severe renal or pulmonary involvement
- Apheresis : rapid removal of pathogenic auto-antibodies (anti-MPO++, anti-PR3?, anti-GBM+++)
- ANCA antibodies are good candidates for apheresis
  - High molecular weight (160 kDa), low synthesis rate (7%), long half-life (22 days)
  - Predominantly intravascular distribution (70-55% Ig G), low organ deposition
- One multicentric, randomized study (Sweden) : 44 patients with RPGN (AAV or anti-GBM), no superiority of IA or PEx on renal and global prognosis
  - *Stegmayr BG et al, Int J Artif Organs 1999;22:81-7*

## Diapositive 2

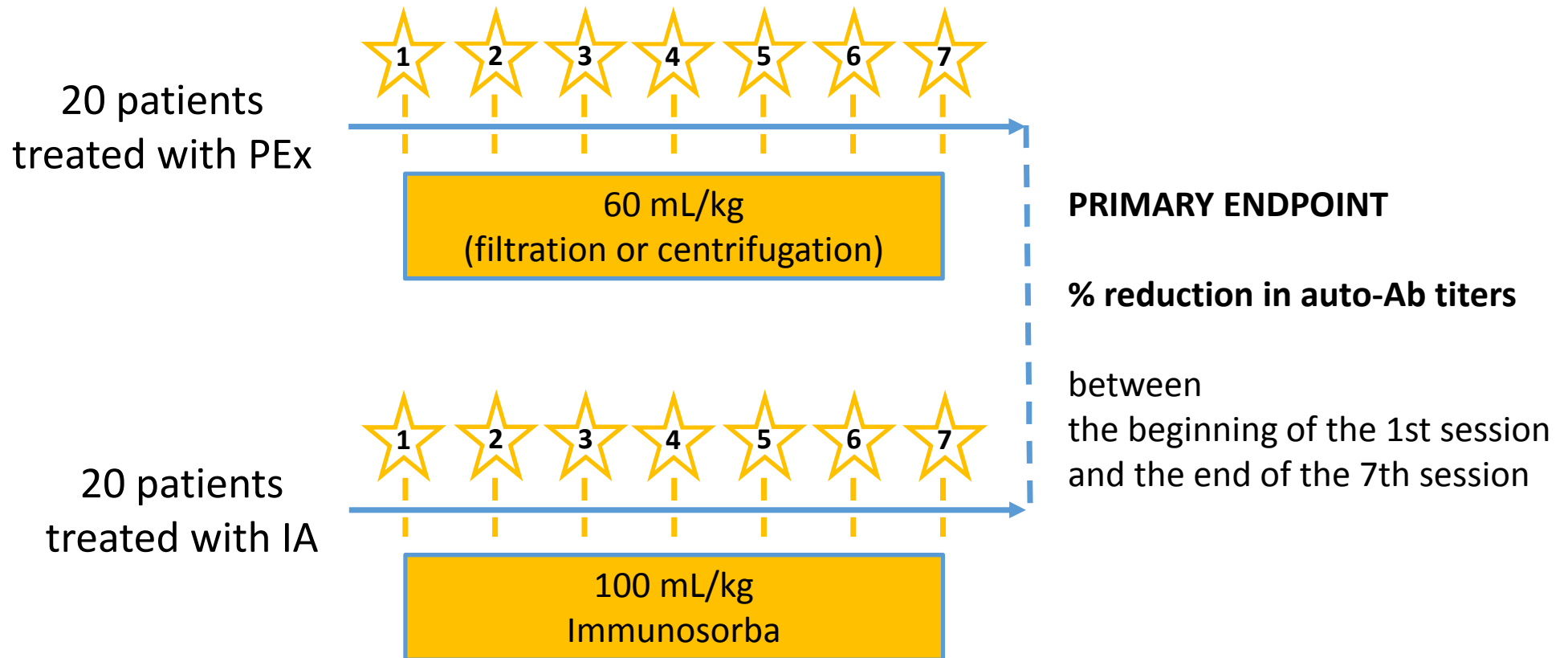
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**j10** 42% et 78% pour IgA et IgM  
dr21560; 14/03/2017

# Apheresis : PEx or IA?

	Plasma Exchange	Immuno Adsorption
<b>Specificity</b>	Non specific	Semi specific
<b>Substitution solute</b>	Albumin or Fresh Frozen Plasma	None
<b>Volume of plasma treated</b>	60ml/kg/session	100ml/kg/session
<b>Anticoagulation</b>	Systemic (heparin) or local	Local (citrate)
<b>Risk of allergy</b>	Yes	No
<b>Complications</b>	Bleeding disorders	Metabolic alkalosis & Fluid overload → IA can be coupled with dialysis
<b>Cost</b>	560 euros for 3.5L of plasma treated substitution Albumin 4% (without FFP)	1209 euros

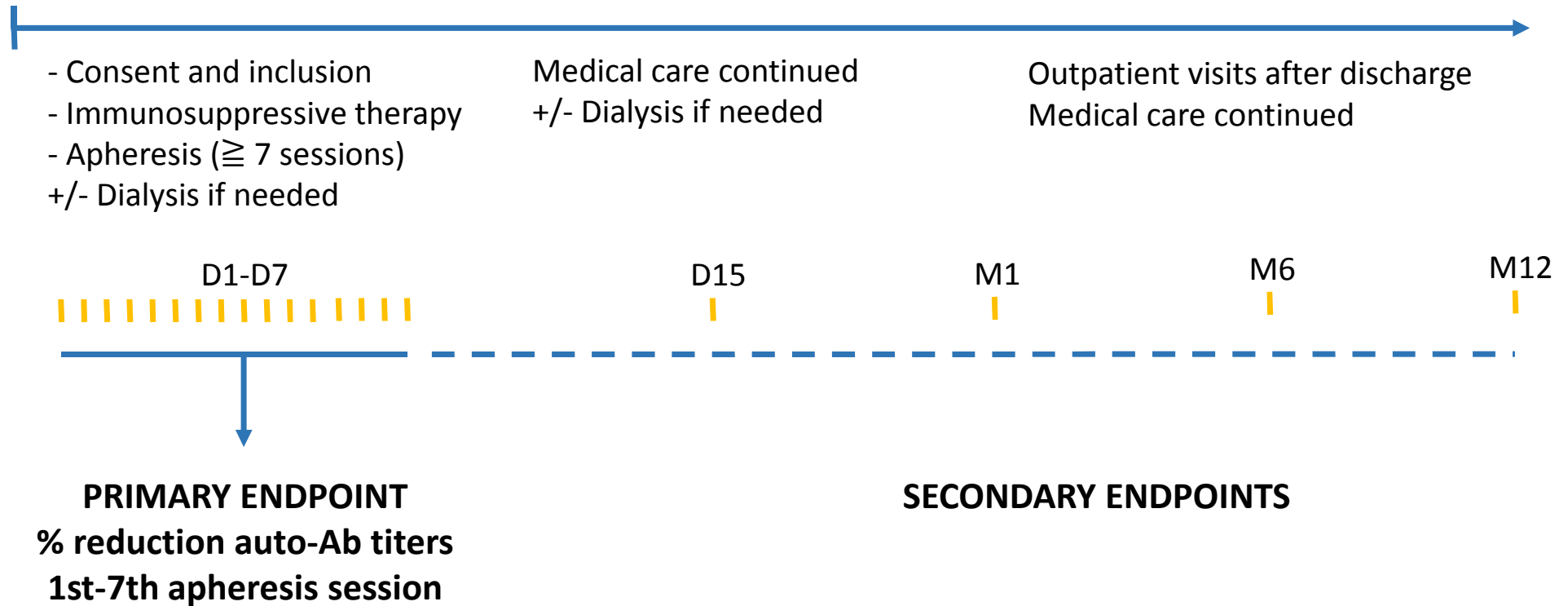
# CINEVAS : a pilot multicentric study



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## Diagnosis and indication for apheresis

Follow-up :  
12 months



# CINEVAS : a pilot multicentric study

## SECONDARY ENDPOINTS:

- Mean % reduction of auto-Ab **per session**
- **N sessions needed** for a 100% reduction in auto-Ab
- **Rebound** of auto-Ab titers between sessions
- Kinetics according to the target of Ab (MPO, PR3, MBG)
- Kinetics of fibrinogen and platelets
- Kinetics of overall IgG, IgA and IgM
- **Patient survival** M1, M6, M12
- **Renal survival** M1, M6, M12
- **Activity (BVAS)** M1, M6, M12
- **Damage (VDI)** M1, M6, M12
- **Adverse events**

# CINEVAS : a pilot multicentric study

## INCLUSION CRITERIA

- Age  $\geq$  18 years
- AAV with anti-MPO + or anti-PR3 +, or anti-GBM disease with anti-GBM + antibodies
- Immunosuppressive induction therapy with corticosteroids and cyclophosphamide/rituximab
- Written informed consent
- Indication for apheresis according to the investigator

## EXCLUSION CRITERIA

- Pregnancy or lactation
- Severe anemia (Hb  $<$  7 g/dL)
- Vasculitis without positive auto-Ab
- Positive ANCA antibodies in non-AAV diseases (i.e. endocarditis...)



## CINEVAS : 10 centers participating

- AP-HM Dr J. MOUSSI-FRANCES, Dr M. SALLEE, Pr N. JOURDE-CHICHE
- AP-HP Dr B. TERRIER (Cochin), Dr C. RAFAT (Tenon)
- CHU BESANCON Dr T. CREPIN
- CHU GRENOBLE Dr L. ROSTAING
- CHU LYON Dr E. KALBACHER (HCL)
- CHU de ROUEN Dr D. BERTRAND
- CHRU STRABOURG Dr T. KRUMMEL
- CHU SAINT ETIENNE Dr N. MAILLARD
- CHU TOULOUSE Dr S. FAGUER

## CINEVAS : results expected & perspectives

- Hypothesis : IA > PEx
  - 1) kinetics : rapid removal of ANCA or anti-GBM
  - 2) +/- tolerance : less adverse events (bleeding)
  
- Randomized controled trial
  - PHRC proposed in 2021 if CINEVAS shows a benefit of IA over Pex
  - Clinical benefit of IA vs PEx in terms of renal and global prognosis
  
- Widening of apheresis indications in AAV if PEXIVAS shows a benefit of PEx



**FRESENIUS  
MEDICAL CARE**

Funding : 83,446 euros



<b>PERSONS WORKING ON THE PROJECT</b>						<b>24 284</b>
<b>INVESTIGATION</b>						<b>6 000</b>
<b>Personnels PROMOTEUR et CENTRE ASSOCIE affectés à la réalisation du projet</b>						
TEC (Technicien d'études cliniques)		150 EUROS/ SUJ	47 500	13%	1,0	6 000
			-			
<b>PROMOTION</b>						<b>9 700</b>
<b>Montage, organisation, coordination projet, réglementaire</b>						
Chef de projet DRCI	APHM	1 mois	58 200	14%	1,0	8 350
ARC	APHM	1 mois	49 000	2%	1,0	750
<b>Vigilance</b>						
Praticien non titulaire	APHM	1 mois	75 000	1%	1,0	600
<b>DATA ANALYSIS</b>						<b>8 584</b>
<b>Traitement des données</b>						
Ingénieur biostatisticien	APHM	1 mois	59 800	8%	1,0	4 784
Data manager	APHM	1mois	47 500	8%	1,0	3 800
			-			
<b>MEDICAL EXPENSES</b>						<b>56 052</b>
<b>PURCHASE OF BIOLOGICAL REAGENTS</b>						<b>7 000</b>
<b>Biologie</b>						
réactifs		kit	350	20	1,0	7 000
<b>NURSE AND LABORATORY ACTS</b>						<b>49 052</b>
<b>Actes médico-techniques</b>						
Actes infirmiers (AMI)		1,5 AMI	4,71	220,00	1,0	1 036
Actes de biologie (B)		B70 (=18,9)anti-M	20,00	40,00	18,9	15 120
Actes de biologie (B)		B66 (=17,82) dosa	20,00	40,00	17,8	14 256
Actes de biologie (B)		B51 (=13,77)	14,00	40,00	13,8	7 711
Actes de biologie (B)		B58 (=15,66)	14,00	40,00	15,6	8 736
Actes de biologie (B)		hémogramme (B2)	7,00	40,00	7,8	2 192
<b>GENERAL EXPENSES</b>						<b>3 110</b>
<b>Printing, Insurance</b>						<b>1 110</b>
<b>Autres dépenses hotelières</b>						
travaux d'impression	APHM	CRF-NI-CE	400	1	1,0	400
assurance (SHAM)	APHM	Assurance	710	1	1,0	710
<b>Publication Cost</b>						<b>2 000</b>
<b>Valorisations</b>						
frais de publication			2 000	1	1,0	2 000
<b>TOTAL Projet</b>						<b>83 446</b>

## CINEVAS : Time Line

- June 2017 Fresenius Medical Care agreed to sponsor CINEVAS : 83,446 euros
- Sept 2017 AP-HM agreed to promote CINEVAS
- Oct-dec 2017 Selection of centers for CINEVAS  
(IA with Fresenius, and/or PEx by filtration/centrifugation)
- Jan-Mar 2018 Legal procedures (CPP and ANSM)
- Mar 2018 REDCap installed at AP-HM
- Apr-May 2018 CINEVAS eCRF elaboration on REDCap
- Fresenius contract signature by AP-HM : the 1st patient will have to be included < 6 months
- Expected duration of inclusions : 24 months