Jun 18th 2026

Università di Brescia

Dipartimento di Scienze Cliniche e Sperimentali

Dottorato di Ricerca in
«Intelligenza Artificiale in Medicina e Innovazione nella Ricerca clinica e metodologica»

Coordinatore: Prof. Domenico Russo

Personalizing treatment in ANCA-associated vasculitis using digital pathology

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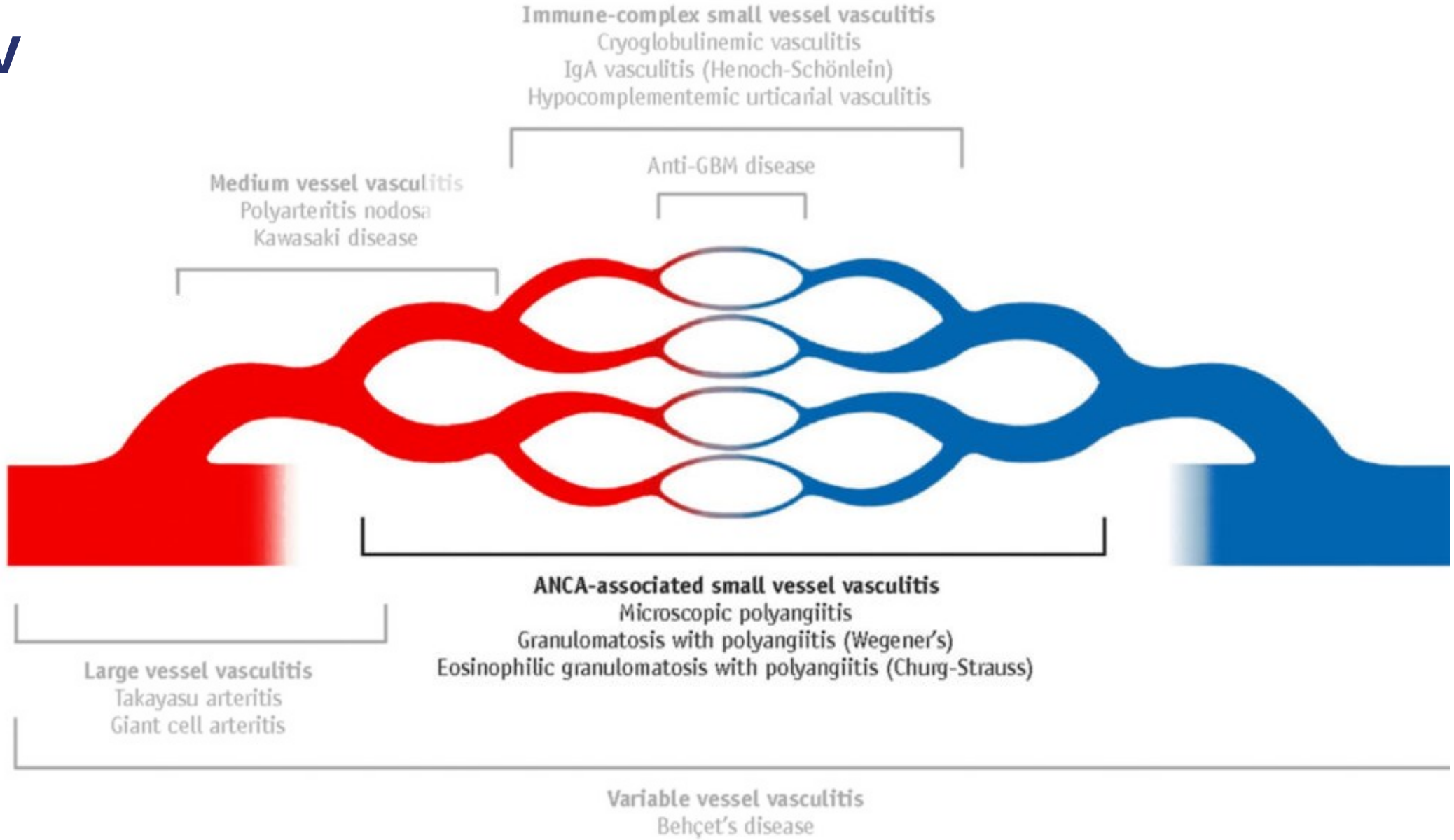
CICLO XLI

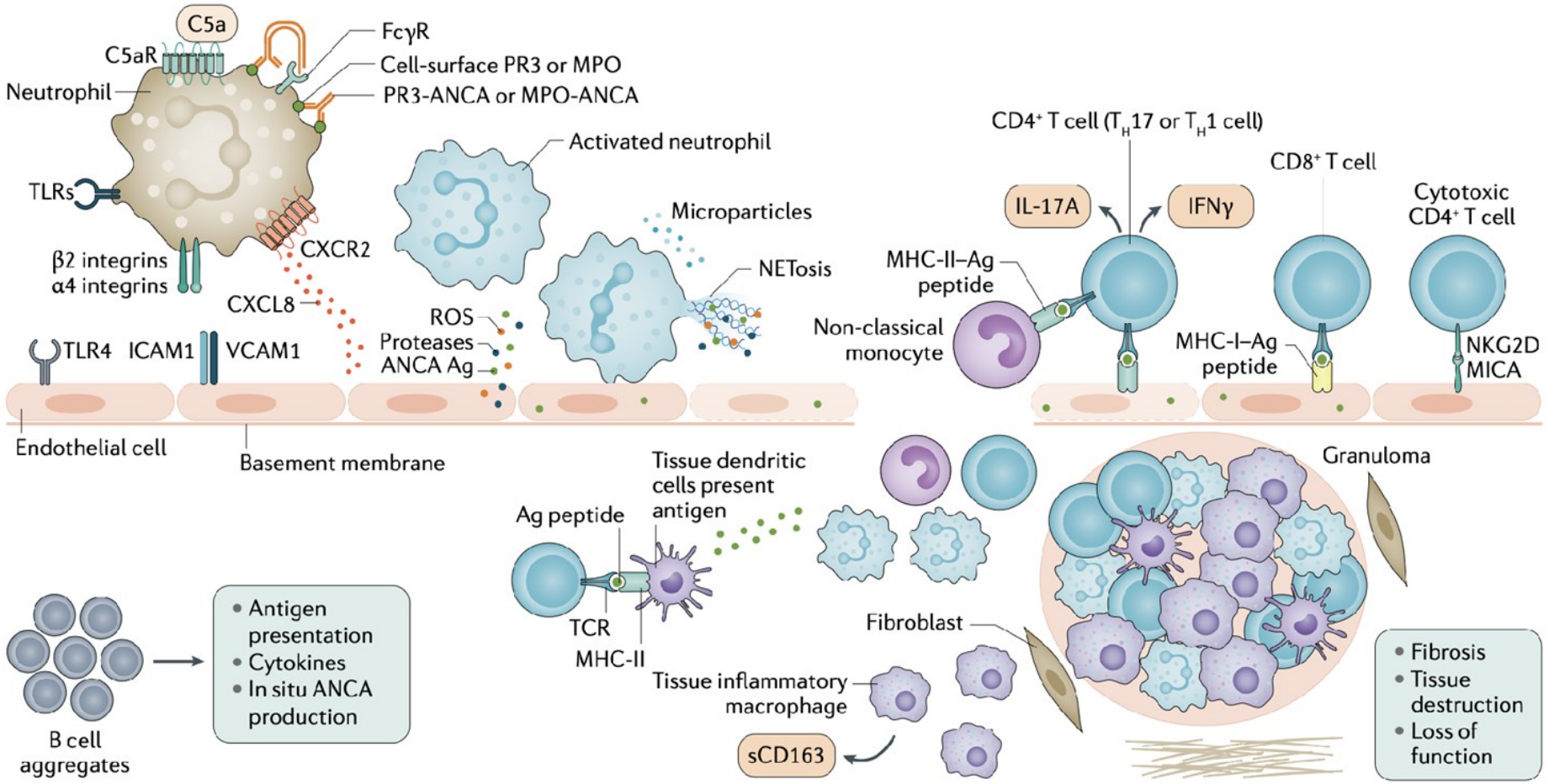
Supervisor: Prof. Federico Alberici

AAV



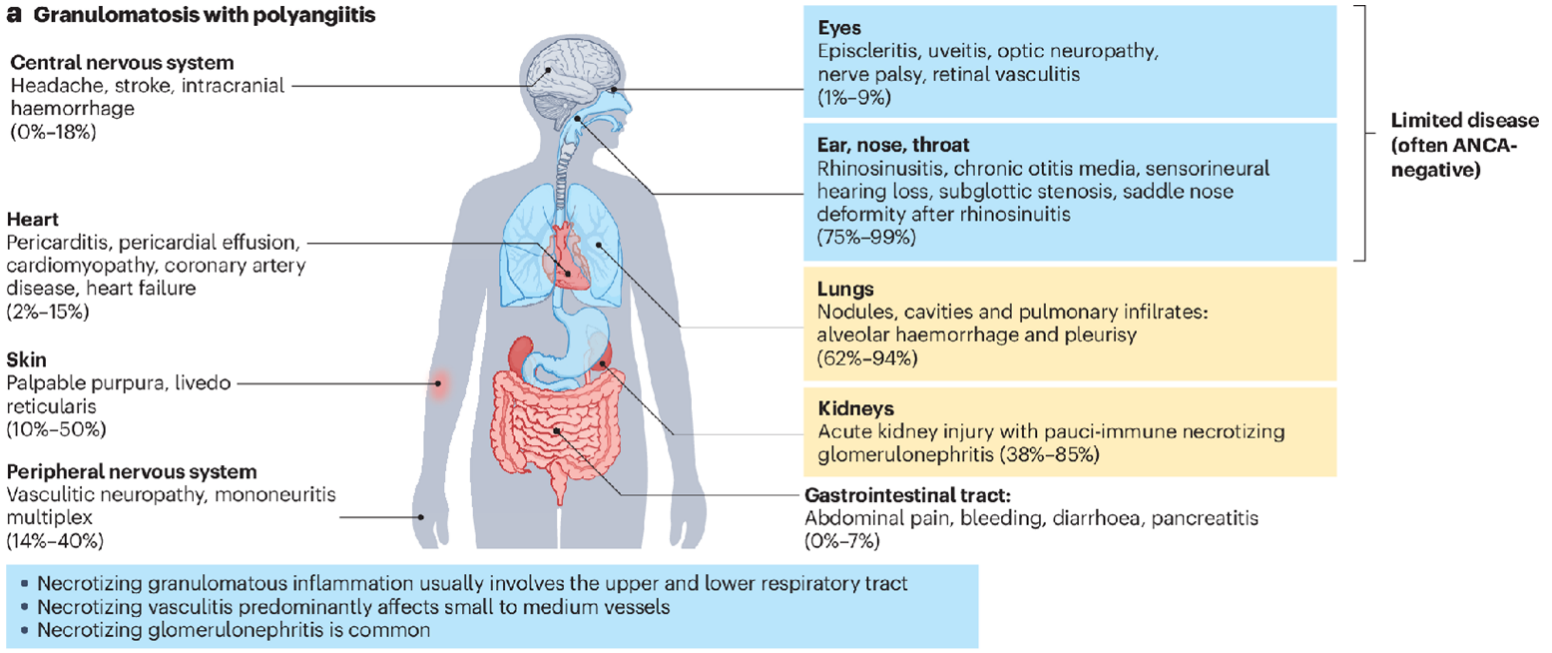
Adapted from Jennette C et al, Clin Exp Neph (2013)

AAV pathogenesis



Kitching R et al, Nat Dis Primers (2020)

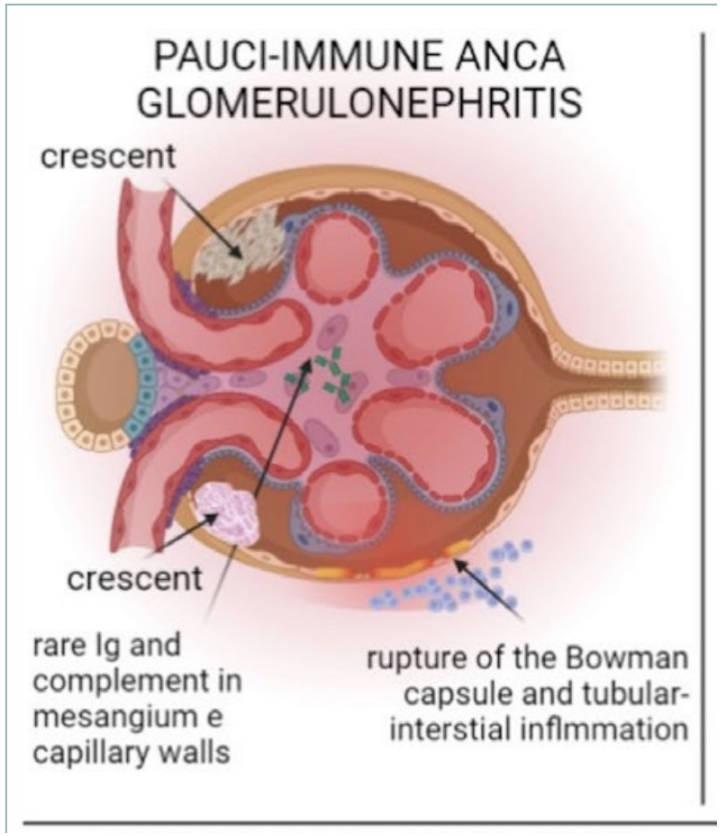
AAV
Clinical features

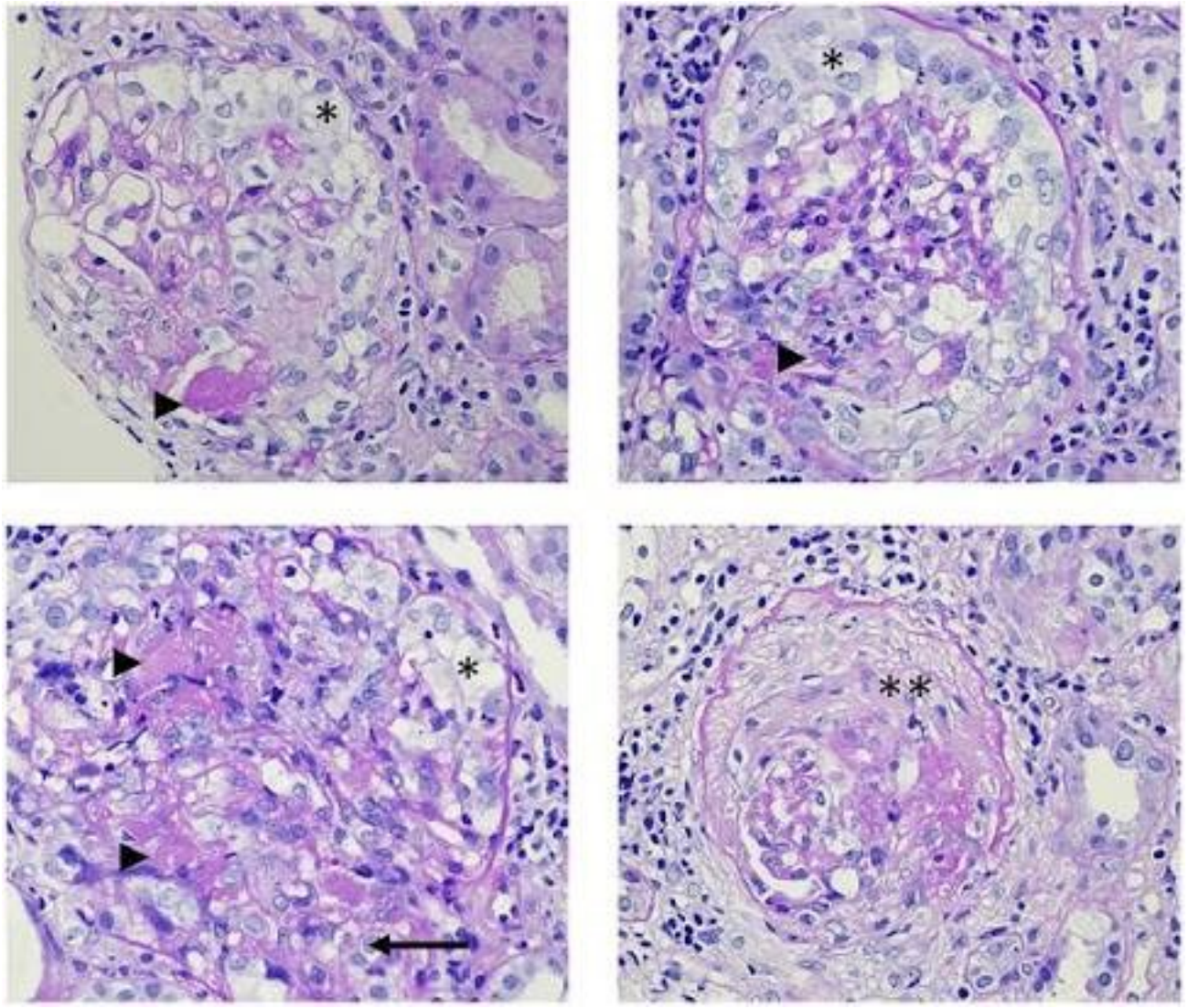


- Jennette et al, CJASN

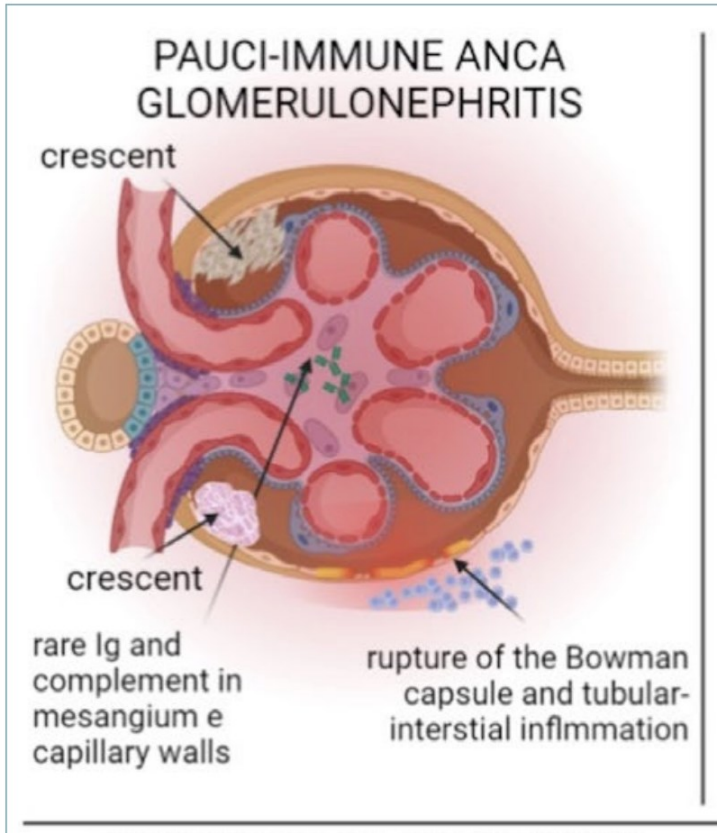
Kitching R et al, Nat Dis Primers (2020)

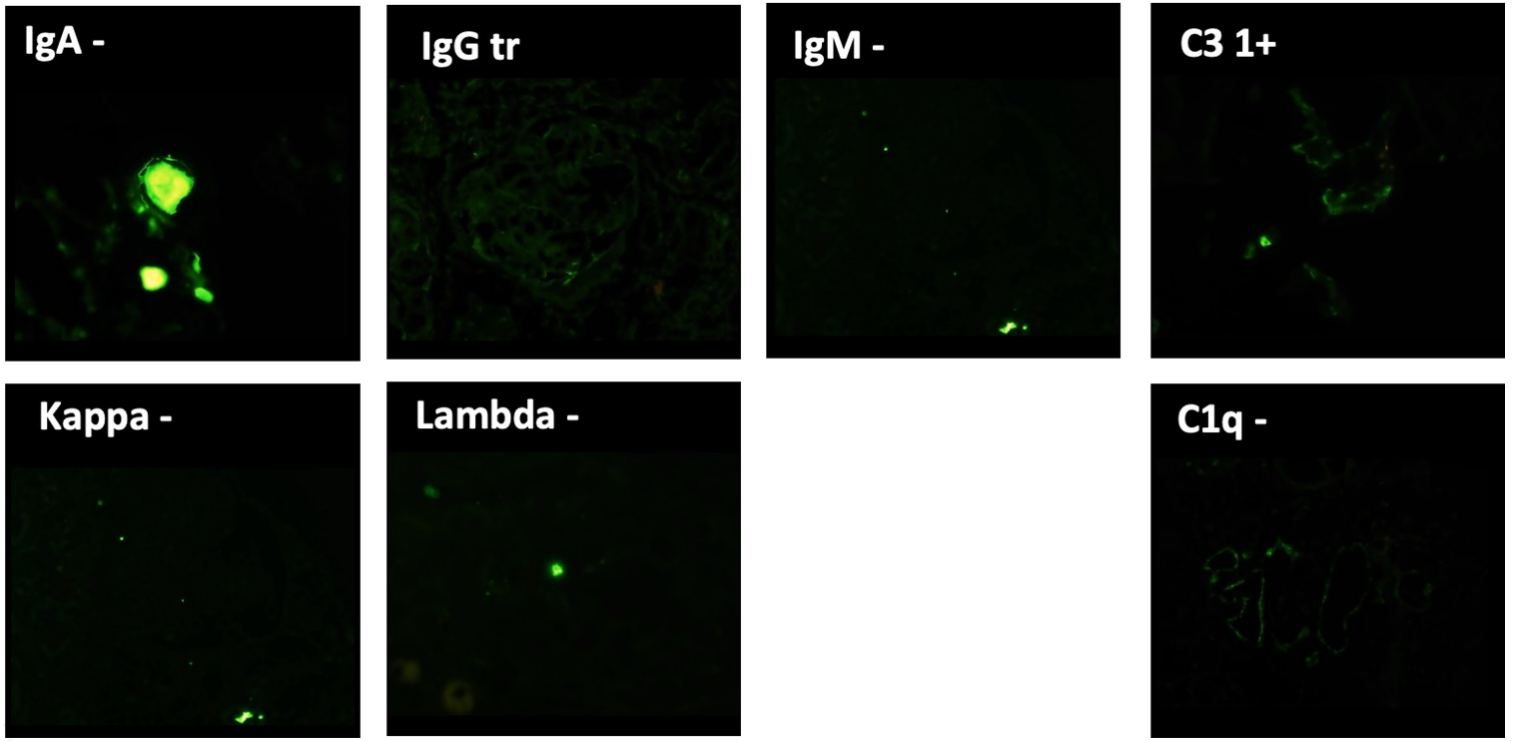
Renal histology in AAV light microscopy



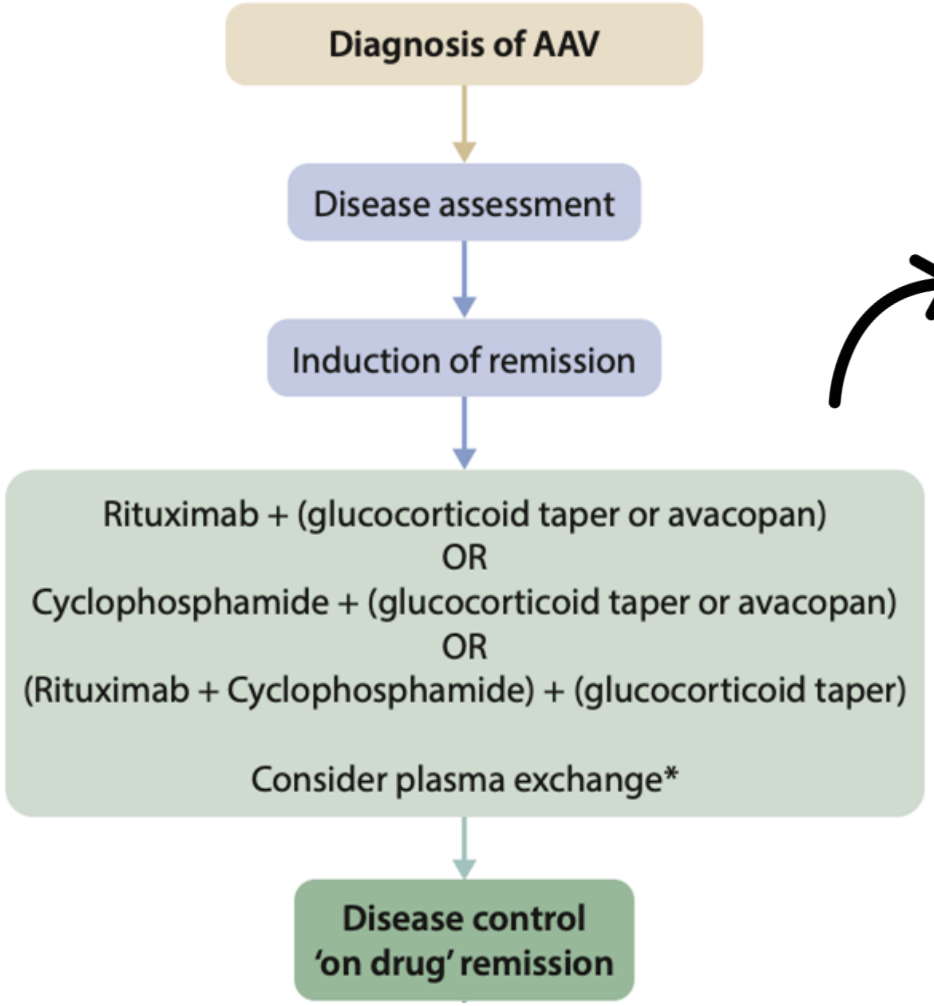


Renal histology in AAV
indirect immunofluorescence





AAV treatment – induction phase

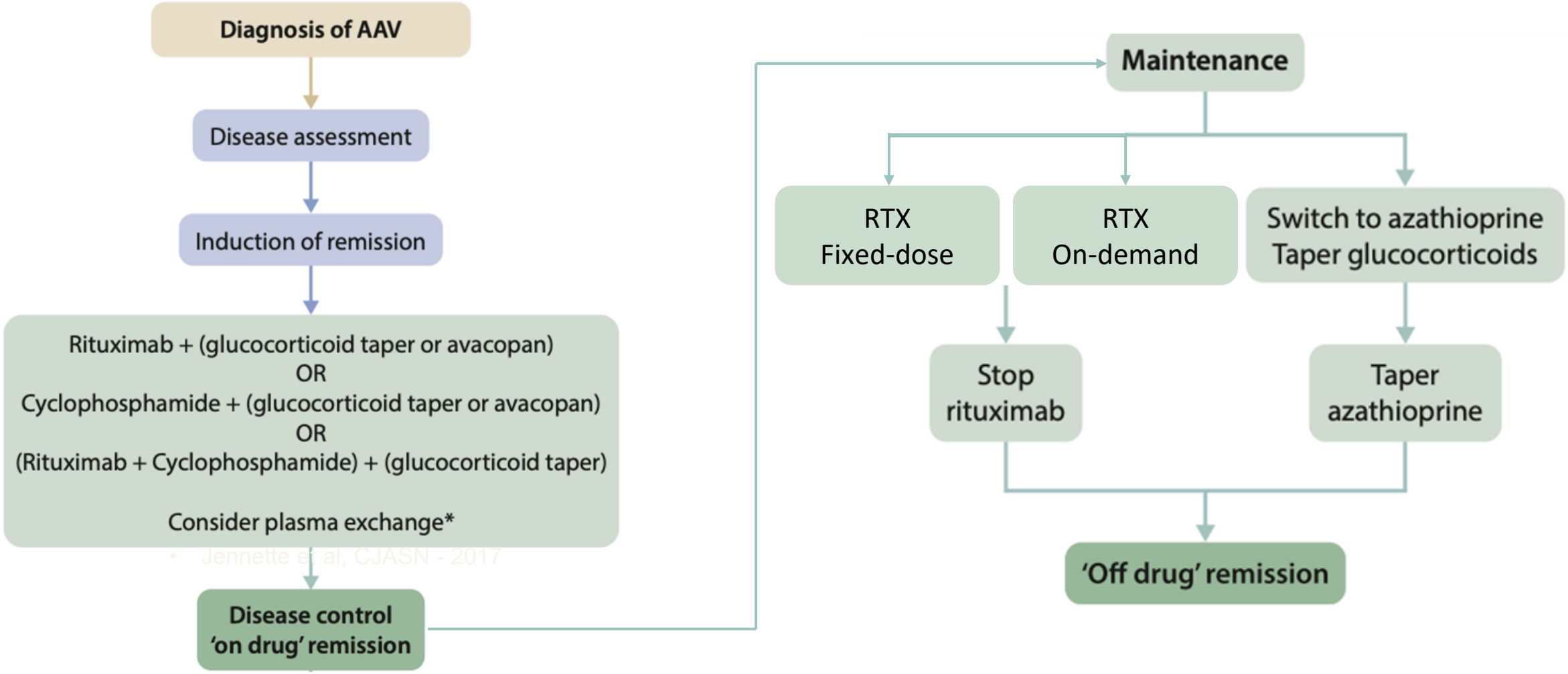


Rituximab preferred	Cyclophosphamide preferred
• Children and adolescents • Pre-menopausal women and men concerned about their fertility • Frail older adults • Glucocorticoid-sparing especially important • Relapsing disease • PR3–ANCA disease	• Rituximab difficult to access • Severe GN (SCr >4 mg/dl [354 µmol/l])*

Figure 7 | Factors for consideration when choosing between rituximab and cyclophosphamide for induction therapy of AAV.
*A combination of 2 intravenous pulses of cyclophosphamide with rituximab can be considered. AAV, ANCA-associated vasculitis; ANCA, antineutrophil cytoplasmic antibody; GN, glomerulonephritis; PR3, proteinase 3; SCr, serum creatinine.

Adapted from Floege J et al, KI (2024)

AAV treatment – maintenance phase



Adapted from Floege J et al, KI (2024)

Renal histology predicts kidney survival in AAV

End-stage kidney disease incidence

Overall 175/848 (21%)

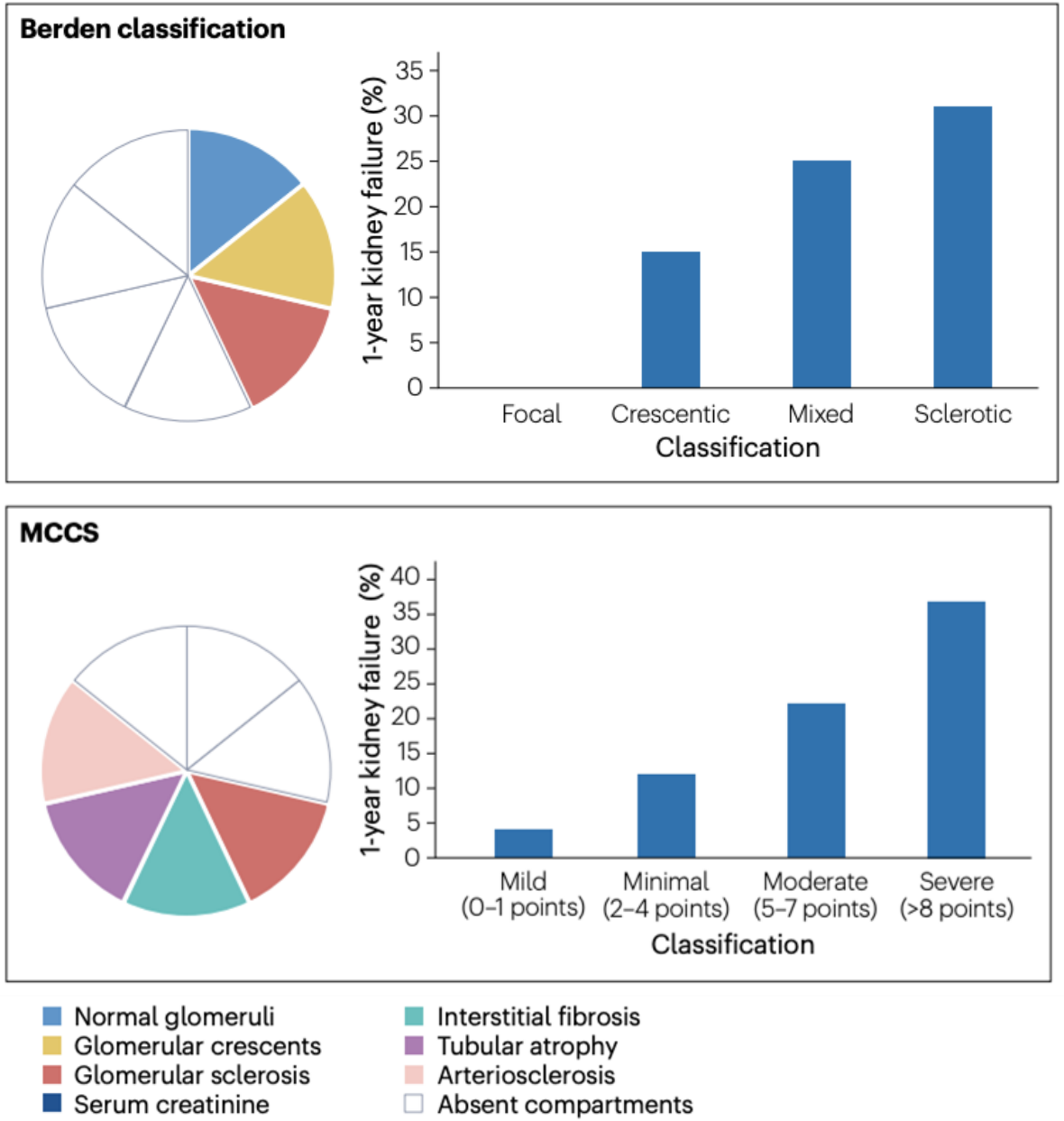
Dialysis	Transplant
n = 140 (80%)	n = 35 (20%)

Factors associated with end-stage kidney disease

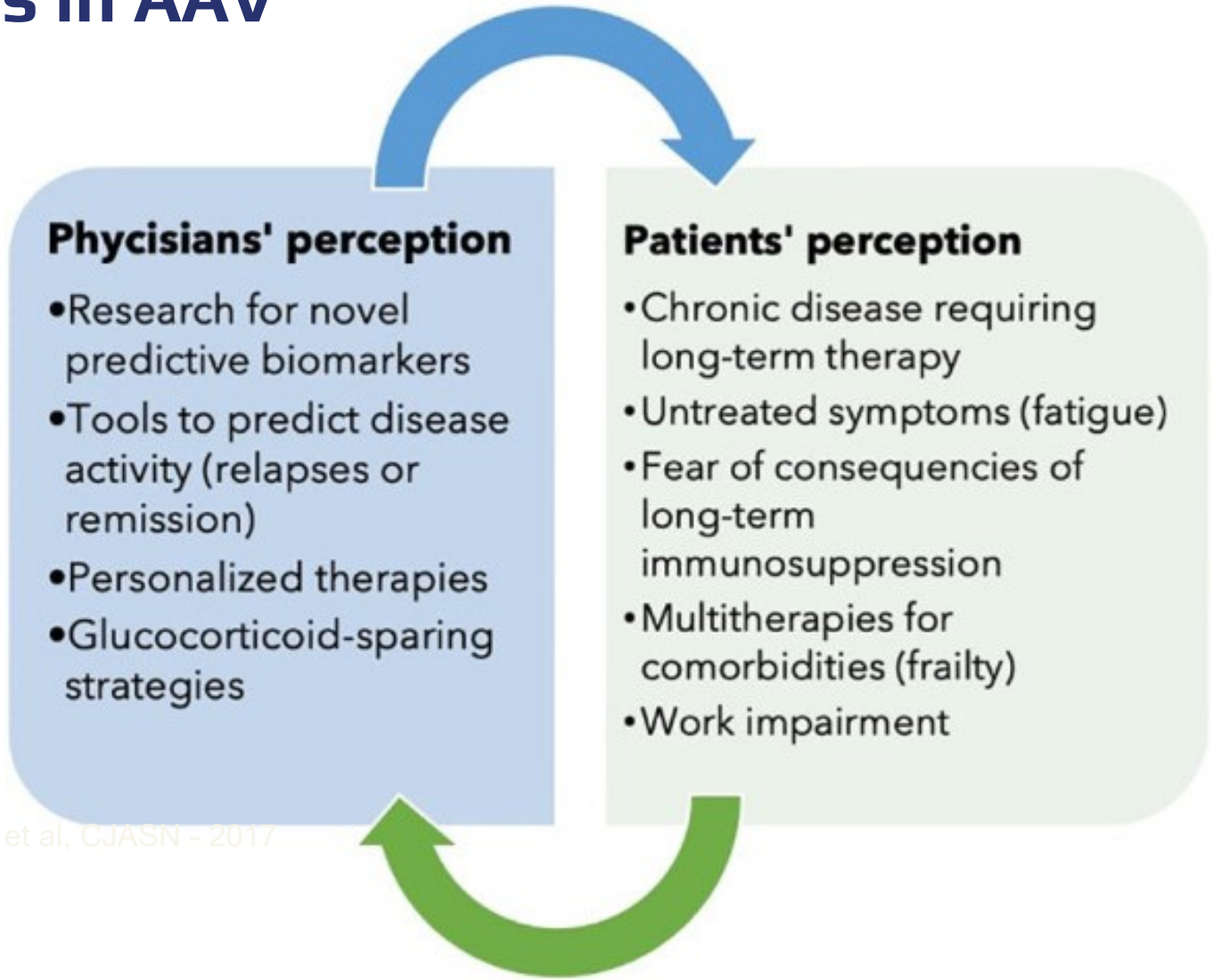
	Age > 65 years	eGFR	Haemoglobin
Hazard ratio (95% CI)	1.68 (1.18–2.41)	0.97 (0.93–0.99)	0.88 (0.78–0.98)

Sanchez-Alamo B et al, NDT (2024)

Casal Moura M et al, Nat Rev Rheum (2025)



Unmet needs in AAV



- Jennette et al, CJASN - 2017

Quartuccio L et al, Front Immunol (2023)

Kidney Outcomes in ANCA-Glomerulonephritis According to Induction Immunosuppression & Histopathology

ISN INTERNATIONAL SOCIETY OF NEPHROLOGY

Multicentric retrospective

Biopsy proven ANCA glomerulonephritis

n=304

Median eGFR
20 ml/min/1.73m²

Berden classification

Mixed	33.2%
Crescentic	31.6%
Focal	23.3%
Sclerotic	11.8%

Induction Treatment

Cyclo	59%
Rituximab	17%
Cyclo + ritux	24%

Kidney outcomes

eGFR Recovery 50%
at 6 months
Crescentic group
Ritux vs Cyclo OR 0.23 (0.05-0.98)

Kidney Failure 19.4 %
median follow-up 42 months
Crescentic group
Ritux vs Cyclo HR 3.42(1.03-11.35)

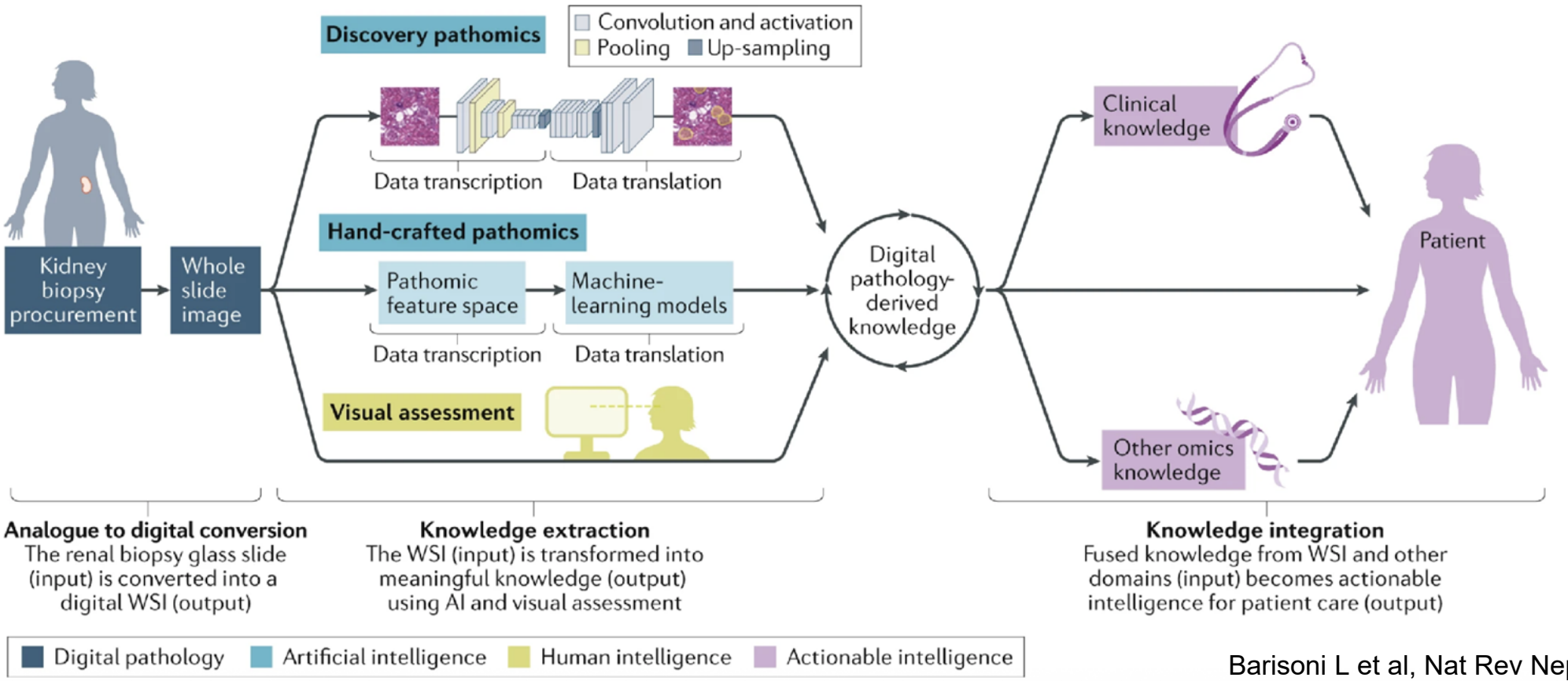
KI REPORTS
Kidney International Reports®

Conclusion: Patients with crescentic class ANCA-glomerulonephritis receiving RTX monotherapy may have worse kidney outcomes than those treated with CYC-based regimens.

Uzzo M et al, 2026. VA by Pallavi Prasad, MD, DNB(nephrology)

Study goal

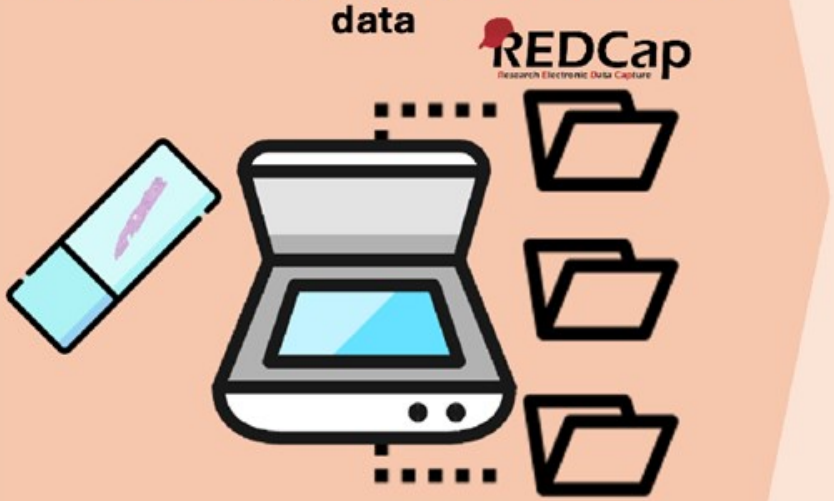
To identify histopathological predictors of efficacy and safety across different induction regimens in patients with AAV and biopsy-proven renal involvement using deep learning



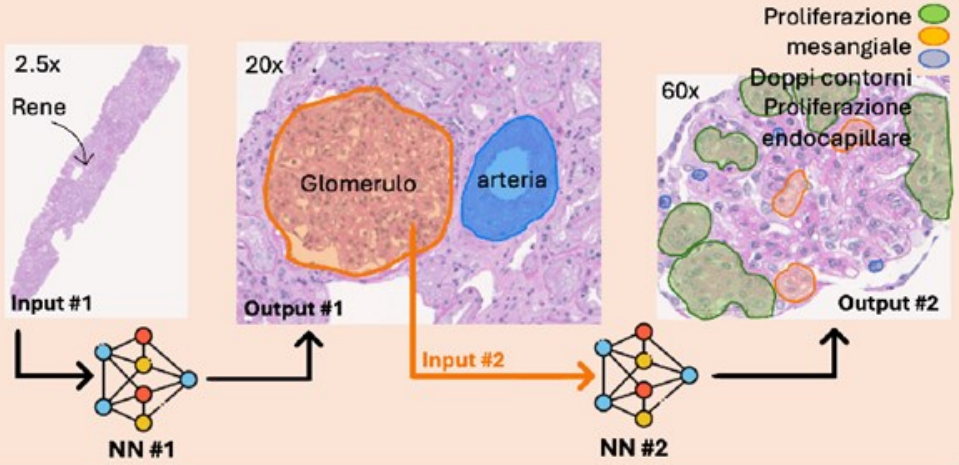
Barisoni L et al, Nat Rev Neph (2020)

STUDY WORKFLOW

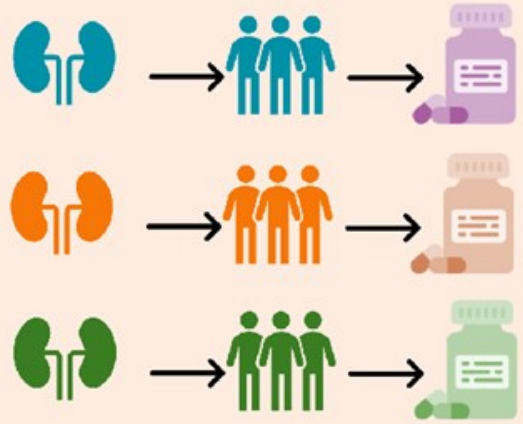
To develop a granular repository of whole-slide digital images and clinical data



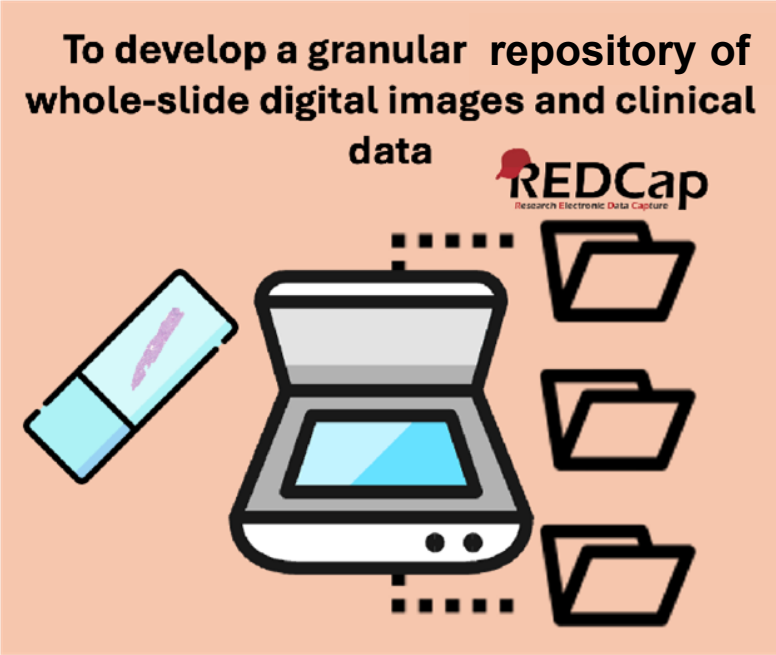
To train and validate neural network pipeline to recognize distinct histological features across multiple magnifications



To identify clinical-histological phenotypes and correlate them with response to induction treatment regimens



STUDY DESIGN: Phase I

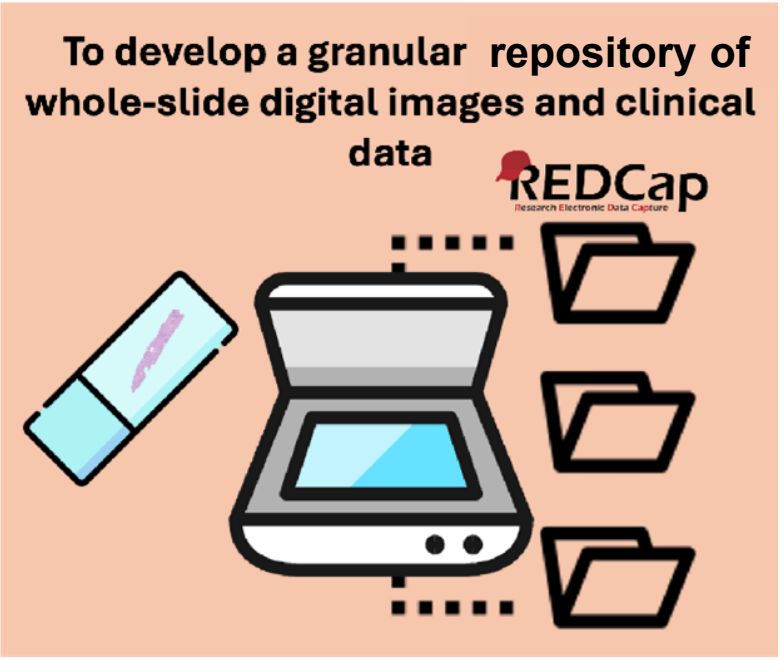


Multicenter (multinational)

Mixed retrospective-prospective observational study

9 participating centers (+2 on the way)

STUDY DESIGN: Phase I



Age at diagnosis ≥ 18 yo
and
ANCA-positive MPA or GPA
and
Biopsy-proven AAV-glomerulonephritis

STUDY DESIGN: Phase I

To develop a granular repository of whole-slide digital images and clinical data

	Instrument name	Fields
	AAV REDCap Cover	2
	Demographic Features And Habits (Baseline)	10
	Charlson Comorbidity Index and other comorbidities (baseline)	15
	Neoplasia (baseline)	6
	Pharmacological exposure (baseline)	2
	Family history (baseline)	3
	AAV features (baseline)	58
	Kidney biopsy (baseline)	37
	Lab tests (baseline)	68
	Other Biopsies (baseline)	8
	Infectious diseases (baseline)	5
	Aav Therapy After Diagnosis	198
	Aav Escalation Therapy	246
	Kidney biopsy (repeat biopsies)	38
	Adverse events and Follow-up	21
	Hospitalizations (follow-up)	5
	Cardiovascular Events (follow-up)	4
	Neoplasia (follow-up)	5
	Infections (follow-up)	7
	Laboratory exams (follow-up) - ALL	39
	Laboratory exams (follow-up) - TIMEPOINTS	13
	ESKD and CKD (Outcome)	7
	Death (Outcome)	5
	Notes	1

- Modular structure:

- Relevant clinical data (baseline)
- Labs
- Histological features
- Treatment modules
- Adverse events and outcome

- Validated scores:

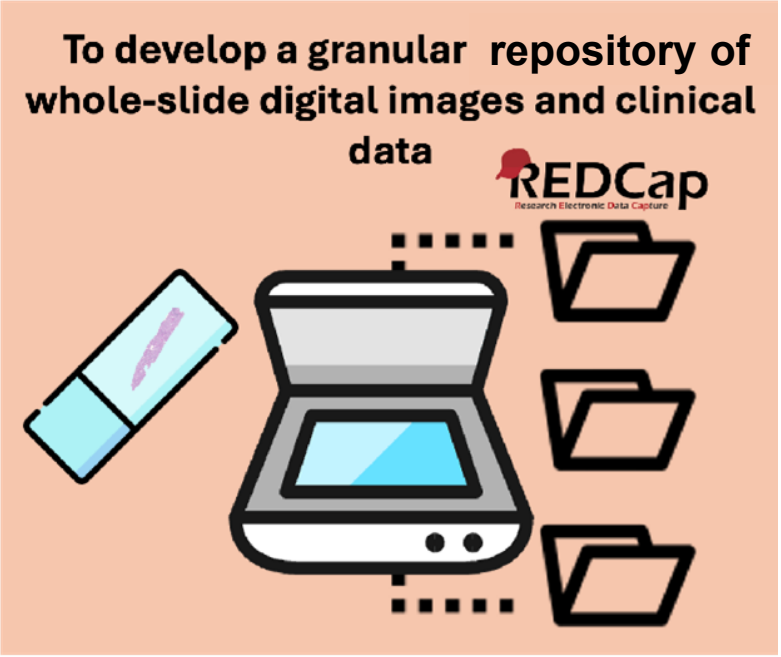
- Charlson comorbidity index
- BVAS v3.0
- Berden classification
- Mayo Clinic chronicity score

- Automated laboratory data capture

- Clear data dictionary

- REDCap built-in features

NEXT STEPS...



- Obtain ethics for other participating centers
- Expand the clinical dataset
- Develop the workflow for WSI scanning

Dr. Tedesco Martina

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