

To the Chairman of the Scientific Jury,  
designated by the Rector  
of the Medical University  
Prof. Dr. Paraskev Stoyanov  
Varna

## **Review**

**By Prof. Zhaneta Georgieva Tianeveva, MD, PhD, Member of the Scientific Jury, determined by order № P-109-166 / 03.06.2020 of Prof. Dr. Valentin Ignatov, PhD, Rector of the Medical University "Prof. Dr. Paraskev Stoyanov", Varna, for the academic position "Associate Professor", specialty "Rheumatology" in higher education 7. "Health and Sports", professional field 7.1. "Medicine" for the needs of the Faculty "Medicine", First Department of Internal Medicine, Management Board "Rheumatology" and Clinic of Rheumatology of UMHAT "St. Marina" EAD Varna**

For participation in the competition, documents have been submitted by one candidate: Assistant Professor **Tanya Kirilova Shivacheva, MD, PhD**, Faculty of Medicine, First Department of Internal Medicine, Rheumatology Department, Medical University of Varna.

The documents submitted by the candidate are in accordance with the requirements of the regulations for holding the academic position of "associate professor" and the regulations of MU Varna.

### **Biographical data:**

Dr. Tanya Kirilova Shivacheva successfully graduated in medicine at MU-Sofia in 1982. Since 1985. works as a resident doctor in the Intensive Care Cardiology Department of the Cardiology Clinic at MHAT "St. Marina" EAD Varna. In 1987 she was appointed a resident doctor at the Rheumatology Clinic. Since 1989 is an assistant in the Department of Internal Medicine, MU "Paraskev Stoyanov", Varna. The same year he acquired the specialty of Internal Medicine, in 1997 - the specialty of Rheumatology.

Dr. Shivacheva is enrolled as a doctoral student in an independent form of education in the doctoral program "Internal Medicine" with the topic of the dissertation: "Study of the clinical activity of rheumatoid arthritis in patients undergoing treatment with biological agents." Defends successfully in 2019.

She is a member of the Bulgarian Medical Association, the Bulgarian Scientific Society of Rheumatology and the Bulgarian Medical Society of Osteoporosis and Osteoarthritis.

### **Research activity**

**Dissertation work for awarding the Educational and Scientific degree "Doctor" - 50 points:** "Study of the clinical activity of rheumatoid arthritis in patients undergoing treatment with biological agents." The dissertation work in-depth studies the activity of RA, the purpose of treatment, the effectiveness of biological agents, concomitant diseases and long-term prognosis in RA patients. For the first time in the country the activity of Rheumatoid arthritis has been described and examined in dynamics, against the background of treatment with biological agents, in the conditions of real clinical practice. An analysis of the risk factors for CVD was made in combination with the factors originating from the inflammatory nature of RA and its treatment in the conditions of real clinical practice. The activity of RA in patients with and without CVD was analyzed. Optimized thresholds of the DAS28 (CRP) activity rating scale are proposed, which can be introduced into daily clinical practice for more accurate reflection of residual RA activity during treatment with biological and synthetic agents. The dissertation can be a basis for a prospective examination of the prognostic model proposed by Dr. Shivacheva.

**Habilitation work-monograph-100 points.** "The patient with Rheumatoid arthritis - present and future" by Dr. Tanya Shivacheva presents the accumulated new evidence and a new approach in the diagnosis and treatment of patients with RA. An in-depth analysis of the evidence in the field of epidemiology, risk factors, pathogenesis, clinical research, clinic, classification and treatment of RA was made. The biological nature of the pathogenetic chain of the local and systemic autoimmune process underlying arthritis has been thoroughly assessed. The goals and strategies in treatment are presented, as well as the individual groups of drugs. The modern immunological markers of the disease and the possibility for them to serve in the diagnostic process are indicated.

The functional characteristics of the patients' condition have been updated and the activity of the disease process with the conducted biological therapy has been monitored in dynamics. A special place is given to the assessments for RA activity and treatment response, modern approaches to disease control, comorbidity and multimorbidity. Own results support the new evidence for the demographic characteristics of patients and the peculiarities of RA.

The monograph synthesizes modern evidence of the disease and is of interest to rheumatologists, internists, general practitioners, specialists.

**Full-text publications in scientific journals, referenced and indexed in world-famous databases with scientific information -212 points.**

Distribution of scientific papers by authorship: individual author - 5 scientific papers, co-authored - 60 scientific papers, of which: first author - in 16 scientific papers, second author - in 11 scientific papers, third author - in 15 scientific papers, subsequent author - in 18 scientific papers.

The presented scientific papers are divided into the following scientific fields: Rheumatoid arthritis; NSAIDs; Reactive arthritis; Slow-acting disease-modifying agents and chondroprotectors, in inflammatory and degenerative joint diseases; Studies in patients with osteoporosis; Studies in autoimmune vascular diseases.

A relationship was found between the presence of some concomitant diseases and higher values of the index scores of RA (A-1; B-3; G-7-7). Dr. Shivacheva points out that the index scores do not only reflect the "residual" activity of Rheumatoid Arthritis (A-1; B-3). An optimized approach in rheumatological practice is proposed and the multimorbid approach in patients with rheumatoid arthritis to treatment with target molecules (B-3) is studied. Current characteristics of accelerated early coronary disease in rheumatoid arthritis have been analyzed (G-7-1, I. 2., II. 16, III. 9). There is a higher proportion of cardiovascular accidents among patients with inflammatory joint disease and a higher overall cardiovascular risk compared with patients with osteoarthritis. (II. 27). The available cardiovascular diseases and traditional risk factors for them in patients with rheumatoid arthritis, long-term treatment with biological agents (A-1; B-3; G-7-7) were analyzed. For the first time in Bulgaria, a cardiovascular risk characteristic was studied in patients with Rheumatoid Arthritis undergoing long-term treatment with biological target molecules (A-1; B-3).

An algorithm has been proposed to reduce the expected cardiovascular morbidity in these patients, which would lead to a better prognosis and longer life expectancy (A-1).

Some issues related to increasing the life expectancy of patients with rheumatoid arthritis in the "biological" era (A-1; B-3; G-7-7) have been resolved.

For the first time in our country an index assessment of the activity of Rheumatoid Arthritis - DAS28 was used in the study of the therapeutic efficacy of Leflunomide in the conditions of long-term follow-up of patients (A-1, I. 3). An optimized DAS 28 scale for categorizing the activity of Rheumatoid Arthritis (A-1) has been proposed in clinical practice. A model for determining the trend of rheumatoid arthritis activity has been developed and an integrated assessment (A-1) has been defined. A register of patients with rheumatoid arthritis for long-term treatment with biological disease-altering drugs has been created on the territory of the Clinic of Rheumatology, University Hospital "St. Marina"-EAD. (A-1, B-3, G-7-6, G-7-7, I. 3.).

Significant regularities in the treatment of patients with rheumatoid arthritis with expensive biological target molecules in real clinical conditions (A-1, B-3, G-7-6, G-7-7) have been revealed: An analysis of data from clinical practice has been made. of treatment with biological drugs, according to the mechanism of action and duration of therapy (A-1; B-3; G-7-7; I. 3). The influence of the "time" factor from diagnosis to "first dose" of a biological drug on the radiographic progression of rheumatoid arthritis and functional motor deficiency (A-1; B-3) has been established. The benefit of long-term treatment with biological drugs has been proven, expressed by a continuing significant decrease in the activity of Rheumatoid arthritis for a 12-month period, on average over 3.5 years after the start of biological therapy (A-1, I. 3). , with a real goal achieved in treatment with biological drugs, in everyday clinical conditions - remission of the disease and its retention for a 12-month period (A-1, B-3, G-7-6). The share of patients on combination therapy has been established. The spectrum of safety and tolerability of a new for the country biological drug - Tocilizumab (II. 24) was analyzed. Rapid and significant positive dynamics of clinical and laboratory indicators of RA activity has been established (G-7-5, II. 20).

Data from real clinical practice were analyzed and the relative share of patients with RA in long-term treatment with biological drugs who continue to take corticosteroids (A-1, B-3, G-7-6 ÷ 7) was studied. A high proportion of patients who are treated with biological drugs and continue to take corticosteroids and / or non-steroidal drugs (A-1, B-3, G-7-6 ÷ 7) has been found. Clinical response and immunological changes after plasmapheresis in patients with rheumatoid arthritis,

treatment with slow-acting disease-modifying drugs without achieving clinical and laboratory remission were studied. Circulating immune complexes were evaluated; immunoglobulins; phagocytic activity (I. 4). For the first time in our country antiperinuclear factor and antikeratin antibodies have been studied as serological markers for RA. (I. 6). Their importance has been proven as diagnostic immunological markers, some of which were later identified as anti-citrullinated protein antibodies in patients with RA. (II. 4, II. 7, II. 9).

### **Professional experience**

Dr. Shivacheva has been working in Internal Medicine and Rheumatology since 1989. It is characterized by emphasized depth, responsibility and professionalism towards patients and the medical-diagnostic process. She has over 30 years of teaching experience. She also teaches English language training.

### **In conclusion:**

According to the requirements of MU Varna and NACID for holding the academic position "Associate Professor" Dr. Tanya Kirilova Shivacheva meets these requirements and can be determined as a researcher capable of independent scientific work in the field of rheumatology, an erudite doctor and a teacher with a strong professionalism.

**Dr. Shivacheva is an established specialist in the field of Rheumatology. As a teacher she is respected and loved by her students. The presented scientific papers and references meet the accepted scientometric criteria provided in the Law for development of the academic staff in the Republic of Bulgaria and the Regulations for development of the academic staff in MU-Varna for holding the academic position "associate professor".**

**I propose with confidence to the Scientific Jury Dr. Tanya Kirilova Shivacheva for the award of the academic position of "Associate Professor" in the professional field of Medicine in the specialty "Rheumatology"**

15.07.2020

Varna

Reviewer  
(Prof. Zh. Georgieva, MD, PhD)

