

VEGETARIAN VERY LOW PROTEIN DIET SUPPLEMENTED WITH KETOANALOGUES MAY REDUCE NEPHROTIC-RANGE PROTEINURIA IN PREDIALYSIS CKD PATIENTS

Liliana Gârneață^{1,2}, Alexandra Stancu², Paula Luca², Gabriel Ștefan¹, Gabriel Mircescu^{1,2}

¹ - "Carol Davila" University of Medicine and Pharmacy, Bucharest; ² - "Dr Carol Davila" Teaching Hospital of Nephrology, Bucharest, Romania

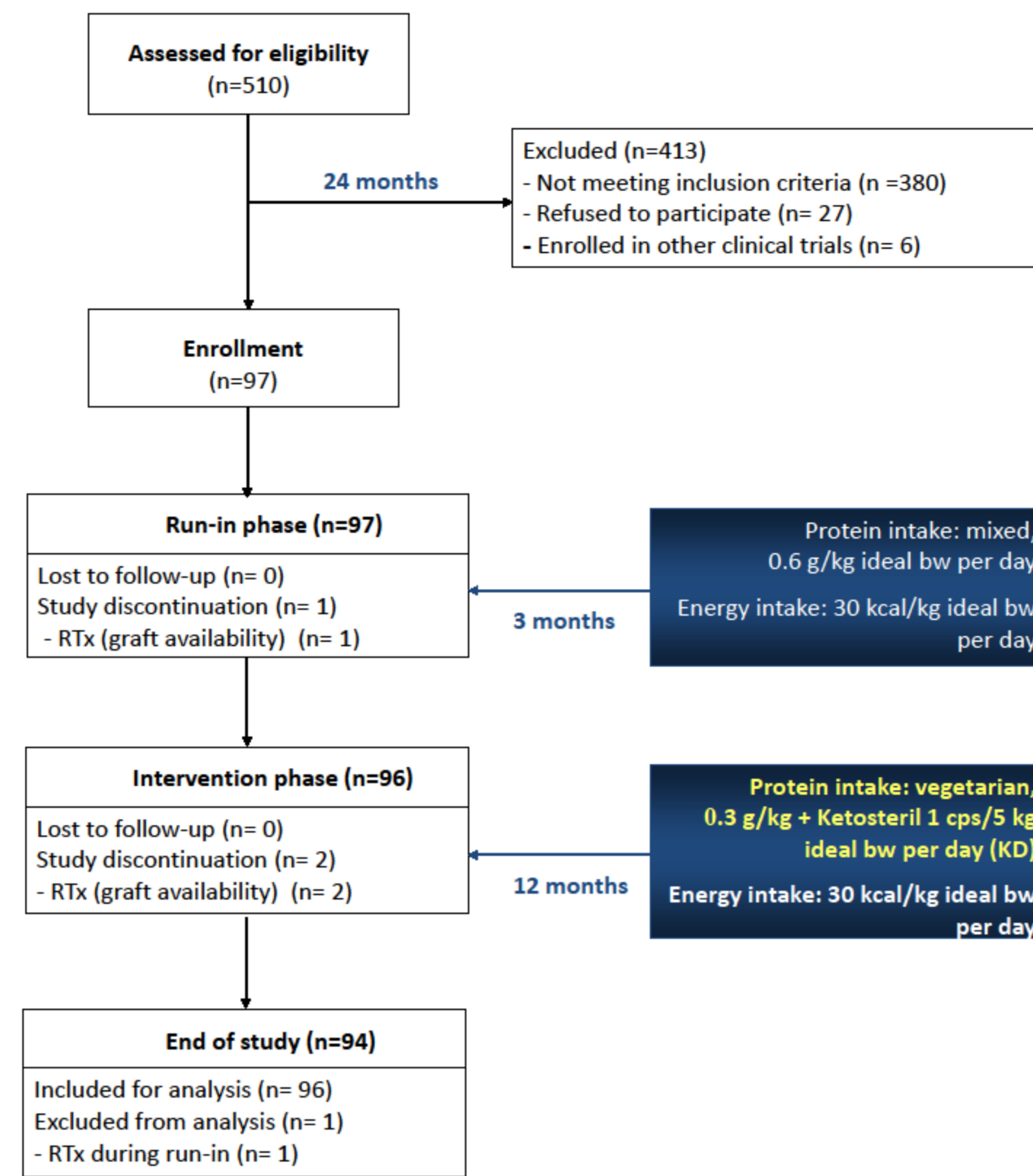
BACKGROUND AND OBJECTIVE

- Background:** Protein-restricted diets were reported as beneficial in advanced Chronic Kidney Disease (CKD) to postpone dialysis, mainly through a better metabolic control [1-7]. Better blood pressure control and decrease in proteinuria with low protein diets were also supported [8-10].
- Objective:** to assess the impact of ketoanalogue-supplemented vegetarian very low protein diet (keto-diet, KD) on nephrotic-range proteinuria in CKD patients.

STUDY DESIGN. SUBJECTS AND METHODS

- Type:** Prospective, interventional, single-center
- Parameters:**
 - Efficacy:
 - Primary:
 - Proteinuria
 - GFR
 - Death of the patient/ESRD
 - Secondary: CKD-related metabolic disturbances
 - Safety: nutritional status, dietary compliance, adverse events

- Selection criteria:**
 - non-diabetic adults, stage 4 CKD (GFR 15-30 mL/min per 1.73m², average of urea and creatinine clearances)
 - proteinuria >3 g/g creatinuria
 - primary glomerulopathies
 - without indication/with contraindications for etiologic/pathogenic treatment
 - good nutritional status



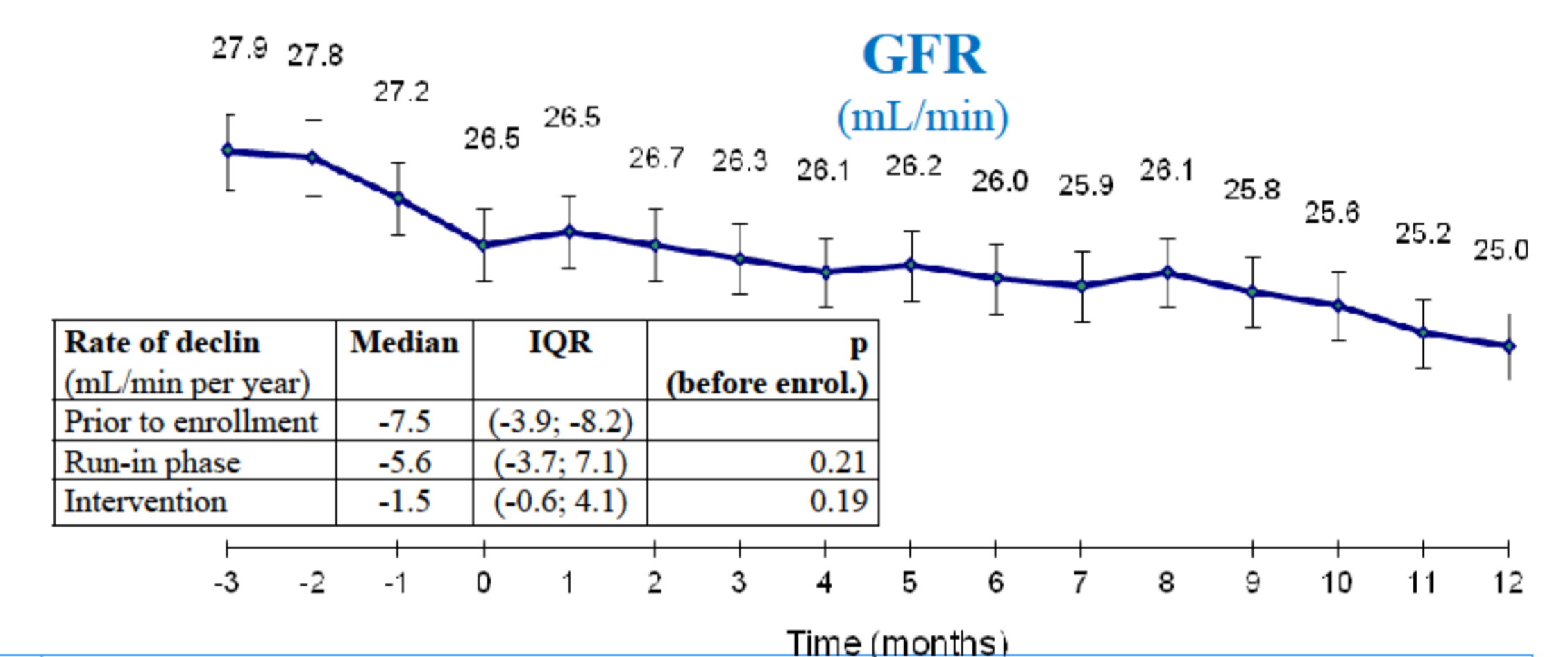
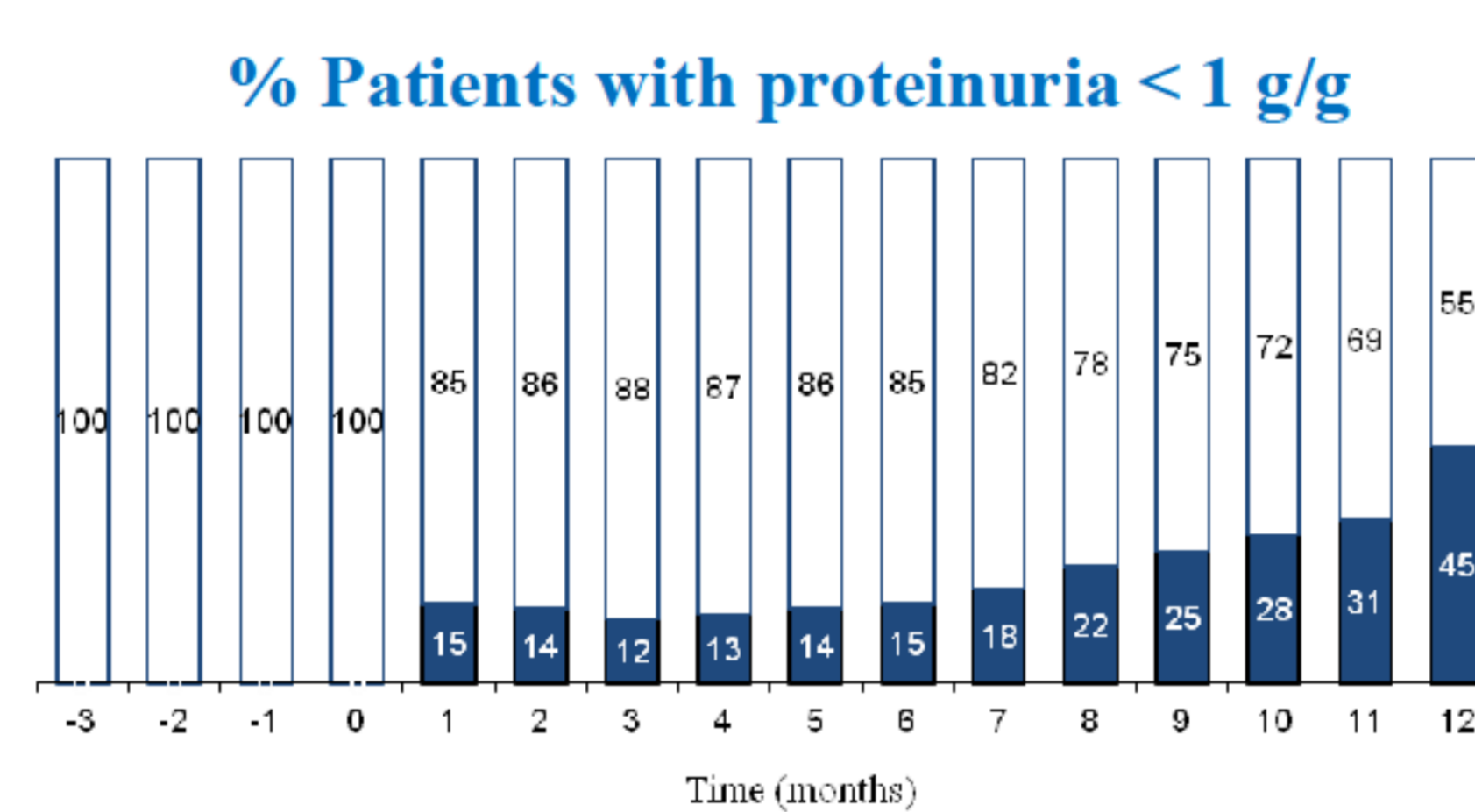
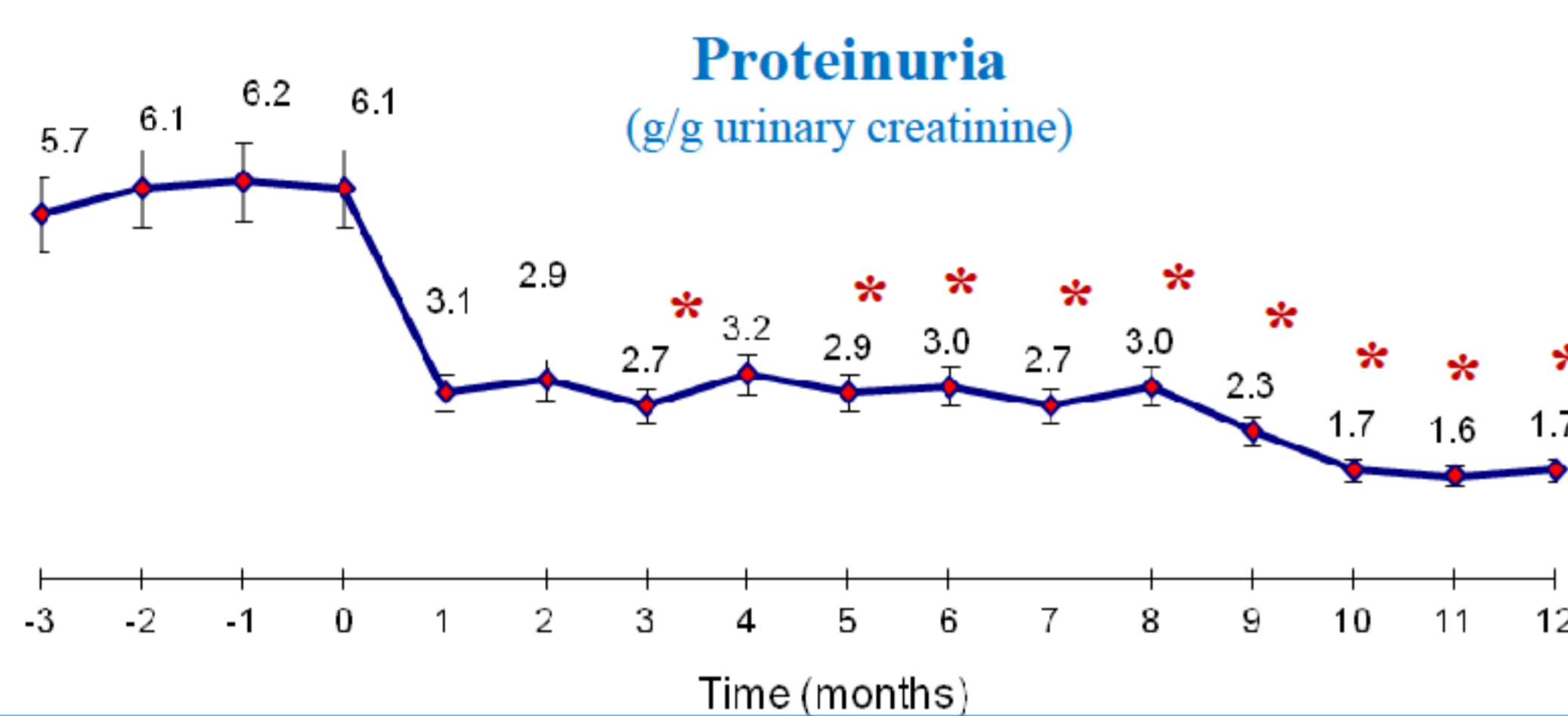
Patients Flowchart

Patients' characteristics

Age (years) [#]	55.0±11.3
Gender (male, %)	63
Parameters of renal function	
Proteinuria (g/g creatinuria)	5.7±2.1
GFR (mL/min/1.73 m ²) [#]	27.9±5.8
Estimated rate of GFR decline (mL/min-yr)	7.5 (5.9-8.2)
Serum creatinine (mg/dL)	2.4±1.1
Blood pressure control	
Patients with optimal BP control (%) ^{##}	71.7
Patients on antihypertensive treatment (%)	92
Patients on ACEIs/ARBs (%)	100
Parameters of nutritional status	
SGA (A, %)	87
Body mass index (BMI) (kg/m ²) [#]	24.9±4.2
Serum albumin (g/dL) [#]	3.7±0.3
Parameters of inflammation	
C - reactive protein (CRP, mg/L)*	4.0 (2.0; 8.0)
Dietary habits prior to enrollment	
Protein intake (g/day)	0.75±0.22
Energy intake (kcal/day)	33.2±3.1

RESULTS

Proteinuria. Progression of Chronic Kidney Disease



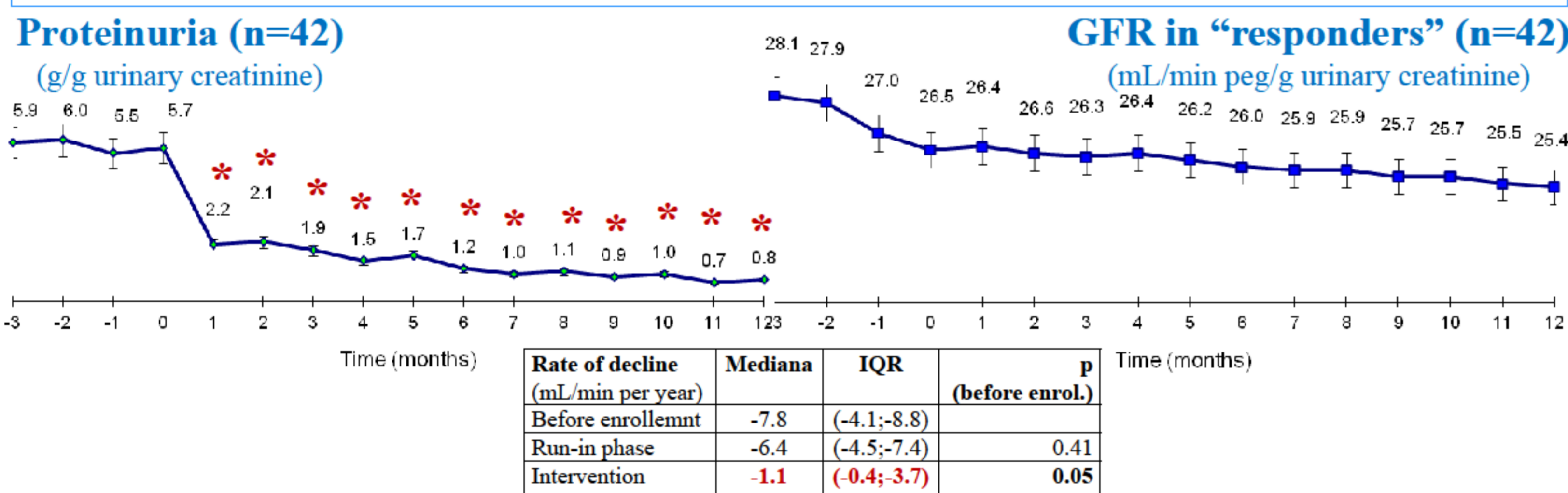
Rate of decline (mL/min per year)	Median	IQR	p (before enrol.)
Prior to enrollment	-7.5	(-3.9; -8.2)	
Run-in phase	-5.6	(-3.7; 7.1)	0.21
Intervention	-1.5	(-0.6; 4.1)	0.19

- Proteinuria did not significantly change during run-in, but significantly decreased starting with the 3rd month of KD (*-p<0.05).

- No patient had proteinuria < 1 g/g at baseline. 12% of patients reached this level ("responders") after 3 months of KD; 45% were "responders" at EOS.

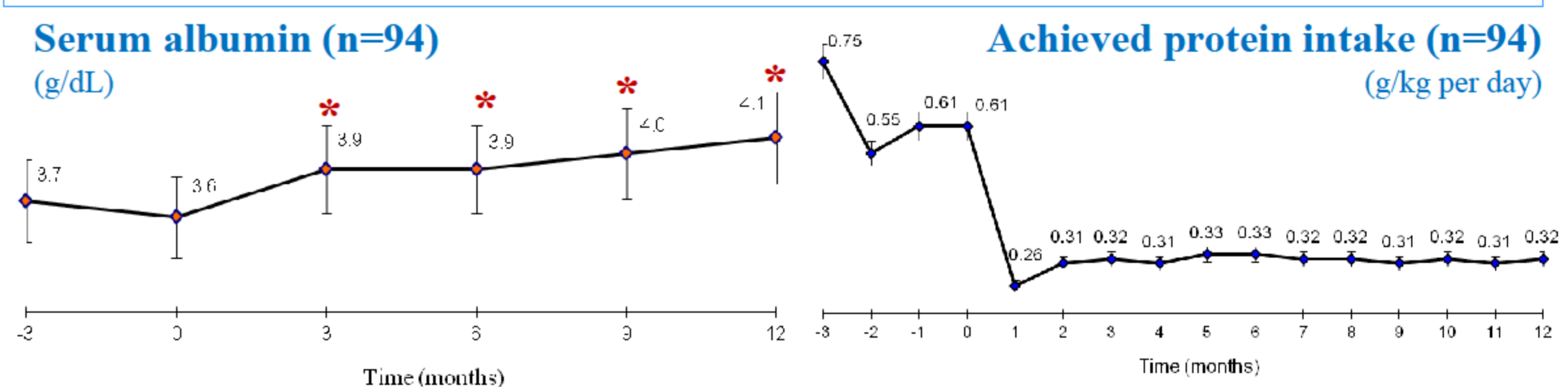
- GFR continued to decrease.
- The rate of decline was reduced, with no statistical significance

Proteinuria and Progression of CKD in "responders"



- In "responders", the rate of decline in renal function significantly decreased.
- There were no differences between "responders" and "non-responders" at baseline in age, gender, proteinuria, GFR, previous rate of decline, nutritional status, BP control, use of ACEI/ARBs or previous dietary habits.

Safety Parameters. Compliance



- Serum albumin significantly increased starting with the 3rd month of KD.
- The protein intake was very close to prescription throughout the study.
- The compliance to KD was good.
- There were no changes in the nutritional status and no adverse reactions.

CONCLUSIONS

- In compliant CKD patients with nephrotic-range proteinuria and no indication for specific therapies, vegetarian very low protein diet supplemented with ketoanalogues could reduce proteinuria and even the rate of decline in renal function in "responders", without any negative influence on the nutritional status.

REFERENCES

- Mitch WE: Dietary protein restriction in chronic renal failure: nutritional efficacy, compliance, and progression of renal insufficiency. *J Am Soc Nephrol* 2:823-831, 1991
- Walser M, Hill S: Can Renal Replacement Be Deferred by a Supplemented Very Low Protein Diet? *J Am Soc Nephrol* 10:110-116, 1999
- Fouque D et al: Low protein diets for CKD in non diabetic adults. *Cochrane Database Syst Rev* 3:CD001892, 2009
- Mircescu G et al: Effects of a supplemented hypoproteic diet in CKD. *J Ren Nutr* 17(3):179-188, 2007
- Brunori G et al: Efficacy and Safety of a Very-Low-Protein Diet When Postponing Dialysis in the Elderly: A Prospective Randomized Multicenter Controlled Study. *Am J Kidney Dis*, 49(5) 569-580, 2007
- Piccoli GB et al: Vegetarian low-protein diets supplemented with ketoanalogues: a niche for the few or an option for many? *Nephrol Dial Transplant* 28:2295-2305, 2013
- Gameata L et al: Ketoanalogue-Supplemented Vegetarian Very Low-Protein Diet and CKD Progression. *J Am Soc Nephrol*. Published online before print January 28, 2016
- Teplan et al: Effects of very low protein diet supplemented with ketoanalogues on proteinuria in diabetic patients. *Klin Biochem Met* 2:70-73, 2003
- Bellizzi V et al: Very low protein diet supplemented with ketoanalogs improves blood pressure control in chronic kidney disease. *Kidney Int*, 2007; 71: 245-251
- Di Iorio et al: Phosphate attenuates the anti-proteinuric effect of very low-protein diet in CKD patients. *Nephrol Dial Transplant*, 2013;28:632-640