

Supplemental material is neither peer-reviewed nor thoroughly edited by CJASN. The authors alone are responsible for the accuracy and presentation of the material.

Supplemental Table 1: Estimated GFR decline and baseline estimated glomerular filtration rate in participants of the EXAMINE trial

	eGFR<15 ml/min/1.73m²	eGFR 15-20 ml/min/1.73m²	eGFR>20 ml/min/1.73m²
Composite Endpoint (n=98)	16.3% (16/98)	8.2% (8/98)	75.5% (74/98)
50% decline in eGFR (n=30)	0.0% (0/30)	0.0% (0/30)	100% (30/30)
ESRD (n=68)*	23.5% (16/68)	11.8% (8/68)	64.7% (44/68)

*ESRD is defined as a decline in eGFR < 15 ml/min/1.73m², initiation of dialysis, or both eGFR < 15 ml/min/1.73m² and dialysis. ESRD = End Stage Renal Disease, eGFR = estimated glomerular filtration rate measured by the CKD-EPI equation (ml/min/1.73 m²).

Supplemental material is neither peer-reviewed nor thoroughly edited by CJASN. The authors alone are responsible for the accuracy and presentation of the material.

Supplemental Table 2: Estimated GFR decline by treatment group in participants of the EXAMINE trial

Characteristic n (%)	Alogliptin (n=2701)	Placebo (n=2679)	P Value
eGFR decline	50/2693 (1.9)	48/2674 (1.8)	0.87
CKD stage 5 or dialysis	33/2693 (1.2)	35/2674 (1.3)	0.78
50% decline in eGFR	26/2701 (1.0)	28/2679 (1.0)	0.76
30% decline in eGFR	126/2701 (4.7)	117/2679 (4.4)	0.60
New microalbuminuria*	149/433 (34.4)	162/466 (34.8)	0.91
New macroalbuminuria**	117/950 (12.3)	145/1049 (13.8)	0.32

Estimated GFR decline was defined as 1. 50% decrease in eGFR from baseline or 2. ESRD with stage 5 CKD eGFR < 15 ml/min/1.73 m² dialysis, or both eGFR < 15 ml/min/1.73m² and dialysis. *Incident microalbuminuria >30-300 mg/g albumin/creatinine. ** Incident macroalbuminuria ≥300mg/g albumin/creatinine.

Supplemental Table 3: Biomarker quartile concentrations at baseline and change over 6 months in participants of the EXAMINE trial

Biomarker	Quartile 1	Quartile 2	Quartile 3	Quartile 4
Baseline				
Cystatin C (mg/L)	≤0.8	>0.80, 0.92	>0.93, 1.13	≥1.13, 4.90
uKIM-1/Cr (ng/mg)	≤0.33	>0.33, 0.60	>0.60, 1.02	≥1.02, 20.97
uNGAL/Cr (ng/mg)	≤6.90	>6.90, 13.40	>13.40, 30.50	≥30.50, 3686.40
Change from Baseline to 6 months*				
uKIM1/Cr (ng/mg)	-16.16, - 0.33	>-0.33, - 0.04	>-0.04, 0.23	≥0.23, 58.23
uNGAL/Cr (ng/mg)	--3500.60, -7.50	>-7.50, - 0.40	>-0.40, 6.10	>6.10, 10961.70

Baseline Cystatin C was available in 5,213 of the 5,367 total individuals, uKIM-1/Cr was available in 4,875 individuals and uNGAL/Cr was available in 4,962 individuals. Serial measurements of uKIM-1/Cr were available in 3,865 individuals and uNGAL/Cr were available in 3,982 individuals. *Subjects with eGFR decline that occurred within 180 days (6 months) are excluded from the calculations of biomarker change over 6 months (n=32). No subjects are excluded for the baseline calculations. uKIM-1/Cr= urinary Kidney Injury Molecule – 1/Creatinine (ng/mg). uNGAL/Cr= urinary Neutrophil Gelatinase Associated Lipocalin/Creatinine (ng/mg).

Supplemental Table 4: Biomarker characteristics at baseline and as a change over 6 months by treatment group in participants of the EXAMINE trial

Biomarker	Alogliptin	Placebo	P Value
Baseline, mean ± SD			
Cystatin C (mg/L)	1.03 ± 0.38	1.03 ± 0.37	0.89
uKIM-1/Cr (ng/mg)	0.84 ± 1.01	0.83 ± 0.85	0.74
uNGAL/Cr (ng/mg)	51.78 ± 179.44	43.65 ± 141.10	0.08
Change over 6 months, mean ± SD*			
uKIM-1/Cr (ng/mg)	-0.04 ± 1.61	-0.05 ± 1.11	0.82
uNGAL/Cr (ng/mg)	7.09 ± 384.62	1.69 ± 152.00	0.56

Baseline Cystatin C was available in 2,625 individuals in the Alogliptin group and 2,588 individuals in the placebo group. Baseline uKIM-1 was available in 2,450 individuals in the Alogliptin group and 2,425 individuals in the placebo group. Baseline uNGAL was available in 2,497 individuals in the Alogliptin group and 2,465 individuals in the placebo group. The change in uKIM-1 over 6 months was available in 1,951 individuals in the Alogliptin group and 1,914 individuals in the placebo group. The change in uNGAL over 6 months was available in 2,001 individuals in the Alogliptin group and 1,981 individuals in the placebo group. uKIM-1= urinary Kidney Injury Molecule – 1/Creatinine (ng/mg). uNGAL= urinary Neutrophil Gelatinase Associated Lipocalin/Creatinine (ng/mg).

* Subjects with CKD progression that occurred within 180 days (6 months) are excluded for the calculations of biomarker change over 6 months (n=32). No subjects are excluded for the baseline calculations.

Supplemental material is neither peer-reviewed nor thoroughly edited by CJASN. The authors alone are responsible for the accuracy and presentation of the material.

Supplemental Table 5: Pearson correlation coefficients of baseline biomarker concentrations and baseline albuminuria in participants of the EXAMINE trial

	Cystatin C	P Value	uKIM- 1/Cr	P Value	uNGAL /Cr	P Value
Microalbuminuria	0.13	<0.001	0.02	0.55	0.03	0.22
Macroalbuminuria	0.36	<0.001	0.49	<0.001	0.48	<0.001

Baseline albumin excretion was measured in 80/98 individuals with and 3048/5269 without eGFR decline. Microalbuminuria 30-300 mg/g albumin/creatinine. Macroalbuminuria <300mg/g albumin/creatinine.