

To the Chairman of the Scientific Jury  
in accordance with Order No. P- 109-88/23.02.2022  
of the Rector of Medical University - Varna

## **R E V I E W**

of the dissertation for the awarding of educational and scientific degree "Doctor" in the scientific specialty "Nephrology" to Dr. Snezhana Atanasova Atanasova Medical University "Prof. Dr. Paraskev Stoyanov - Varna, Faculty of Medicine, Department of Internal Medicine on the topic

"Assessment and dynamic monitoring of hyperphosphatemia - a predictor of bone mineral disorders in dialysis patients"

by Assoc. Prof. Dr. Alexander Ivanov Osichenko, PhD,

scientific specialty - nephrology, Head of Dialysis Clinic, Acibadem City Clinic, Tokuda University Hospital, Sofia

Bone mineral disorders (BMD) in chronic kidney disease (CKD) are a main risk factor for the development of spontaneous fractures, cardiovascular disease and high mortality in patients on hemodialysis (HD).

This determines the relevance of the presented dissertation of Dr. Snezhana Atanasova Atanasova, which aims to analyze the diagnostic, clinical and therapeutic aspects of bone mineral metabolism disorders in CKD in the course of conservative and hemodialysis treatment.

In order to realize the set goal, 6 main tasks are clearly and precisely formulated.

It is hypothesized that the developed constellation of diagnostic and therapeutic methods contributes both to the elucidation of the etiopathogenetic mechanisms of BMD in patients with CKD on conservative and hemodialysis treatment and to the increase of the effectiveness of the individualized approach to these patients.

The dissertation contains 134 standard pages and is illustrated with 45 tables, 29 figures and 1 appendix. The reference list includes 206 references, 8 in Cyrillic and 198 in Latin.

Dr. Snezhana Atanasova Atanasova has a good knowledge of the nature of the problem and has presented a creative assessment of the analyzed literature.

The dissertation covers 116 patients with CKD: 30 patients in the pre-dialysis stage (control group) and 86 patients on HD in the Clinic of Nephrology and Dialysis at the University Hospital "St. Marina" followed clinically and examined by routine methods for a period of 3 years (1.II.2019 and 31.I.2022).

A detailed medical history and objective physical status were taken. The following laboratory parameters were studied: parathyroid hormone (PTH), calcium, phosphorus, alkaline phosphatase, vitamin D, sclerostin. Quality of life of patients on hemodialysis was studied with a specialized questionnaire (KDQOL-36) modification of S. Staykova. Statistical data were processed using BM SPSS v.25, and Jamovi v.2.1.1. A variety of modern methods were used to suit the objectives of the study.

The results were interpreted in depth and in comparison, with data from published studies in the literature, where available. The results show that: 1) HD patients have higher phosphorus and PTH values and lower calcium values compared to pre-dialysis patients. 2) Treatment with calcium carbonate and a combination of sevelamer and cinacalcet shows significant significance regard to hyperphosphatemia and secondary hyperparathyroidism (SHPT). 3) More than half of patients on etelcalcetide on HD achieved more than 30% reduction in PTH in the first quarter, and more than 60% in the first year of treatment. 4) Dialysis patients have up to 3 times higher serum sclerostin compared to pre-dialysis patients. 5) In patients undergoing hemodiafiltration, phosphorus elimination increases from 67% to 76%, whereas it is a constant value in patients on convection dialysis. 6) Correction of BMD have determining importance for improving quality of life in patients on dialysis treatment.

The contributions of the dissertation are of a certain scientific-theoretical and applied-practical nature.

Contributions of theoretical nature 1) For the first time in Bulgaria the serum biomarker sclerostin in dialysis and pre-dialysis patients has been studied and interpreted 2) For the first time in Bulgaria a correlation between etelcalcetide and elevated concentrations of the serum biomarker sclerostin in dialysis patients has been proven. 3) High efficacy and comparative safety of Sevelamer and Cinacalcet in controlling hyperphosphatemia of patients with CKD-BMD have been established. 4) The advantage of hemodiafiltration in patients with hyperphosphatemia for prevention and treatment of SHPT has been proven. 5) It has been shown that CKD significantly affects physical activity, emotional and mental stability in patients, as well as their perception of general health.

Contributions of practical-applied nature: 1) The serum biomarker sclerostin studied for the first time in Bulgaria in patients with CKD allows to detect and interpret significant disturbances in bone-mineral metabolism and prevention of cardiovascular diseases. 2) The application and advantages of intravenous etelcalcetide as well as its effect on serum sclerostin and PTH in hemodialysis patients with SHPT were evaluated. 3) Measuring and assessing quality of life in patients with CKD and hyperphosphatemia allows a more complete understanding of their specific needs and assists in enhancing the effectiveness of clinical management.

In relation to the dissertation topic Dr. Snezhana Atanasova Atanasova has 3 publications in scientific journals.

The presented materials fully comply the requirements of the Law On The Development Of The Academic Composition In The Republic Of Bulgaria, the Regulations for its application and that Medical University – Varna for the awarding of educational and scientific degree "Doctor".

In conclusion, I think that the dissertation of Dr. Snezhana Atanasova Atanasova is complete, modern, thorough, well-structured and well-formed, with clear and accurately formulated and executed tasks, with certain conclusions and contributions to both modern science and practice. All this gives me grounds to recommend to the members of the esteemed scientific jury to award to Dr. Snezhana Atanasova Atanasova the educational and scientific degree "Doctor" in the scientific specialty of nephrology in the professional field 7.1. Medicine by field of higher education 7. Health and Sport.

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PhD  
Sofia

Assoc.Prof.Alexander Ivanov Osichenko, MD,

