

Hyperlipidemia affects the efficacy of the ACE- inhibitors: an Italian multicenter study on GLYCOGEN STORAGE DISEASE TYPE 1

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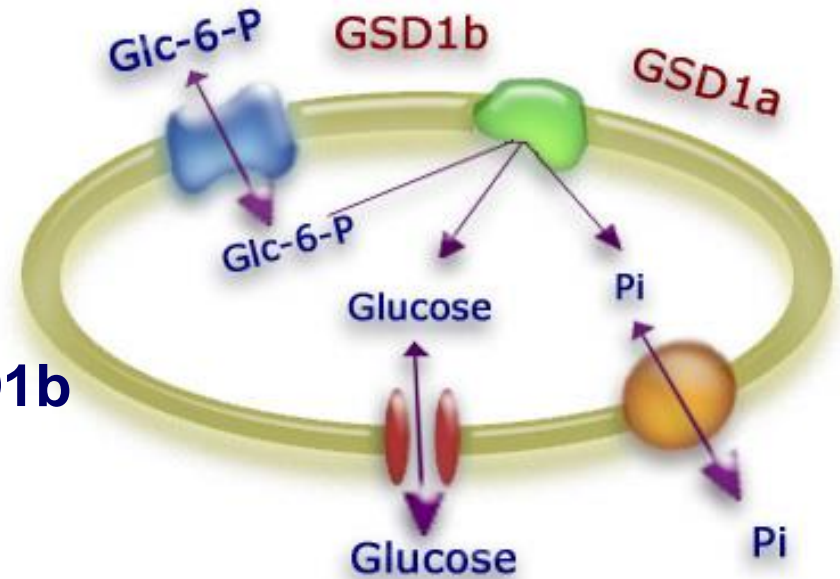
Glycogen storage disease type 1

Genetic and molecular bases

Frequency 1:100.000 newborns

Autosomal recessive

Two types → GSD1a and GSD1b



Chromosomal loci

GSD1a → Glucose-6-phosphatase (G6-Pase α) 17q21

GSD1b → Glucose-6-phosphate Translocase (G6-PT) 11q23

Glycogen storage disease type 1

Clinical features

GSD1a/GSD1b

Short stature - delayed puberty
Liver and kidney enlargement
Fasting hypoglycemia
Hyperlipidemia and hyperuricemia

Chronic renal disease

Liver adenoma
Osteoporosis

GSD1b

Neutropenia/Neutrophil dysfunction
Recurrent infections

Inflammatory bowel disease



Chronic renal damage: pathogenesis

G6-Pase deficiency in proximal tubular cells

(Pan et al., 1998)

Hyperlipidemia

(Yokoyama et al., 1995)

Hyperuricemia

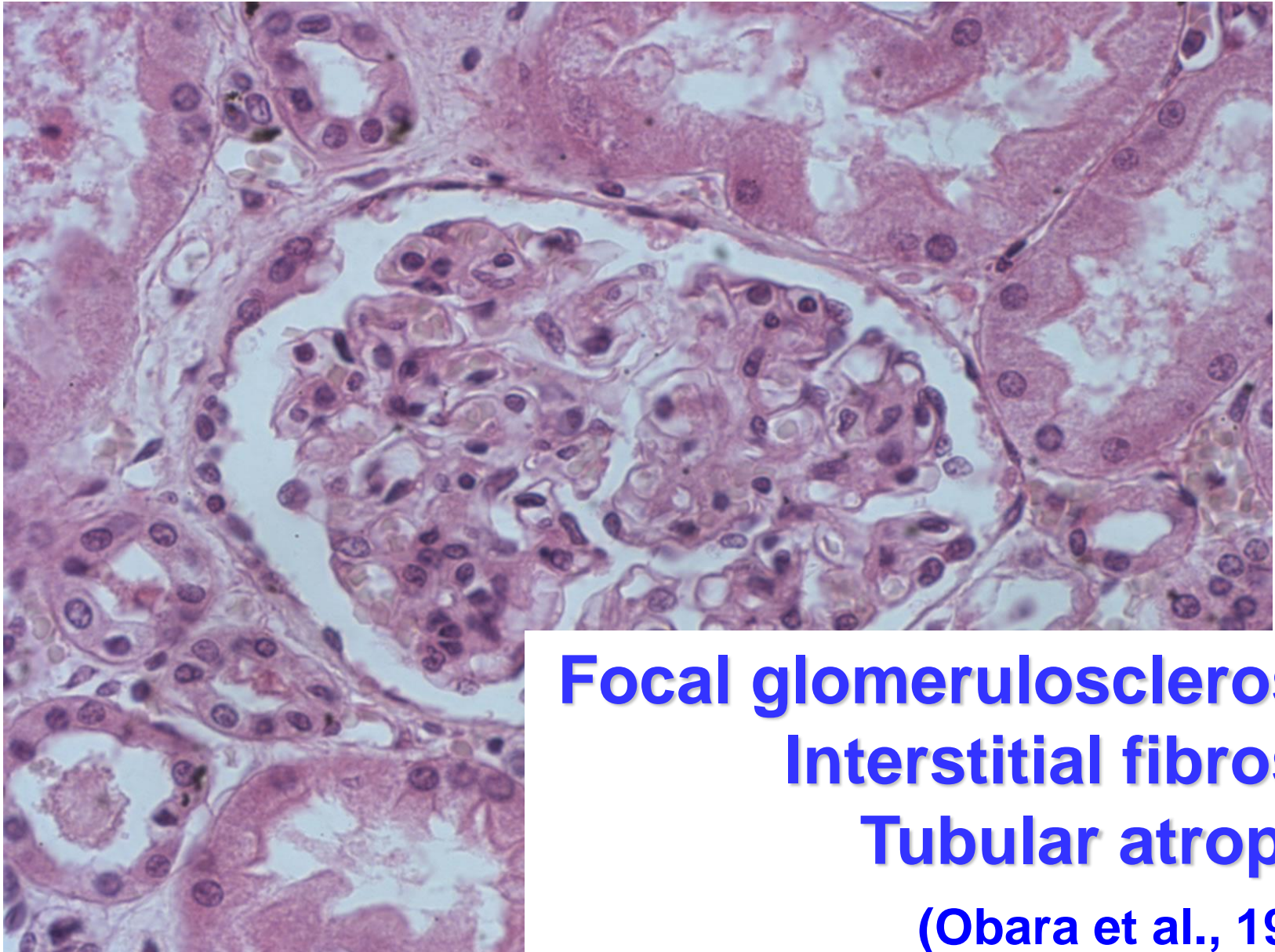
(Mazzali et al., 2001; Kang et al., 2002)

Activation of the angiotensin system

(Yiu et al., 2008)

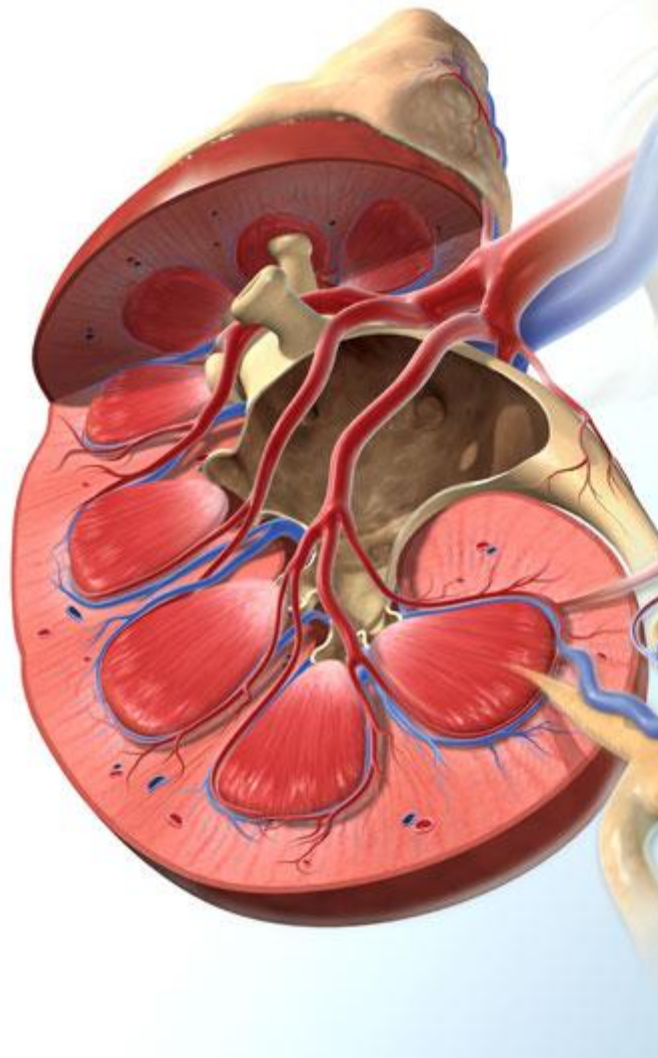


Chronic renal damage: histology



Focal glomerulosclerosis
Interstitial fibrosis
Tubular atrophy
(Obara et al., 1993)

Chronic renal damage: evolution



Glomerular damage

Hyperfiltration

Microalbuminuria

Proteinuria



Similarity to

Diabetic nephropathy

Chronic renal damage: therapy

ACE-inhibitors



Anecdotal reports: Improvement of renal damage

(Baker et al., 1988; Ozen et al., 2000; Pela et al., 2001; Gianni et al., 2002)



Case-control study: Improvement of glomerular hyperfiltration No effect on microalbuminuria and proteinuria

(Melis et al., 2005)



Aim of the study

- 1- To evaluate the efficacy of ACE-inhibitors on renal damage of GSD1 patients**
- 2- To investigate the role of the metabolic control on the initiation and progression of GSD1-related nephropathy**
- 3- To analyze the interference of the altered metabolic environment on the efficacy of the ACE-inhibitors**

Patients

86 patients

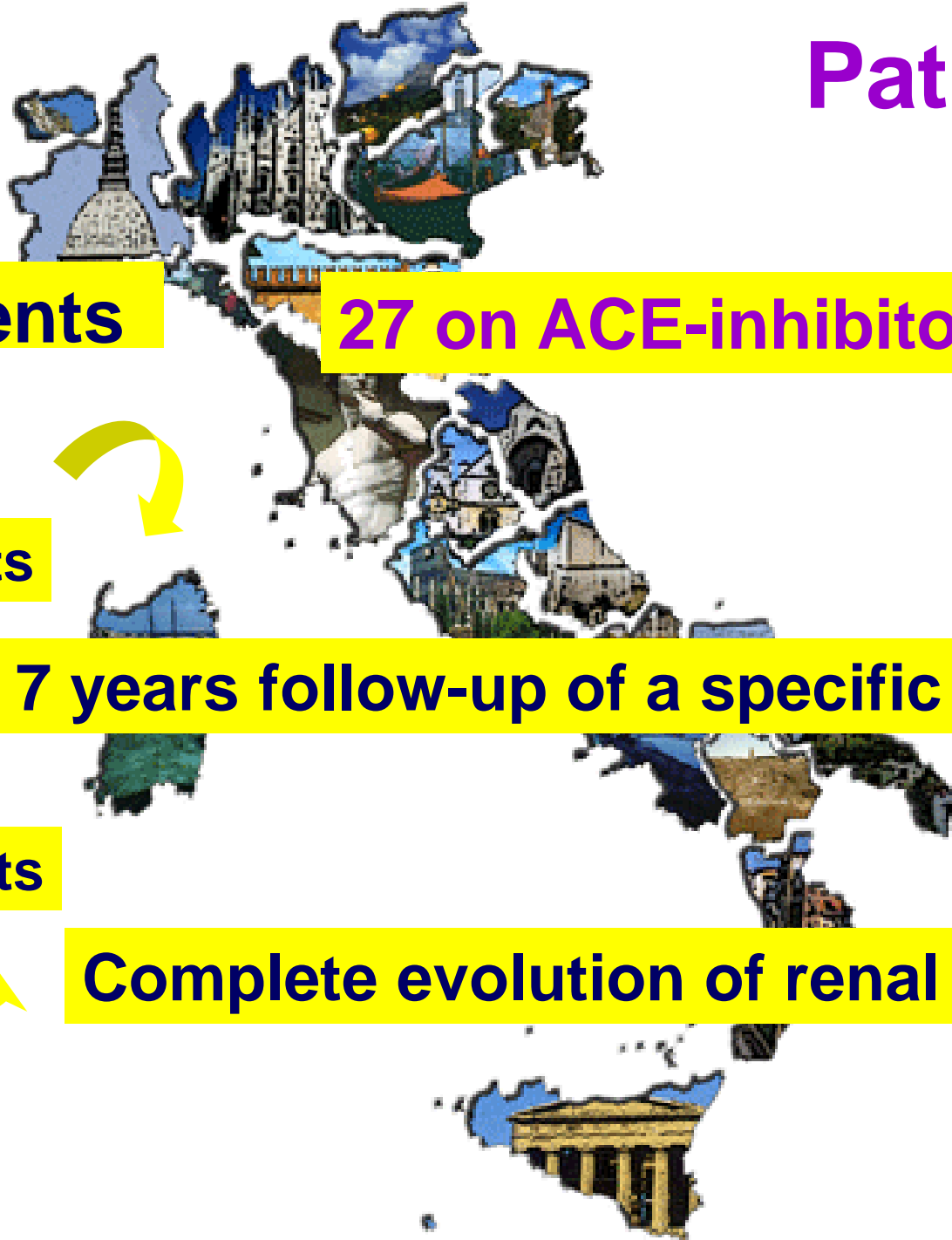
27 on ACE-inhibitors

52 patients

7 years follow-up of a specific parameter

30 patients

Complete evolution of renal damage



Methods and study design

Retrospective-prospective observational study

Biochemical parameters of metabolic control

Glomerular filtration rate, microalbuminuria and proteinuria

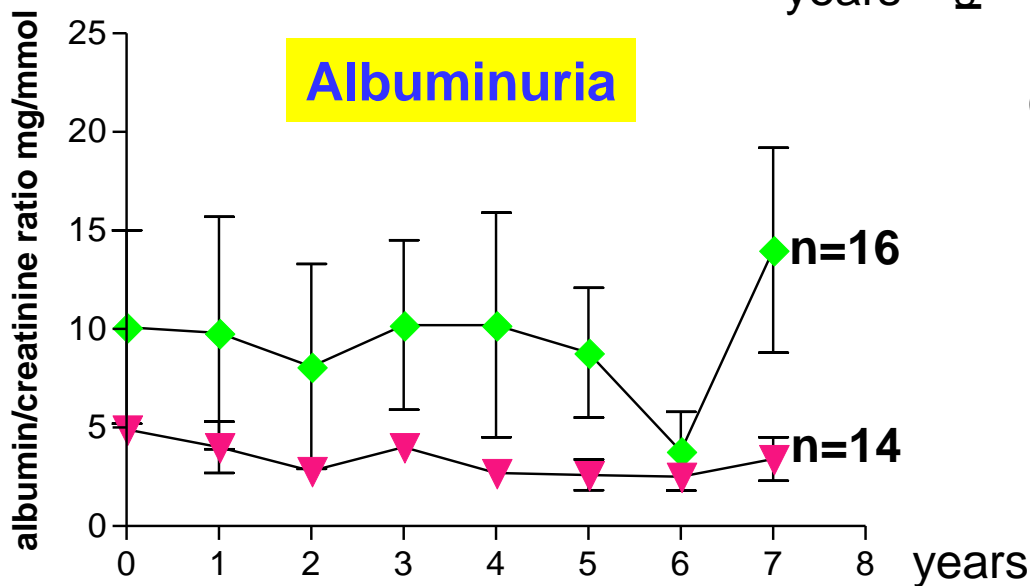
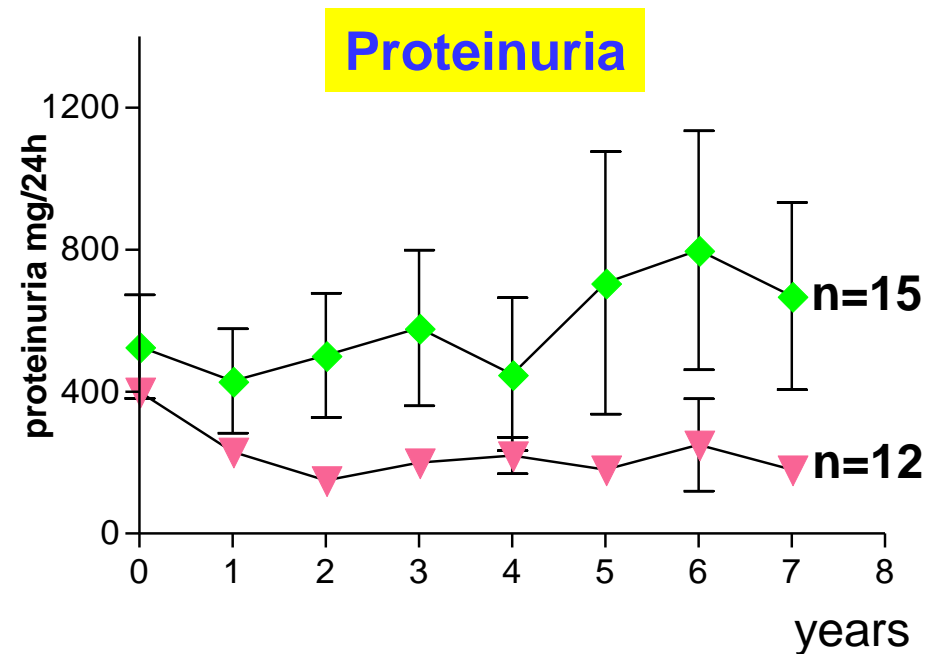
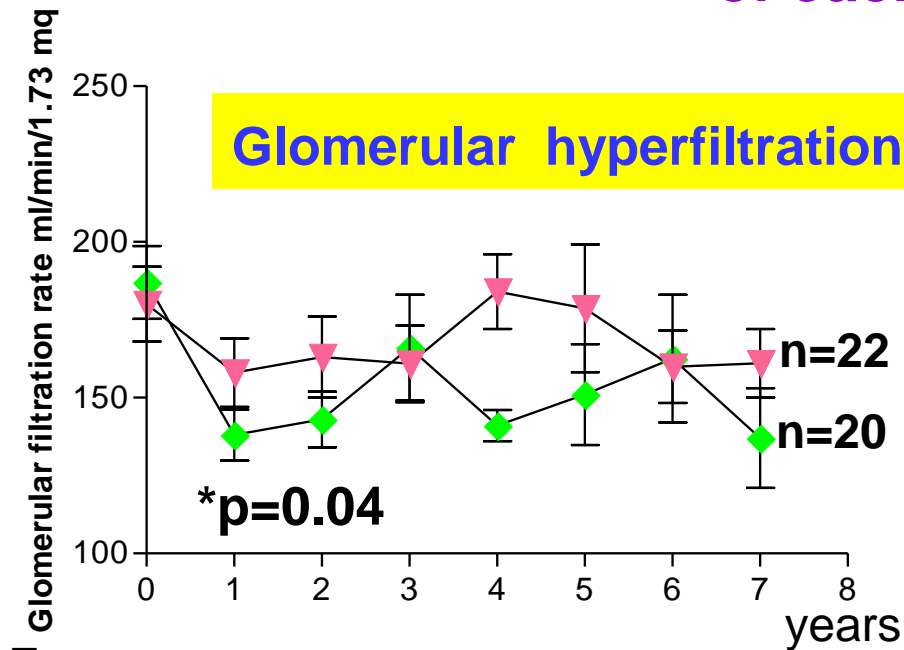
Statistical analysis

Mann Whitney and Wilcoxon rank tests

Spearman correlation and chi square tests

Linear regression analysis

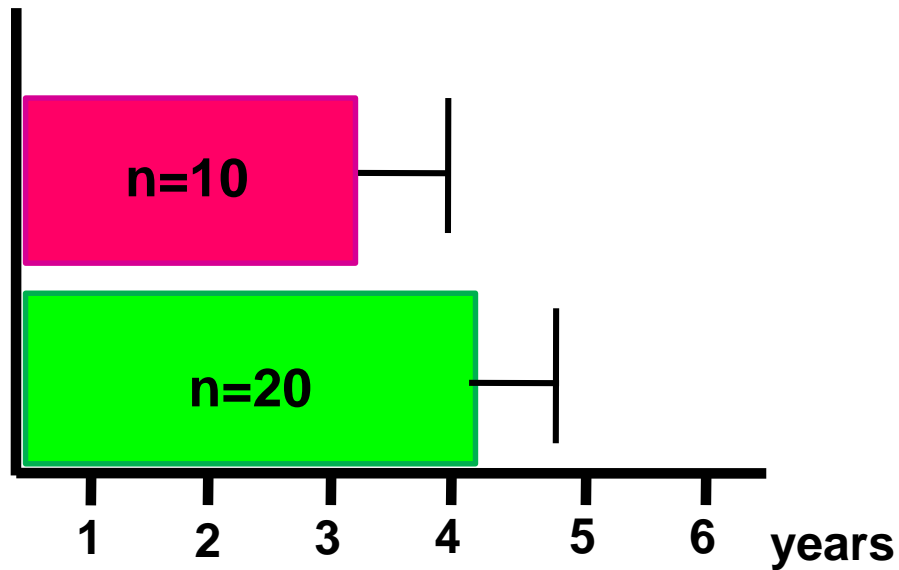
RESULTS (1): efficacy of ACE-inhibitors on the evolution of each parameter



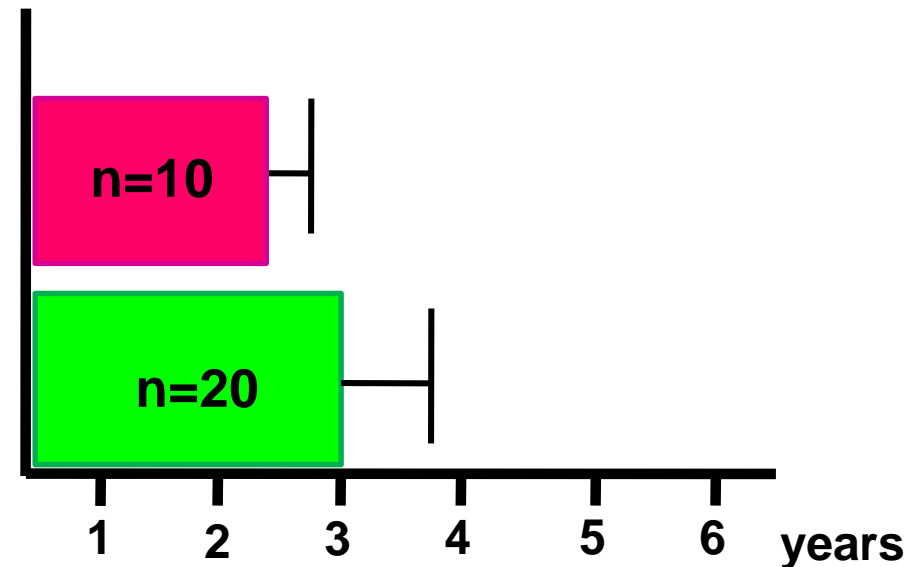
Treated
Untreated

RESULTS (1): efficacy of ACE-inhibitors on the progression of renal damage

Glomerular hyperfiltration → microalbuminuria



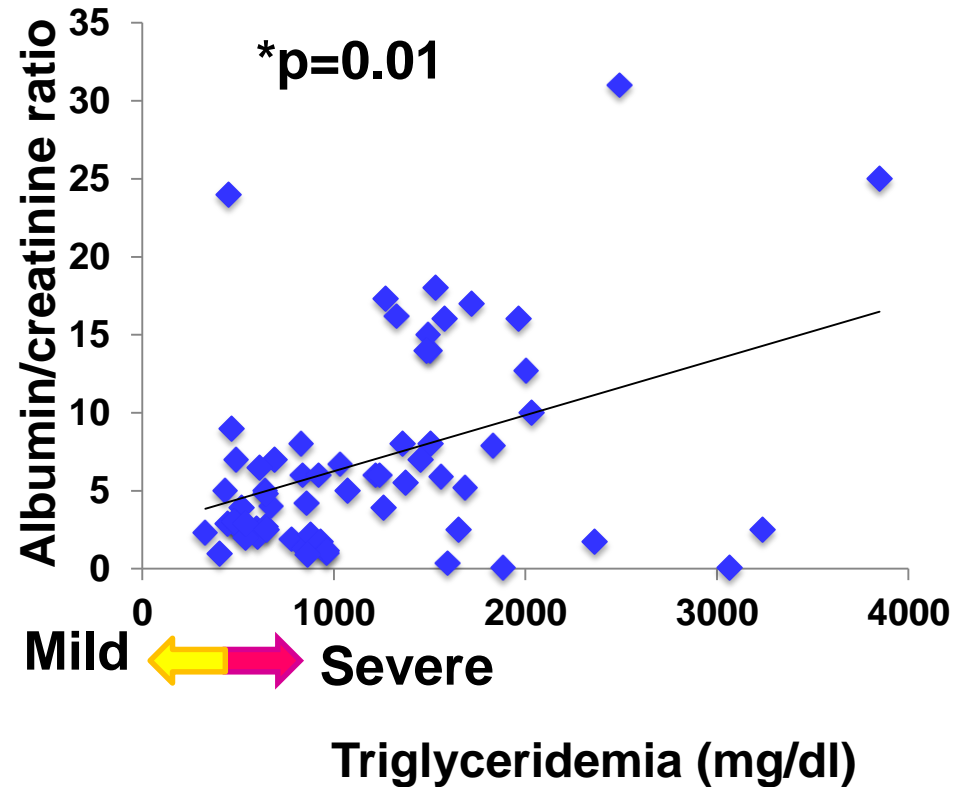
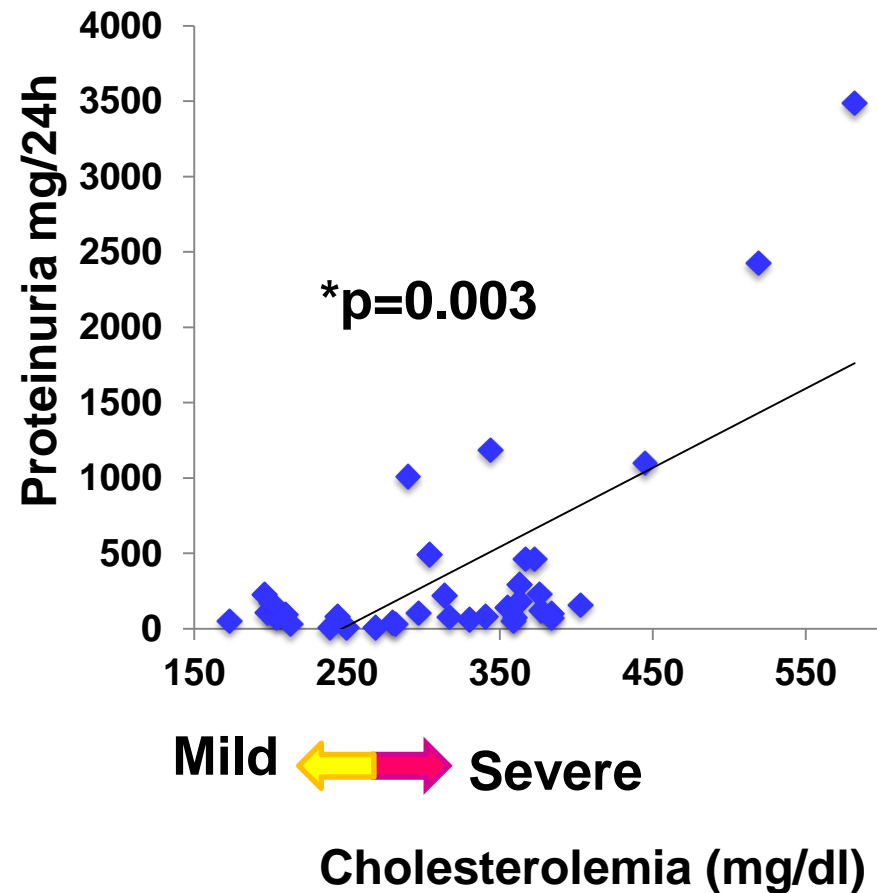
Microalbuminuria → proteinuria



— Treated
— Untreated

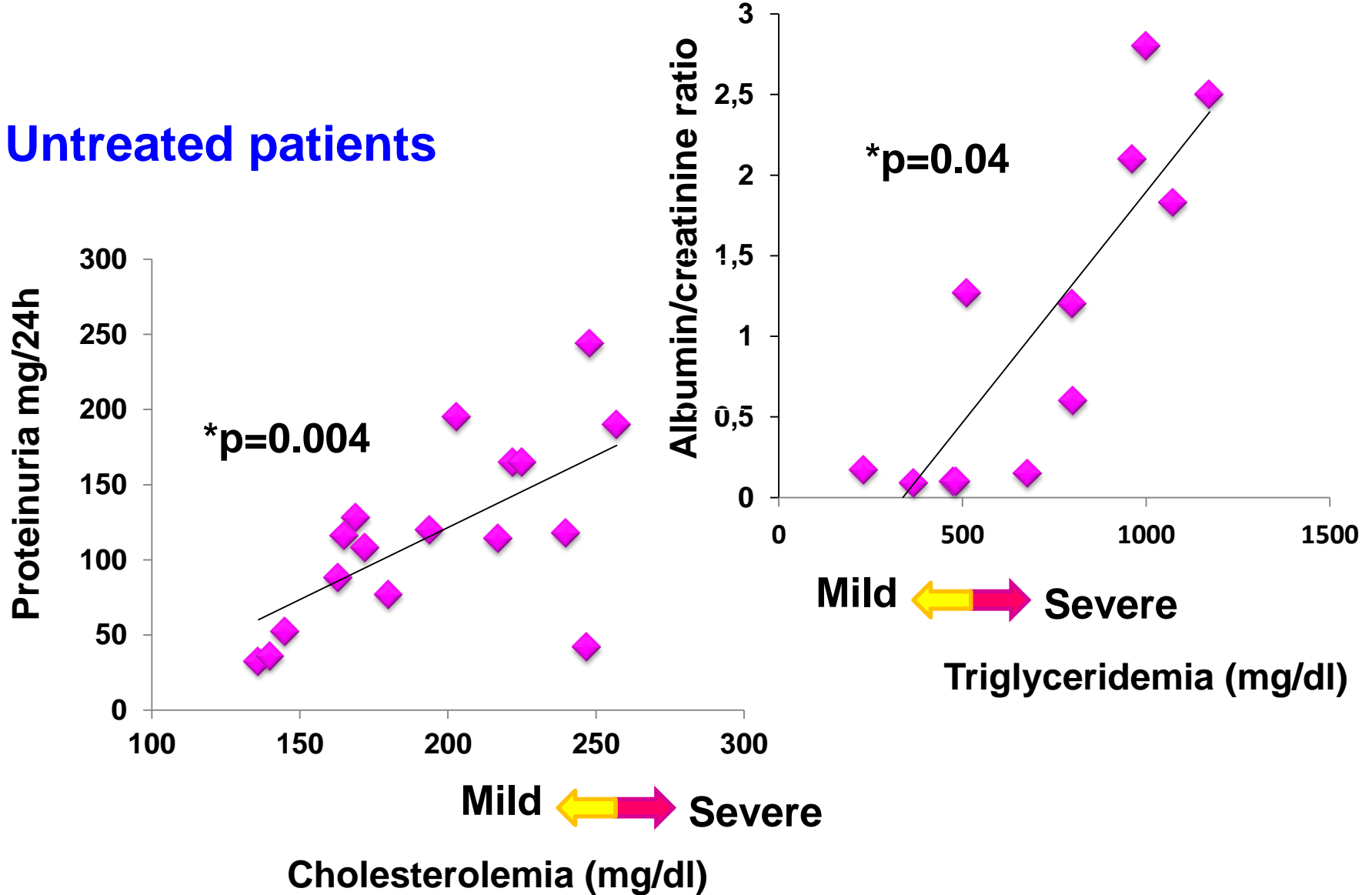
RESULTS (2): role of the metabolic control

Treated patients



RESULTS (2): role of the metabolic control

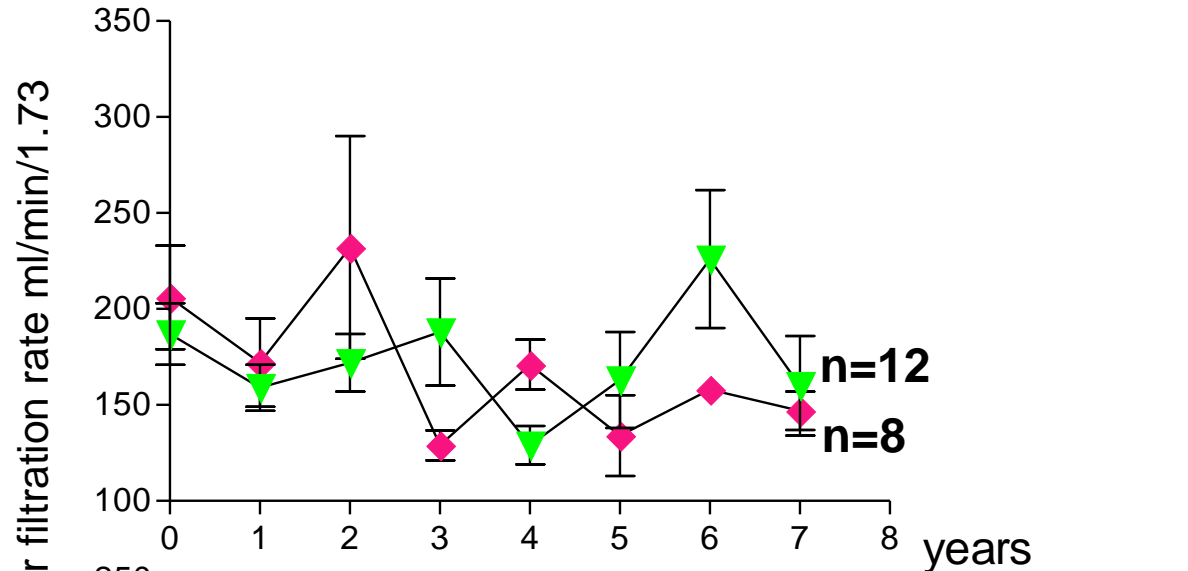
Untreated patients



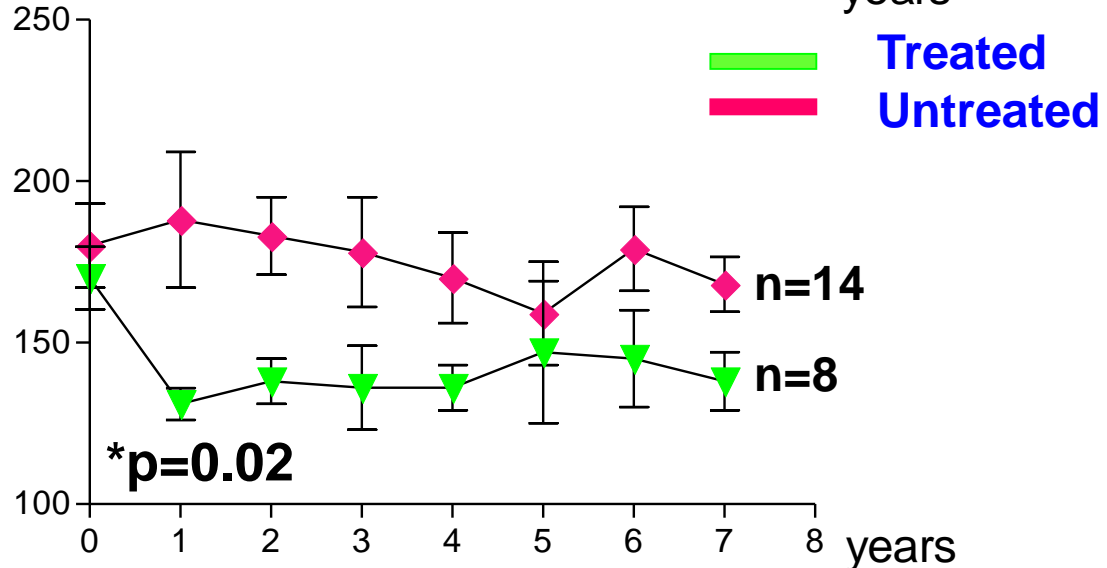
RESULTS (3a): interference of the altered metabolic environment on the efficacy of the ACE-inhibitors

Glomerular hyperfiltration

Severe hyperlipidemia



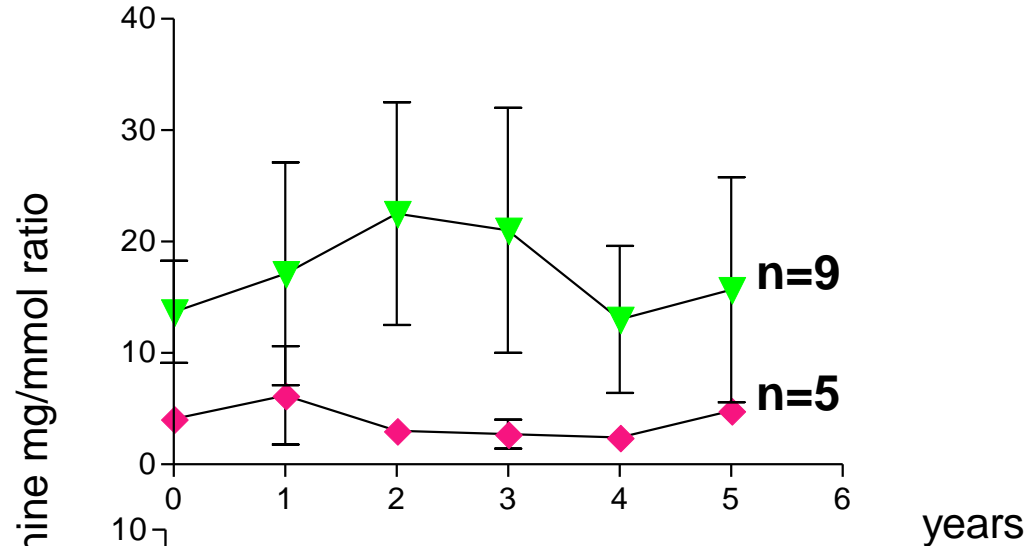
Mild hyperlipidemia



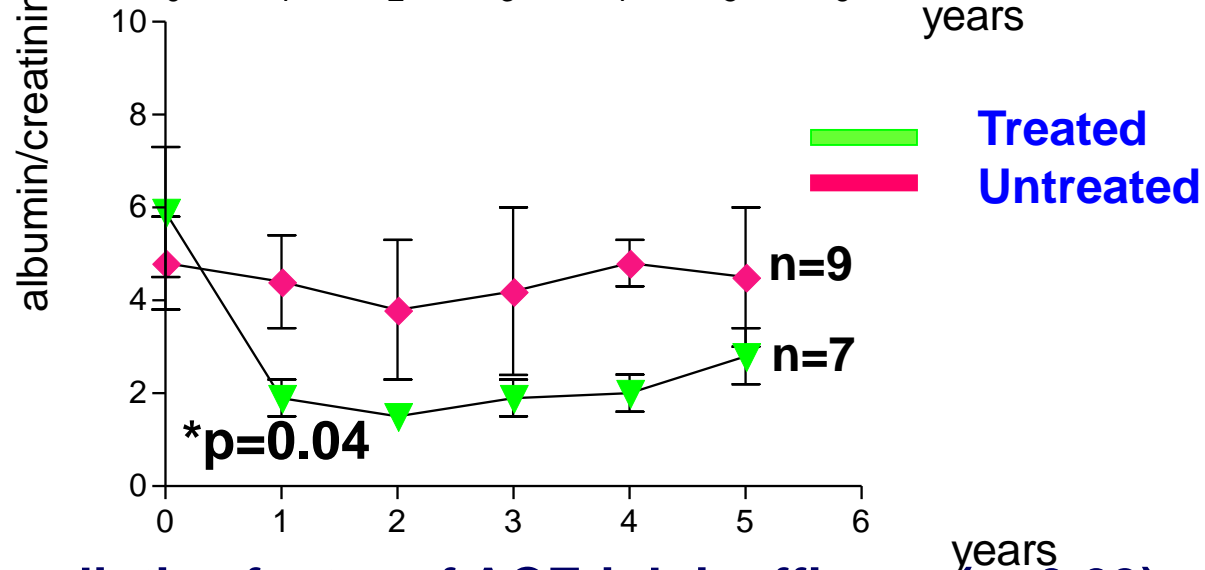
RESULTS (3b): interference of the altered metabolic environment on the efficacy of the ACE-inhibitors

Microalbuminuria

Severe hyperlipidemia



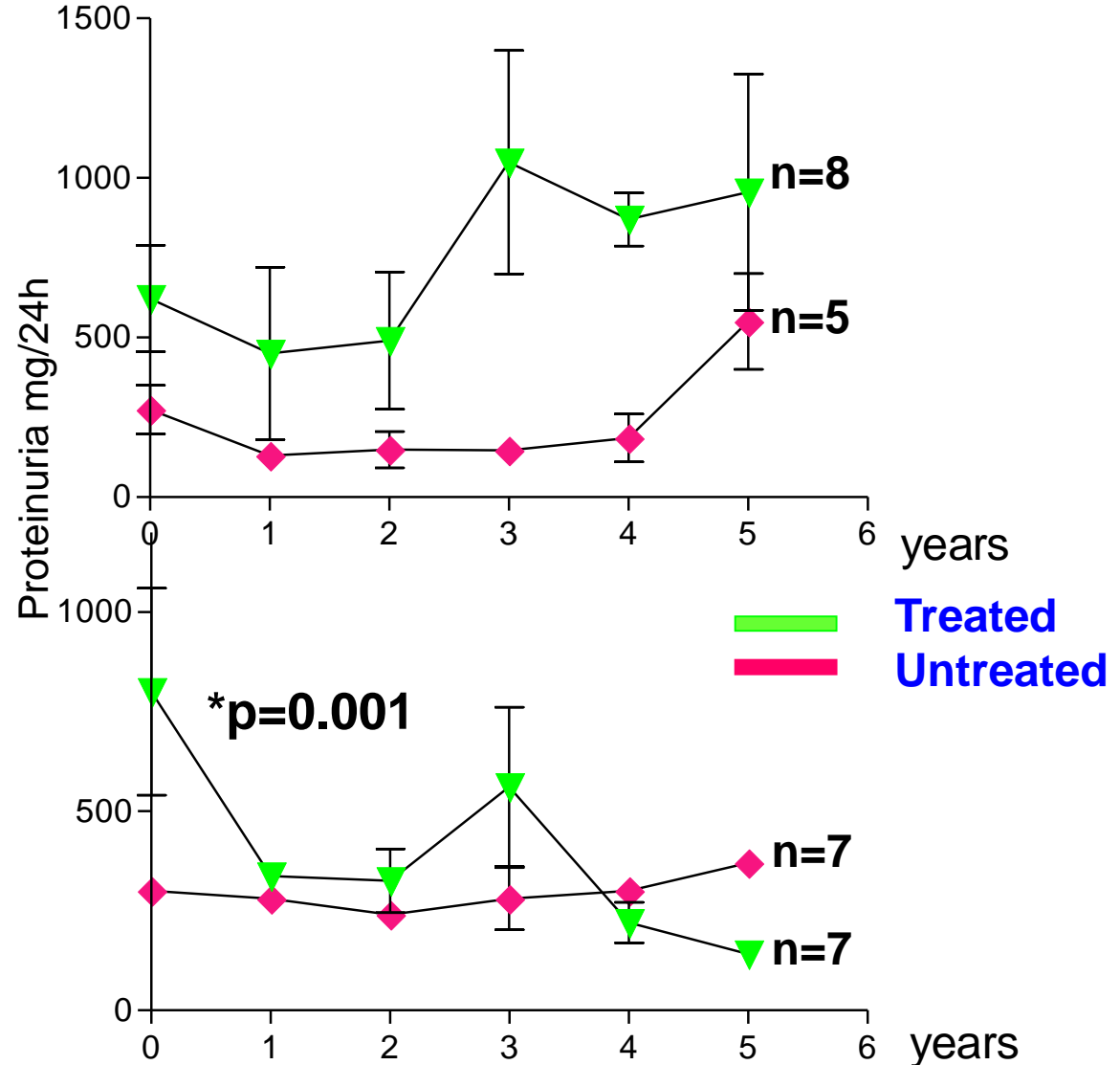
Mild hyperlipidemia



Hypertriglyceridemia → predictive factor of ACE-inh inefficacy ($p=0.03$).

RESULTS (3c): interference of the altered metabolic environment on the efficacy of the ACE-inhibitors

Proteinuria



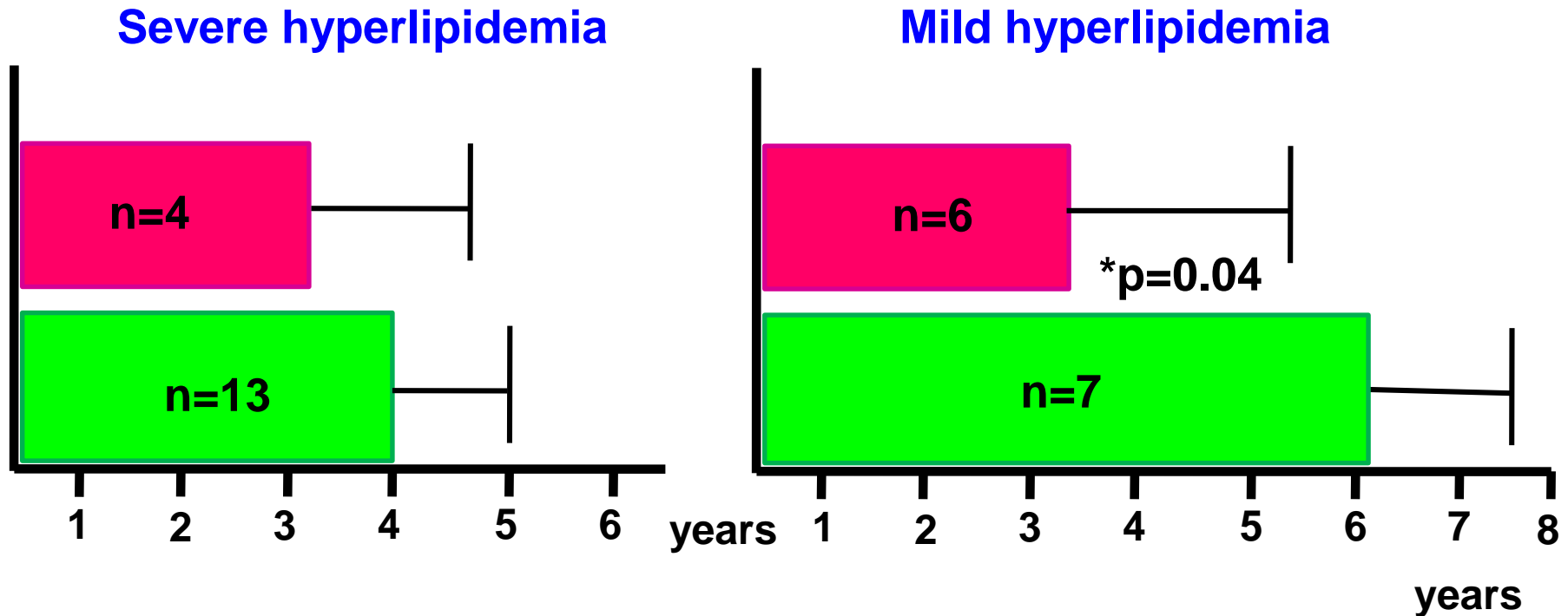
Severe hyperlipidemia

Mild hyperlipidemia

Hypercholesterolemia → predictive factor of ACE-inh inefficacy (p=0.02).

RESULTS (3d): interference of the altered metabolic environment on the efficacy of the ACE-inhibitors

Glomerular hyperfiltration → microalbuminuria



Hypertriglyceridemia → predictive factor of ACE-inh inefficacy (p=0.04).

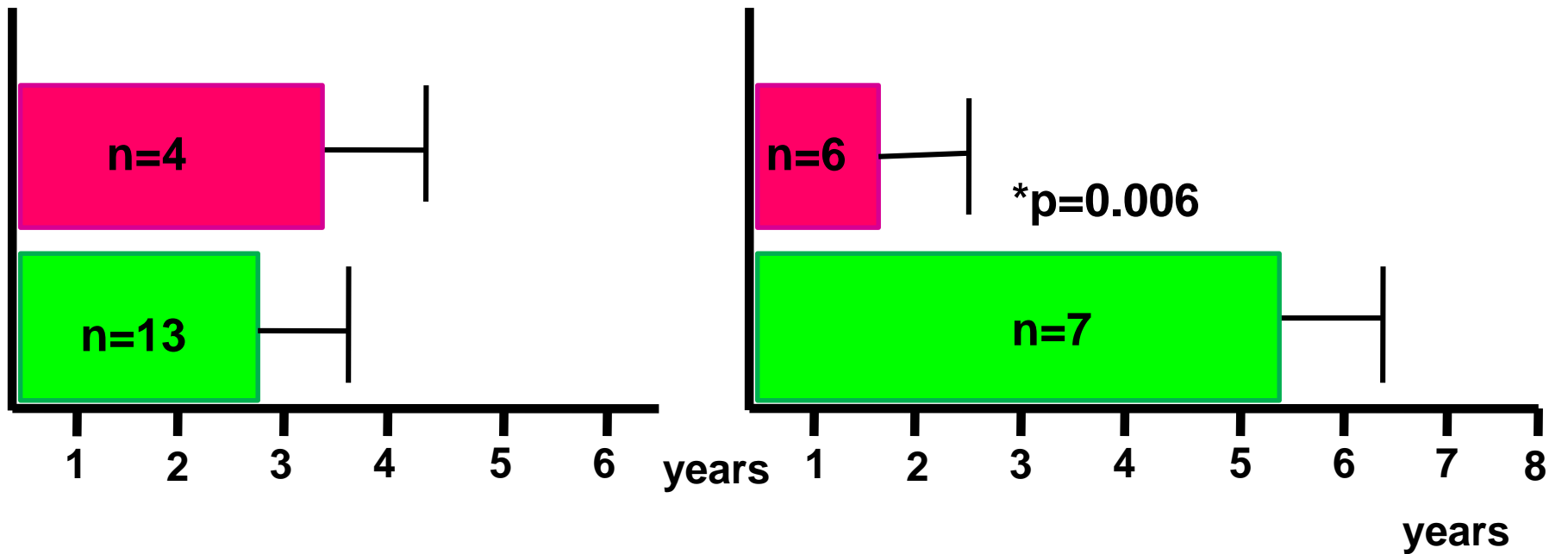
— Treated
— Untreated

RESULTS (3e): interference of the altered metabolic environment on the efficacy of the ACE-inhibitors

Microalbuminuria → proteinuria

Severe hyperlipidemia

Mild hyperlipidemia



Legend:
Treated (green)
Untreated (red)

CONCLUSIONS

ACE-inhibitors improve and delay the progression of renal damage in GSD1 patients with mild hyperlipidemia

Suggestions

Importance of a strict follow-up of chronic kidney disease

Need for a precocious start of ACE-inhibitors treatment

Possible effect of a lipid reduction treatment

Italian study group on GSD1

Naples

G. Andria
R. Della Casa
D. Melis
G. Parenti

Monza

R. Parini
M. Rigoldi

Siena

A. Benedetti
P. Marcolongo

Milan

M. Giovannini
S. Paci

Genoa

M. Di Rocco



Rome

C. Dionisi Vici
F. Deodato

Padoa

A. Burlina
B. L. Giordano

Palermo

L. Iapichino
M. Caserta
C. Castana

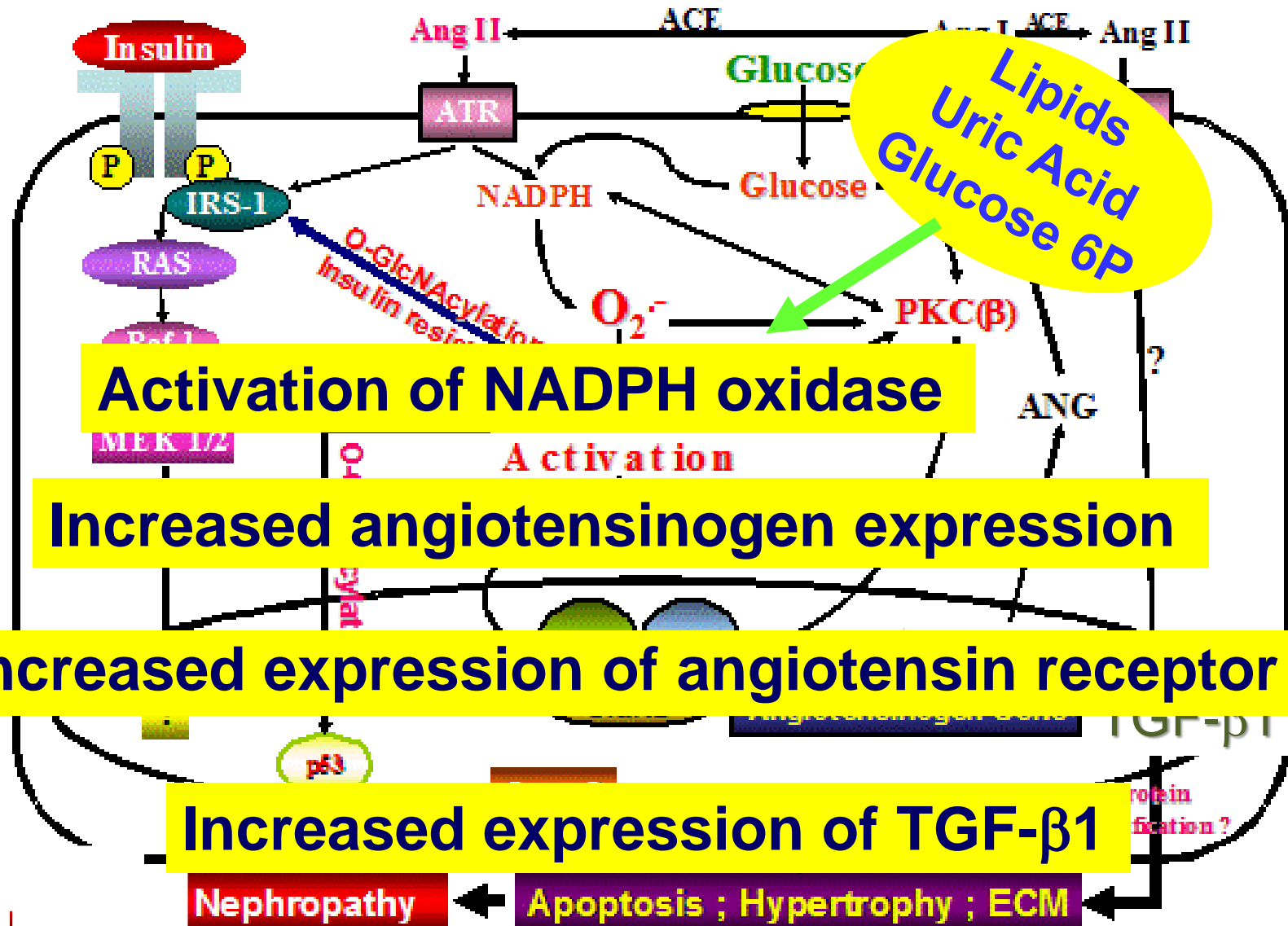
Bari

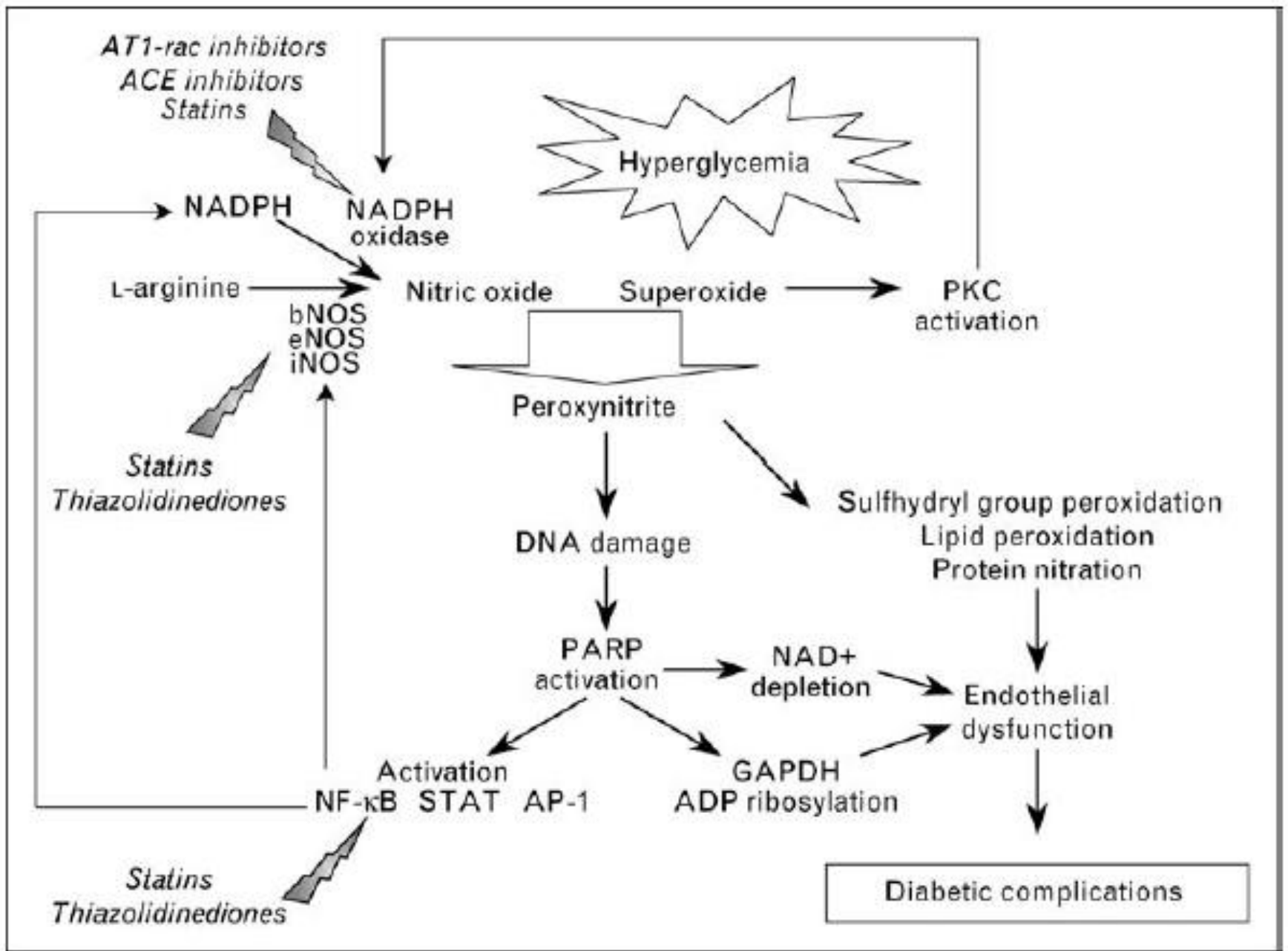
F. Papadia

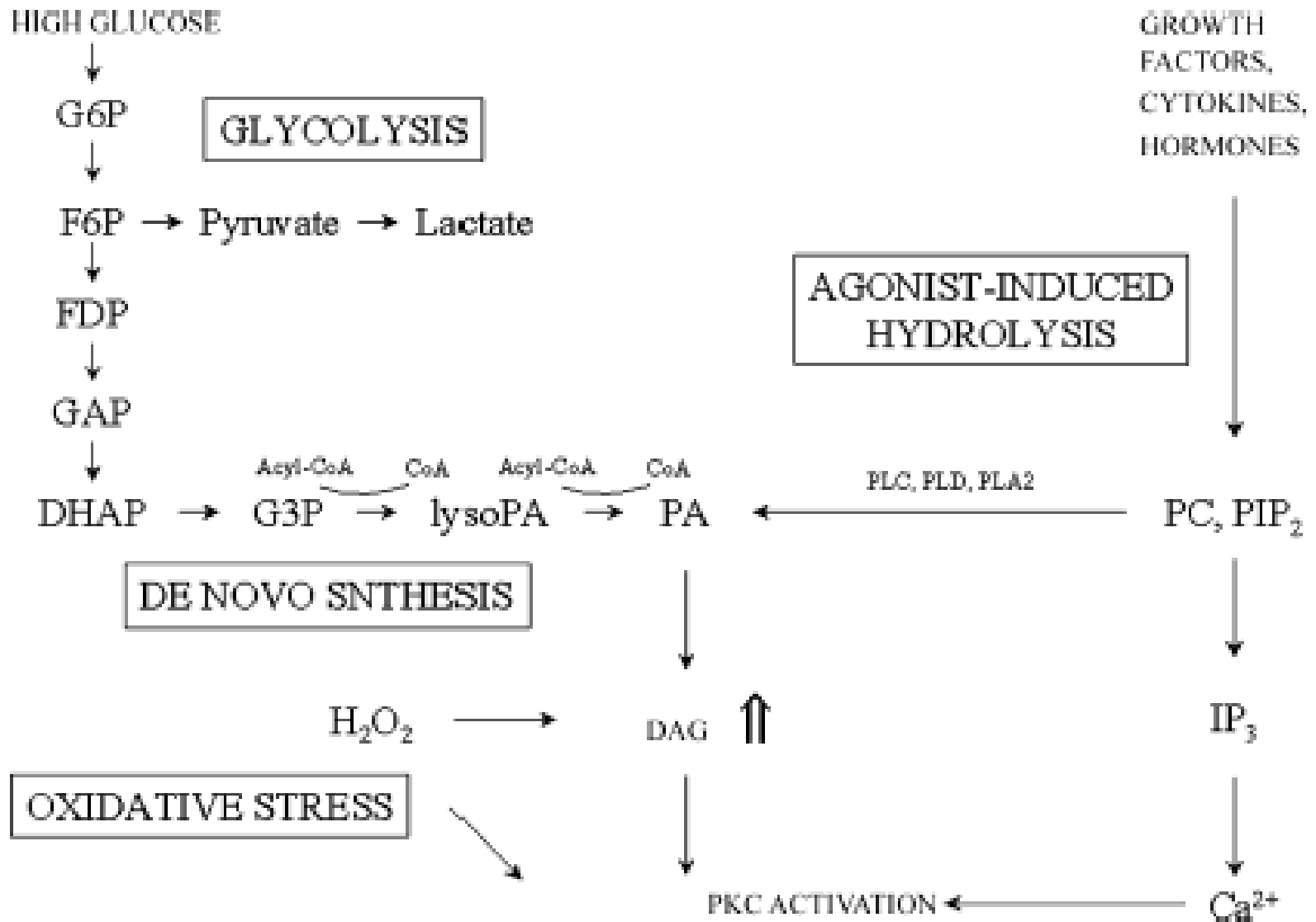
Florence

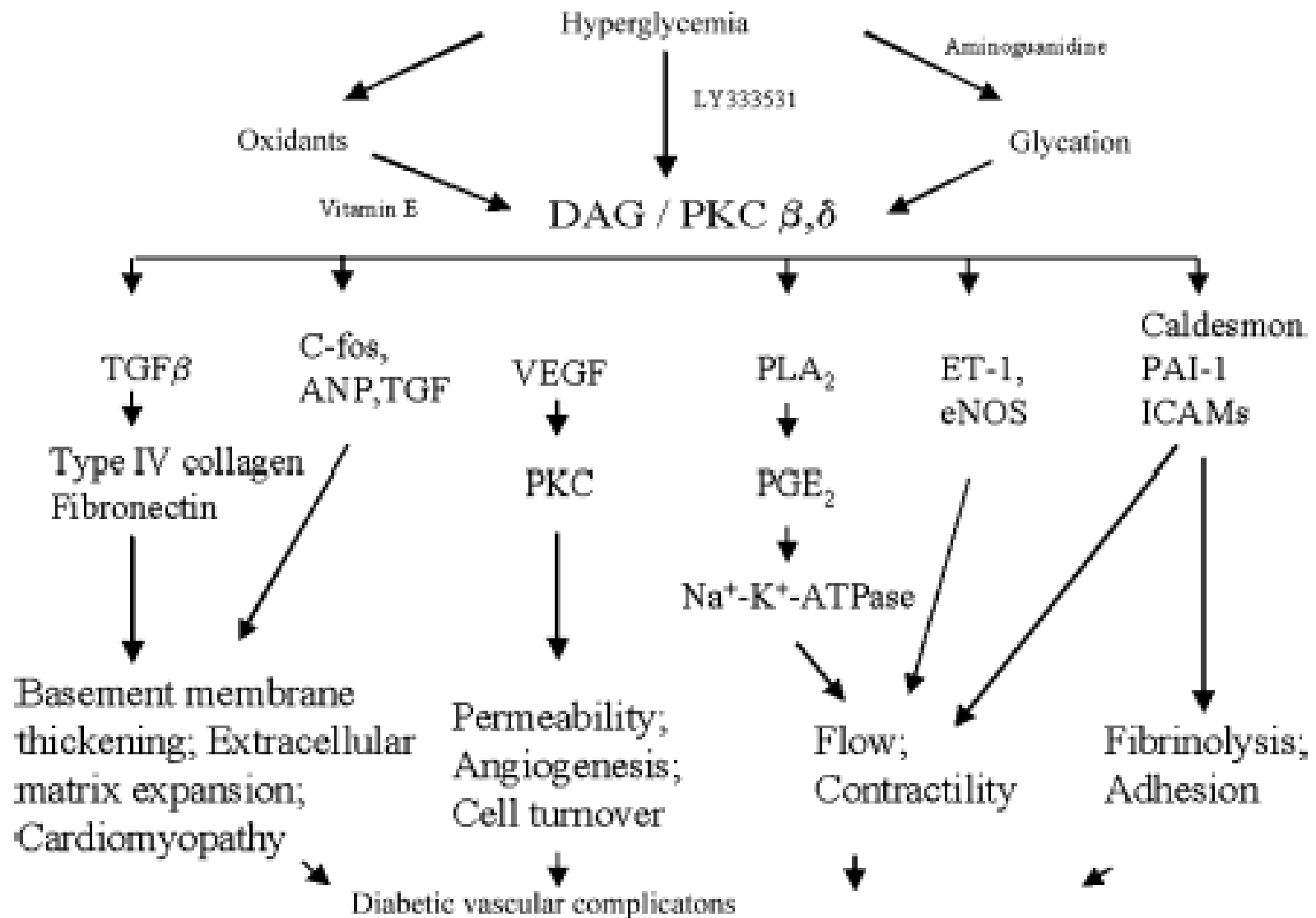
A. Donati

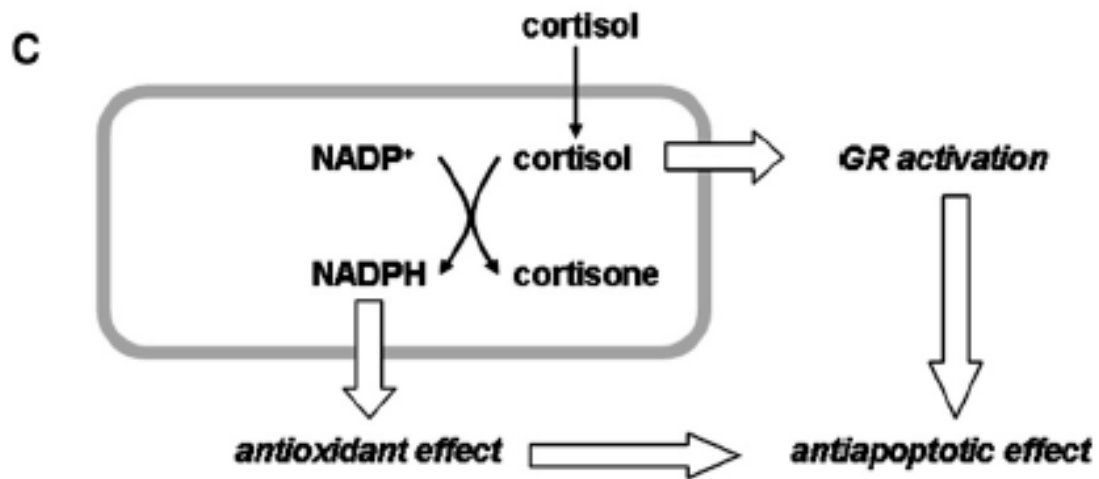
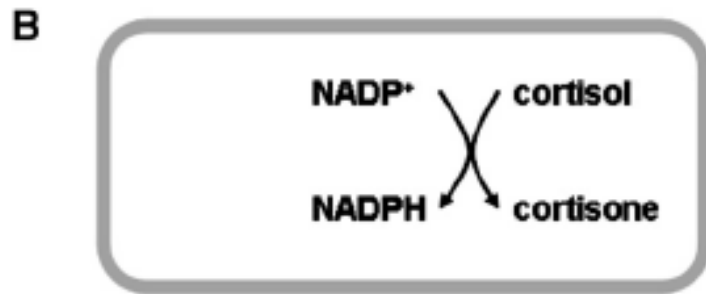
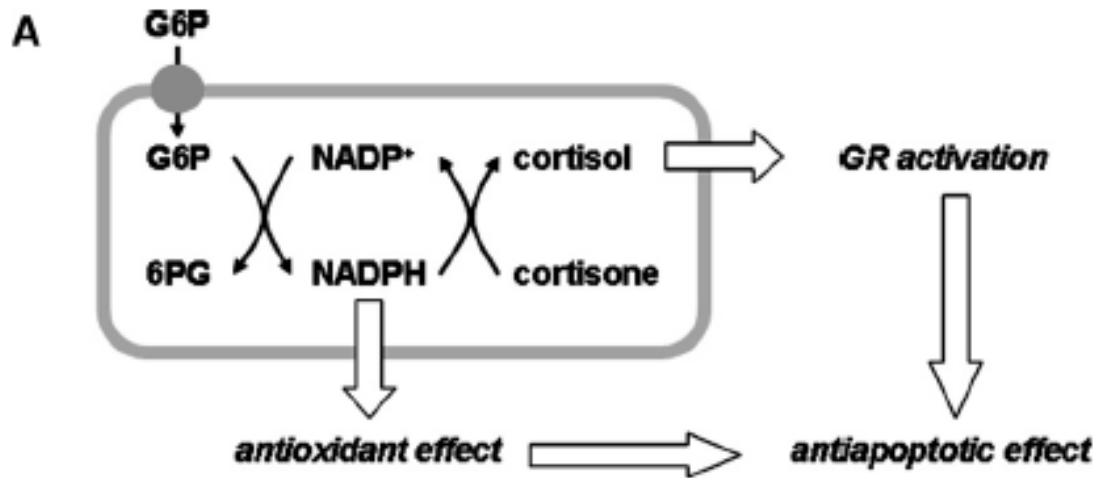
Hypotheses

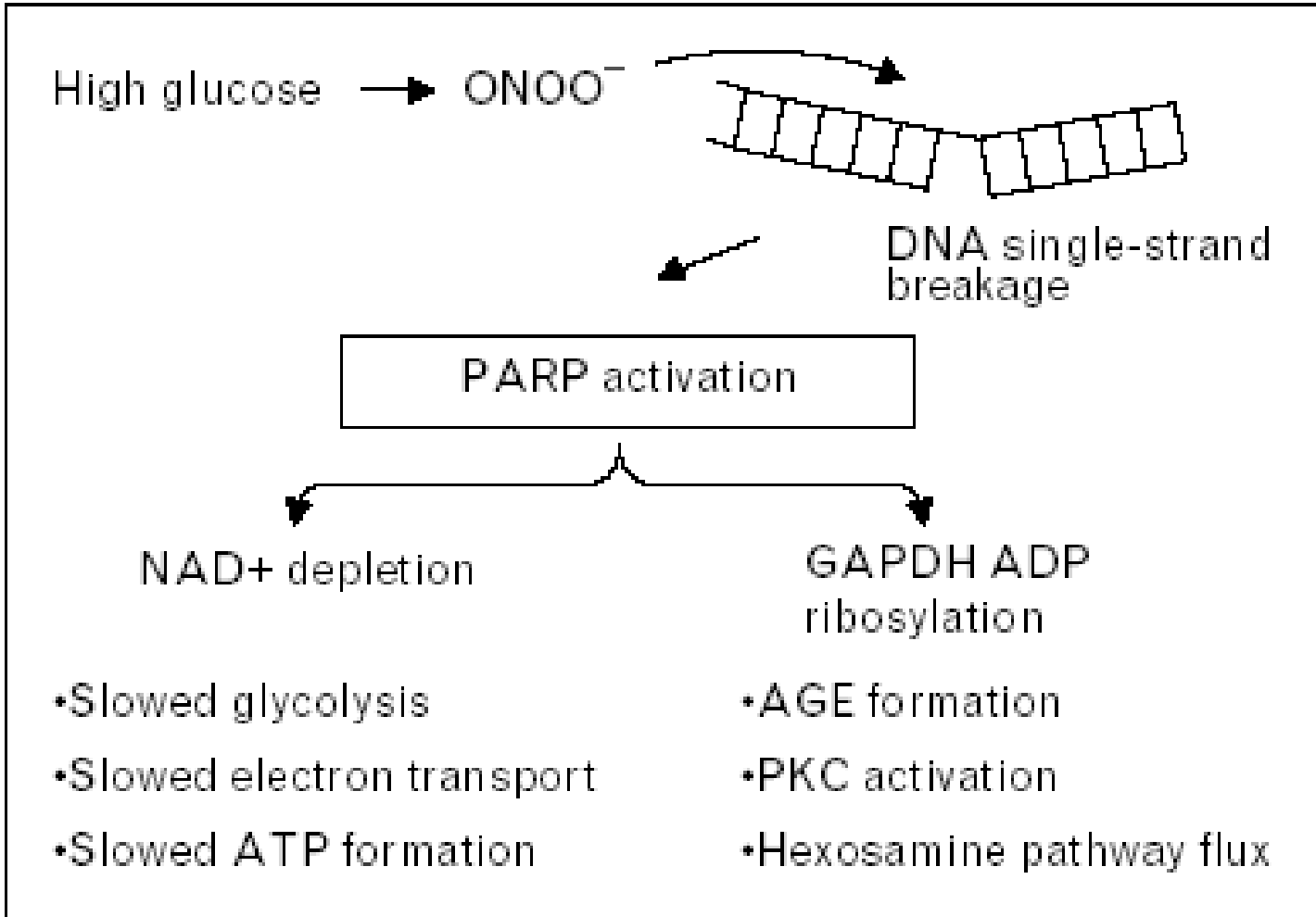


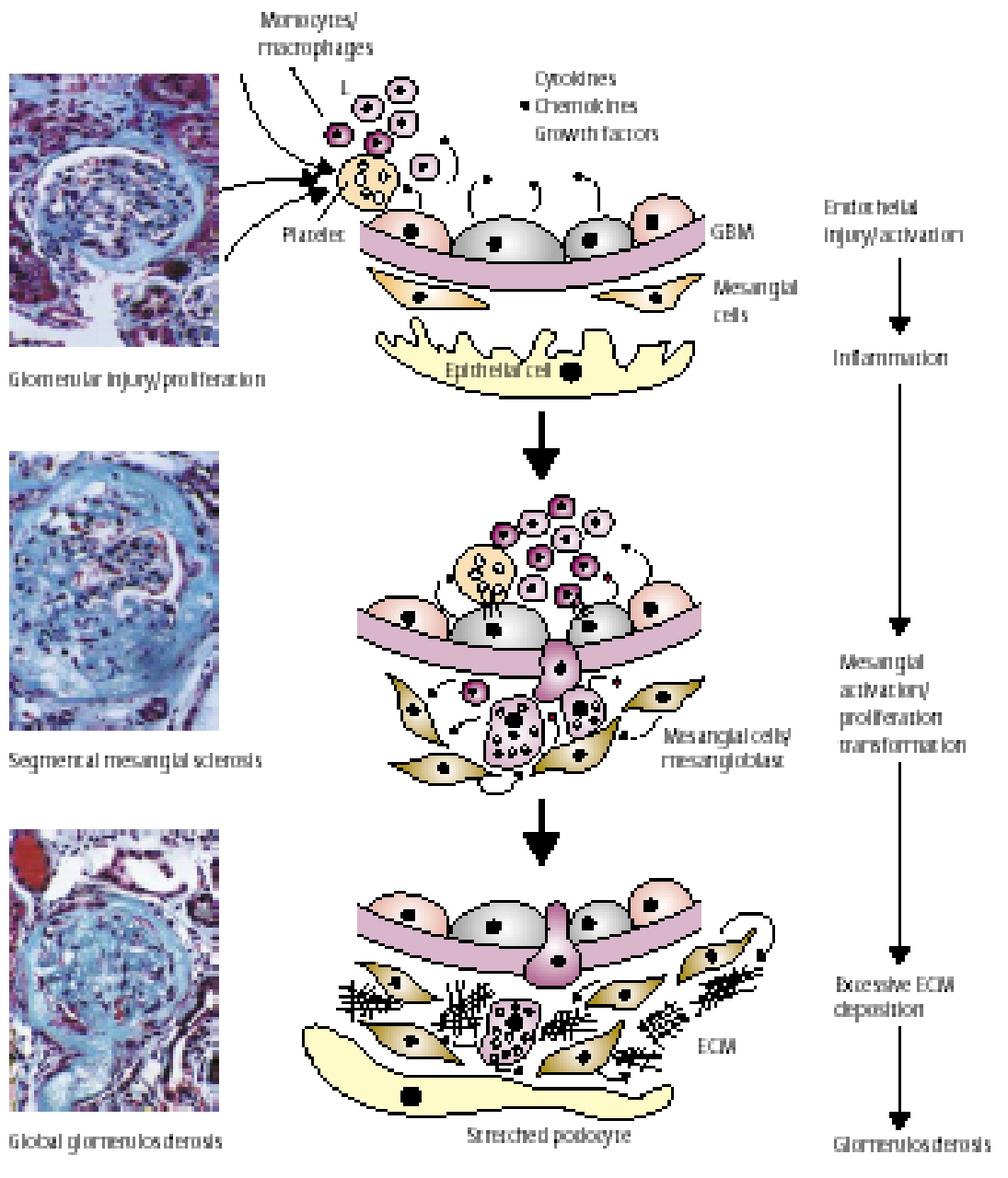


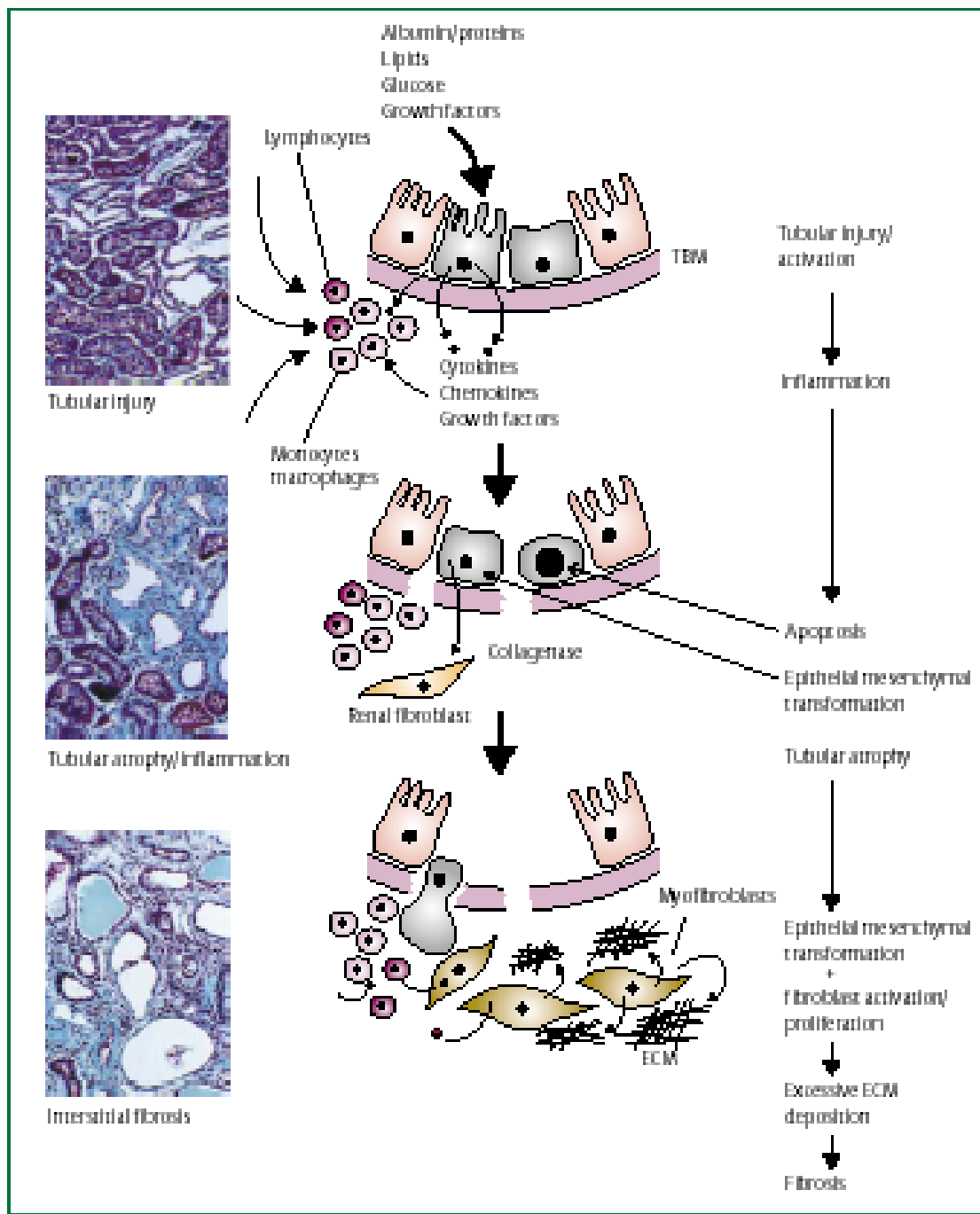




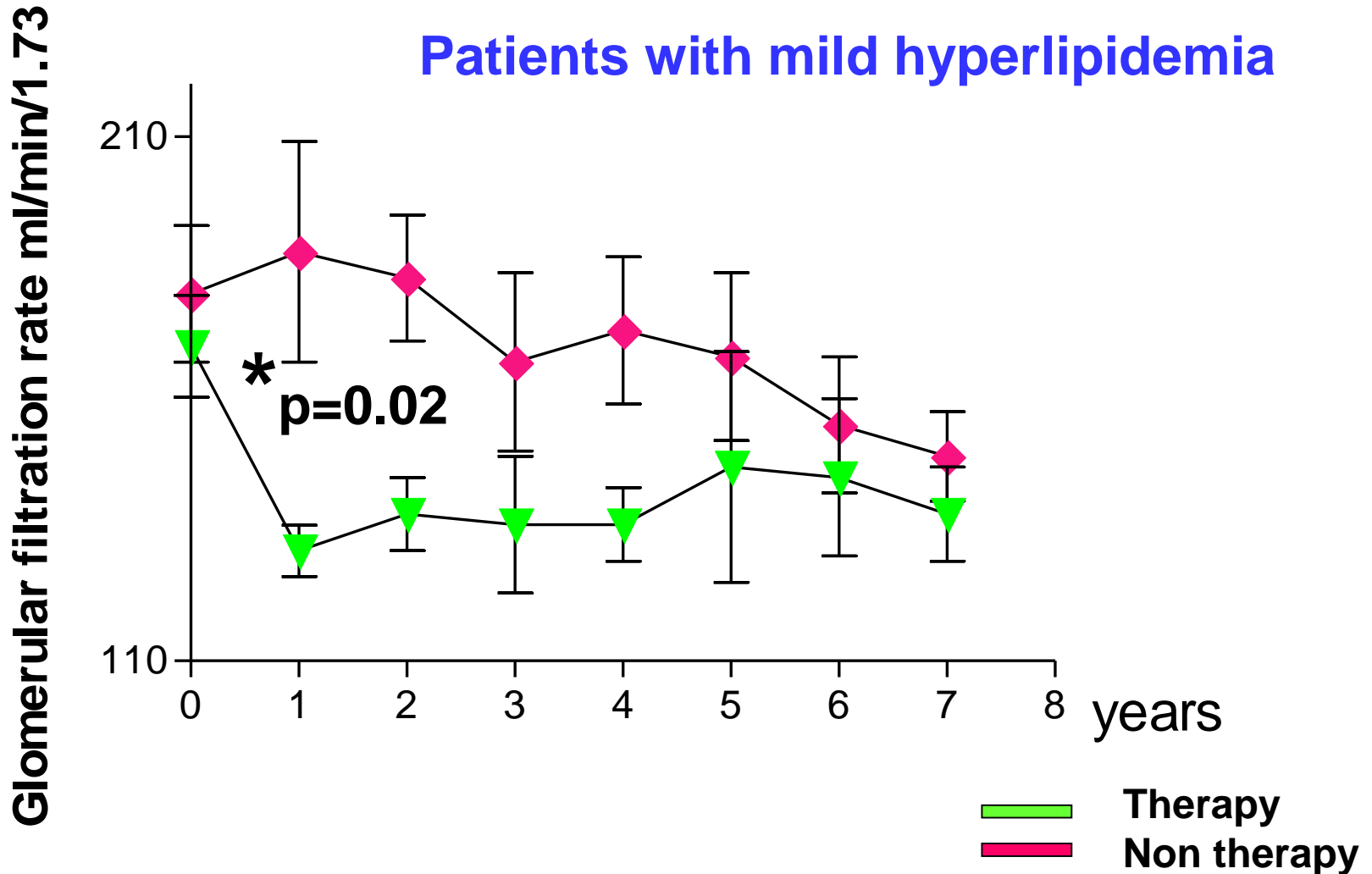






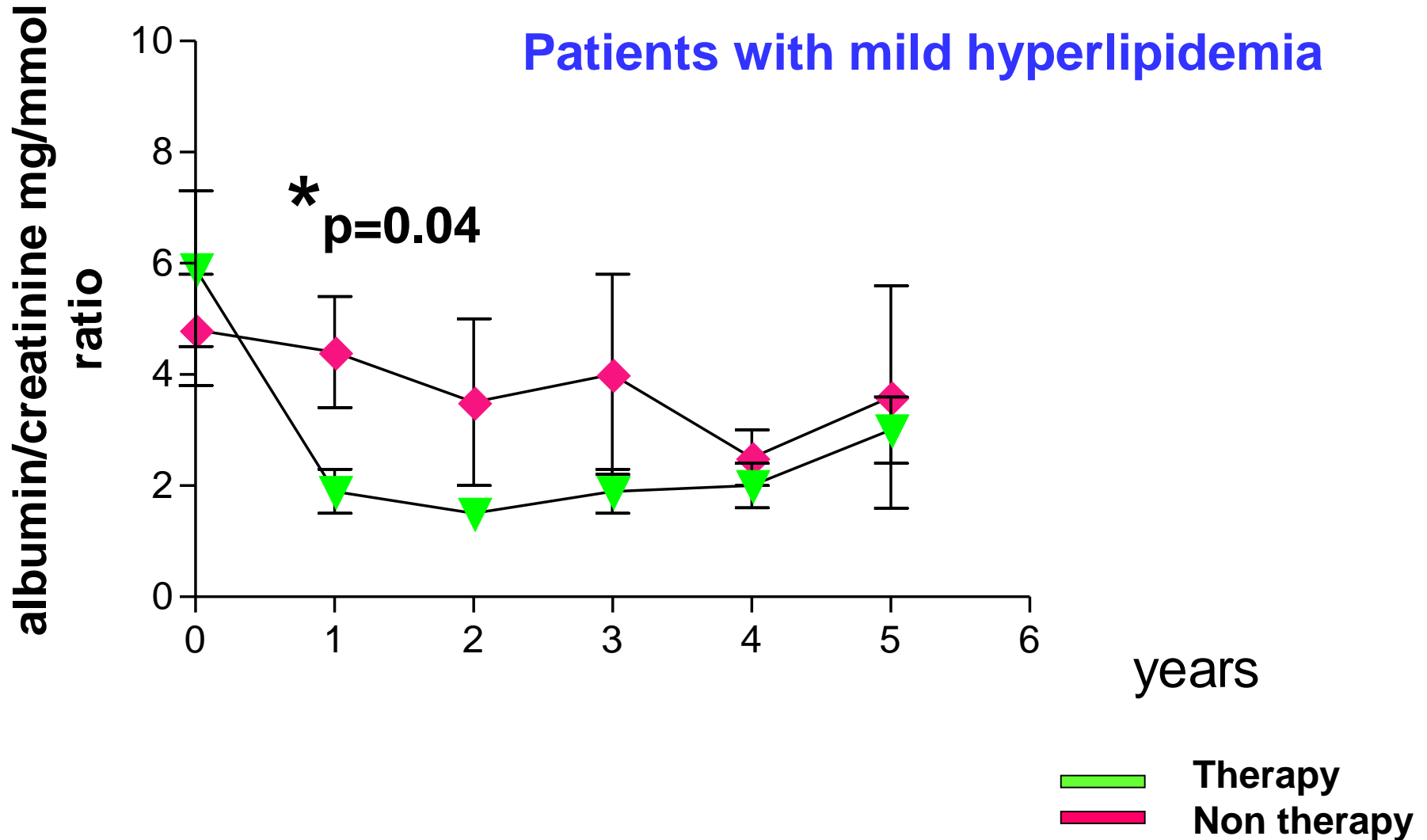


RESULTS (3): interference of the altered metabolic environment on the efficacy of the ACE-inhibitors



Results (4): interference of the altered metabolic environment on the efficacy of the ACE-inhibitors

Patients with mild hyperlipidemia



RESULTS (5): interference of the altered metabolic environment on the efficacy of the ACE-inhibitors

