Kidney Phenotype in Interstitial Lung Disease in ANCA-associated Vasculitis: European Multicentre Study

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Background

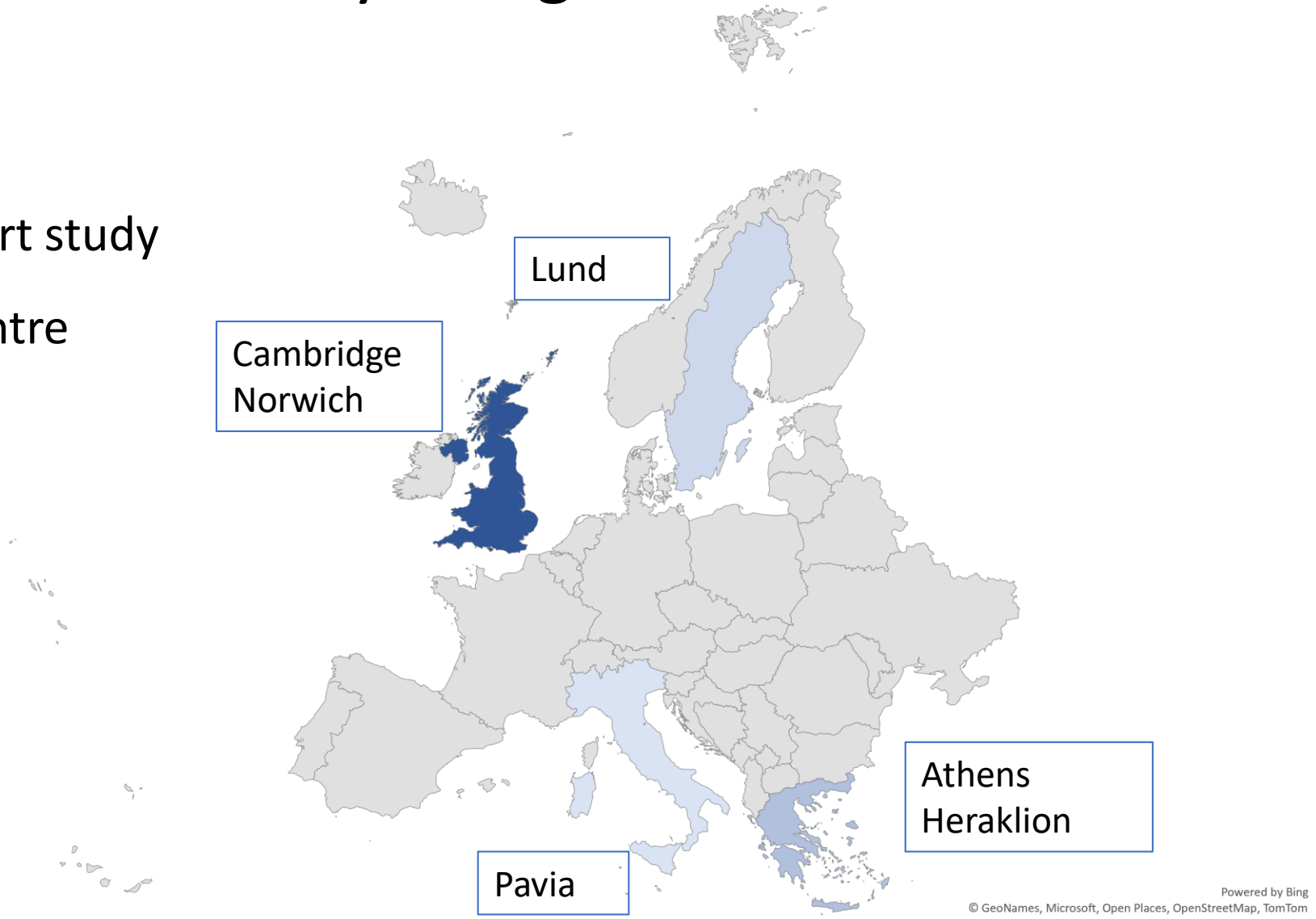
- Interstitial Lung Disease (ILD) can co-occur in ANCA-associated Vasculitis.
- ILD is a fibrotic disease and associated with MPO-ANCA.
- Not-well defined the long term outcome.
- Not-well established the immunosuppressive effectiveness.
- MPO-ANCA is associated with a more fibrotic phenotype in the kidney.

Educational Objectives

- Understanding the association of clinical subtype of ANCA-associated vasculitis (AAV) with pulmonary fibrosis and the consequences of fibrosis on organ damage and long-term patient outcomes.
- We hypothesised that there would be more fibrosis in the kidneys of AAV patients with ILD than those without ILD.

Study Design

- Retrospective cohort study
- European multi-centre
  - 4 European countries
  - 6 Centres



Eligibility Criteria

Inclusion Criteria

- Patients with ILD in the context of AAV and patients with ILD and PR3 or MPO-ANCA without vasculitis.
- At least one CT scan available
- Follow-up > 6 months
- **Subgroups:**
  1. **AAV-ILD**: ANCA positive ILD with features of vasculitis
  2. **ANCA-ILD**: ANCA positive ILD without features of vasculitis

Exclusion Criteria

- Non–ANCA-type vasculitis or other autoimmune conditions.
- Alternative explanations for ILD (eg radiation treatment, drugs, pneumoconiosis, infection-related).

ILD definition (Clinical Practice Guideline 2022 for IPF); UIP: Usual Interstitial pneumonia (possible, definite, indeterminate); NSIP: Non specific interstitial pneumonia; Cryptogenic Organized pneumonia ; Chronic hypersensitivity pneumonia

Study Design

Central radiological re-evaluation
Ongoing process

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Images obtained from Cambridge Cohort

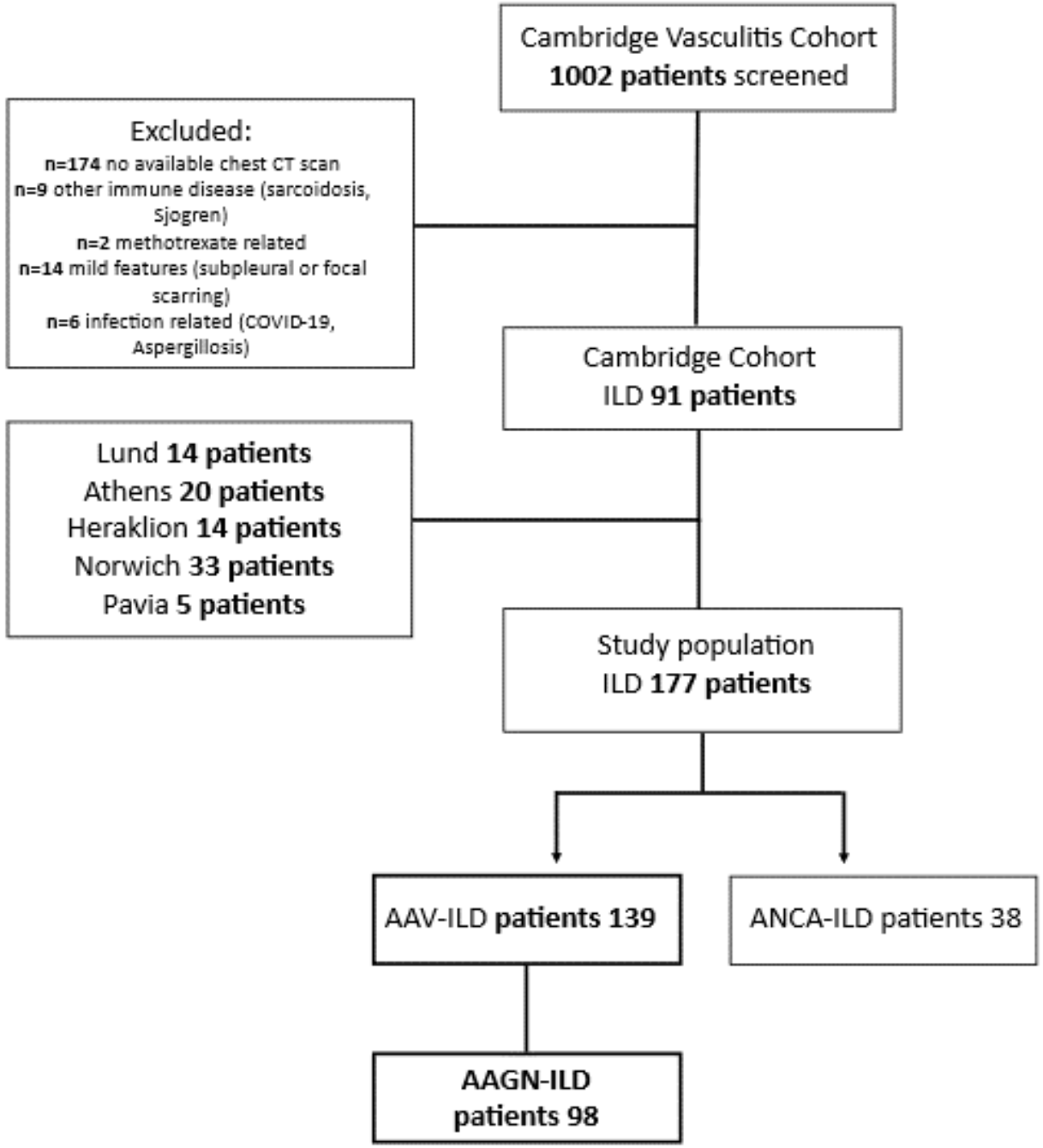
Study Objectives

Primary Objective

- Long-term outcome
  - Survival
  - Respiratory survival

Secondary Objectives

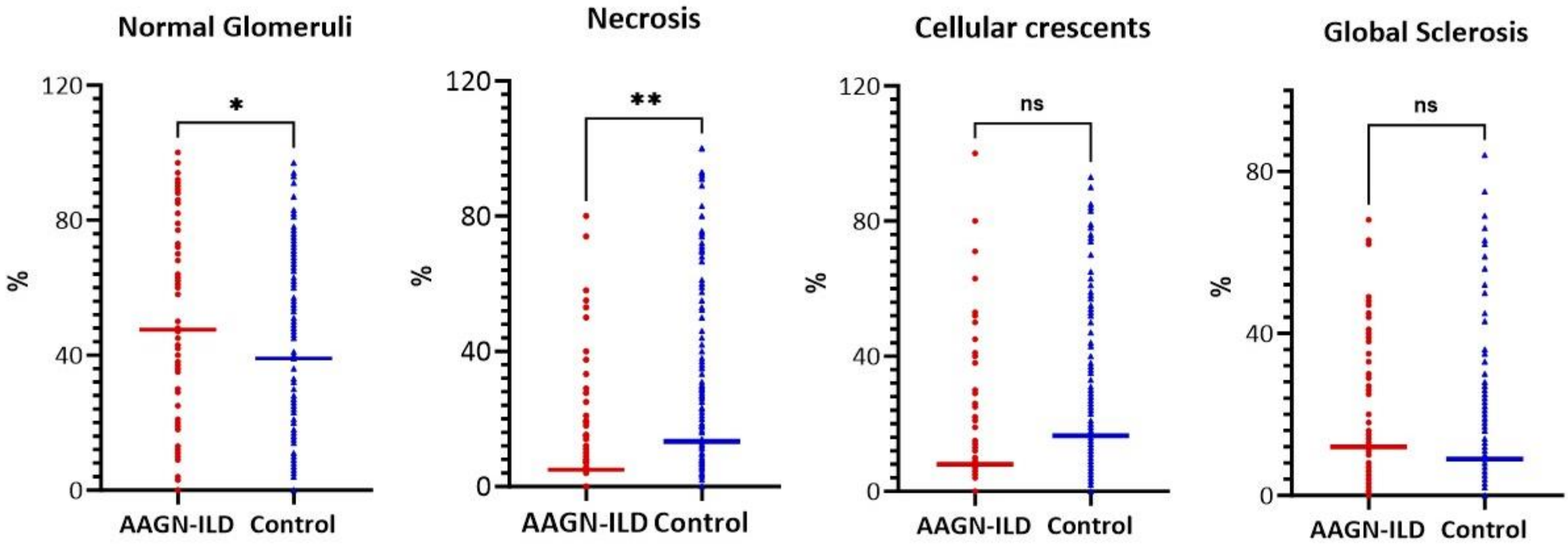
- Respiratory progression
  - Lung function tests (LFTs)
- Treatment effectiveness
  - -Direct effect on LFTs pre and post treatment (T0 and T12)
- Renal phenotype
  - -Histology
  - -Renal progression
  - -Comparison group: ANCA-associated glomerulonephritis without ILD (Cambridge AAV cohort).


Cambridge Vasculitis Cohort
1002 patients screened
Excluded:
n=174 no available chest CT scan
n=9 other immune disease (sarcoidosis, Sjogren)
n=2 methotrexate related
n=14 mild features (subpleural or focal scarring)
n=6 infection related (COVID-19, Aspergillosis)
Cambridge Cohort
ILD 91 patients
Lund 14 patients
Athens 20 patients
Heraklion 14 patients
Norwich 33 patients
Pavia 5 patients
Study population
ILD 177 patients
AAV-ILD patients 139
ANCA-ILD patients 38
AAGN-ILD
patients 98

Clinical Characteristics

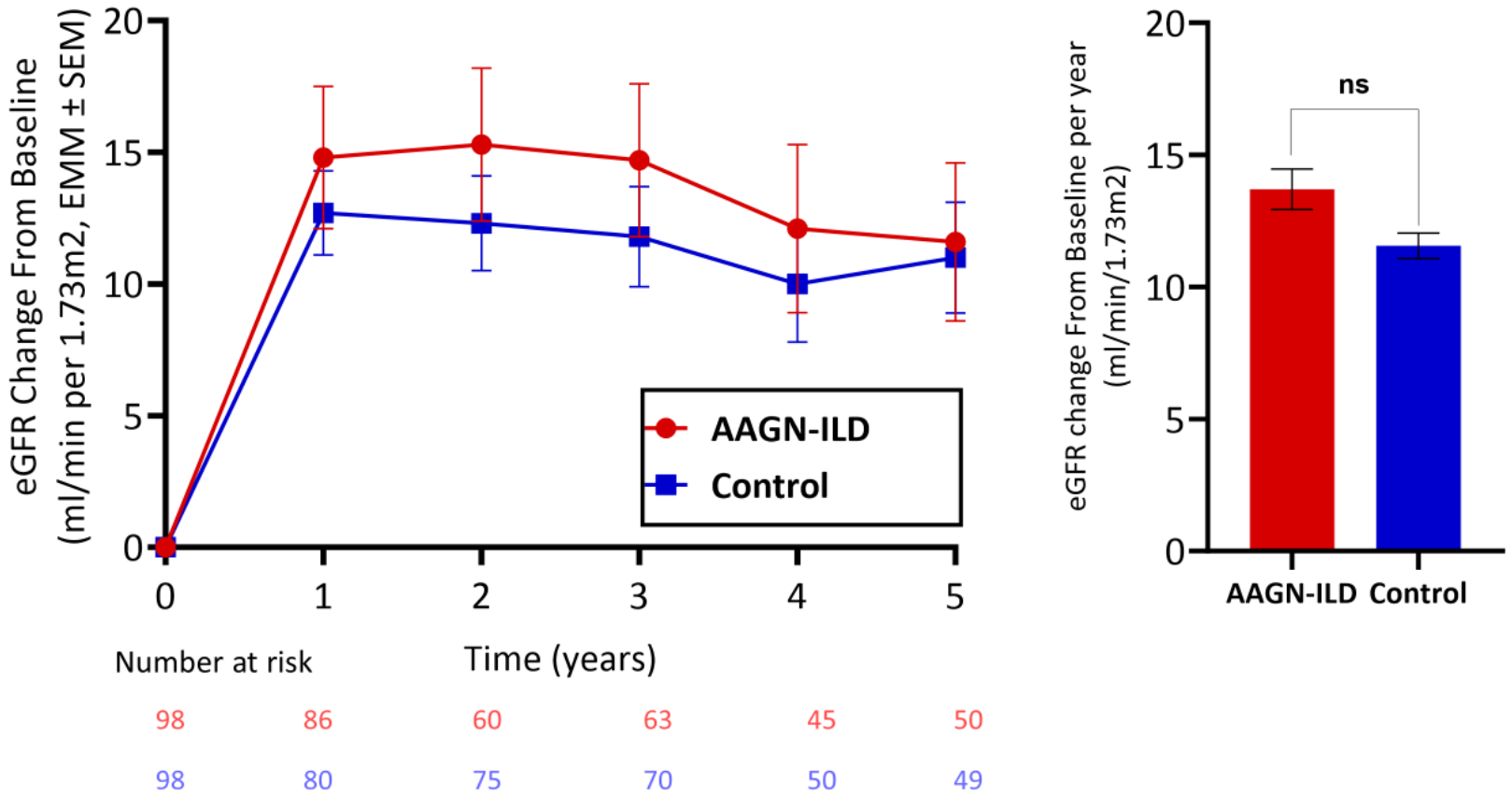
	AAGN-ILD N=98	Unmatched Control N=183	p value
Age (years), mean± SD	**71±11**	64±14	<0.001
Serological phenotype			<0.001
MPO % (n)	**88 (84)**	51 (93)	
PR3 % (n)	12 (12)	48 (87)	
Kidney function at diagnosis			
GFR ml/min/1.73m2 median (IQR)	**28 (12-50)**	20 (9-40)	0.043
ACR mg/mmol, median (IQR)	**18 (8-95)**	79 (26-192)	0.001
Haematuria % (n)	**86 (70)**	98 (165)	0.001
Berden Classification			0.599
Focal class % (n)	45 (34)	40 (68)	
Mixed class % (n)	32 (24)	31 (53)	
Crescentic class % (n)	19 (14)	21 (36)	
Sclerotic class % (n)	4 (3)	8 (14)	
Follow-up (years), median (IQR)	4.9 (2-8)	3 (1-6)	0.025

Glomerular changes



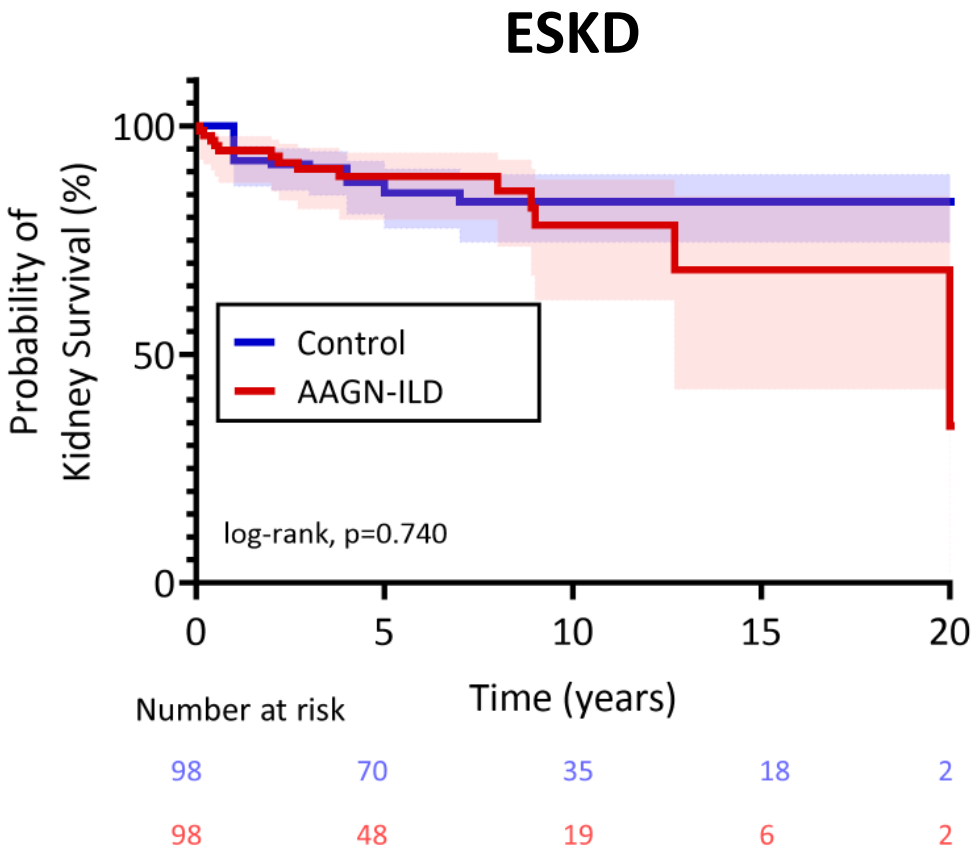
Scatter dot plot represent medians and interquartile range (IQR) with individual data points. ns, non-significant; * $p<0.05$, **$p<0.001$. matched cohort study by sex, age, ANCA type (1:1)

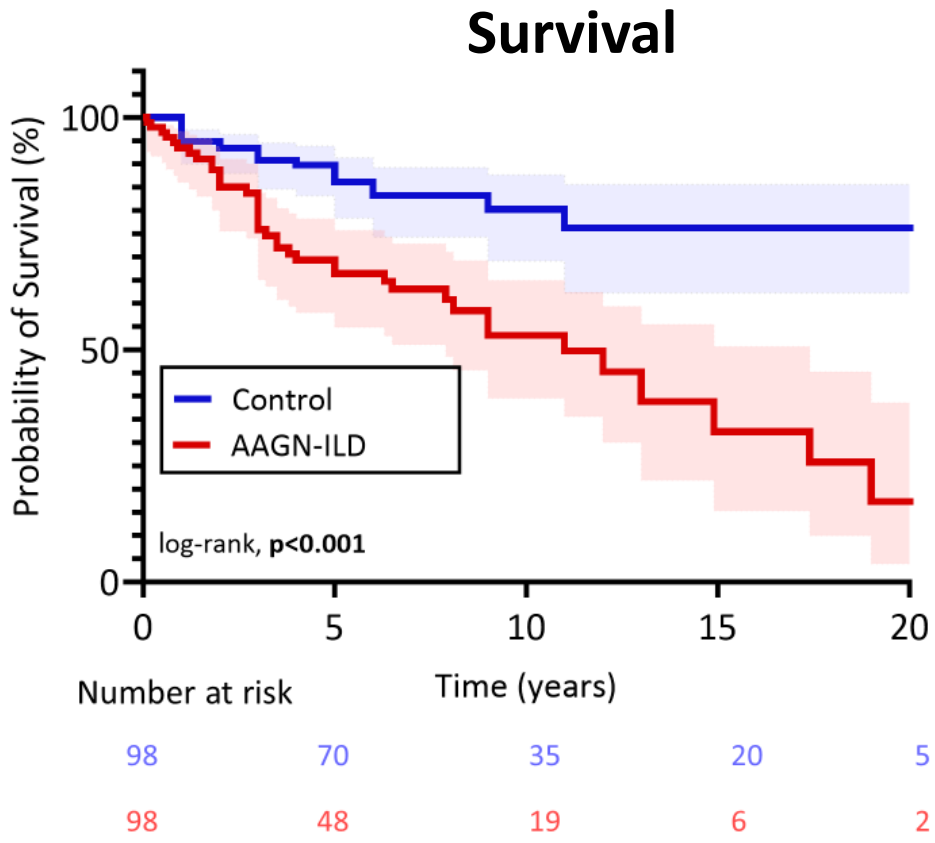
Change in Glomerular Filtration Rate (GFR)



Estimated marginal means (EMMs) ± SEM (standard of error) delta GFR between AAGN-ILD and control groups over 5 years and (B) delta GFR per year over 5 years obtained by mixed effects model for repeated measures analysis with fixed effects ILD, time, ILD and time interaction as factors, and baseline GFR and age as covariates. Column bar graph showing the estimated marginal means± SEM. matched cohort study by sex, age, ANCA type (1:1)

Long-term Outcome





Kaplan Meier analysis of kidney survival according to the presence of ILD . Shaded areas represent 95% CIs
matched cohort study by sex, age, ANCA type (1:1)

Risk factors for Mortality

Variable	Univariable		Multivariable	
	HR (95% CI)	P value	HR (95% CI)	P value
Age	1.0 (1.06 to 1.12)	<0.001	1.0 (1.05 to 1.11)	<0.001
ILD	2.3 (1.41 to 3.66)	0.001	1.6 (0.99 to 2.66)	0.05
ESKD	4.2 (2.54 to 7.12)	<0.001	3.4 (1.95 to 5.92)	<0.001

Adjusted for: age, gender, GFR at diagnosis, Berden classification, Induction treatment

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Conclusions

- In ILD-AAV, kidney involvement is frequently observed exhibiting a kidney phenotype marked by better preserved kidney function and **fewer inflammatory component.**
- Despite well-preserved kidney function at the initial presentation, the long-term progression to **ESKD** was observed at a similar rate among patients with and without interstitial lung disease (ILD) nephritis.
- Notably, the presence of ILD was identified as an **independent risk factor for mortality** in patients with AAGN.

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