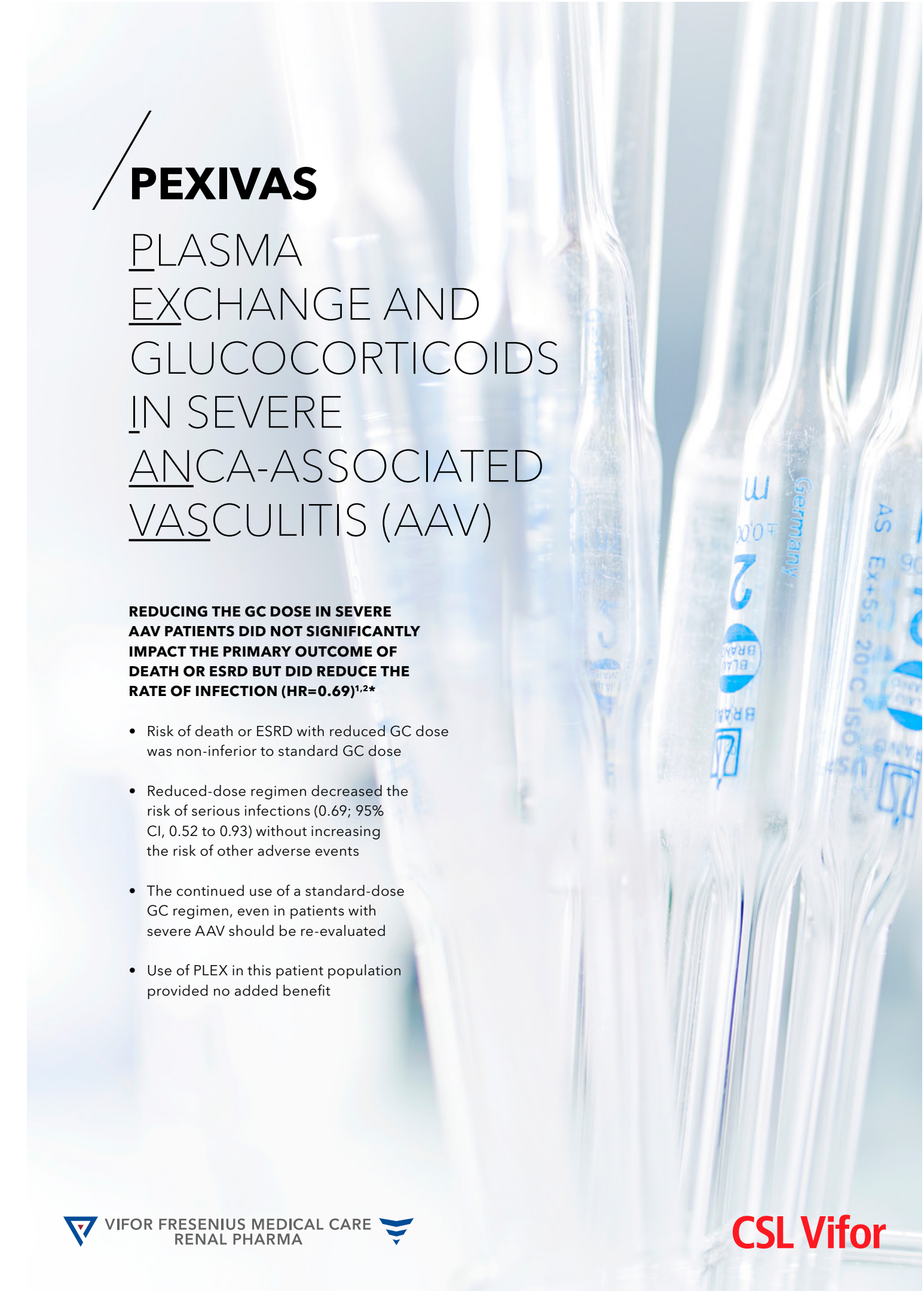
PEXIVAS

PLASMA EXCHANGE AND GLUCOCORTICOIDS IN SEVERE ANCA-ASSOCIATED VASCULITIS (AAV)



REDUCING THE GC DOSE IN SEVERE AAV PATIENTS DID NOT SIGNIFICANTLY IMPACT THE PRIMARY OUTCOME OF DEATH OR ESRD BUT DID REDUCE THE RATE OF INFECTION (HR=0.69)[1,2]*

- Risk of death or ESRD with reduced GC dose was non-inferior to standard GC dose
- Reduced-dose regimen decreased the risk of serious infections (0.69; 95% CI, 0.52 to 0.93) without increasing the risk of other adverse events
- The continued use of a standard-dose GC regimen, even in patients with severe AAV should be re-evaluated
- Use of PLEX in this patient population provided no added benefit

VIFOR FRESENIUS MEDICAL CARE RENAL PHARMA

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INTRODUCTION

PEXIVAS assessed the use of PLEX and two GC doses in severe AAV patients. For patients with severe AAV, ESRD and premature death are common outcomes. Previous trials have suggested PLEX is beneficial in severe AAV, but further evidence is needed to understand the benefits on clinically important outcomes such as death and ESRD.[1]

STUDY AIM

Evaluate the incidence of death or ESRD in severe AAV patients treated with PLEX vs no PLEX and standard- vs reduced-dose GC regimens.[1]

The sponsor of this study was:
University of Pennsylvania

STUDY DESIGN

Randomised, open-label, two-by-two factorial design, multicentre trial[1]

Patients with newly diagnosed or relapsing GPA, MPA (N=704)
All patients treated with induction therapy CYC or RTX, 1–3 consecutive days of methylprednisolone pulses up to a maximum cumulative dose of 1–3 g
Half of the patients received; PLEX (n=352) 60 mL albumin replacement per kg or bodyweight, 7 treatments within 14 days of randomisation OR no PLEX (n=352)

0.5 to 5.5 months

Reduced GC dose (n=353):
Oral prednisone or prednisolone at 50% of the standard GC dose

Standard GC dose (n=351):
Oral prednisone or prednisolone, dose determined by patient's weight (<50 kg, 50–75 kg, or >75 kg)

5.5–12 months

All patients received 5 mg per day of oral prednisone or prednisolone

>12 months

GC dose determined by local investigators

PRIMARY OUTCOME: DEATH OR ESRD
(≥12 CONTINUOUS WEEKS OF RRT OR BY KIDNEY TRANSPLANTATION)

STEROID TAPERING SCHEDULE:[1,2]

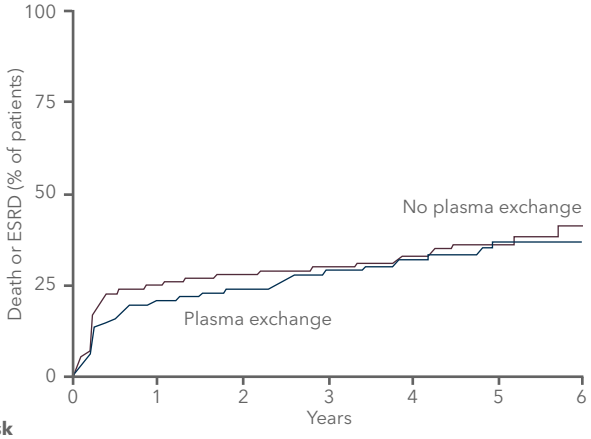
	Standard oral GC dosing			Reduced-dose oral GC dosing		
Week	<55 kg	50–75 kg	>75 kg	<55 kg	50–75 kg	>75 kg
1	50	60	75	50	60	75
2	50	60	75	25	30	40
3–4	40	50	60	20	25	30
5–6	30	40	50	15	20	25
7–8	25	30	40	12.5	15	20
9–10	20	25	30	10	12.5	15
11–12	15	20	25	7.5	10	12.5
13–14	12.5	15	20	6	7.5	10
15–16	10	10	15	5	5	7.5
17–18	10	10	15	5	5	7.5
19–20	7.5	7.5	10	5	5	5
21–22	7.5	7.5	7.5	5	5	5
23–52	5	5	5	5	5	5
>52	Investigators' local practice			Investigators' local practice		

PRELIMINARY RESULTS

The reduced-dose GC regimen was non-inferior to standard-dose in relation to risk of death or ESRD, 25.5% vs 27.9% (absolute risk difference, 2.3%; 95% CI, -4.5–9.1), and the reduced-dose resulted in a lower risk of serious infections in the first year of treatment, 27.2% vs 33.0%.

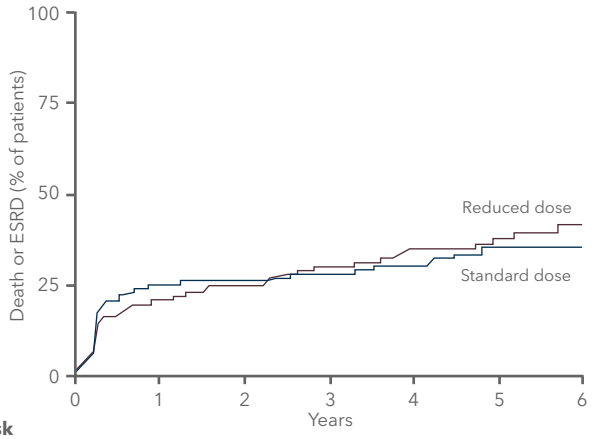
The use of PLEX did not result in a significantly lower incidence of death or ESRD vs the no PLEX group, 28.4% vs 31.0%. There was no interaction between the GC regimen and PLEX assignment.

Risk of death or ESRD reduced dose vs standard GC dose



No. at risk							
No plasma exchange	352	244	183	136	82	44	10
Plasma exchange	352	252	186	135	82	43	10

Risk of death or ESRD PLEX vs no PLEX



No. at risk							
Reduced dose	353	256	185	133	80	48	9
Standard dose	351	240	184	138	84	39	11

CONCLUSION

Use of a reduced-dose GC regimen was non-inferior to a standard-dose regimen at reducing the risk of death or ESRD. There was a significant reduction in the rate of serious infections in the first 12 months. The addition of PLEX to standard therapy was not found to be beneficial.[1]

In summary, in severe AAV patients, reduced exposure to GCs was non-inferior to standard GC exposure and the use of PLEX provided no added benefit.[1]

RISK OF DEATH OR ESRD WITH REDUCED GC DOSE WAS NON-INFERIOR TO STANDARD GC DOSE[1]

References & footnotes

AAV, ANCA-associated vasculitis; ANCA, anti-neutrophil cytoplasmic antibody; CYC, cyclophosphamide; eGFR, estimated glomerular filtration rate; ESRD, end-stage renal disease; GC, glucocorticoid; GPA, granulomatosis with polyangiitis; HR, hazard ratio; MPA, microscopic polyangiitis; MPO, myeloperoxidase; PLEX, plasma exchange; PR3, proteinase 3; RRT, renal replacement therapy; RTX, rituximab

*Patients with newly diagnosed or relapsing GPA or MPA with a positive test for MPO or PR3, and kidney involvement; severe AAV defined by an eGFR <50 mL per min per 1.73 m^2 of body surface area or diffuse pulmonary haemorrhage. Patients enrolled between June 2010 and September 2016 and randomised in a 1:1:1:1 ratio to receive PLEX and standard-dose GCs, PLEX and reduced-dose GCs, no PLEX and standard-dose GCs and no PLEX and reduced-dose GCs.[1]

1. Walsh M, et al. *N Engl J Med* 2020;382(22)2169. doi: 10.1056/NEJMc2004843.
2. Walsh M, et al. *N Engl J Med* 2020;382(22)2169. doi: 10.1056/NEJMc2004843. [Supplementary appendix].