Abstract 1104 Table 1   Effect of BEL 10 mg/kg IV on PERR and CRR at Week 104 and time to renal-related event or death in newly diagnosed and relapsed pts with LN

Table. Effect of BEL 10 mg/kg IV on PERR and CRR at Week 104 and time to renal-related event or death in newly diagnosed and relapsed pts with LN

	Relapsed		Newly diagnosed	
	PBO (n=75)	BEL 10 mg/kg IV (n=75)	PBO (n=148)	BEL 10 mg/kg IV (n=148)
PERR at Week 104, n (%)	17 (22.7)	27 (36.0)	55 (37.2)	69 (46.6)
OR (95% CI) vs PBO	2.31 (1.07, 5.01)		1.36 (0.85, 2.20)	
p-value	0.0331		0.2036	
CRR at Week 104, n (%)	8 (10.7)	17 (22.7)	36 (24.3)	50 (33.8)
OR (95% CI) vs PBO	3.11 (1.16, 8.31)		1.49 (0.88, 2.51)	
p-value	0.0237		0.1355	
Time to renal-related event or death*, n (%)	23 (30.7)	12 (16.0)	40 (27.0)	23 (15.5)
HR (95% CI) vs PBO	0.47 (0.23, 0.95)		0.55 (0.33, 0.93)	
p-value	0.0354		0.0242	

*Time to renal-related event or death is a composite endpoint defined as the first event occurring after Day 1 among the following: 1) death, 2) end-stage kidney disease, 3) doubling of serum creatinine, 4) renal worsening as evidenced by increased proteinuria and/or impaired renal function, or 5) renal disease-related treatment failure

OR, 95% CI and p-value are from a logistic regression model run within the subgroup level for the comparison between BEL and PBO with covariates of induction regimen (CYC vs MMF), race (Black African descent vs other), baseline uPCR, and baseline eGFR

HR, 95% CI and p-value from Cox proportional hazards model for the comparison between BEL and PBO adjusted for induction regimen (CYC vs MMF), race (Black African descent vs other), baseline uPCR, and baseline eGFR

CI, confidence interval; HR, hazard ratio; OR, odds ratio

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| 1105 | RESPONSE GENE TO COMPLEMENT-32 EXPRESSION IS UPREGULATED IN THE KIDNEY AND PROMOTES RENAL FIBROSIS IN LUPUS NEPHRITIS |

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Background RGC (Response Gene to Complement)-32 is a cell cycle regulator widely expressed in normal tissues, multiple tumors and in a variety of cell lines. RGC-32 is localized in the cytoplasm and translocates to the nucleus upon upregulation by complement activation, growth factors and cytokines. Depending on the cell type, physiological or pathological conditions, RGC-32 can stimulate cell growth through increased p34CDC2 kinase activity and Akt phosphorylation or suppress it via arrest in mitotic progression. We have shown that RGC-32 is critical for murine and human Th17 cell differentiation. RGC-32 is induced by TGFβ in fibroblasts and human proximal tubular epithelial cells (PTEC) and mediates TGFβ dependent profibrotic pathways that contribute to renal fibrosis. RGC-32 expression has been described in tubules of normal human kidneys and its upregulation was reported in tubules from patients with IgA nephropathy. The expression patterns and function of RGC-32 in lupus nephritis (LN) have not yet been investigated.

Methods In situ expression and localization of RGC-32 was assessed by immunohistochemistry in kidney biopsies from 25 lupus patients with proliferative lupus nephritis and 11 patients with other nephropathies (IgA nephropathy, minimal change disease, ANCA-associated glomerulonephritis, nephrosclerosis, acute tubular necrosis). In vitro, the expression of RGC-32 in human PTEC cells was assessed by Flow cytometry, Western blot and RT-PCR in the presence or absence of cytokines with known nephritogenic potential such as IL-1, TNFα, IFNγ and TGFβ.

Results Consistent with the staining distribution reported in normal kidneys, RGC-32 immunostaining was predominant in proximal and distal tubules and was detected in a focal or diffuse pattern. Tubular mean staining intensity was significantly higher in SLE than in non-SLE specimens (2.0±0.23 vs 1.30±0.49; p=0.04) and was noted both in areas of normal appearing as well as damaged tubules. RGC-32 expression was also detected in glomeruli and in inflammatory cells in the interstitium of LN biopsies and colocalized with CD4+ T cells and CD68+ macrophages, respectively. Staining intensity was significantly higher in glomeruli and interstitium of LN

specimens compared to disease controls (2.4±1.4 vs.1.6±0.8 and 1.8± 0.9 vs. 0.96±0.4 respectively) and correlated with the activity (r=0.4), chronicity (r=0.5) and interstitial fibrosis scores (r=0.5). In vitro, RGC- 32 mRNA and protein expression was upregulated in PTEC by nephritogenic cytokines including IL-1 (7.8 fold), TNFα (5 fold), TGFβ (3.1 fold) and to a lesser extent by IFNγ (2.1 fold). TGFβ induced mRNA production of Collagen 1a1 and collagen III by in vitro cultured human PTEC was increased in RGC-32 transfected cells vs. control.

Conclusions RGC-32 expression is increased in glomeruli and tubulointerstitium in kidneys of patients with lupus nephritis. Upregulation of RGC-32 is mediated by proinflammatory cytokines and may play pathogenetic role in organ damage in SLE by promoting manifestations of progressive renal disease such as interstitial fibrosis. Thus RGC-32 is a potential therapeutic target in the treatment of lupus nephritis.

Acknowledgments

Trial Registration

Lay summary RGC-32 expression is increased in glomeruli and tubulointerstitium in kidneys of patients with lupus nephritis. Upregulation of RGC-32 is mediated by proinflammatory cytokines and may play pathogenetic role in organ damage in SLE by promoting manifestations of progressive renal disease such as interstitial fibrosis. Thus RGC-32 is a potential therapeutic target in the treatment of lupus nephritis.

Lupus Nephritis

1106 STABILITY OF NOVEL URINARY BIOMARKERS USED FOR LUPUS

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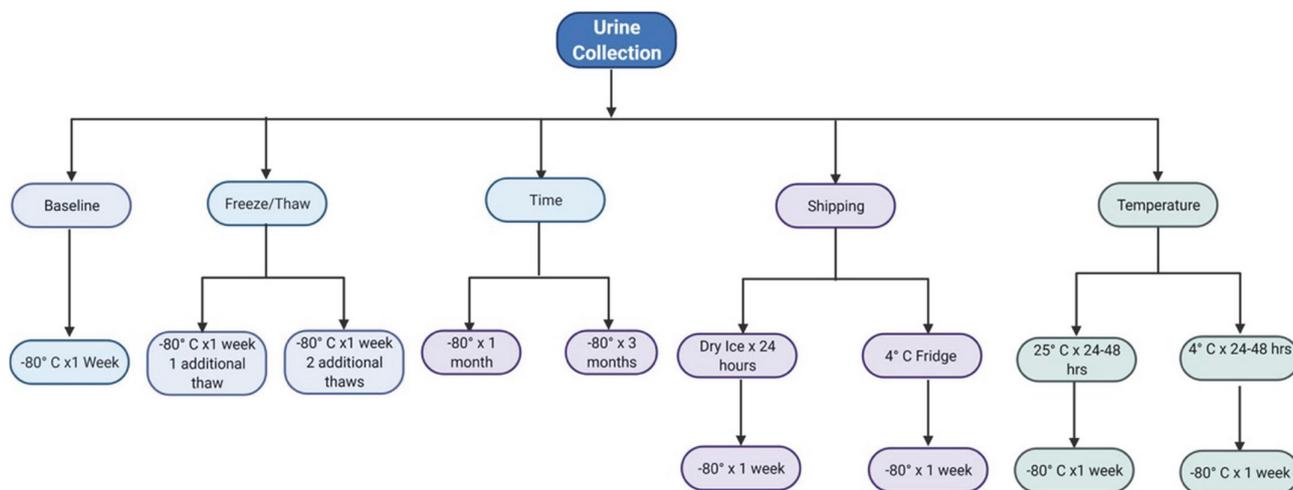
Background We have developed and validated the Renal Activity Index for Lupus (RAIL), a composite score of six urinary

Abstract 1106 Table 1

	Condition	Mean	Spearman Correlation Coefficient	P-value
Adiponectin	Baseline	1.94	0.97	<0.01
	Dry Ice	1.90	0.99	<0.01
	Shipping	2.05	0.96	<0.01
	Fridge	2.13	1.00	<0.01
	RT	2.03	0.89	<0.01
	FT1	1.86	0.98	<0.01
	FT2	1.98	0.99	<0.01
	1MO	1.95	0.98	<0.01
	3MO	1.63	0.91	<0.01
Ceruloplasmin	Baseline	3.62	0.99	<0.01
	Dry-Ice	3.55	1.00	<0.01
	Shipping	3.55	1.00	<0.01
	Fridge	3.48	0.98	<0.01
	RT	3.61	1.00	<0.01
	FT1	3.69	0.87	<0.01
	FT2	3.49	1.00	<0.01
	1MO	3.80	1.00	<0.01
	3MO	4.25	0.95	<0.01
Hemopexin	Baseline	5.52	0.92	<0.01
	Dry Ice	5.52	0.99	<0.01
	Shipping	5.53	0.98	<0.01
	Fridge	5.51	0.96	<0.01
	RT	5.41	0.96	<0.01
	FT1	5.49	0.96	<0.01
	FT2	5.47	0.97	<0.01
	1MO	5.54	0.97	<0.01
	3MO	5.82	0.92	<0.01
MCP-1	Baseline	4.56	1.00	<0.01
	Dry Ice	4.60	1.00	<0.01
	Shipping	4.56	1.00	<0.01
	Fridge	4.50	1.00	<0.01
	RT	4.43	1.00	<0.01
	FT1	4.55	1.00	<0.01
	FT2	4.47	1.00	<0.01
	1MO	4.67	0.99	<0.01
	3MO	4.61	0.10	<0.01

Abbreviations: RT: Room Temperature, FT: Freeze Thaw, MO: Month

Abstract 1106 Figure 1