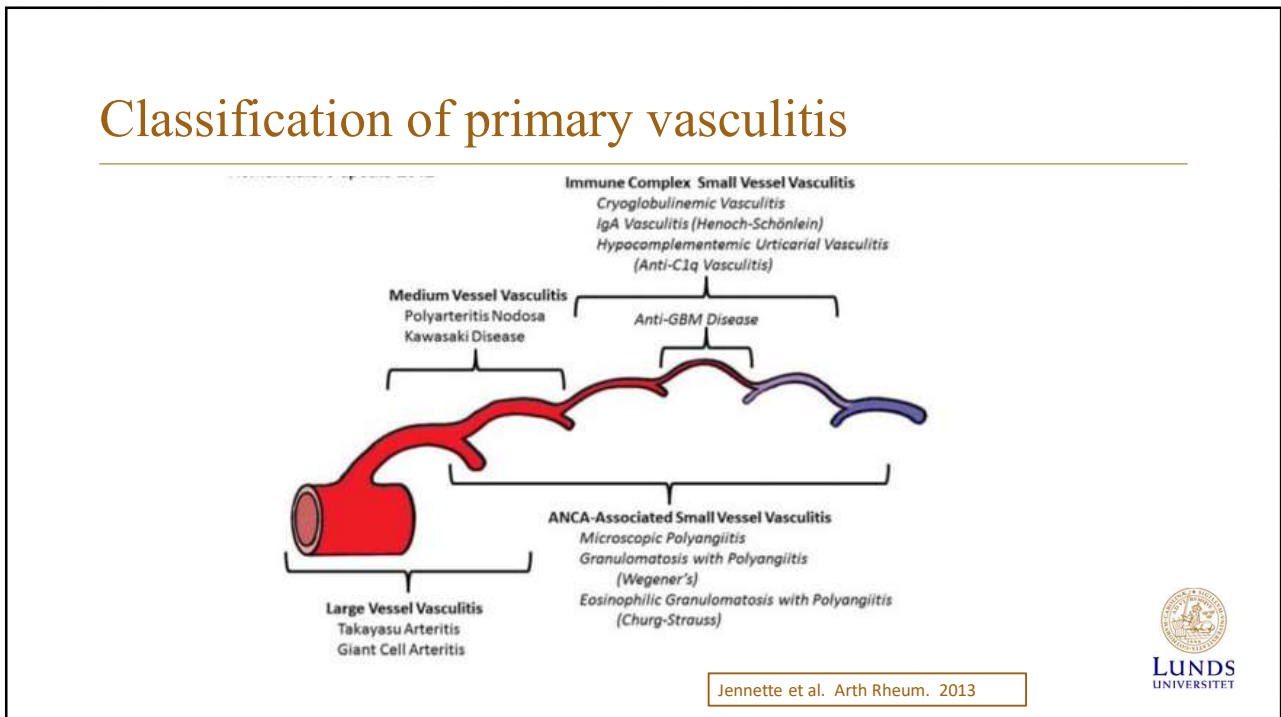


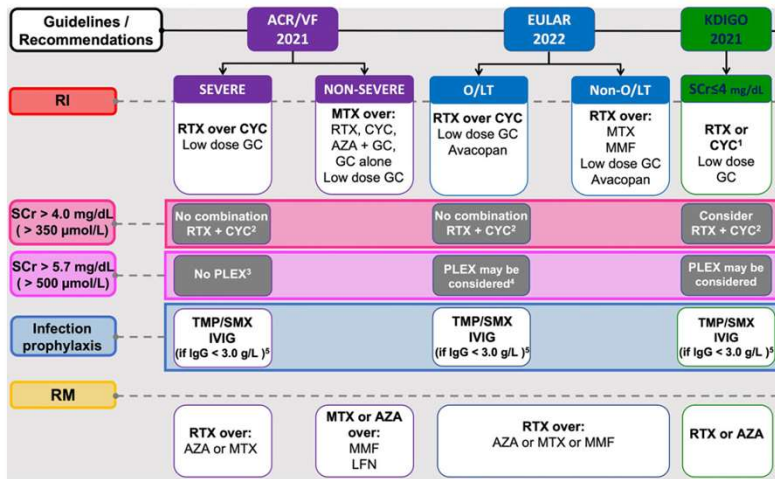


1



2

ACR – EULAR – KDIGO – Region Skåne



- ACR 2021 (?)
- EULAR 2022 (2009)
- KDIGO 2024 (2013)
- Region Skåne 2025 (1998)

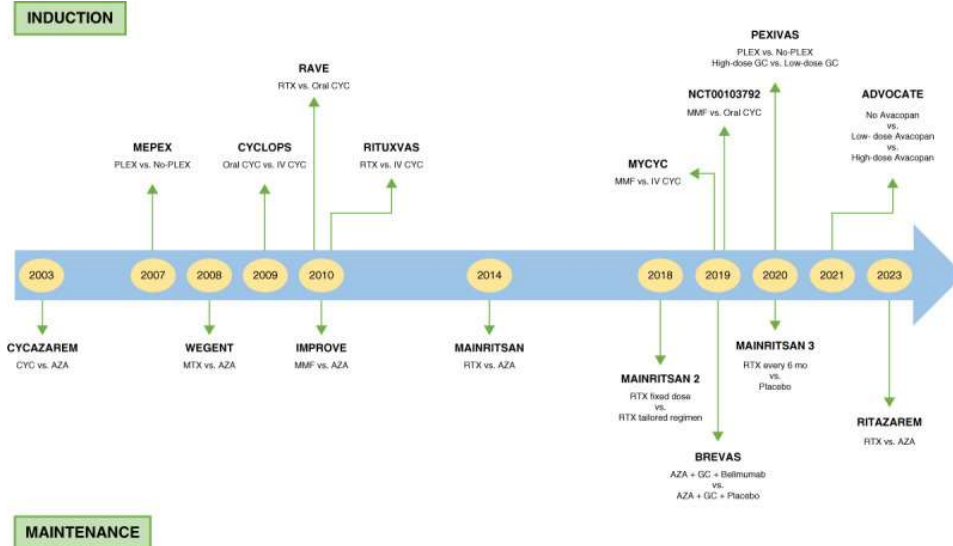
<https://vardgivare.skane.se/siteassets/1.-vardriktlinjer/regionala-varprogram--fillistning/systemisk-vaskultit---engagerande-sma-och-medelstora-karl--vardprogram.pdf>

Casal Maura M. et al. NDT, 2023 Oct 31;38(11):2637-2651



3

Trials in ANCA-associated vasculitis



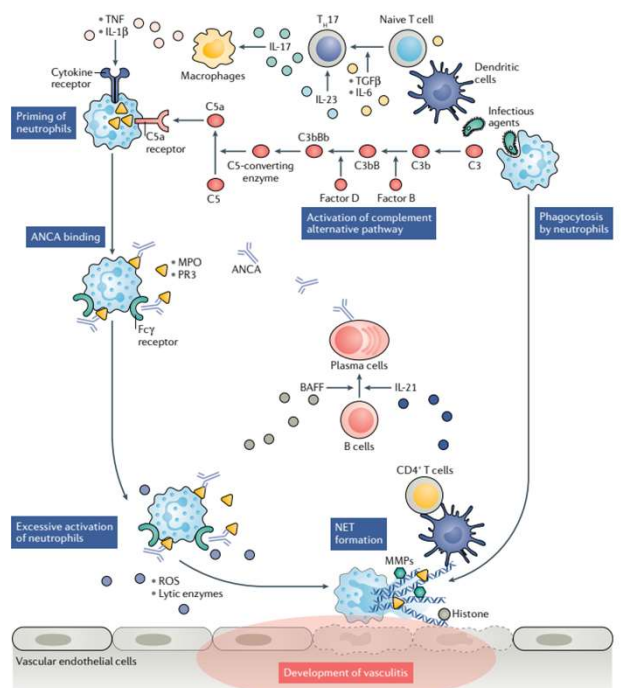
4

Pathogenesis of ANCA vasculitis

Key steps:

- Break of tolerance
- ANCA production
- Complement activation
- Priming of neutrophils
- Neutrophil degranulation and NET-osis

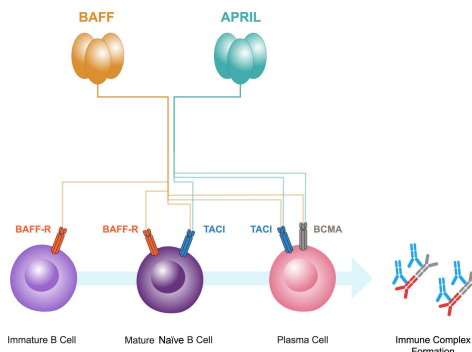
Nakazawa D. Nat Rev Rheumatol. 2019 Feb;15(2):91-101.



5

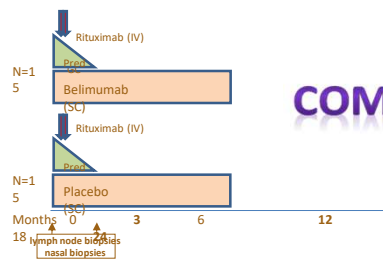
B-cell cytokine inhibition

- Belimumab
 - BAFF antagonist
- Telitacicept and Povetacicept
 - Dual antagonist of BAFF and APRIL



Cheung CK et al. Front Nephrol. 2024 Feb 1;3:1346769

- RUBY- 3 USA (Povetacicept) fully recruited
- TEST-T-AAGN, China (Telitacicept) fully recruited
- Combivas UK, (Belimumab) completed

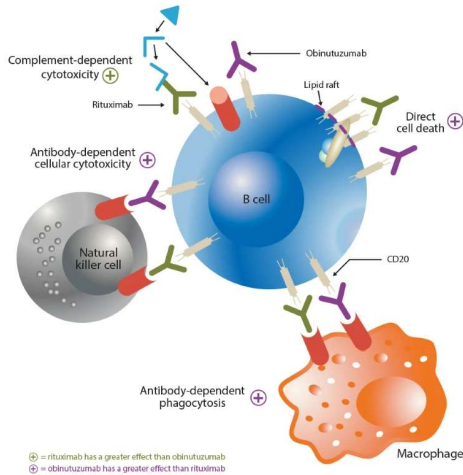


COMBIVAS



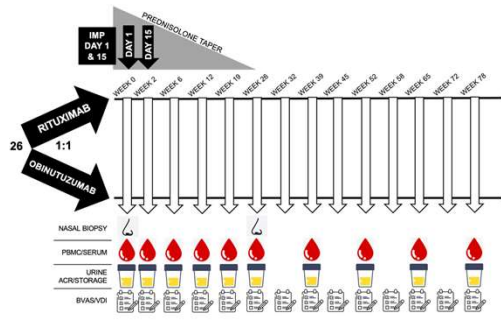
6

Enhanced B cell depletion



Hernandez et al, Nature Portfolio

Obinutuzumab



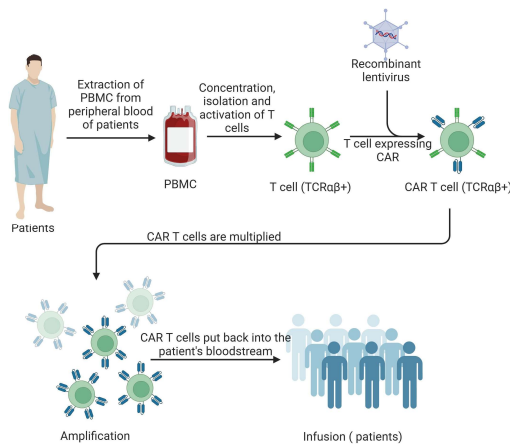
Primary endpoint: Change in CD19+ B cells in NALT

ObiVas



7

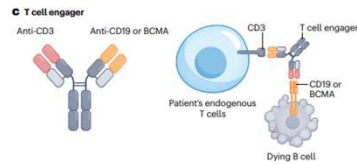
CAR-T cells and Bispecific antibodies



Kong Y et al. Front Immunol. 2025 Jan 9;15:1519671.

CAR-T cell studies in AAV listed in Cincialtrials.gov NCT06590545

- NCT06277427
- NCT06548607
- NCT06508346
- NCT07315087
- NCT06614270
- NCT06549296
- NCT06680388
- NCT06375993
- NCT06285279
- NCT06056921
- NCT07203404
- NCT07339540
- NCT06316791
- NCT06316076
- NCT06828042
- NCT06978647
- NCT07305116
- NCT06350110
- NCT06775912
- NCT06794008



Huji Xu. Nature Reviews Rheumatology, 2025

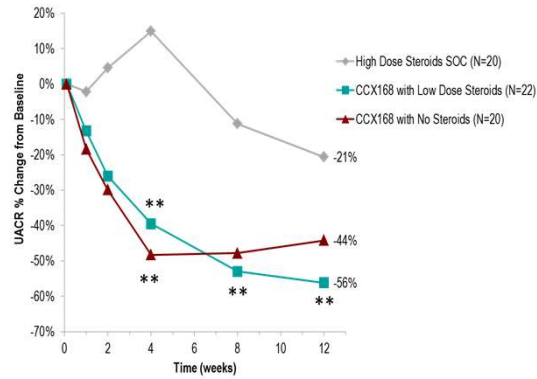
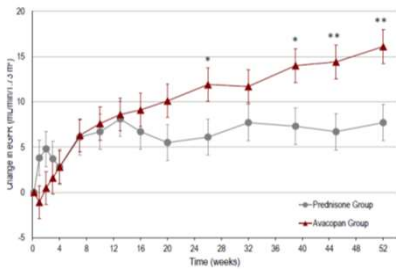


8

First complement active drug - Avacopan

CLEAR¹ och ADVOCATE²

- Rapid steroid tapering¹
- Fewer relapses than placebo^{1,2}
- Better renal recovery, most for those with low GFR³



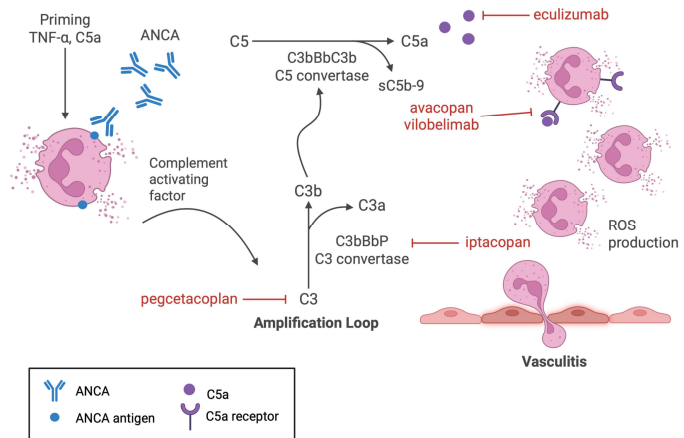
¹Jayne et al, JASN. 2021 Feb 18;384(7):599-609.
²Jayne et al, N Engl J Med. 2021 Feb 18;384(7):599-609.
³Cortazar et al. Kidney Int Rep. 2023 Feb 3;8(4):860-870..



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New complement drugs in vasculitis

- Avacopan –licensed in EU
- Iptacopan- factor B inhibition,
 - Phase 2 study, fully recruited
- Pegcetacoplan- C3 binding and blocking,
 - No studies in vasculitis yet

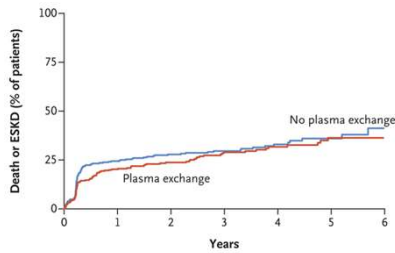


Wu et al. Kidney Int Rep. 2025 Jul 21;10(11):3747-3756



10

Plasma exchange- PEXIVAS and metaanalys



plasma-exchange group 28.4%
control group 31%
hazard ratio with plasma exchange, 0.86;
95% CI 0.65 to 1.13; P=0.27

Study	Yes/No		Risk ratio (95% CI)	Weight (%)	Risk ratio (95% CI)
	Treatment	Control			
Rifle 1980	2/4	7/1	0.38	9.75	0.38 (0.12 to 1.22)
Pusey 1991	1/24	5/18	0.18	3.31	0.18 (0.02 to 1.46)
Cole 1992	3/13	5/11	0.60	8.51	0.60 (0.17 to 2.10)
Guillevin 1997	3/16	1/12	2.05	3.08	2.05 (0.24 to 17.63)
Jayne 2007	10/60	22/45	0.44	24.11	0.44 (0.22 to 0.85)
Szpirt 2011	0/16	4/12	0.01	0.19	0.01 (0.00 to 81.26)
Walsh 2020	48/304	59/293	0.81	51.04	0.81 (0.57 to 1.16)
Overall			0.62	100.00	0.62 (0.39 to 0.98)

Test for heterogeneity: $\tau^2=0.04$;
 $I^2=14.84\%$; $H^2=1.17$

Walsh M et al. N Engl J Med 2020 Feb 13;382(7):622-631;

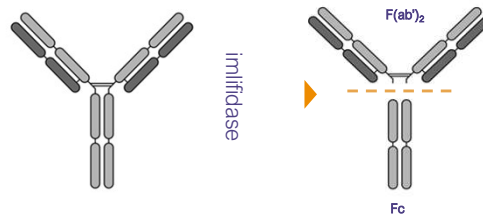
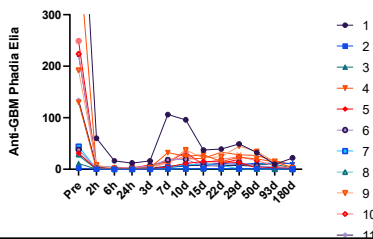
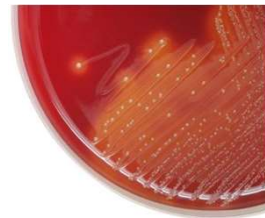
Walsh M, et al. BMJ. 2022 Feb 25;376:e064604



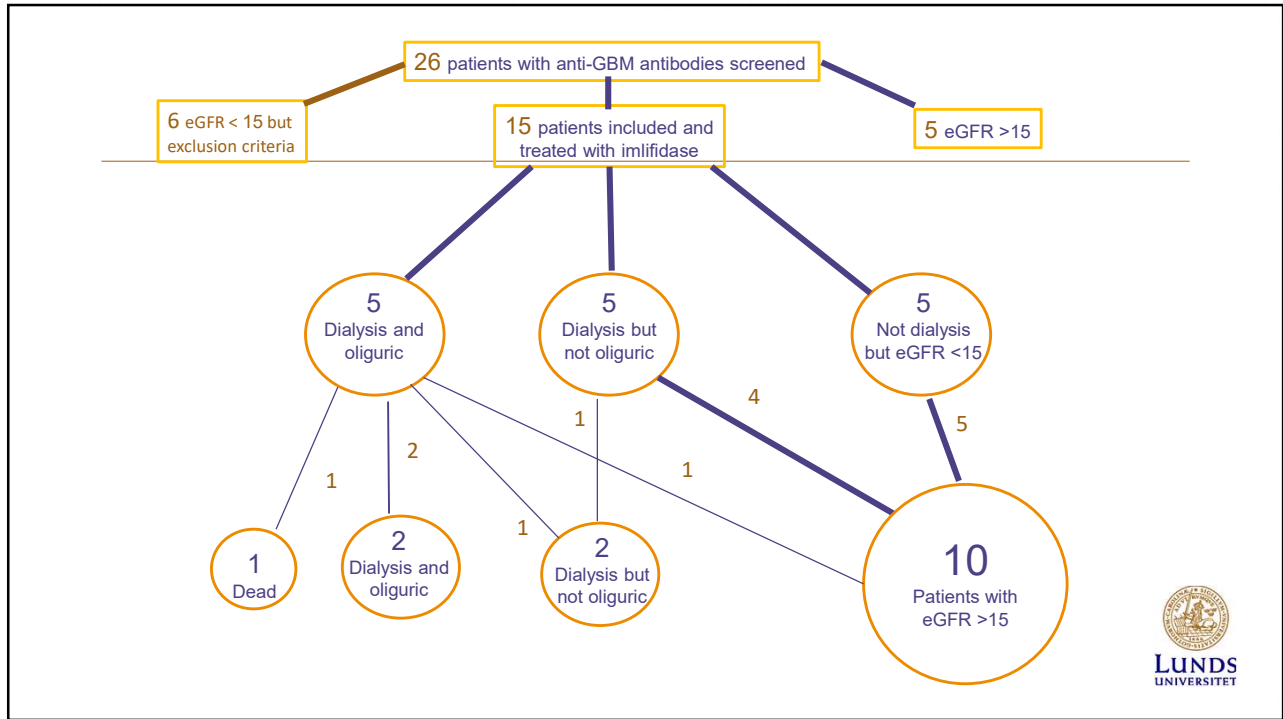
11

IdeS = imflidase

- Immunoglobulin degrading enzyme of *Streptococcus pyogenes*
 - Detected in 2001 by Lars Björck in Lund
 - Interacts with Fc-part of IgG with extremely high specificity and cleaves IgG at the hinge region,



12



13

GOODIDES-02 Phase III Design

- Open-label, multi-centre trial in EU and US
- 50 patients randomised 1:1
- Stratified according to current dialysis need (Yes/No)

Potential Pre-Study SoC	Protocol specific SoC (PLEX/CYC/Corticosteroids)	Long-Term Follow-Up
Screening	Randomisation	1 st PLEX following randomisation
Potential Pre-Study SoC	Protocol specific SoC (PLEX/CYC/Corticosteroids)	Long-Term Follow-Up

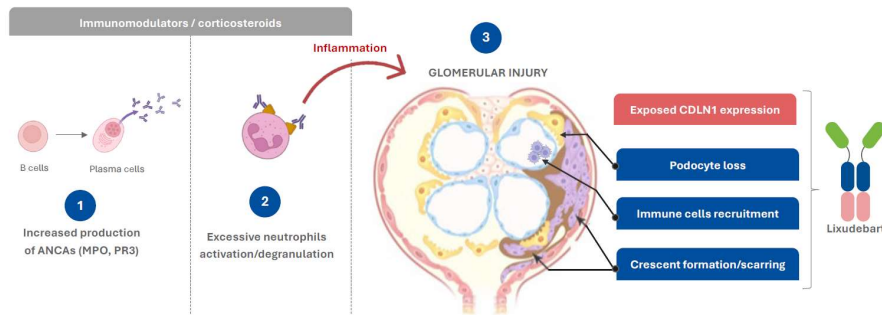
Imlifidase (0.25 mg/kg BW) 15 min infusion
Study Visit: Day 1 Day 2 Day 5 Day 8 Day 15 Day 22 Day 29 Day 50 Day 92 Day 183 12 Months 18 Months 24 Months
 Core-Trial Completion Visit End-of-Trial Visit

14

14

Protecting glomerular cells

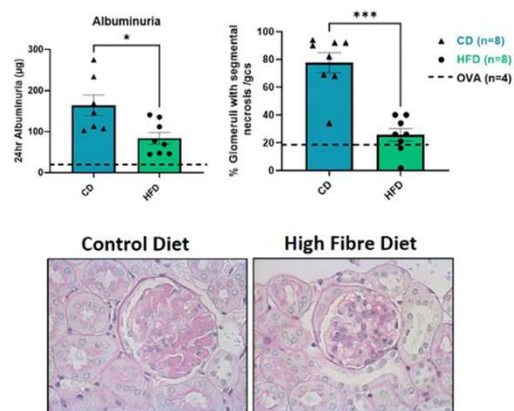
Lixudebart (ALE.F02): anti-CLDN1 antibody
Clinical study recruiting



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Inhibiting neutrophil NET-osis

- **Short Chain Fatty Acids (SCFAs):**
 - (acetate, butyrate etc)
 - Mucosal barrier
 - Monocyte differentiation
 - Tregs
 - Inhibits neutrophil NET-osis
- SCFAs in the diet:
 - Reduced injury in AAV-kidney model
 - Similar effect with diet rich in fibers



Tan D et al, Int J Mol Sci. 2024 Apr 28;25(9):4817

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