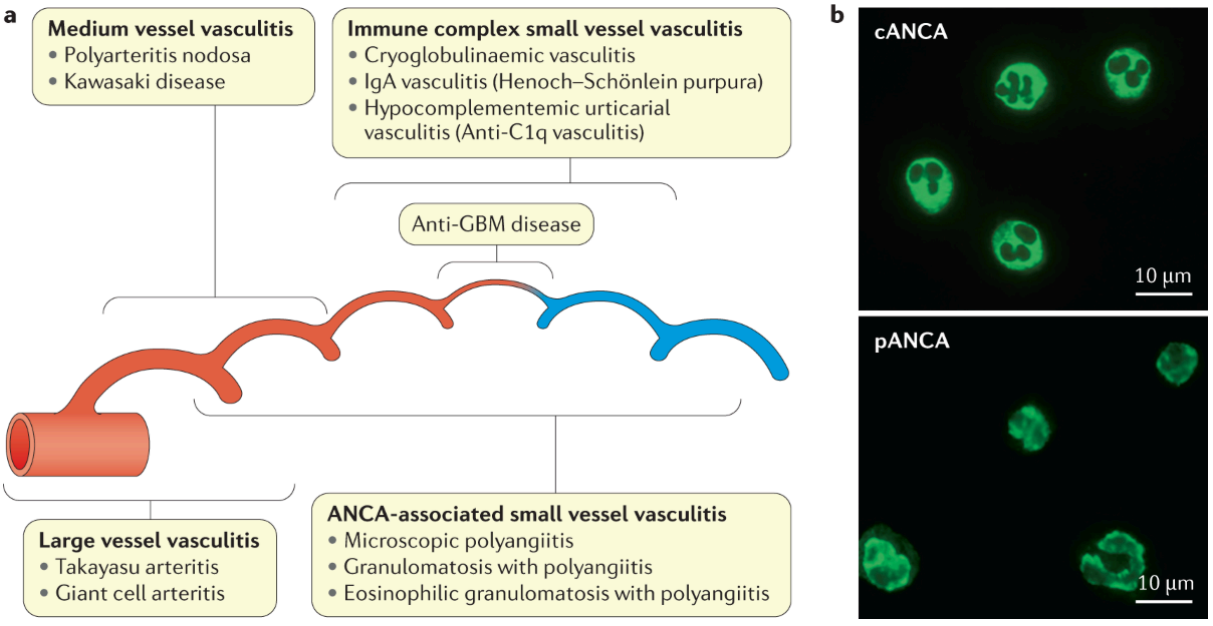
CINEVAS Trial Tweetorial
IA vs. PEx in ANCA Vasculitis: The Battle of Filters

1/ 🔥 Poll 1:
Imagine you're designing a "dream team" of ANCA vasculitis treatments. If you could "supercharge" one part of the treatment, what would you choose?

1. "Boost" Antibody Removal
2. Minimize Side Effects
3. Speed up Recovery
4. Focus on Organ Healing

2/ While building your dream team, picture your blood vessels under siege! That's ANCA-associated vasculitis (AAV), where inflammation ravages tiny vessels, leading to organ damage.

Adapted from : *ANCA-associated vasculitis | Nature Reviews Disease Primers*



3/ 🔬 In AAV, the immune system misfires, producing neutrophil-attacking ANCA antibodies. AAV is rare at 200-400 cases/million. Serologic tests can detect ANCA. Early diagnosis and treatment are crucial!

👉 [ANCA-Associated Vasculitis: An Update - PubMed]

Disease	Incidence * [7]	ANCA-Positivity	PR3-ANCA	MPO-ANCA	Predominant Organ Involvement	Rate of Renal Involvement [77]	RPGN [77]
GPA	1.9–13	~90%	~75%	~20%	Nose and sinuses, lungs, kidneys, joints, eyes	~70%	~50%
EGPA	0.8–4	~40%	<10%	30–40%	Lungs, upper airways, peripheral nerves, heart, skin	~25%	<15%
MPA	1.5–16	~90%	~25%	~60%	Kidneys	>90%	~65%

* per million person-years. Abbreviations: AAV: ANCA-associated vasculitis. ANCA: Antineutrophil cytoplasmic antibody. PR3: leukocyte proteinase 3. MPO: myeloperoxidase. RPGN: rapidly progressive glomerulonephritis. GPA: granulomatosis with polyangiitis. EGPA: eosinophilic granulomatosis with polyangiitis. MPA: microscopic polyangiitis.

4/ AAV leads to pauci-immune necrotizing crescentic glomerulonephritis (NCGN), a severe kidney condition defined by an estimated glomerular filtration rate of <50 ml/min/1.73 m2 of body surface area or the presence of diffuse pulmonary hemorrhage.

👉 [Plasma Exchange and Glucocorticoids in Severe ANCA-Associated]

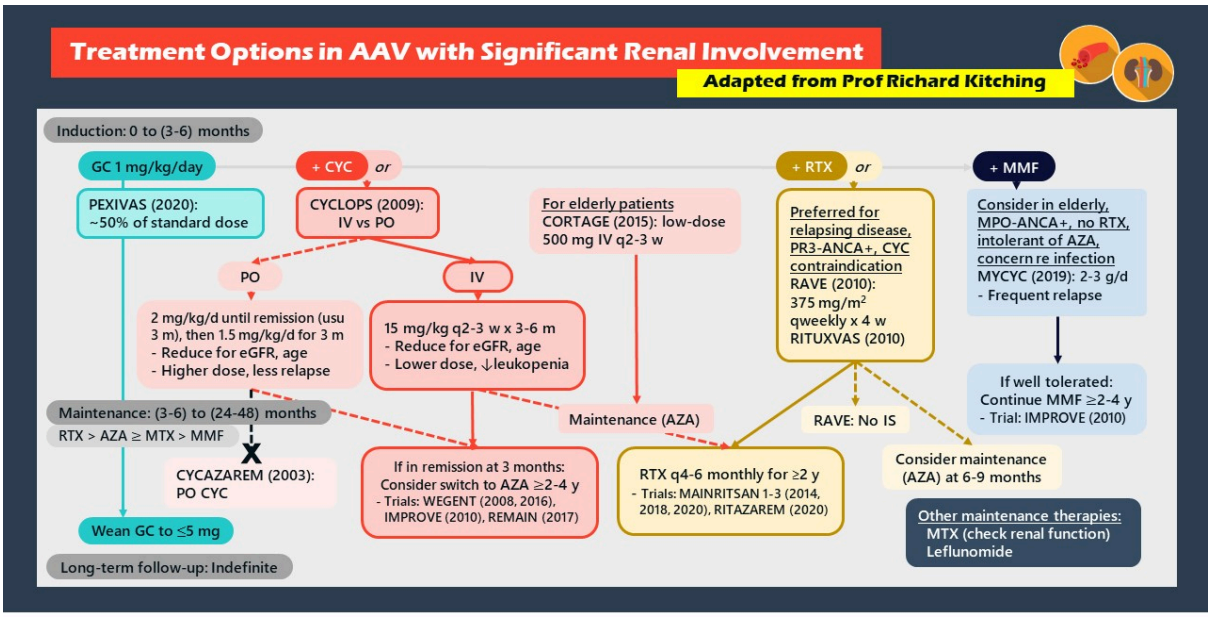
5/ Poll 2:

Which approach do you prefer for treating severe ANCA-associated vasculitis? A. Rituximab-based therapy B. Cyclophosphamide-based therapy
C. Plasma exchange (PLEX) D. Combination of immunosuppressants and glucocorticoids

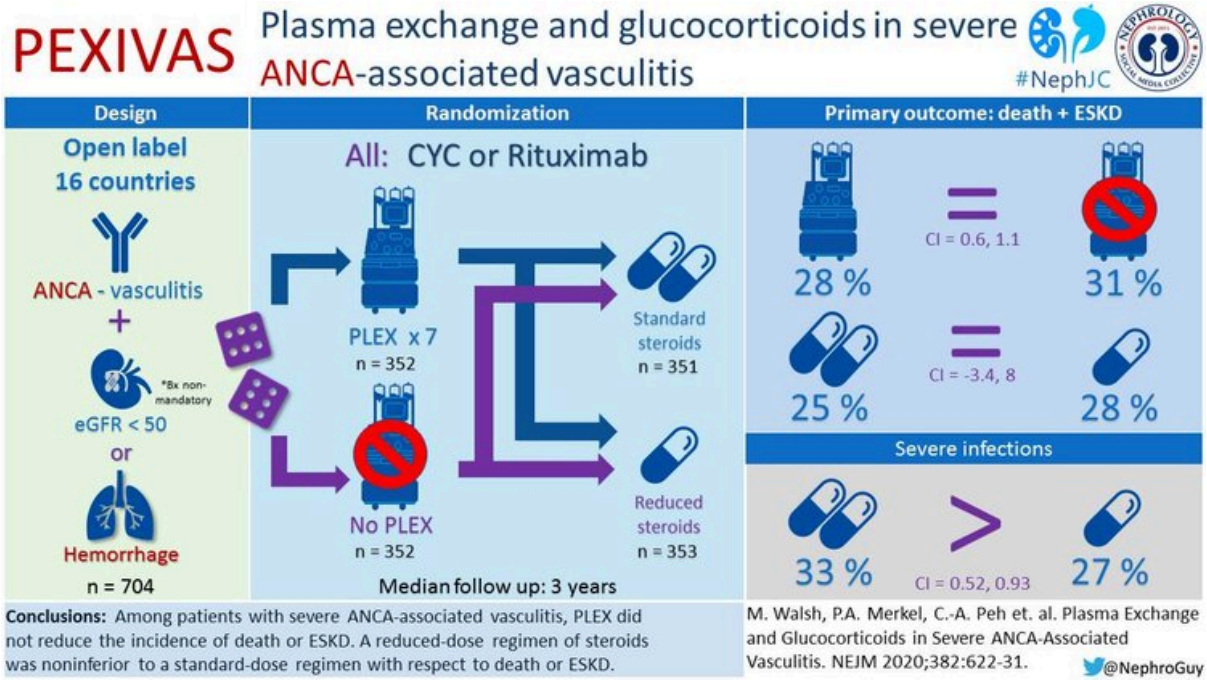
Options:
A
B
C
D

6/ 💡 Treatment strategies for severe ANCA vasculitis vary upon clinical

presentation 👇



7/ 🚩 Plasma exchange showed no benefit in preventing kidney failure or death in the PEXIVAS trial.



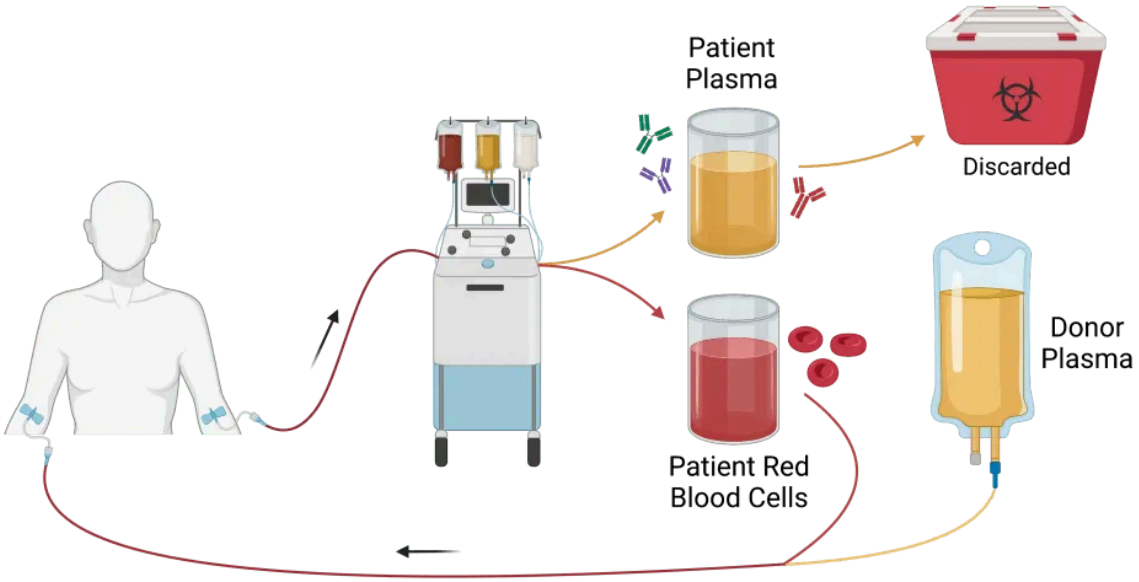
8/ 🚩 KDIGO guidelines recommend considering plasma exchange for patients with severe renal impairment requiring dialysis, alveolar hemorrhage with hypoxemia, overlap with anti-GBM disease, or refractory cases. 👉 KDIGO 2024 KDIGO 2024 Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease

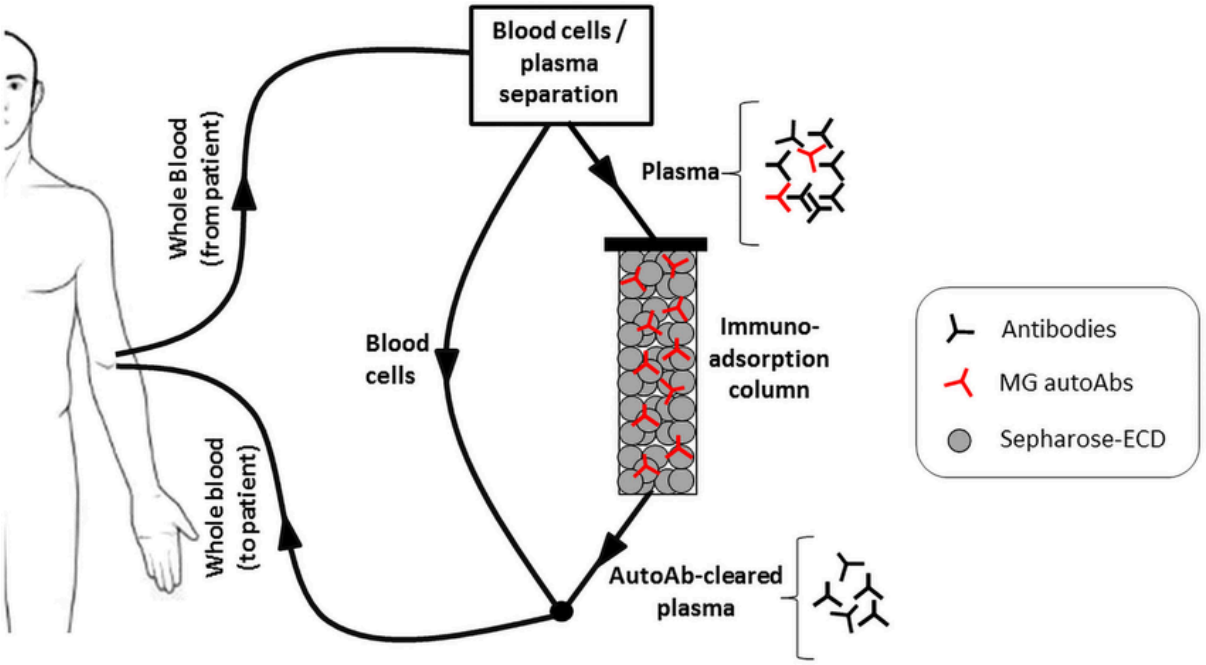
9/ 💣 However, the role of plasma exchange techniques like filtration or immunoadsorption (IA) remains controversial.

10/ How do PEx and IA differ? 👫

🌼 Plasma exchange (PEx), also called plasmapheresis, removes plasma from blood and replaces it with albumin or fresh frozen plasma (FFP).

11/ 🌸IA offers advantages over PEX by selectively removing circulating antibodies while preserving vital plasma components. This targeted approach may enhance patient outcomes. Fig👇treatment - Autoimmune Encephalitis , Myasthenia Gravis: Autoantibody Specificities and Their Role in MG ...



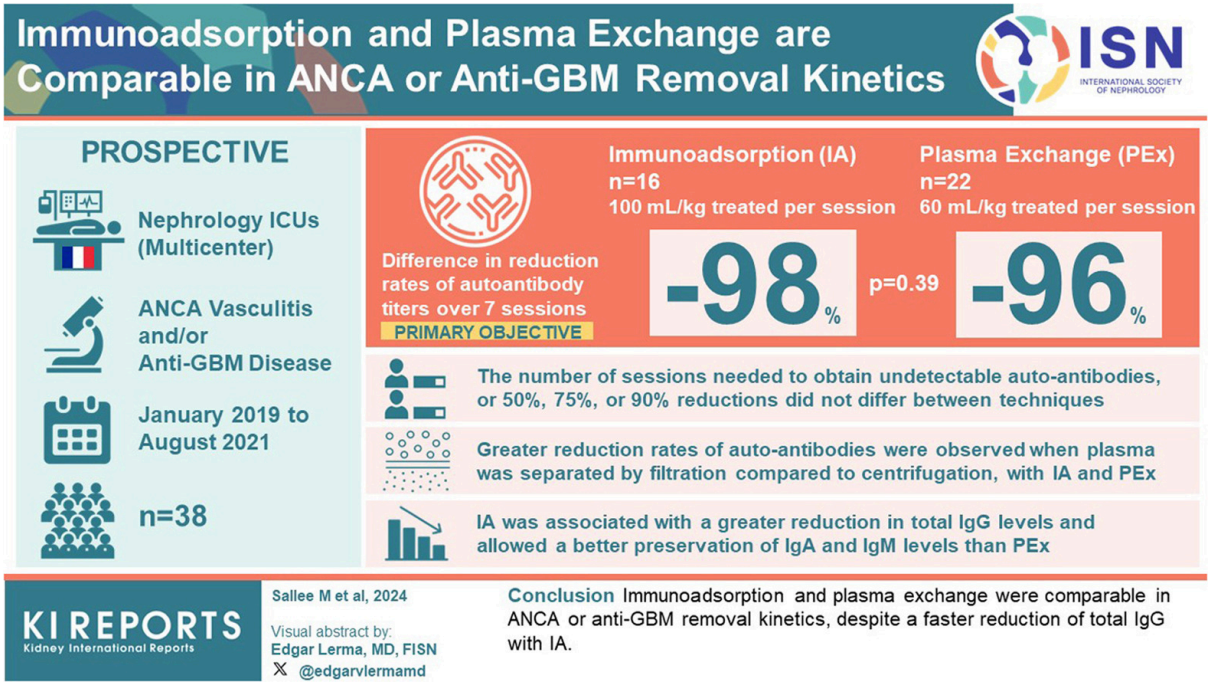


12/ Poll 3:

How frequently do you use immunoadsorption in managing refractory ANCA-associated vasculitis?

- Typically in refractory cases
- If PEX contraindicated
- Rarely or never
- Unfamiliar with use

13/ Got confused !!!! 😢
Here enters the **CINEVAS trial!** Immunoadsorption and Plasma Exchange are Comparable in Anti ...
This French study compared IA and PEx in 38 patients with AAV or anti-GBM disease. Beautiful VA by @edgar



14/ The primary endpoint was the reduction rate in autoantibody titers between the beginning of the first apheresis session and the end of the seventh session.

Table 2. Comparison of the reduction rates in autoantibody levels between immunoadsorption (IA) and plasma exchanges (PEx), considering all autoantibodies, and specifically anti-MPO, anti-PR3 or anti-GBM antibodies

Auto-antibodies and sessions	IA	PEx	*P*-value
All autoantibodies	$n = 19$	$n = 24$	
Over 7 sessions	98 (90–100) ($n =$ 19)	96 (78–100) ($n =$ 24)	0.39
Session #1 ($n = 31$)	42 (5–70) ($n = 16$)	53 (41–62) ($n = 15$)	0.56
Session #2 ($n = 37$)	70 (55–83) ($n = 17$)	52 (21–65) ($n = 20$)	0.035
Session #3 ($n = 34$)	75 (67–84) ($n = 16$)	53 (24–62) ($n = 18$)	0.028
Session #4 ($n = 35$)	68 (56–84) ($n = 16$)	67 (38–71) ($n = 19$)	0.42
Session #5 ($n = 34$)	76 (62–88) ($n = 14$)	57 (32–66) ($n = 20$)	0.054
Session #6 ($n = 32$)	77 (58–94) ($n = 15$)	52 (32–66) ($n = 17$)	0.031
Session #7 ($n = 32$)	67 (56–81) ($n = 13$)	65 (38–73) ($n = 19$)	0.36
Anti-MPO antibodies	$n = 7$	$n = 12$	
Over 7 sessions	93 (90–99)	93 (73–98)	0.58
Anti-PR3 antibodies	$n = 7$	$n = 10$	
Over 7 sessions	98 (97–100)	98 (85–100)	0.65
Anti-GBM antibodies	$n = 5$	$n = 2$	
Over 7 sessions	98 (84–100)	66 (32–100)	0.84

GBM, glomerular basement membrane; IA, immunoadsorption; MPO, myeloperoxidase; PEx, plasma exchange; PR3, proteinase 3.

15/ 📊 Results showed **no significant difference** in ANCA reduction between IA and PEx, both achieving over 90% reduction.

	IA	PEx	p
All auto-antibodies	n= 19	n=24	
Session 1 (n=43)	0 (n=19)	0 (n=24)	-
Session 2 (n=39)	47 [0-55] (n=19)	43 [15-51] (n=20)	0.96
Session 3 (n=38)	58 [18-75] (n=17)	56 [23-68] (n=21)	0.54
Session 4 (n=38)	65 [42-79] (n=17)	66 [20-79] (n=21)	0.96
Session 5 (n=35)	73 [59-82] (n=14)	74 [25-82] (n=21)	0.58
Session 6 (n=34)	75 [66-86] (n=15)	78 [27-90] (n=19)	0.93
Session 7 (n=32)	74 [53-87] (n=13)	73 [42-90] (n=19)	0.98

16/ Interestingly, **filtration-based plasma separation** was **more effective** than centrifugation in removing antibodies. **It's important to note that the trial does not elaborate on why filtration is more effective than centrifugation for antibody removal. Further research might provide more insight into this finding.**

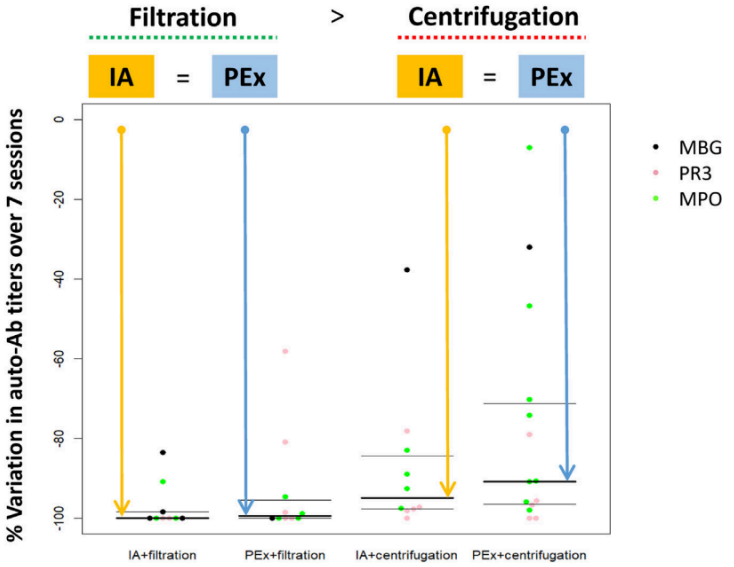


Figure 1. Percent reduction of autoantibody titers ($n = 43$) over 7 sessions of apheresis, with immunoadsorption (IA) or plasma exchange (PEx), after plasma separation by filtration or by centrifugation. Ab, antibody; GBM, glomerular basement membrane; MPO, myeloperoxidase; PR3, proteinase 3.

17/ We can't overlook the side effects!

🛑 IA preserves IgG, IgM, and IgA levels better than PEx.

🛑IA sessions require higher plasma volumes, longer durations, and larger citrate volumes compared to PEx.

🛑Overall, IA sessions tend to be longer than those for PEx.

Table 4. Adverse events and technical parameters with immunoadsorption (IA) and plasma exchanges (PEx)

Outcome and technical parameters	IA	PEx	*P*-value
Patients' outcome	*N*=16 patients	*N*=22 patients	
Death < M12	3 (of sepsis, septic shock, or respiratory failure)	0	0.066
Serious infections (nonfatal)	1 zoster	1 SARS-COV2 infection	>0.99
Serious bleeding	5 (4)	6 (6)	>0.99
(requiring transfusion)			>0.99
Poor tolerance of apheresis session	7 episodes in 5 patients	2 episodes in 2 patients	0.11
Apheresis sessions	*n* = 112 sessions Median (Q1–Q3)	*n* = 154 sessions Median (Q1–Q3)	*P*
Duration, minutes	224 (189–272)	104 (93–122)	6.2e-10
Plasma volume treated, l	6.5 (5.9–7)	4 (4.3–3.4)	1.1e-10
P. volume treated, ml/kg	98 (89–99)	53 (47–56)	1.75e-10
Citrate infusion volume, ml	662 (432–1282)	296 (237–418)	1.5e-05
Plasma infusion volume, ml	0 (0–0)	3415 (573–3882)	1.7e-06
Fibrinogen infusion dose, g	0 (0–0)	0 (0–0)	0.94

IA, immunoadsorption; PEx, plasma exchange.;

18/ ⚖️ Despite some differences, **no overall advantage** was observed for either IA or PEx in terms of antibody reduction or clinical outcomes. There was no difference between IA and PEx in the evolution of the Birmingham Vasculitis Activity Index

(BVAS)

	IA N=16 patients	PEx N=22 patients	p
BVAS	Median [Q1-Q3]	Median [Q1-Q3]	
Inclusion	18.5 [12-22.3]	16 [14-20]	0.84
Day 15	8 [6-12]	12 [11.5-12.5]	0.12
Day 30	8 [8-12]	11 [8-12.8]	0.64
6 months	4 [0-9]	0 [0-7]	0.51
12 months	0 [0-8]	0 [0-2.5]	0.52

19/ Looking ahead: 🔭
❓ Which apheresis technique is superior for AAV?
🔬 More RCTs are needed to compare IA and PEx across AAV subtypes.
💡 CINEVAS offers valuable insights. Choosing the best technique should factor in individual patient characteristics and disease severity.

20/ This has been an X-torial by @DrMedhavi_G POD 3 Glomke3pers @NSMCInternship NephEdC 2024 Interns