patients, highlighting the urgent need for more effective drugs. The aim of this study was to investigate the LN transcriptome in depth to gain insights into underlying molecular mechanisms and to identify new potential drug targets for LN.

Methods We analysed differentially expressed genes in peripheral blood from active LN (n=41) and active non-renal lupus (n=62) patients versus healthy controls (n=497) from the European PRECISESADS project (NTC02890121) and dysregulated gene modules in a discovery (n=26) and a replication (n=15) set of active LN cases. Replicated gene modules qualified for correlation analyses with serological markers, and regulatory network and druggability analysis.

Results Unsupervised co-expression network analysis revealed 20 dysregulated gene modules; seven showed prominent dysregulation in three distinct subgroups of LN patients (figure 1A). These subgroups were classified based on the 'interferon' (IFN) gene module upregulation into low, intermediate, and high IFN subgroups and showed differential dysregulation of the 'B cell' and 'plasma cells/immunoglobulins' modules. Drugs annotated to the IFN network included CC-motif chemokine receptor 1 inhibitors, programmed death-ligand 1 inhibitors, and irinotecan, while the anti-CD38 daratumumab and proteasome inhibitor bortezomib showed potential for counteracting the transcriptomic signature associated with the 'plasma cells/immunoglobulins' module. In silico analysis demonstrated that the low-IFN subgroup may benefit from calcineurin inhibitors while the intermediate-IFN subgroup may benefit from B cell targeted therapies (figure 1B). High-IFN patients exhibited greater anticipated response to anifrolumab while the intermediate-IFN and high-IFN subgroups displayed greater anticipated response to daratumumab.

Conclusion Interferon upregulation and B and plasma cell gene dysregulation patterns revealed three distinct LN patient subgroups, providing a conceptual framework for precision medicine in LN.

Conflicts of Interest IP has received research funding and/or honoraria from Amgen, AstraZeneca, Aurinia, Bristol Myers Squibb, Elli Lilly, Gilead, GlaxoSmithKline, Janssen, Novartis, Otsuka, and Roche. The other authors declare that they have no conflicts of interest related to this work. The funders had no role in the design of the study, the analyses or interpretation of data, or the writing of the manuscript.

024 *APOL1* GENOTYPE IS A MAJOR DETERMINANT OF LUPUS NEPHRITIS SEVERITY IN PATIENTS OF AFRICAN ANCESTRY

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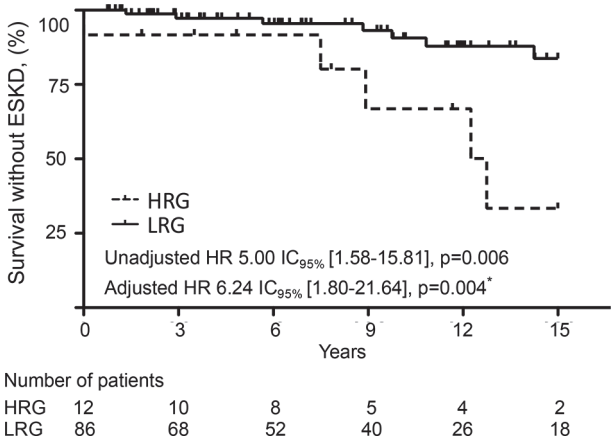
Objective G1 and G2 polymorphisms of *APOL1* gene, exclusively found among patients of African ancestry, have been associated with chronic kidney disease (CKD) and collapsing glomerulopathy. We investigated their impact on lupus nephritis (LN).

Methods We included patients from 6 hospitals in Paris and Marseille in France, between January 2017 and March 2020, with biopsy-proven LN, African ancestry and age >18 years at the time of inclusion. We excluded those with HIV infection. The data were retrospectively collected at LN diagnosis, 1 year after diagnosis and at last follow-up. *APOL1* genotyping was performed and we divided patients in 2 groups: the high-risk genotype (HRG) group with 2 risk alleles and the low-risk genotype (LRG) group with 1 or 0 risk allele. All patients signed a consent form for the genetic analysis and protocol approval was obtained from the ethic committee CERAPHP (Comité d'Ethique de la Recherche AP-HP Centre), registration number 00011928.

Results Ninety-nine patients were included, 13 in the HRG group and 86 in the LRG group. At LN diagnosis, clinical and biological characteristics were similar except for kidney function that was more impaired in the HRG group compared to the LRG group with a median serum creatinine of 131µmol/L [73–641] versus 66µmol/L [53–128] (p=0.01). Patients in the HRG group were more likely to have a serum creatinine above 200µmol/L compared to the LRG group (46% versus 11%, p=0.01, OR 7.1[1.8–28.6]), and required acute haemodialysis more frequently (31% versus 1% respectively, p = 0.001, OR 34.7[3.5–345.1]). Collapsing glomerulopathy was more frequent in the HRG group (46% of patients, versus 5%, OR 17.5[3.3–91.9], p=0.001). Patients in the HRG group were more likely to develop CKD at 1 year follow-up (33% versus 5%, OR 9.6[2.0–46.1]) (table 1). Survival without kidney failure was poorer in the HRG group with a hazard ratio (HR) of 4.6 [1.5–14.2], p=0.006, even after adjusting with the kidney response at 12 months (adjusted HR 6.24[1.8–21.6], p=0.004) (figure 1).

Conclusion *APOL1* high risk genotype was associated to a worse kidney function at diagnosis, development of collapsing glomerulopathy and higher risk of subsequent kidney failure.



Abstract O24 Figure 1 Patient survival without end-stage kidney disease. Legends: Data were censored at 15 years after LN diagnosis. Kaplan Meyer curve was analyzed with the log rank test. ESKD: End stage kidney disease; HRG: High risk genotype; LRG: Low risk genotype; HR: Hazard Ratio. *Hazard ratio was calculated based on the Cox regression, and was adjusted with the kidney response at 12 months (overall response versus none).

Abstract O24 Table 1 Data at Lupus nephritis diagnosis, at 1 year follow-up and at last follow-up

Variables	HRG N=13	LRG N=86	OR $CI_{95\%}$	P value
Data at LN diagnosis				
Age at LN diagnosis, median [IQR]	26 [21–32]	25 [20–34]	-	0.9
Inaugural LN, N (%)	7/13 (54)	38/86 (44)	1.5 [0.5–4.8]	0.6
Serum creatinine (µmol/L), median [IQR]	131 [73–641]	66 [53–128]	-	**0.01**
eGFR, median [IQR]	44 [8–103]	107 [52–126]	-	**0.006**
Serum creatinine > 200µmol/L, N (%)	5/11 (46)	8/76 (11)	**7.1 [1.8-28.6]**	**0.01**
Need for haemodialysis, N (%)	4/13 (31)	1/79 (1)	**34.7 [3.5-345.1]**	**0.001**
Proteinuria (g/g), median [IQR]	3.7 [1.6–5.9]	4.4 [2.0–7.1]	-	0.5
Nephrotic syndrome, N (%)	7/12 (58)	47/74 (64)	0.8 [0.2–2.8]	0.8
Type ISN/RPS I or II, N (%)	1/13 (8)	11/83 (13)	0.6 [0.1–4.6]	0.9
Type ISN/RPS III or IV (± V), N (%)	11/13 (85)	48/83 (58)	4.0 [0.8–19.3]	0.08
Isolated Type ISN/RPS V, N (%)	0/13 (0)	24/83 (29)	**0.09 [0.0-1.6]**	**0.03**
Type ISN/RPS VI, N (%)	1/13 (8)	0/83 (0)	20.0 [0.8–520.0]	0.1
Glomerulosclerosis, N (%)*	4/12 (33)	5/67 (7)	**6.2 [1.4-28.0]**	**0.03**
Interstitial fibrosis, N (%)**	5/11 (46)	14/68 (21)	3.2 [0.9–12.1]	0.1
FSGS, N (%)	7/11 (64)	22/69 (31)	3.7 [1.0–14.1]	0.09
CG, N (%)	5/11 (46)	3/66 (5)	**17.5 [3.3-91.9]**	**0.001**
MCTD, N (%)	3/10 (33)	5/67 (8)	5.3 [1.0–27.2]	0.06
Outcomes at 1 year follow-up				
RAASi treatment, N (%)	5/10 (50)	43/58 (74)	0.35 [0.1–1.4]	0.2
eGFR, median [IQR]	99 [63–106]	116 [92–126]	-	**0.02**
Proteinuria g/g, median [IQR]	1.8 [0.3–3.8]	0.6 [0.1–2.6]	-	0.2
Overall kidney response, N (%)*	7/12 (58)	62/81 (77)	0.43 [0.1–1.5]	0.3
CKD III-V, N (%)	4/12 (33)	4/81 (5)	**9.6 [2.0-46.1]**	**0.009**
Kidney failure, N (%)	1/12 (1)	0/84 (0)	22.0 [0.9–574.3]	0.1
Outcomes at last follow-up				
Years of follow-up, median [IQR]***	7.9 [2.7–18.1]	7.7 [3.3–13.8]	-	0.7
eGFR, median [IQR]	22 [10–98]	99 [54–118]	-	**0.02**
			HR $CI_{95\%}$	
Kidney failure at last follow-up, N (%)	5/12 (42)	7/86 (8)	4.6 [1.5–14.2]	**0.006**

Legends N: Number of patients; IQR: Interquartile range; LN: Lupus nephritis; eGFR: estimated Glomerular Filtration Rate; ISN/RPS: International Society of Nephrology/Renal Pathology Society; FSGS: Focal and Segmental Glomerular Sclerosis; CG: Collapsing glomerulopathy; MCTD: microcystic tubular dilatation; RAASi : Renin-angiotensin-aldosterone system inhibitors ; HRG: High-risk genotype; LRG: Low-risk genotype; OR $CI_{95\%}$: Odds ratio with 95% interval of confidence ; HR $CI_{95\%}$: Hazard ratio with 95% interval of confidence

*Glomerulosclerosis is considered if above or equal 10% of the glomeruli

**Interstitial fibrosis is considered if above or equal to 10% of the kidney parenchyma

*** Number of years between lupus nephritis diagnosis and last follow-up (end of study, loss of sight or end stage kidney disease)

**** Related to duration of follow-up in years

025 LUPUS PODOCYTOPATHY: A RARE FORM OF LUPUS NEPHRITIS – AN ITALIAN RETROSPECTIVE MULTICENTER STUDY

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Objective To describe clinical-morphological features and outcomes of lupus podocytopathy (LP) and compare relapsing and non-relapsing (NR) forms.

Methods Inclusion criteria for LP were SLE diagnosis and: 1) ISN/RPS Class I or Class II at kidney biopsy (KB); 2) with or without mesangial immunoglobulin/complement deposition; (3) >70% foot processes effacement at electron microscopy (EM). In the absence of EM, presence of nephrotic syndrome and complete remission to corticosteroids are needed. Complete remission: normal kidney function, proteinuria<0.5g/day; partial remission: persistence of non-nephrotic proteinuria.

Results (tables 1 and 2) 26 patients (24 Females, median age 45 [16–53] years) were enrolled in this retrospective study. Nephrotic syndrome (84.6%), acute kidney injury (AKI) (38.5%) and arterial hypertension (41.7%) were the clinical