

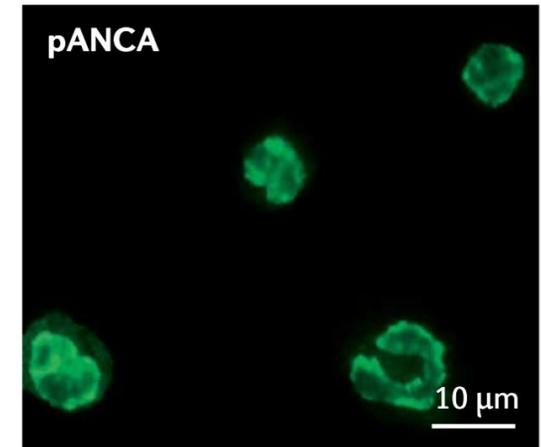
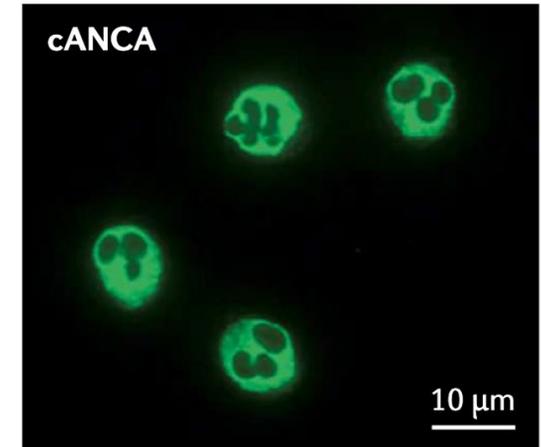
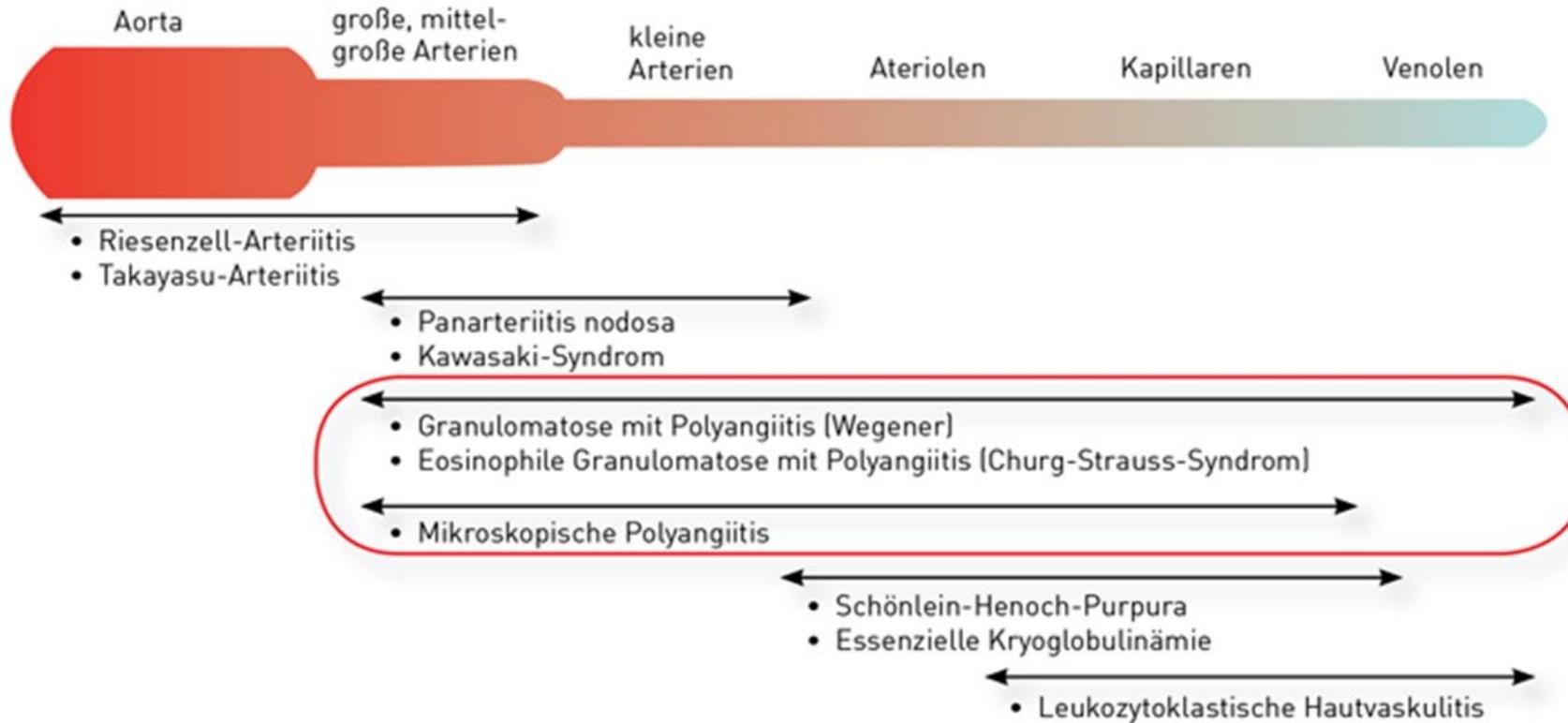
ANCA-assoziierte Vaskulitiden – ein Update

PD Dr. M. Becker, Klinik für Rheumatologie, Universitätsspital Zürich

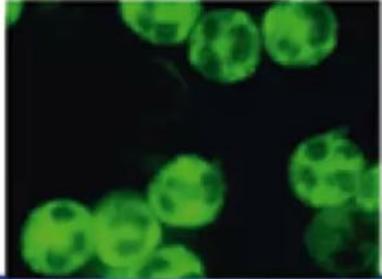
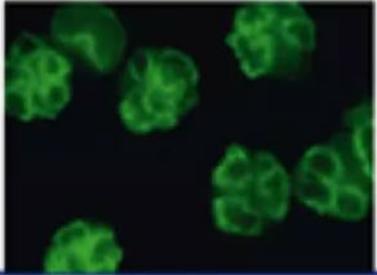
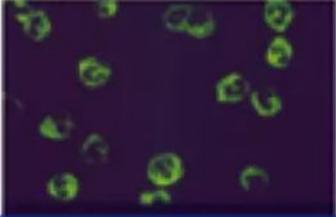
GPA/MPA

Vaskulitiden

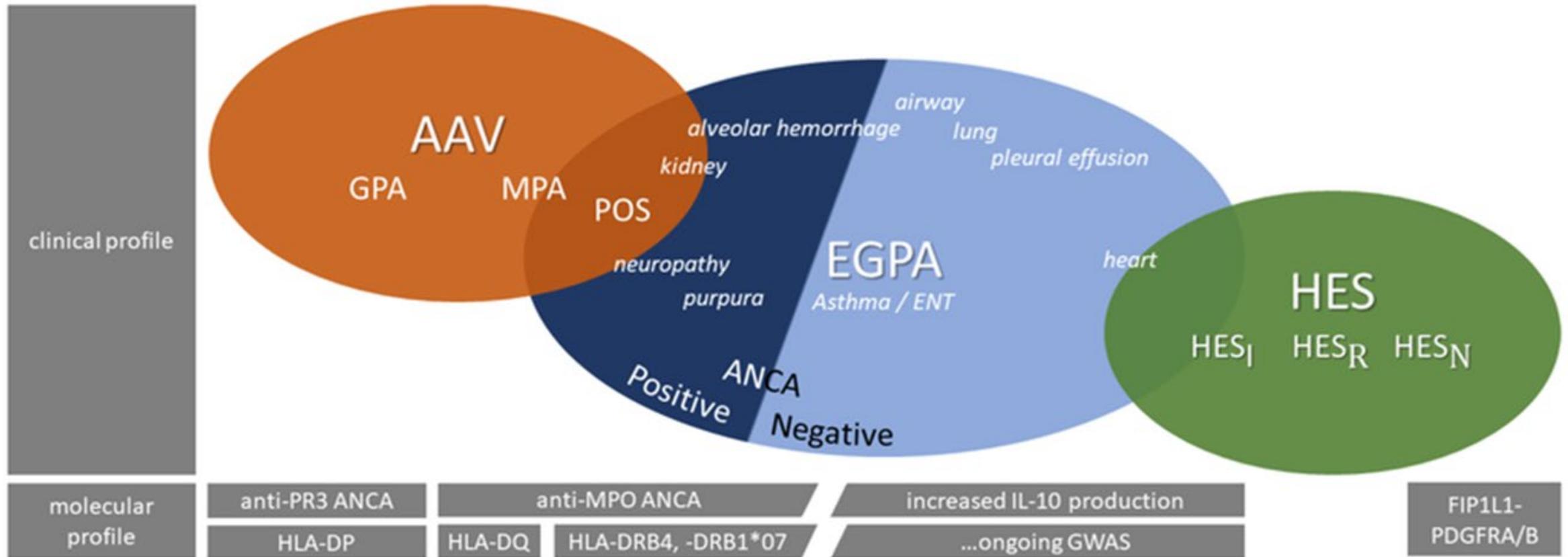
Primäre Vaskulitiden



Anti-Neutrophile cytoplasmatische Antikörper (ANCA)

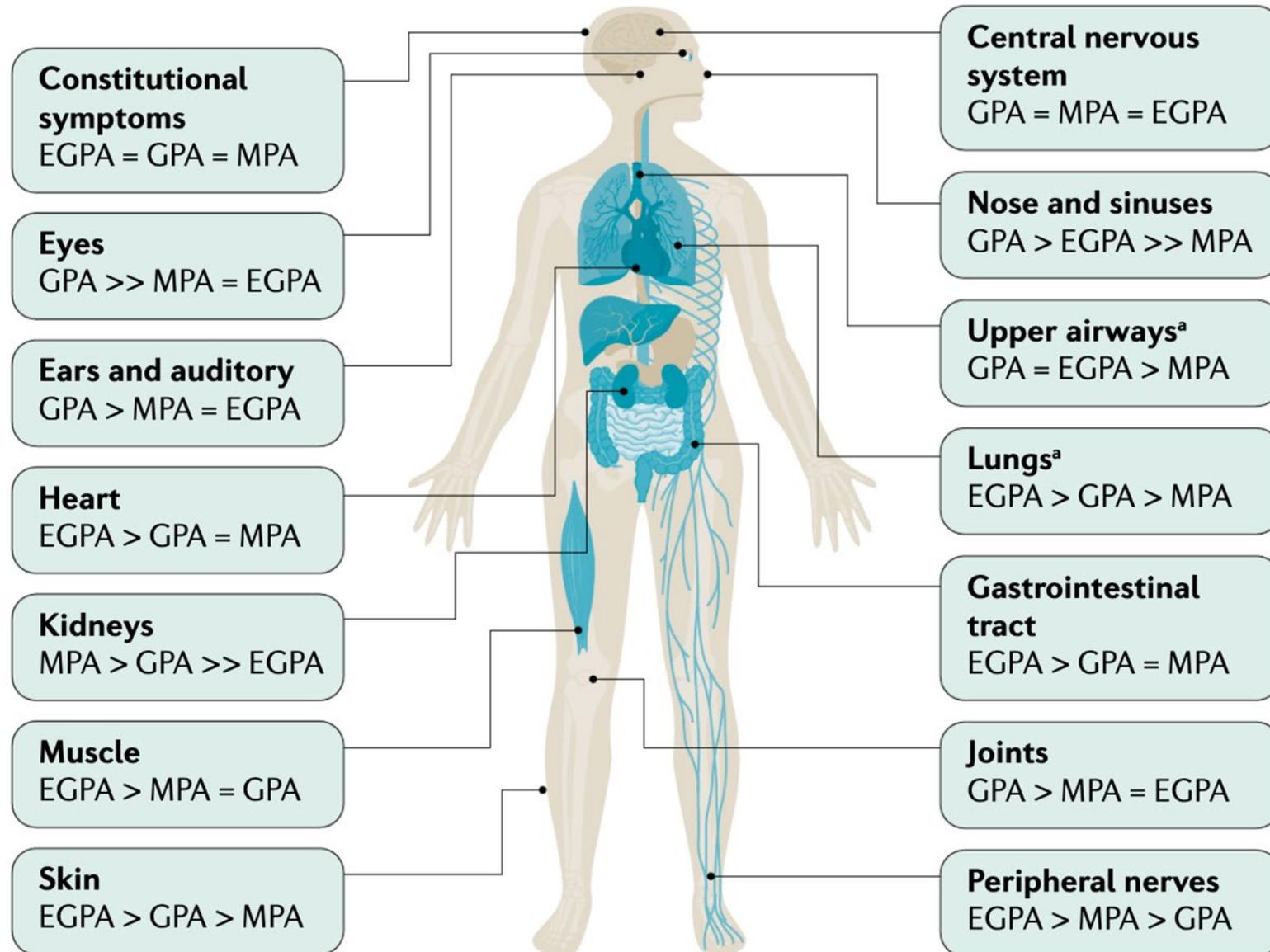
	cANCA	pANCA
Ethanolfixierung		
Formalinfixierung (granuläres Muster)		
Immunoassay	PR3 ~ 85% MPO ~ 10%	MPO ~ 85% PR3 ~ 10%
Formalinfixierung (negativ/unspezifisch) PR3/MPO negativ	atypische cANCA (aANCA)	atypische pANCA (aANCA)

Spektrum der ANCA-assoziierte Vaskulitiden



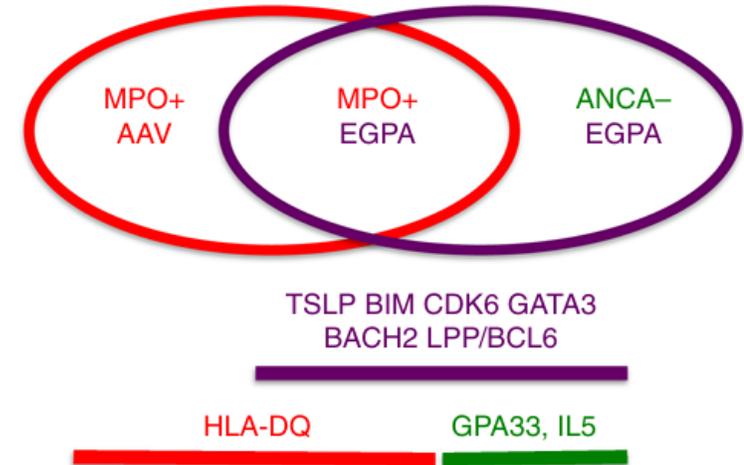
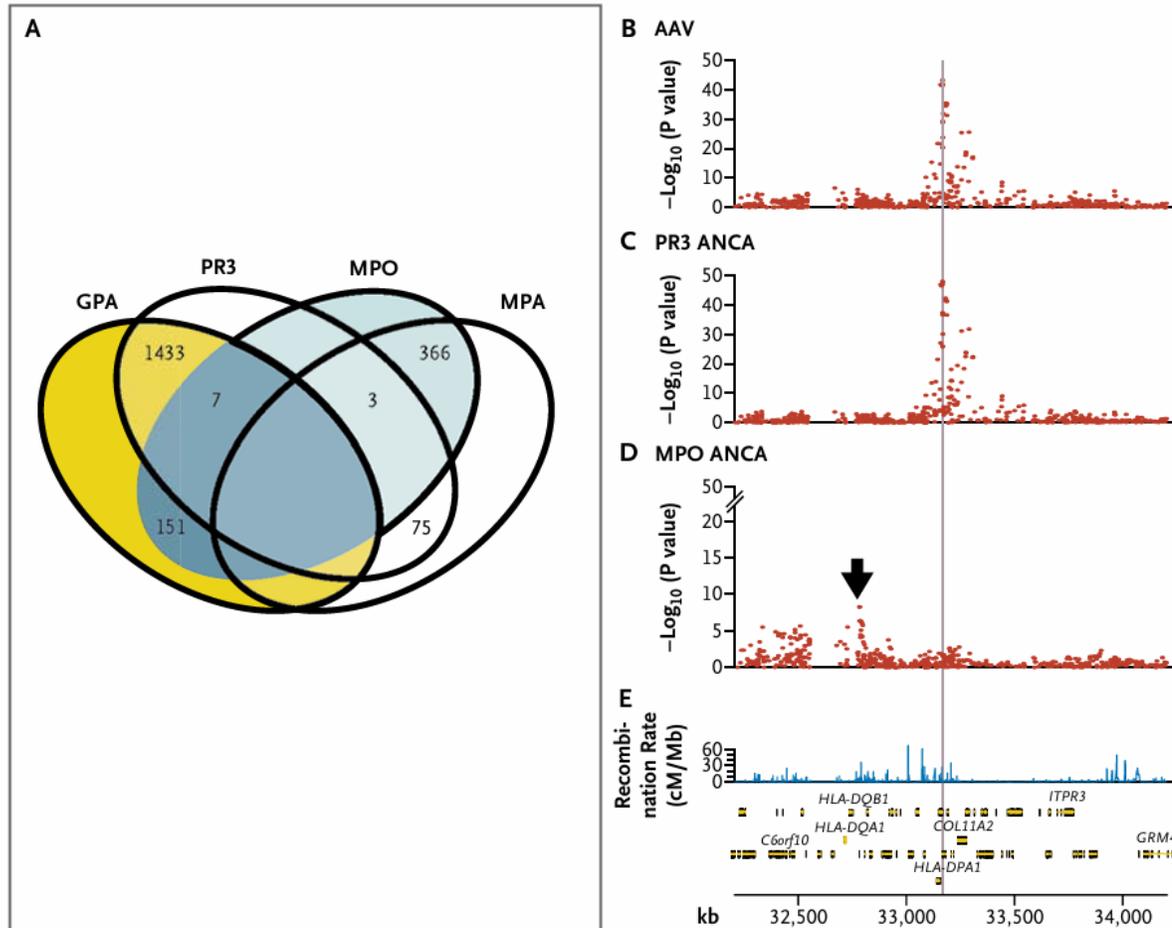
HES, hypereosinophilies Syndrom (I = idiopathisch, R = reaktiv, N = neoplastisch)

Organbeteiligung der ANCA-assoziierte Vaskulitiden



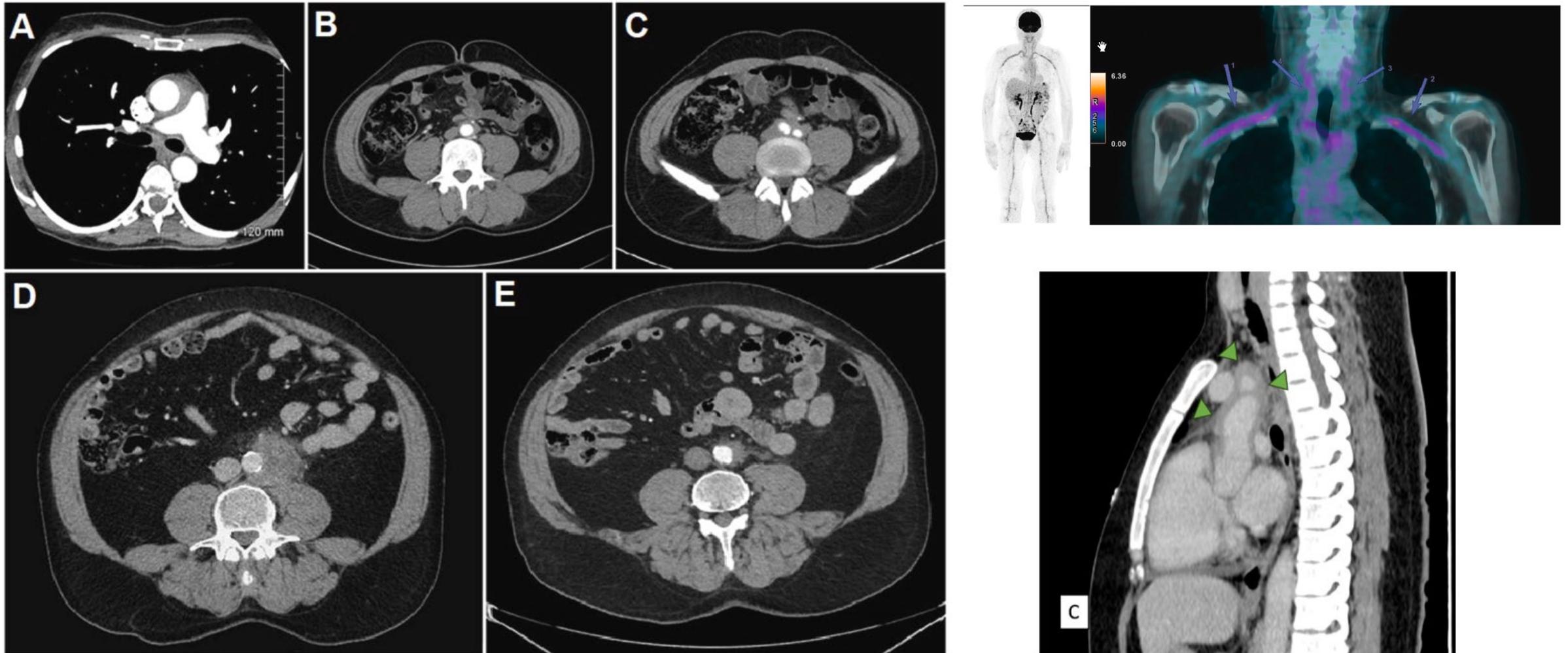
Nat Rev Dis Primers 6, 71 (2020).

ANCA-assoziierte Vaskulitiden – Gemeinsamkeiten/Unterschiede

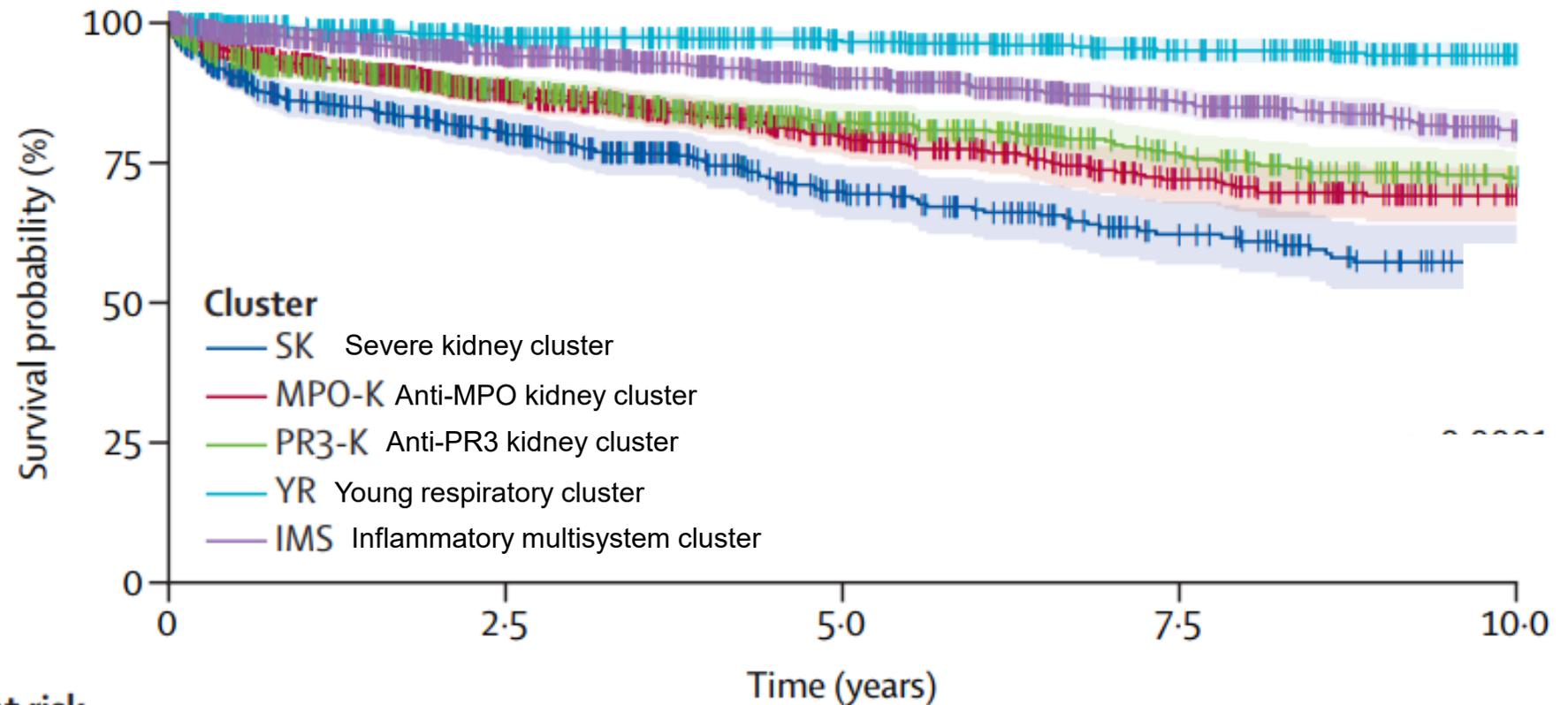


Clinical feature	% of patients with feature		
	MPO+ AAV (non EGPA)	MPO+ EGPA	ANCA-EGPA
Glomerulonephritis	85	29*	9
Neuropathy	20	79*	57
Asthma	n.d.	100	100
Eosinophilia	4.5	100	100
Pulmonary hemorrhage	17	4	4
Ear nose or throat	32	81	88
Pulmonary infiltrates	20	45	61*
Cardiac involvement	3	15	30*
Rituximab response	98	80	38

«Not by the books»: Grossgefässvaskulitis bei AAV



AAV-Analyse von 3868 Patienten: Überleben

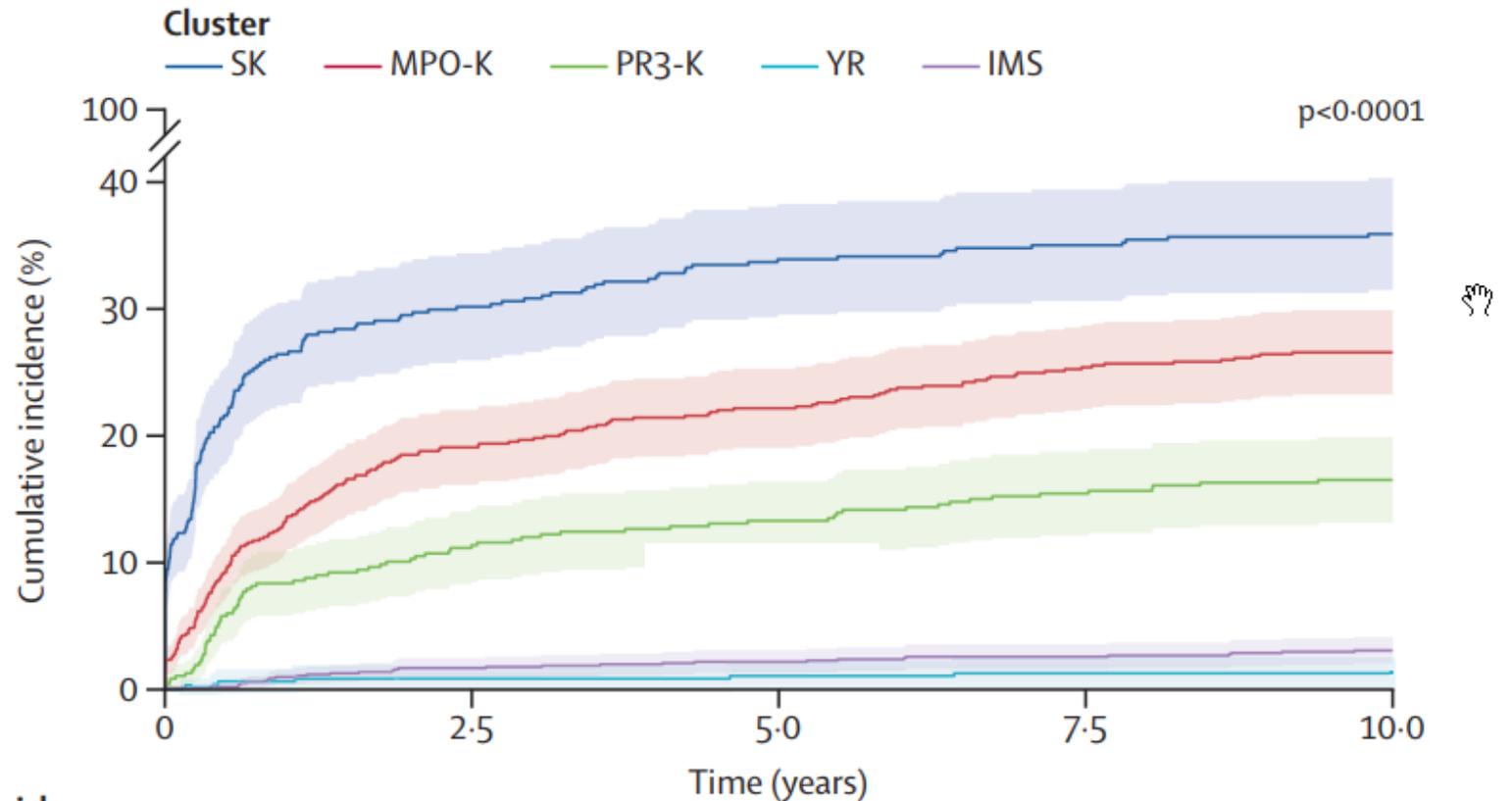


**Number at risk
(number censored)**

	0	2.5	5.0	7.5	10.0
SK	555 (0)	303 (158)	166 (264)	100 (315)	64 (408)
MPO-K	782 (0)	460 (240)	279 (386)	163 (481)	100 (638)
PR3-K	683 (0)	451 (159)	308 (276)	210 (357)	147 (556)
YR	646 (0)	452 (180)	363 (266)	268 (356)	186 (622)
IMS	1202 (0)	809 (332)	590 (522)	422 (667)	281 (1067)

AAV-Analyse von 3868 Patienten: Niereninsuffizienz

- Cluster:
 SK=severe kidney cluster.
 MPO-K=anti-MPO kidney involvement cluster.
 PR3-K=anti-PR3 kidney involvement cluster.
 YR=young respiratory cluster.
 IMS=inflammatory multisystem cluster.



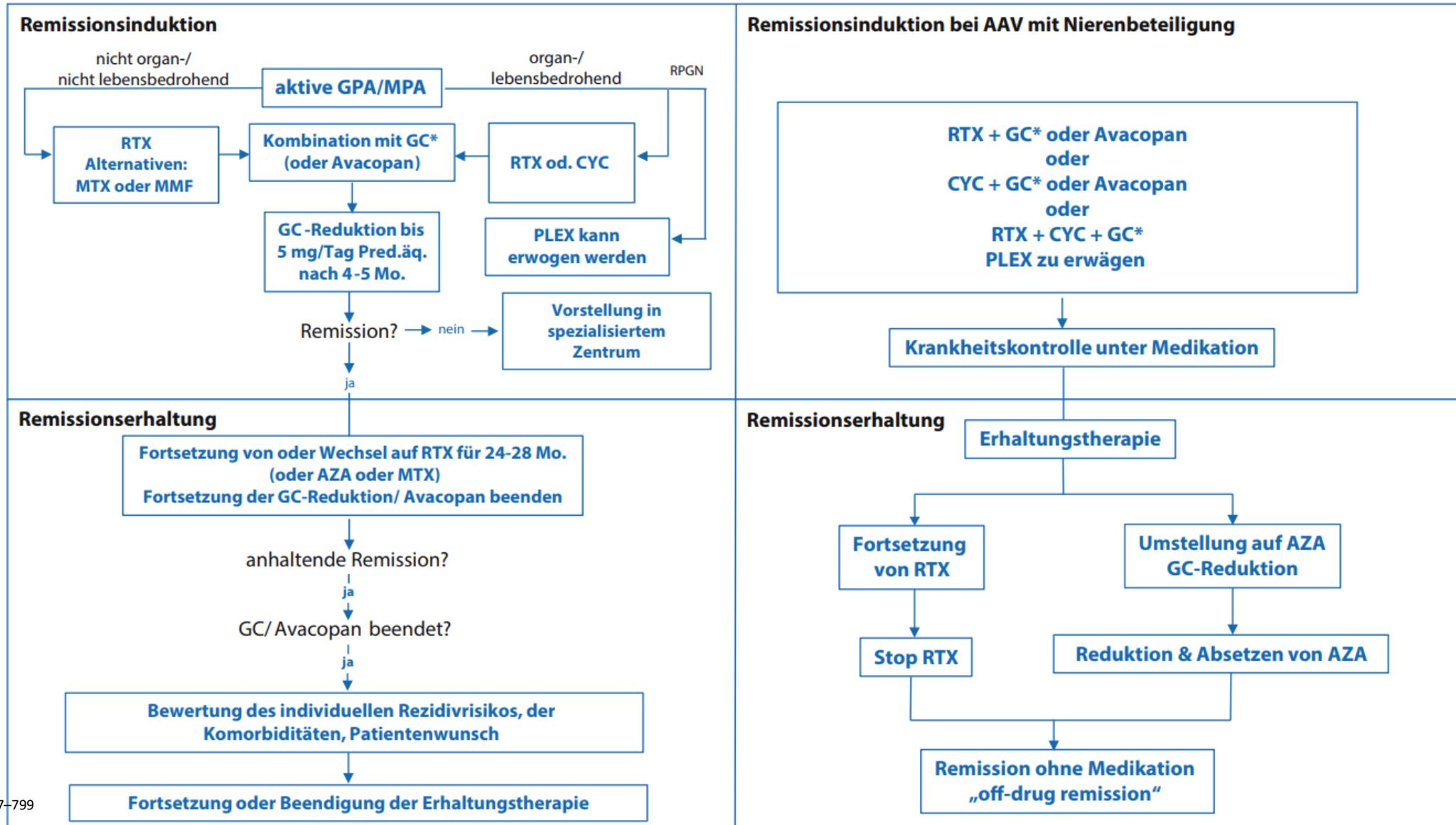
Number at risk
(number dead,
number censored)

Cluster	0	2.5	5.0	7.5	10.0
SK	454 (0, 0)	178 (84, 55)	97 (111, 92)	58 (123, 114)	33 (130, 161)
MPO-K	681 (0, 0)	327 (75, 149)	186 (109, 235)	108 (127, 273)	64 (133, 367)
PR3-K	466 (0, 0)	267 (50, 96)	182 (70, 152)	119 (85, 190)	84 (91, 298)
YR	467 (0, 0)	315 (9, 139)	254 (10, 198)	187 (14, 260)	132 (15, 446)
IMS	1008 (0, 0)	670 (52, 269)	492 (78, 416)	362 (96, 524)	243 (118, 859)

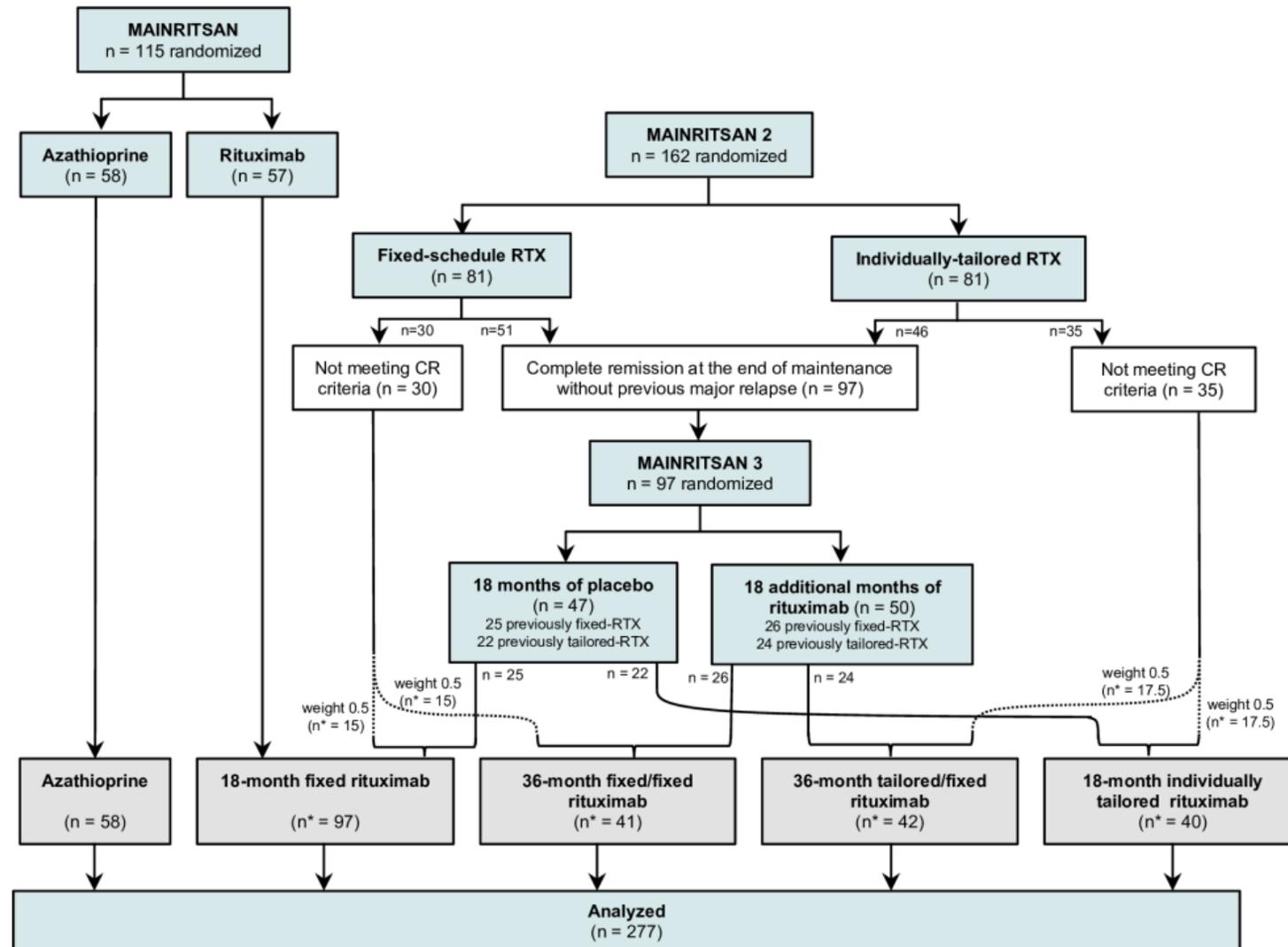
Therapie-Empfehlungen bei AAV (GPA/MPA)

EULAR 2023

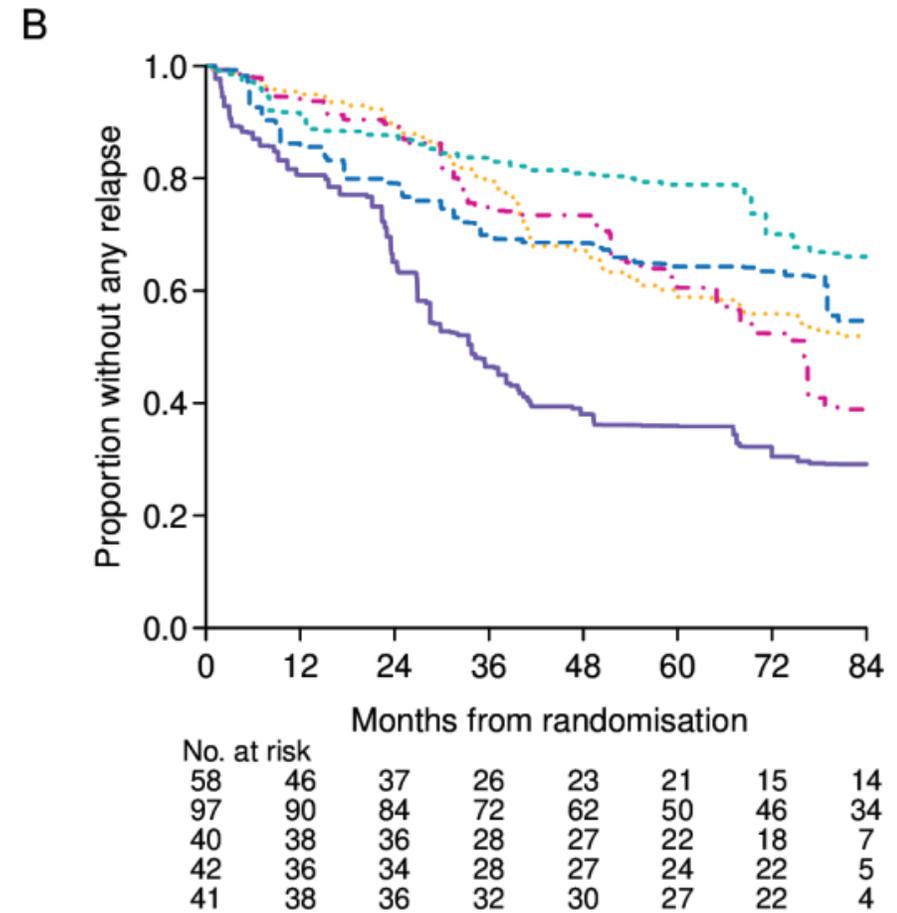
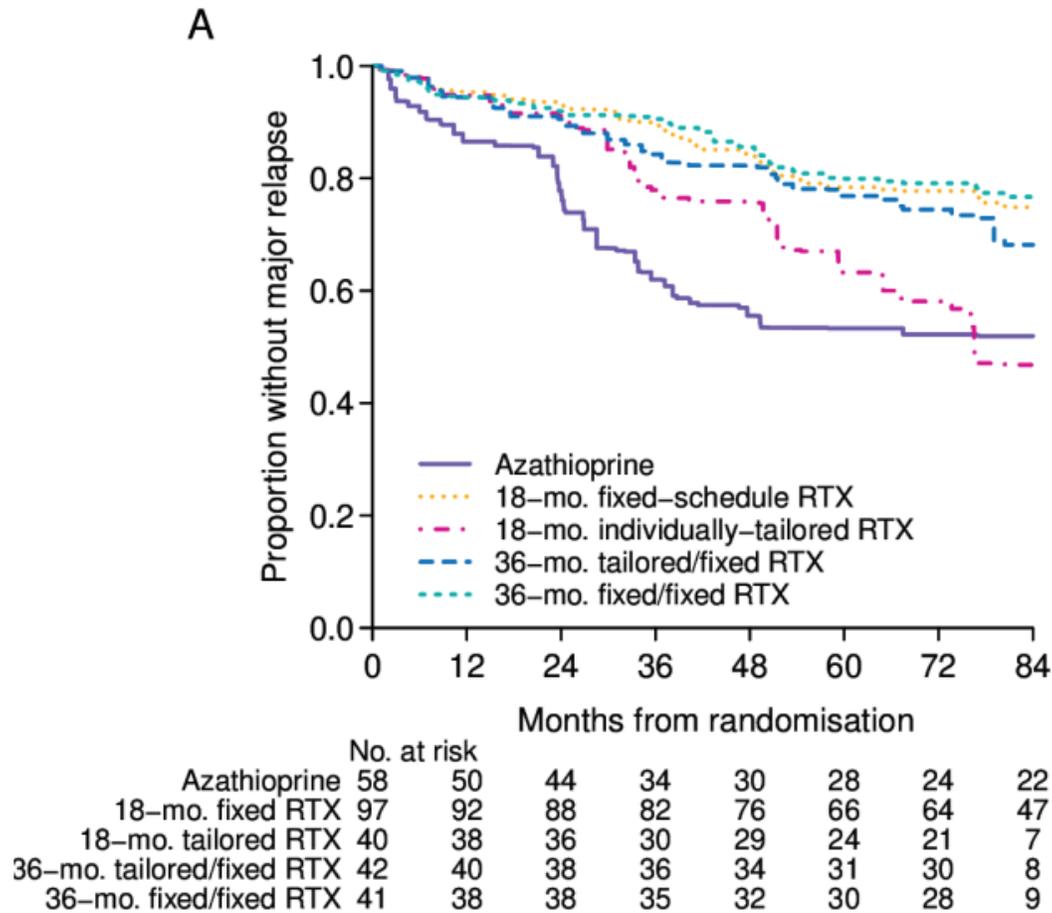
KDIGO 2024



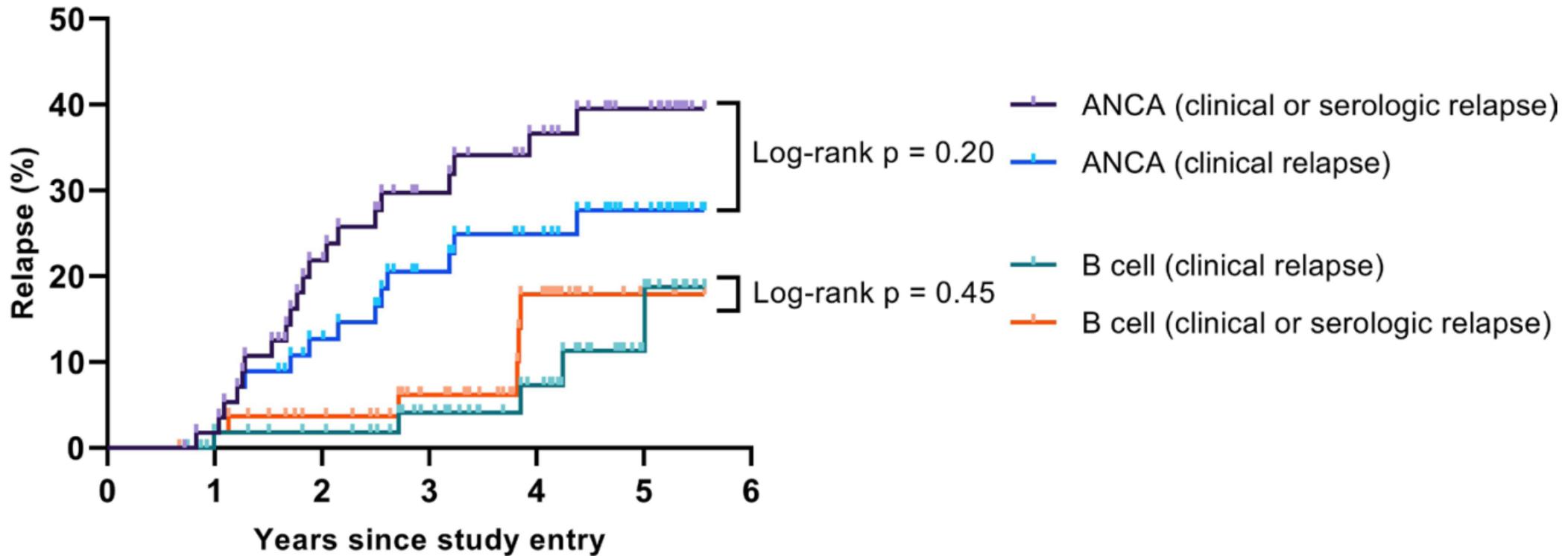
MAINRITSAN-Studien: AZA/RTX



MAINRITSAN-Studien: AZA/RTX



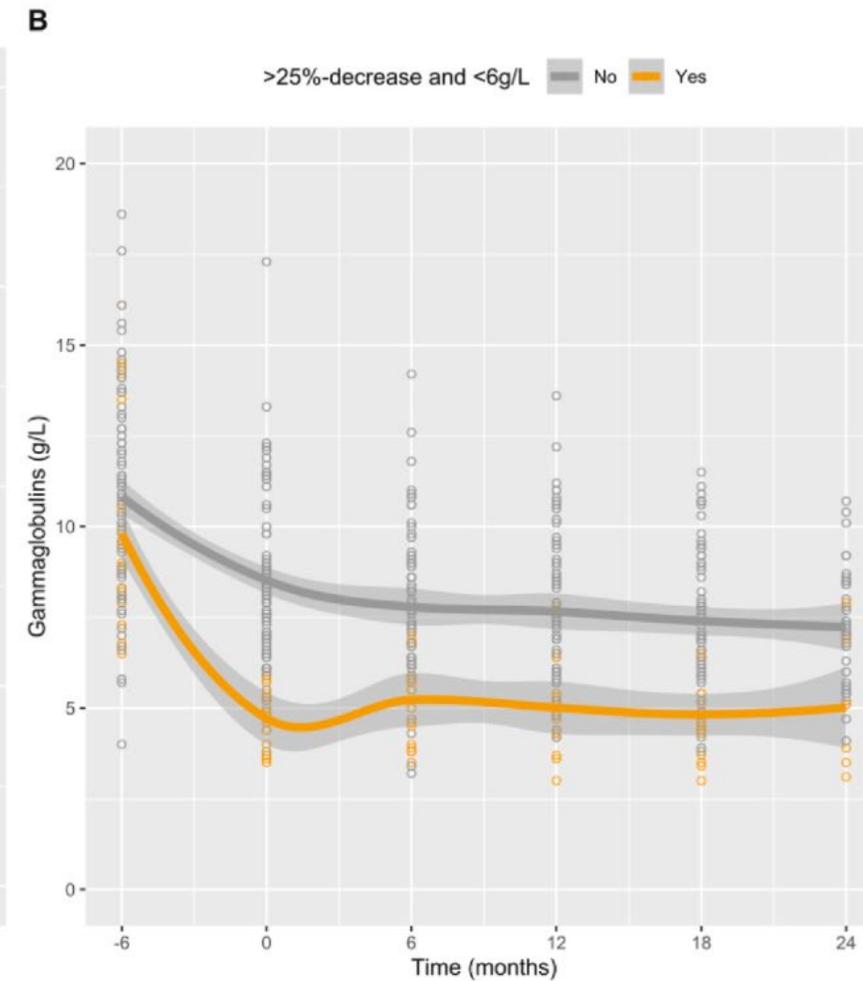
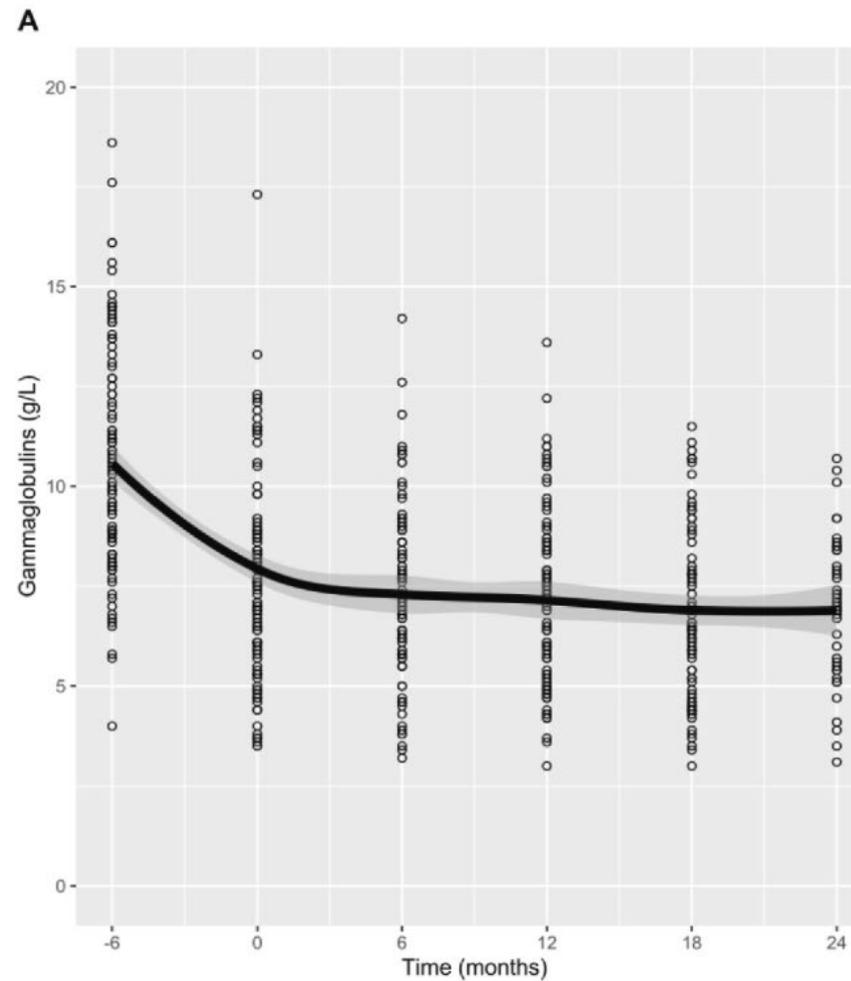
Re-Infusion von RTX: B-Zell-Repopulation vs. ANCA



- ANCA-Gruppe: Anstieg des ANCA-Titers auf das 4 (PR3) bis 5-fache (MPO) des cut-offs
- B-Zellgruppe: Anstieg der peripherin B-Zellen ≥ 10 Zellen/ul

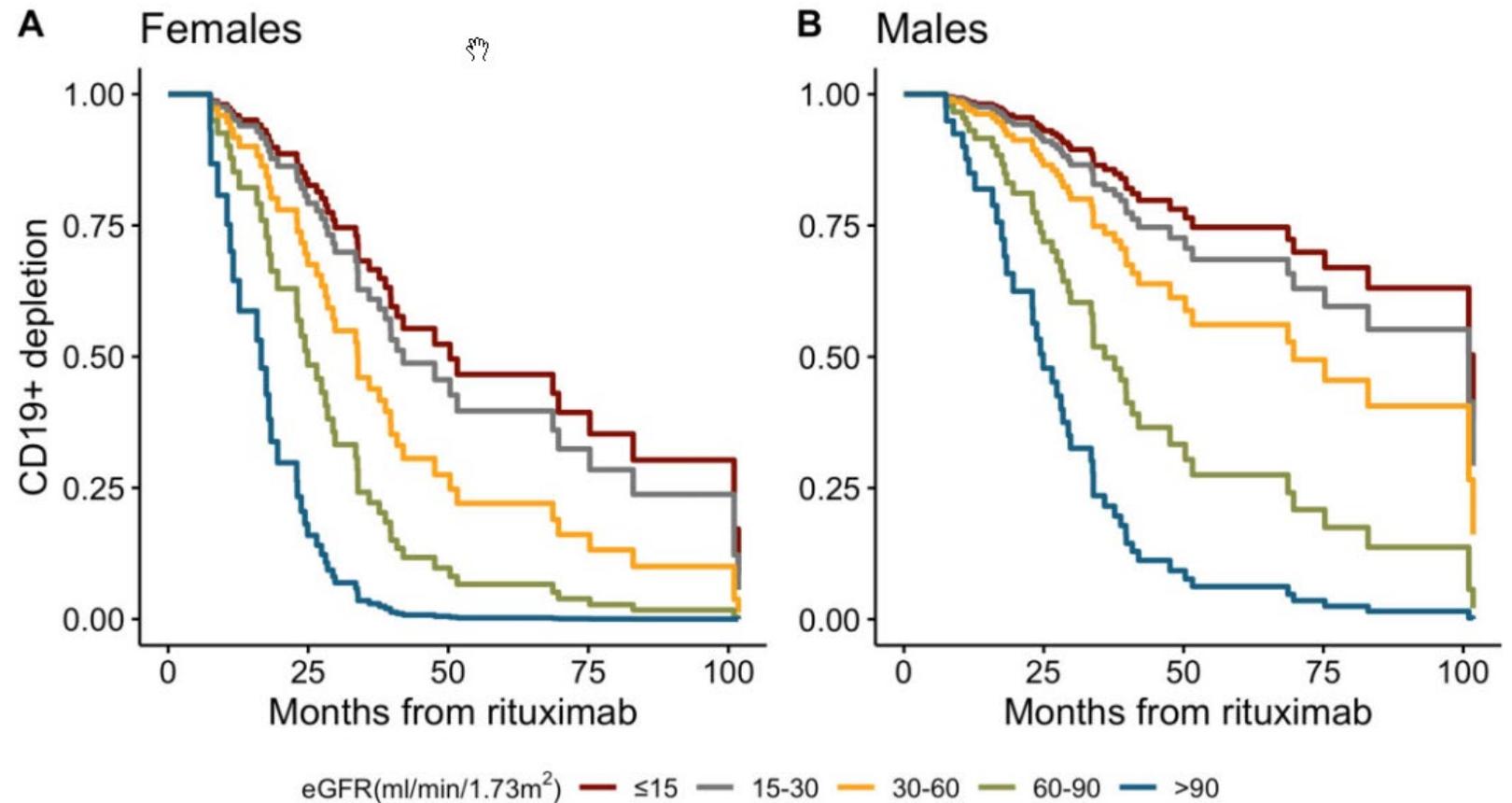
Hypogammaglobulinämie nach RTX

- Beobachtungsstudie mit 98 Pat.
- Risikofaktoren für IgG-Reduktion >25% oder IgG <6g/l
 - Alter
 - Baseline IgG <10g/l
 - Methylprednisolon-Pulse
- Infektionen:
 - Methylprednisolon-Pulse
 - IgG <6g/l oder IgG-Reduktion >25%

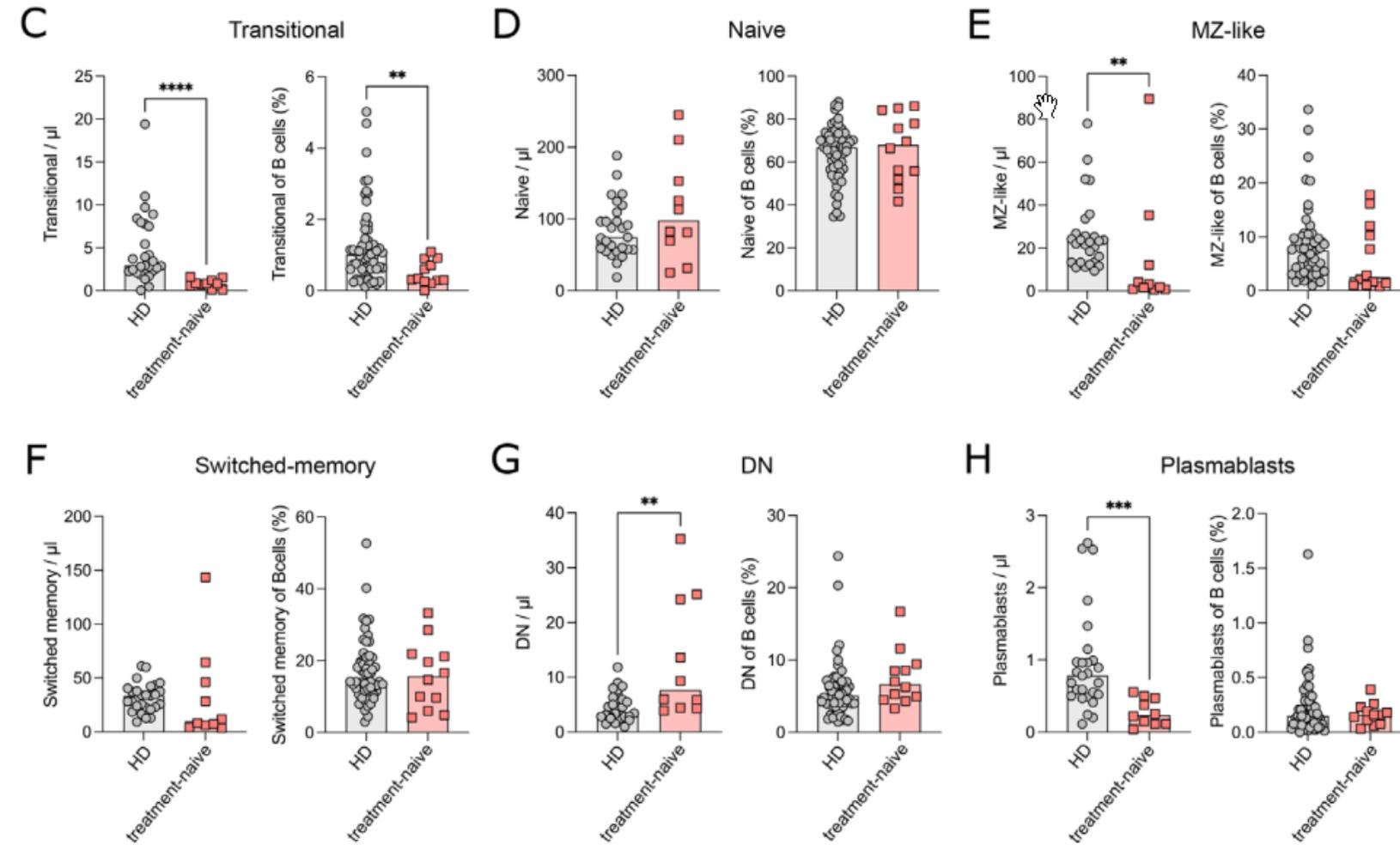


Repopularisierung von B-Zellen nach RTX

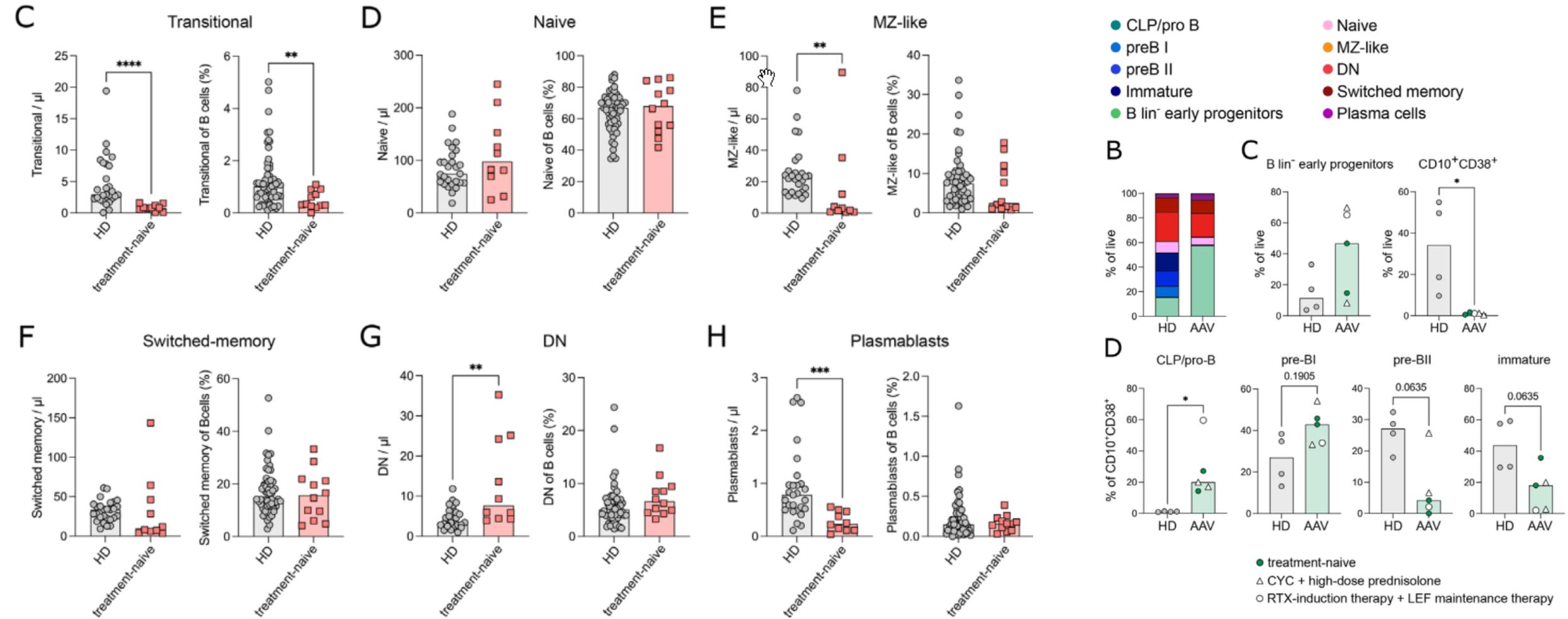
- Repopularisierung mit B-Zellen:
- Abhängig von der GFR (je niedriger, desto länger)
- Abhängig vom Geschlecht (Männer > Frauen)



B-Zell-Veränderungen bei AAV



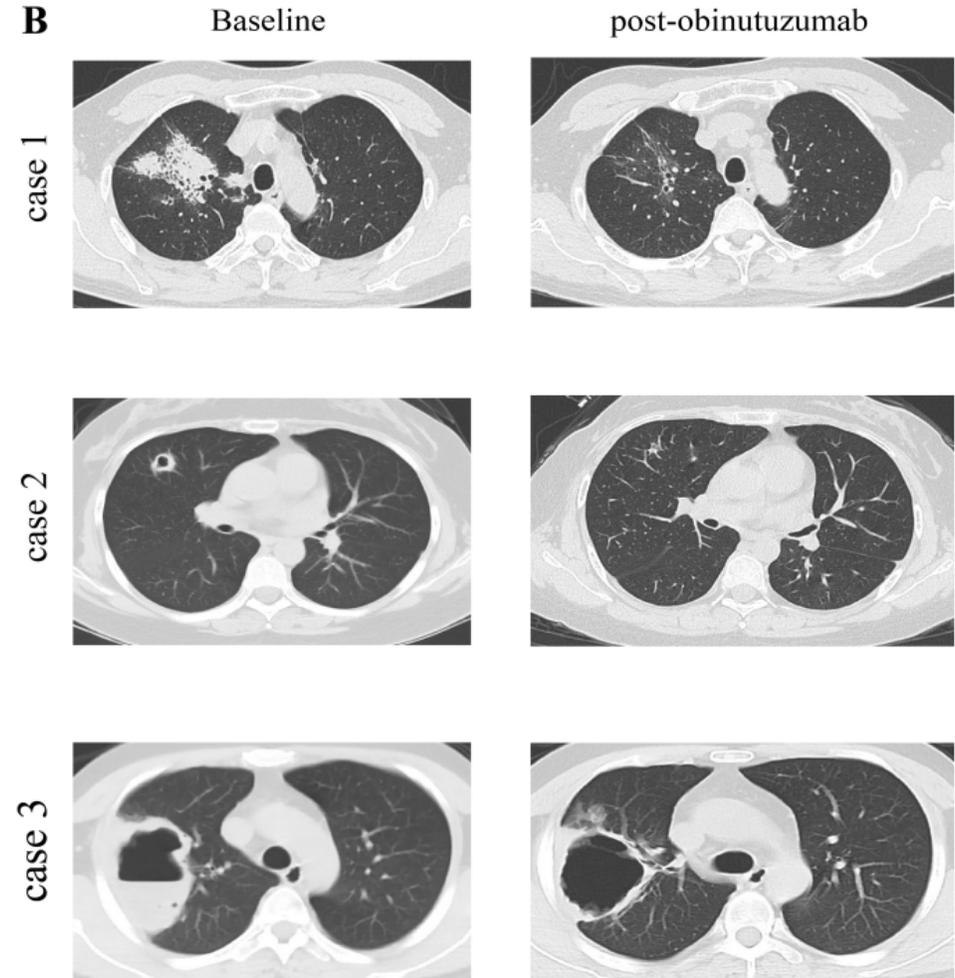
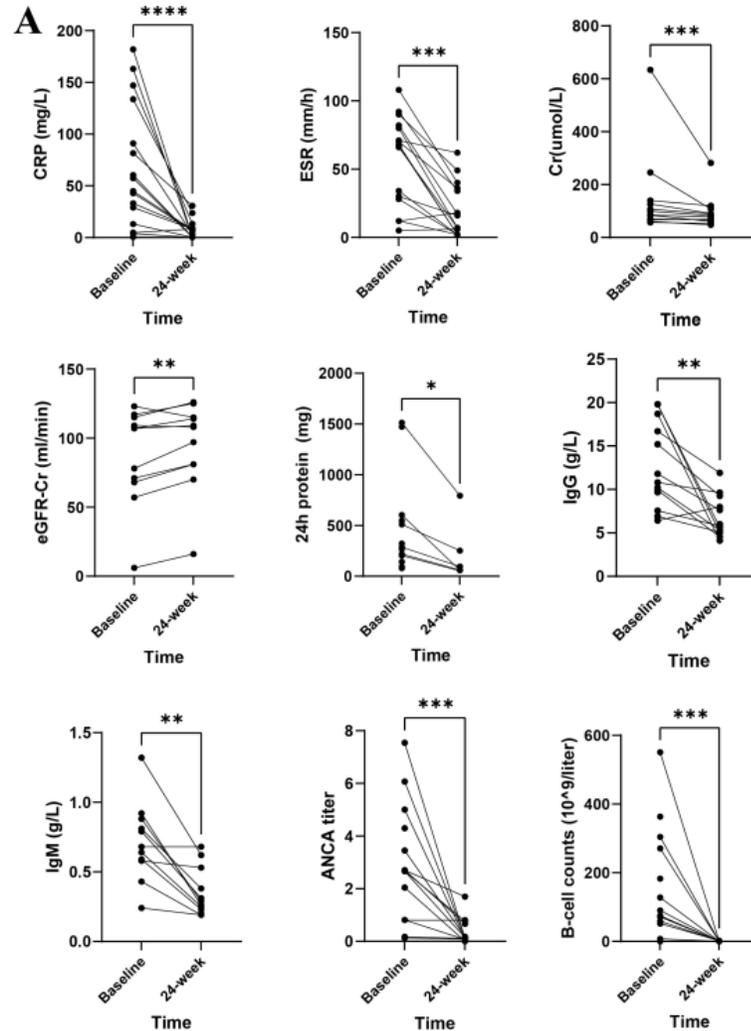
B-Zell-Veränderungen bei AAV



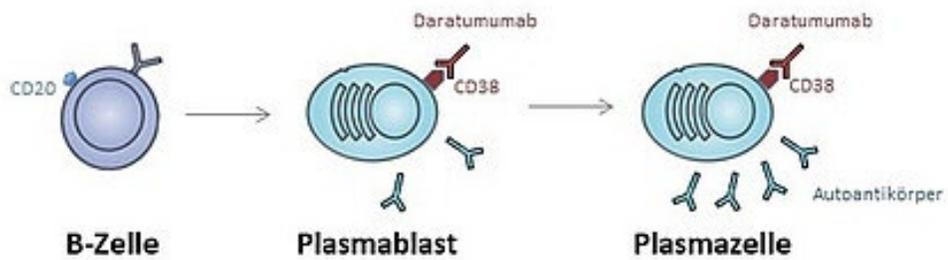
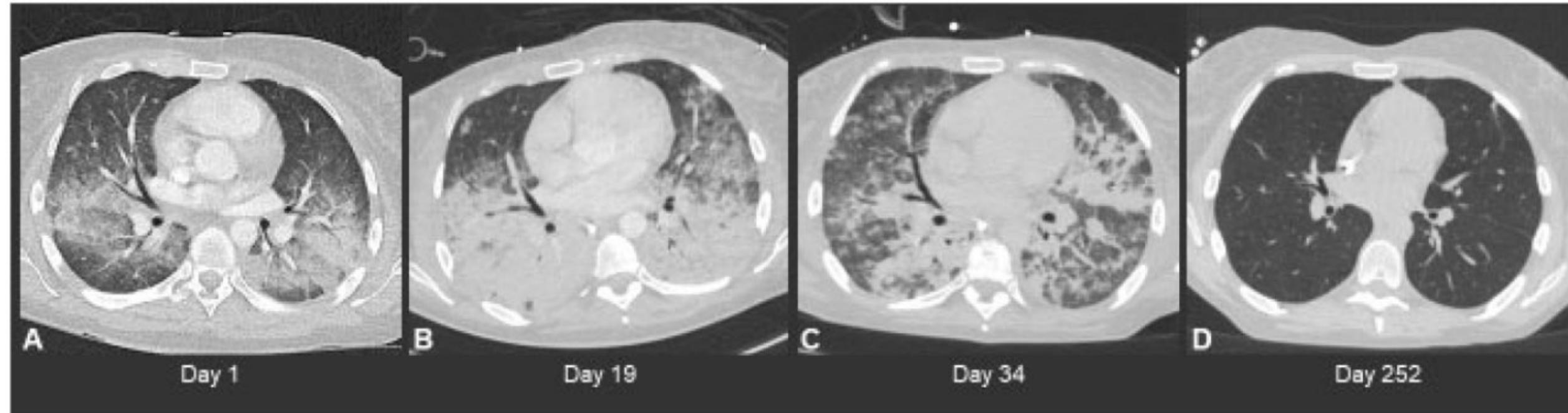
Obinutuzumab (anti-CD20 – 2. Generation) bei AAV:

- 16 Pat. Refraktär auf CYC/RTX
- Meist single dose 1000mg

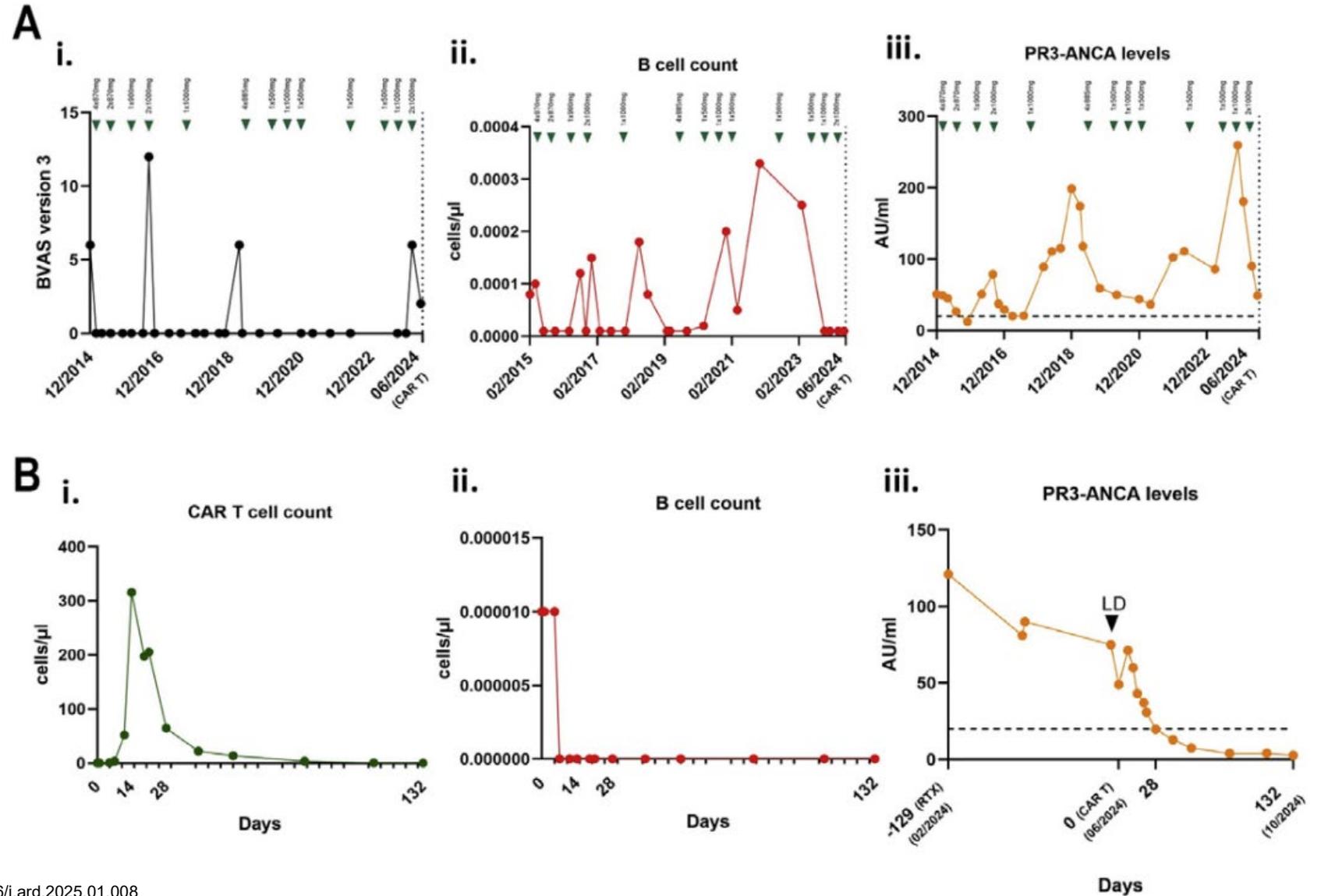
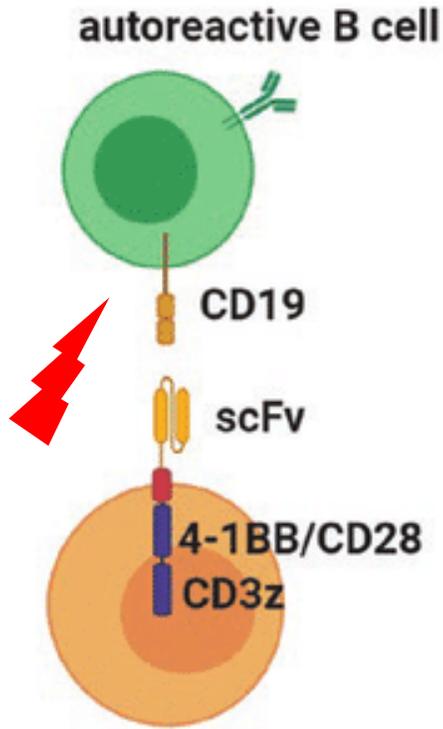
-> ObiVAS Studie (BMJ Open 2024;14:e083277)



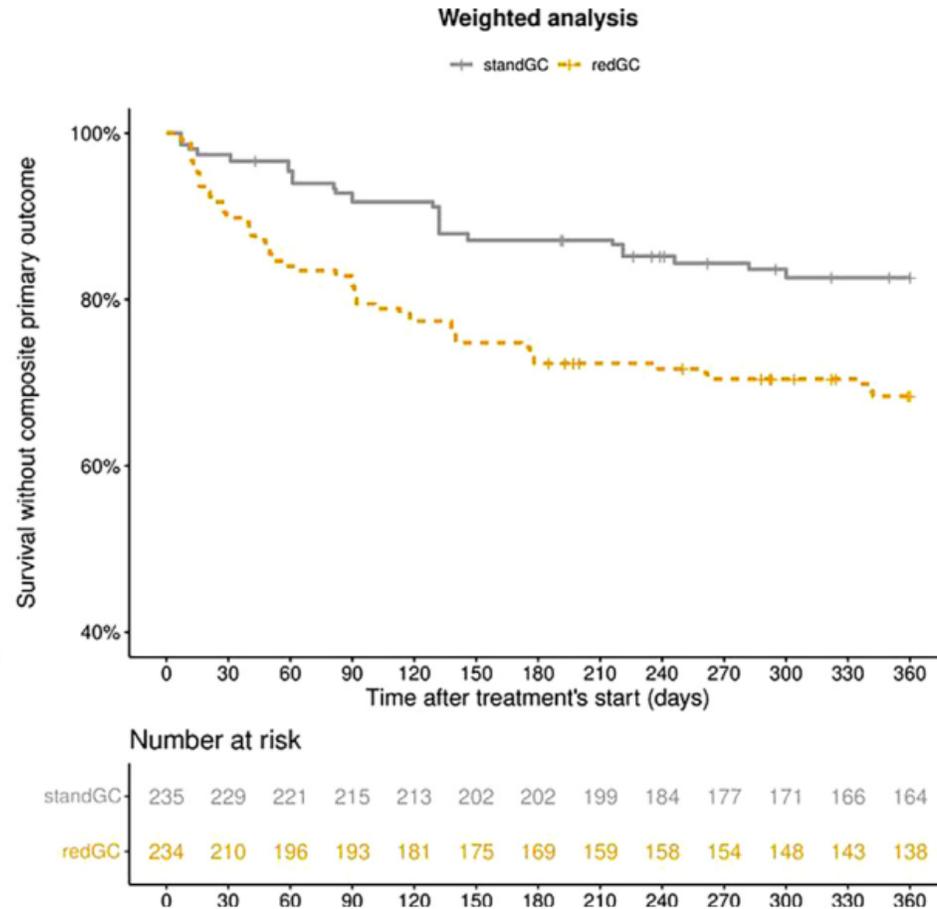
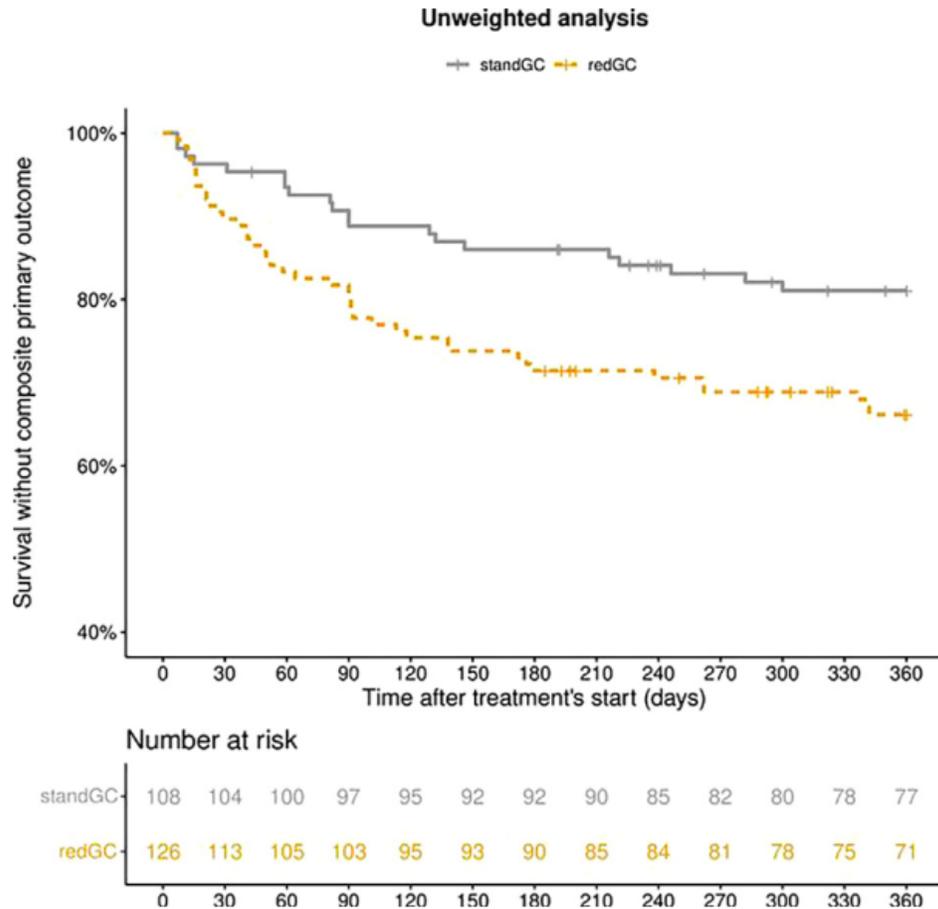
Daratumumab (anti-CD38) bei AAV:



CAR-T bei AAV:

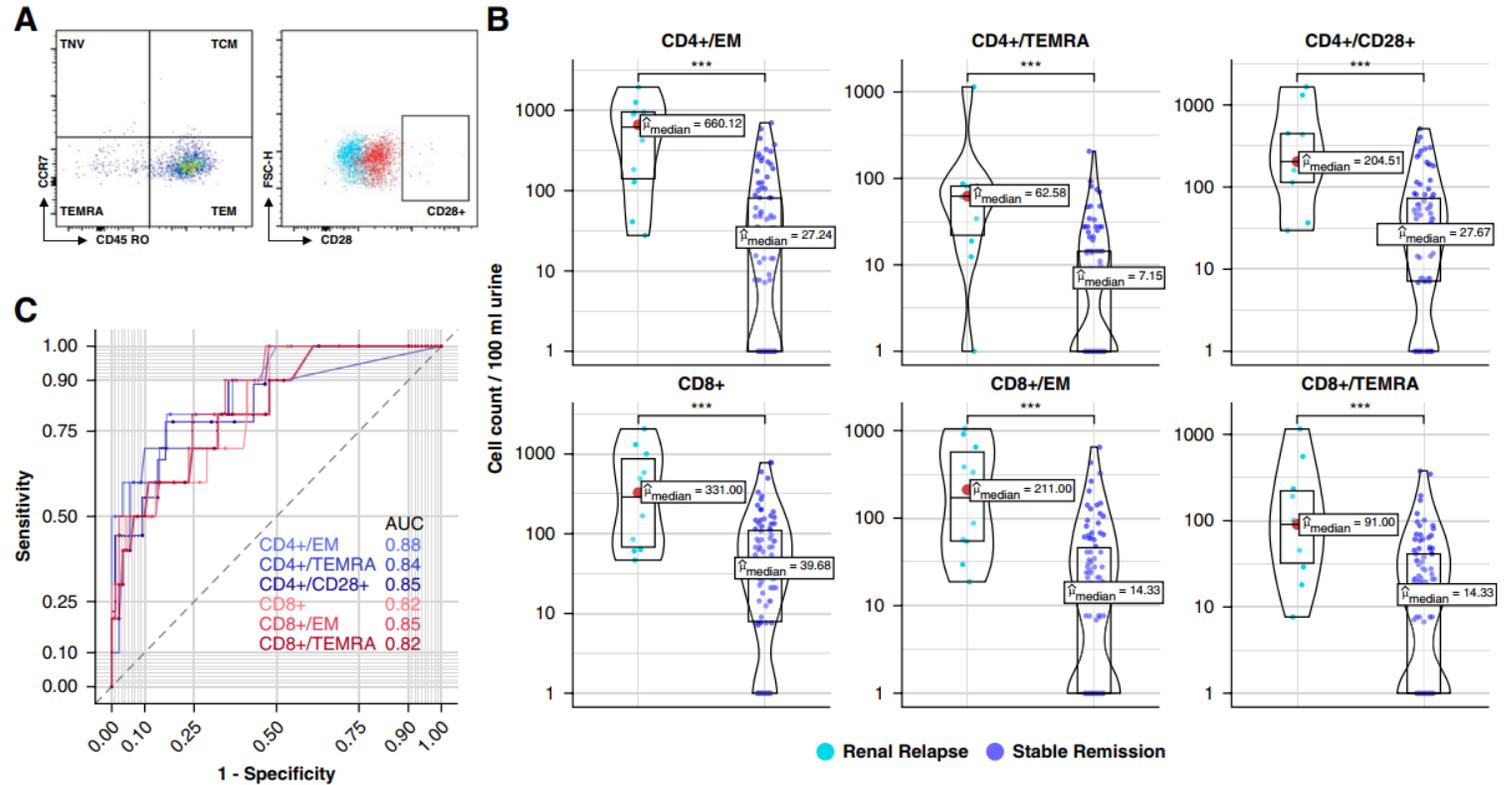
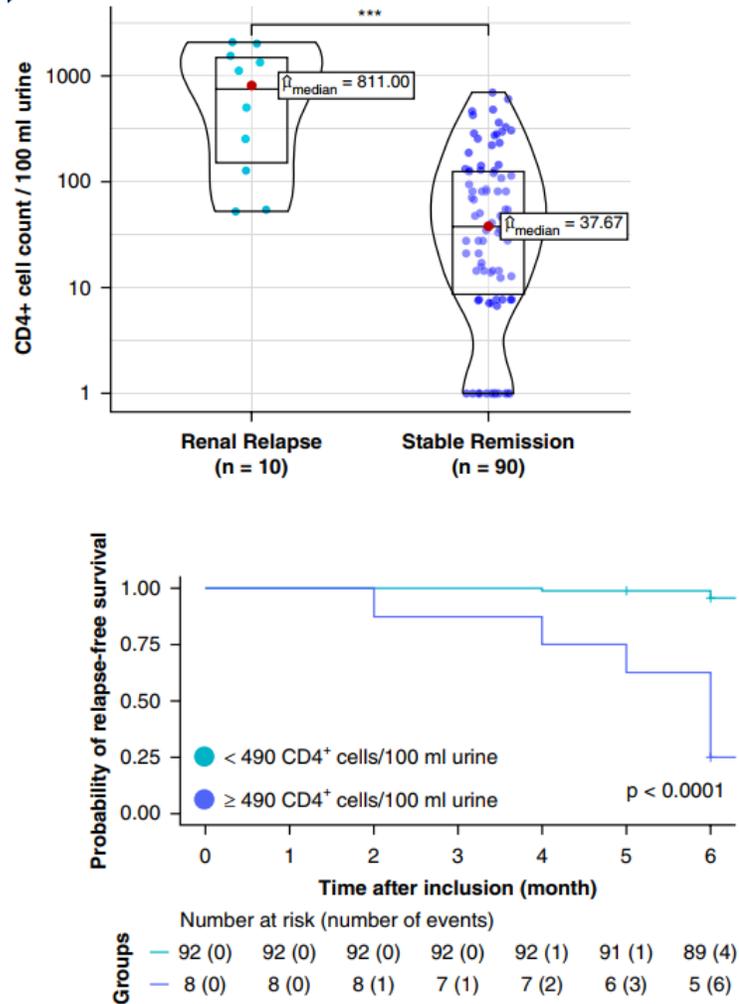


Reduzierte Glukokortikoide: PEXIVAS in real life



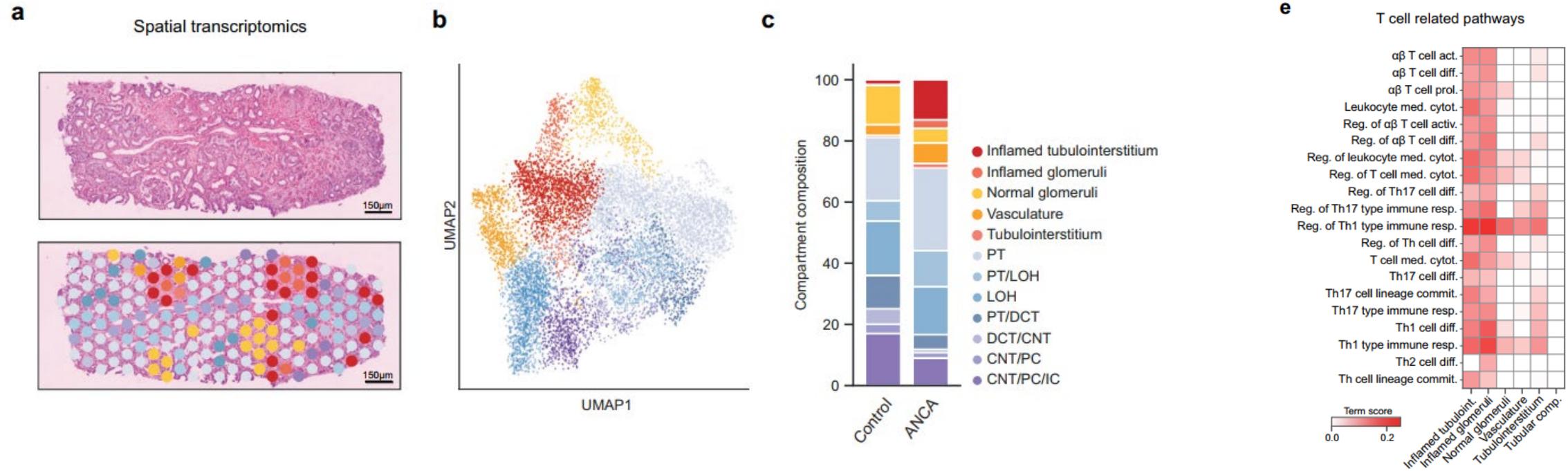
- Reduziertes GC-Schema mit mehr Endpunkten assoziiert (v.a. getrieben durch AAV Progression vor Remission)
- Risikopatienten: RTX und Kreatinin >300umol/l

T-Zellen bei AAV-Glomerulonephritis im Urin

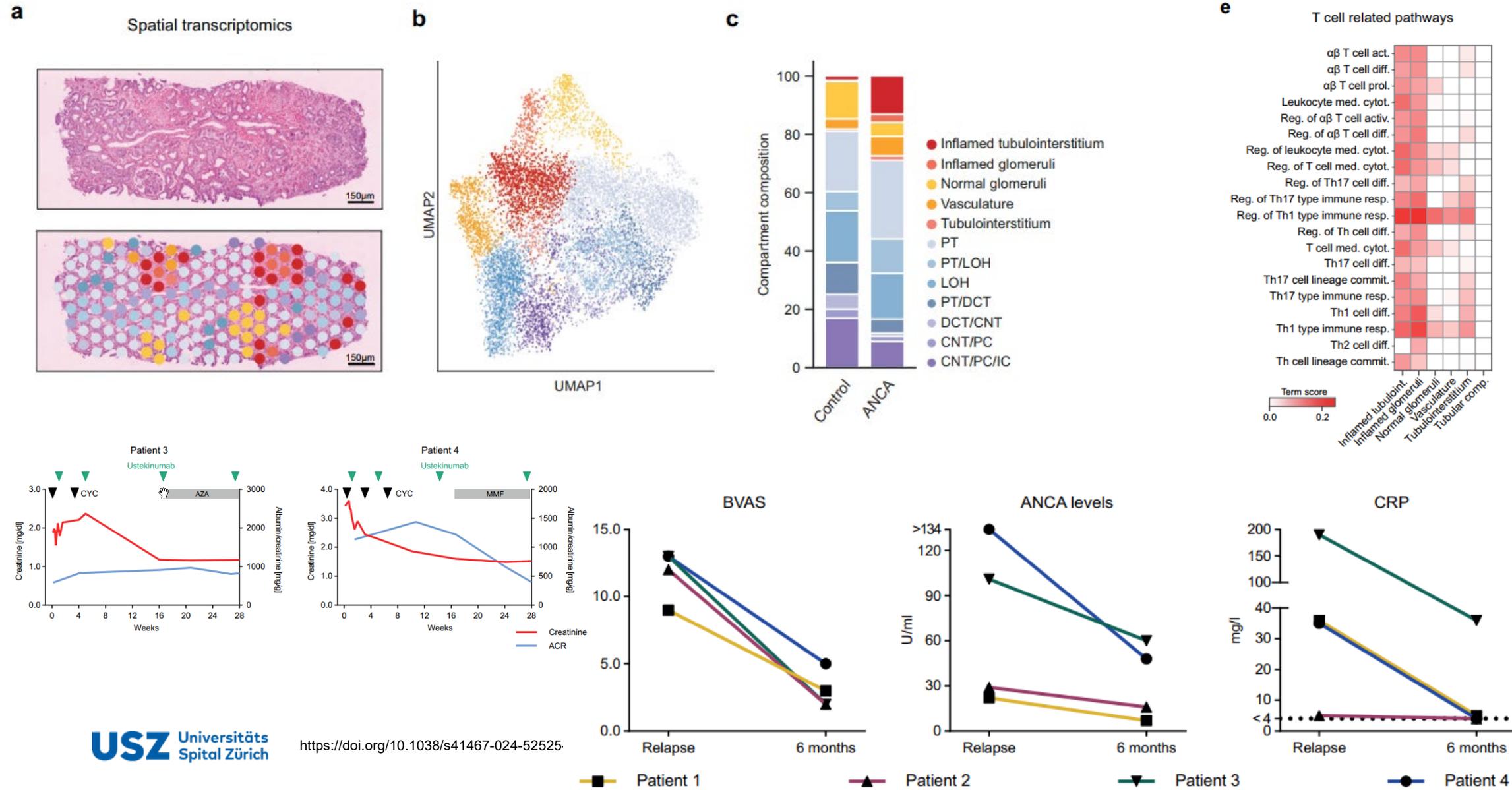


- Erhöhte Anzahl von v.a. CD4+ Effektor-T-Zellen im Urin bei Patienten mit AAV-Glomerulonephritis

Th17-Zellen bei AAV-Glomerulonephritis?



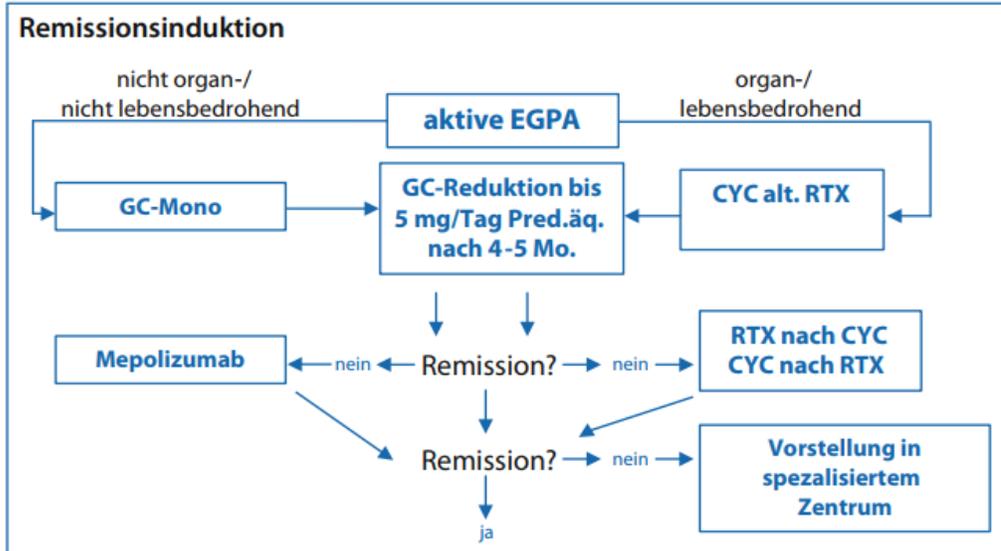
Th17-Zellen bei AAV-Glomerulonephritis?



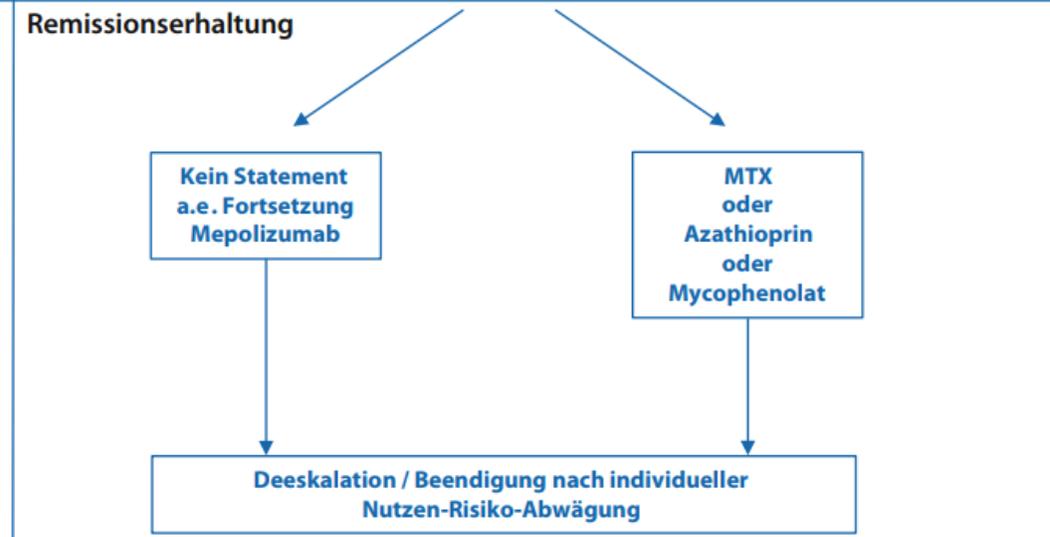
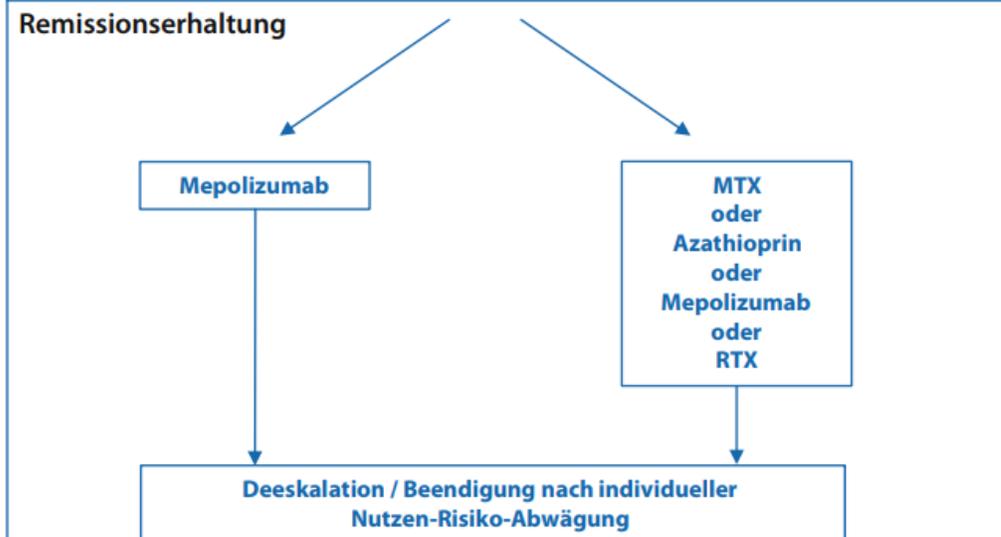
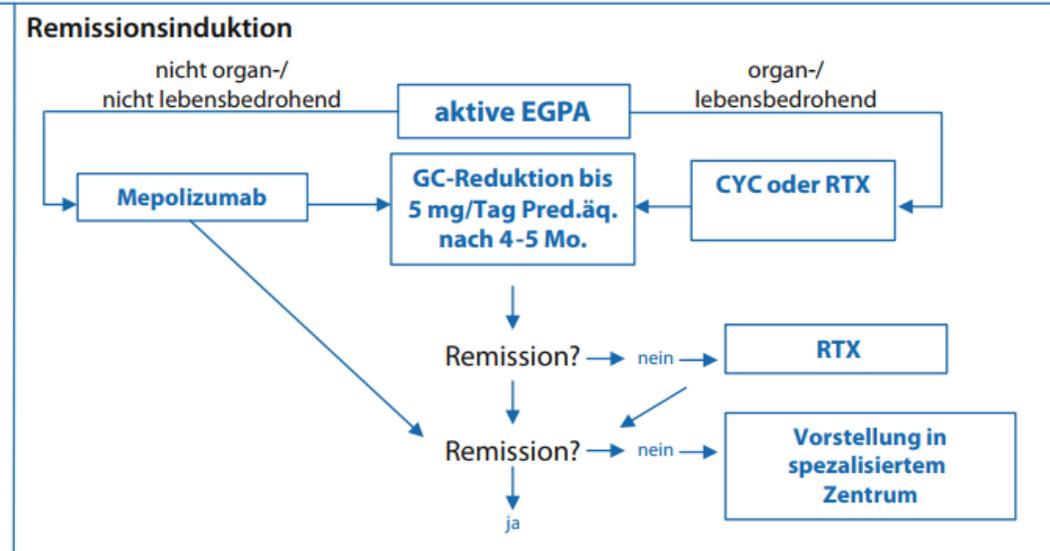
EGPA

Therapie-Empfehlungen bei AAV (EGPA)

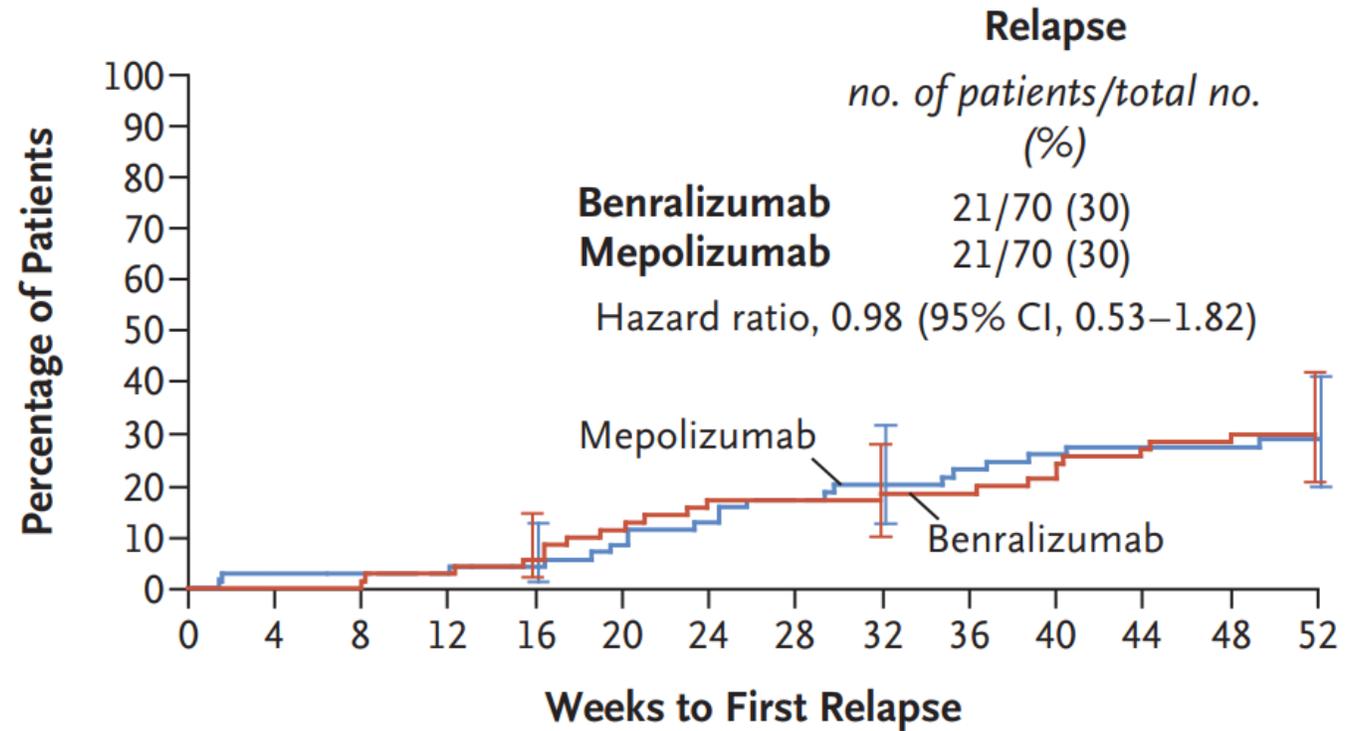
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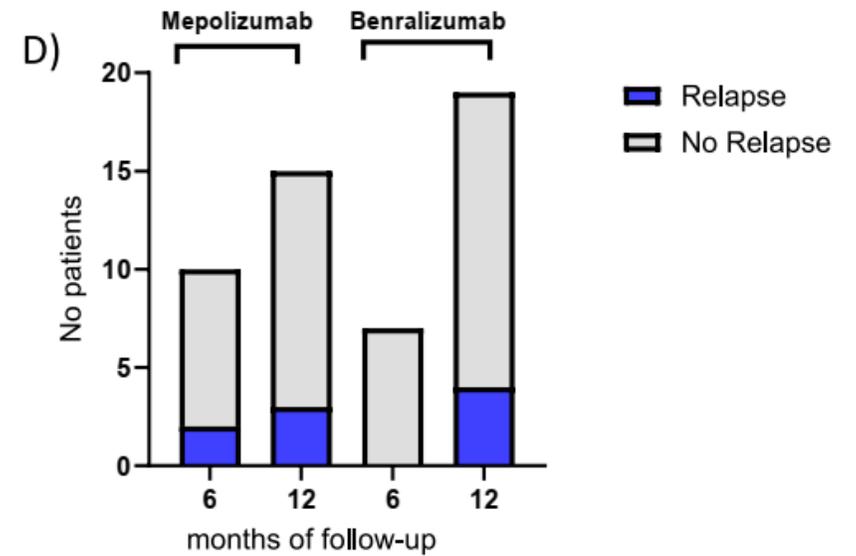
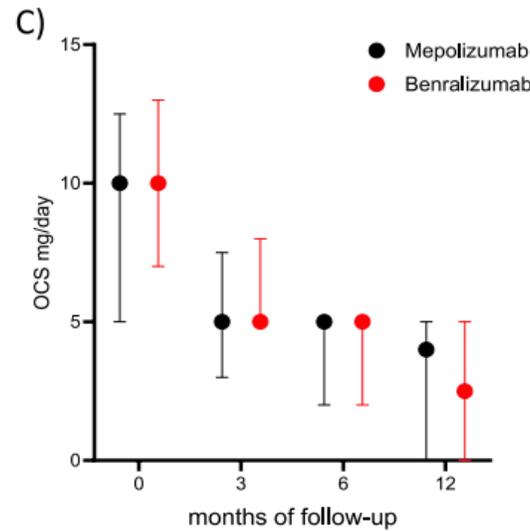
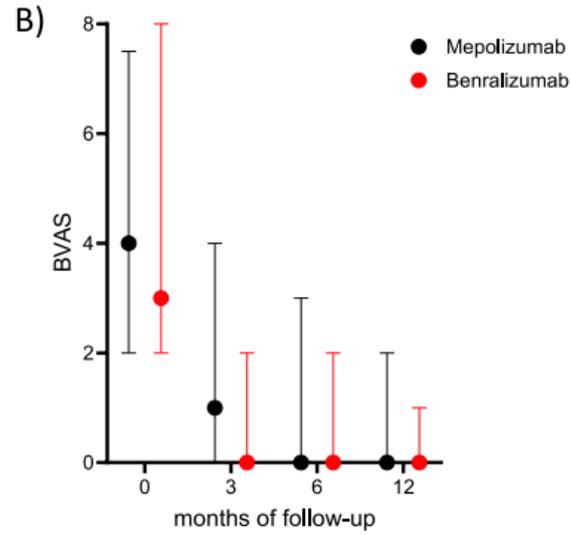
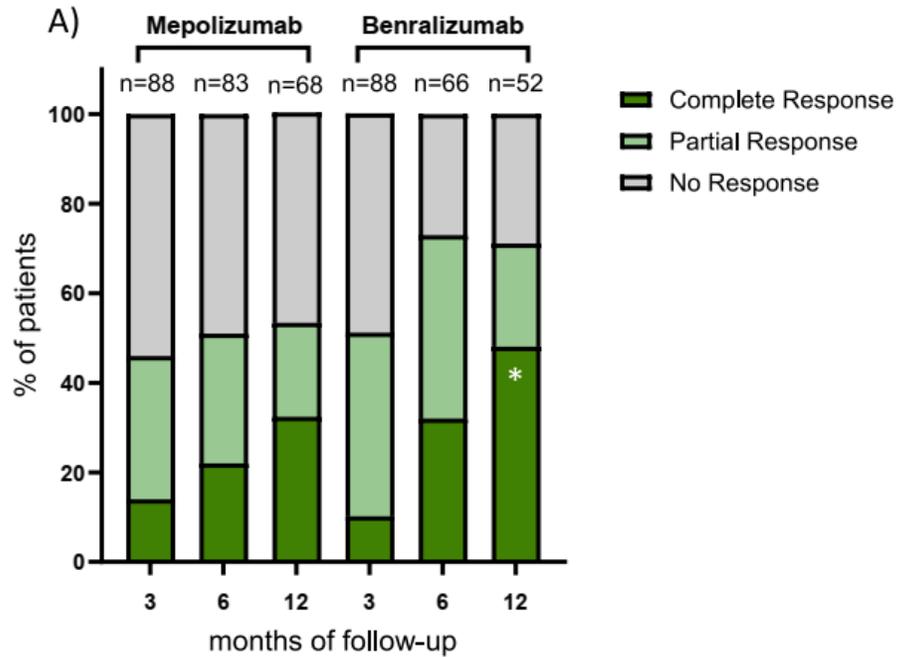
MANDARA Studie: Benralizumab vs. Mepolizumab bei EGPA



No. at Risk

Benralizumab	70	70	68	66	62	58	58	58	57	55	51	50	41
Mepolizumab	68	68	66	66	63	60	57	54	52	50	49	49	38

Beobachtungsdaten: Benralizumab vs. Mepolizumab bei EGPA



Vielen Dank

