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University "Prof. Dr. Assen Zlatarov"
8010 Burgas, NI "Prof Yakimov" Blvd.
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REVIEW

By Prof. Dr. Konstantin Nikolov Ramshev, DM

Chief of Intensive therapy Clinic,
Chief of "Cardiology, Intensive therapy and Internal Medicine"
Ward, Military Medical Academy - Multidisciplinary Hospital for Active
Treatment – Sofia

Concerning: procedure for obtaining an academic position "Associate professor" in the field of Higher education 7. Health and sports; professional sphere 7.1. Medicine, scientific specialty „Internal medicine“ for the needs of University "Prof. Dr. Assen Zlatarov" – Burgas. The competition was published in the Government Newspaper № 90/ 20 Oct 2020.

As per decision of the Faculty Board of "Social health and healthcare" at University "Prof. Dr. Assen Zlatarov" – Burgas, summarized in protocol № 1/04 Jan 2021 and as per Act № ПД 243 / 21 Dec 2020 of the Rector of University "Prof. Dr. Assen Zlatarov" – Burgas, I was elected as an external member of the Scientific board (SB) for the procedure of acquisition of academic degree "Associate professor" at the University. At the first session of the SB I was assigned to write a Review for the competition. The only one candidate, admitted to the competition, is **Dr. Assia Andrianova Konsulova-Kirova, DM.**

I was given a set of documents, which are in compliance with the required by the Law and the Act for graduation of the academic staff in Republic of Bulgaria as well as by the University Regulation for acquisition of above-mentioned academic degree. There are no procedural failures.

I declare no conflicts of interests.

I. SHORT BIOGRAPHIC DATA AND PROFESSIONAL DEVELOPMENT

Dr. Assia Konsoulova was born in 1978 in Sofia. She graduated with excellence higher education in Medicine in 2003 at the Medical University "Prof. Dr. Paraskev Stoyanov" – Varna (diploma № 3343/2003). In 2004 she started working as physician at the Medical oncology clinic at the

Multidisciplinary Hospital for active treatment, “Sveta Marina”- Varna where she was working until January 2019. Further on since January 2019 until present, the applicant continued her professional career at the Medical oncology department at Comprehensive cancer center (CCC) – Burgas where she continues working until present.

Dr. Konsoulova is physician with two medical specialties: Internal Medicine, recognized in 2011 (diploma № 3065/2011) and Medical Oncology, recognized in 2015 (diploma № 3640/2016). She successfully defended a PhD thesis in 2016 on „*Expression of some plasma and tissue biomarkers as potential predictors for antiangiogenic treatment with bevacizumab in metastatic colon cancer*“. This led to the acquisition of a scientific and educational degree “Doctor” in the scientific specialty “Oncology”.

II. RESEARCH ACTIVITY AND SCIENTIFIC CONTRIBUTIONS

Dr. Konsoulova has prepared a list of 71 publications in order to take part in the competition. I acknowledge 39 of them for participation in the competition. 18 of these are in English and are published in books or journals with indexation in world databases with scientific information as Web of science and Scopus. 21 of the publications are in nonrefereed Bulgarian journals with scientific peer-review and 3 of them are chapters in national peer-review scientific books and oncological guidelines. 2 of them are international collaborative works and publications. A significant critical note is that the scientific production of Dr. Konsoulova are predominantly within the field of “Medical oncology”.

The total IF of the suggested for habilitation scientific work is 13.803 and as per SJR it is 8.132. The abstracts have IF 45.19 and SJR 19.135.

III. CHARACTERISTICS AND SCIENTIFIC INFLUENCE OF THE PUBLICATIONS

The scientific publications of Dr. Konsoulova fall within the following areas:

- 1. Rare tumors in clinical oncology – 14 publications (articles B 1-13 and Г 21);**
- 2. Breast cancer management – 10 publications (articles 2, 3, 5, 6, 12, 21 – 24, B 7)**
- 3. Translational medicine and biomarkers – 13 publications (articles 1, 6, 8, 13-17, 19, 20 B1, 3, 12)**
- 4. Immunotherapy – 3 publications (articles 7, 10, 11)**
- 5. Rare tumors in the clinical oncology – 14 articles (article W1-13 and article Г 21).**

The listed 14 articles, presented instead of monography, cover different aspects of the management of rare tumors in the clinical oncology. The scientific achievements of these publications summarize the clinical management of the rare tumors in the oncological practice. The conclusions on staging, surgery, management, treatment and follow-up of these cancers are a result of analysis and comprehensive understanding of the problem, guiding the real-world clinical management. As rare cancers, which in definition are < 1% of all cases, their treatment often creates confusion and mandates further diagnostic detailing and therapeutic step-up approach. The summary of these data assists in the better identification of the rare tumor diseases and provides an option for their more adequate treatment without further delay. The review of literature identifies that the treatment of such rare cancers is often delayed due to a lack of knowledge, need of further diagnostic work-up and difficulties in the clinical decisions. In view of this, the description and the systematization of all available cases are of great help to the better diagnostic and treatment approach. This was done with comprehension and understanding. The most recent immunologic markers are also studied with the aim to differentiate common etiological and pathogenetic mechanisms as well as clinical presentations. The role of the histological morphology is identified as a “gold standard” as a basis for the diagnosis of the oncological diseases. Additionally, the search of potential predictive or prognostic biomarkers, valid for the treatment of these rare oncological diseases is also discussed.

Practical algorithms for adequate diagnosis and identification of potential risk groups for rare gynecological tumors as well as for male breast cancer are being presented for the first time in Bulgaria. Several series of rare cancers are presented such as: lymphoepithelioma-like uterine cervix cancer (articles B5 and B12), mucoepidermoid cancer (article B1), smooth muscle uterine tumors with unknown malignant potential - STUMP – (article B6), warty carcinoma of the uterine cervix (article B2), synchronous primary tumors (articles B7 and B9) or more rare localizations of frequent malignant diseases (article B8) or sex-specific incidence differences (article 21) present data for the potential diagnostic and therapeutic management.

The treatment of precancerous conditions is given a special attention (articles B3, B4 and B11) with an emphasis on the early prophylaxis before development of the malignant diseases and this has a clear clinical implication. The conservative management of highly symptomatic conditions, typically managed with surgery, is discussed. A successful conservative treatment has led to a regression of the precancer conditions in their further follow-up and this gives a further direction for potential scientific research work with a longer follow-up.

The current perception of the heterogeneous rare tumors is analyzed. Based on personal experience, clinical guidance for diagnosis, treatment and follow-up work-up of patients with rare difficult to treat cancers are given. This gave the opportunity to draw. Additional scientific contribution of the above-mentioned publications is the comparison with similar in histology but different in localization tumors. The summary of data for histologically similar but with different localization rare primary cancers gives a valuable guidance on the clinical management and the sensitivity to different treatment methods. The discussed similarities give an opportunity to test similar therapeutic strategies, as chemo- or radiotherapy.

The publications publish for the first-time information on these rare cancers in Bulgaria. Additionally, some of them (articles B1, B2) are currently the largest data base, published in the scientific literature.

The last 2 publications (B13 and B14) are a result of long-years collaborative international groups work where the applicant is a national representative for Bulgaria. At several phases, the gaps in the care for different patient groups are identified and this has a logical clinical significance; these groups are teenagers and young adults (article B13) and patients with lung cancer (article B14). The need of specialized care teams for the management of the transitional and relatively rarely affected by cancer teenagers and young adults is discussed as currently there is no specialized care for them in Bulgaria. As a result, creation of specialized centers, dedicated to the specific care was initiated in Bulgaria. A scientific and clinical contribution is the suggested algorithm for improvement of the treatment for this subgroup of patients.

The contribution for the structuring of the management and treatment strategy for patients with lung cancer is similar (article B14). The large co-author collaboration with equal contribution in both B13 and B14 articles, due to the national representation of many countries, resulted in an intellectual achievement of 3 years of research. The rarity of the discussed topic is a reason to include them in the publications instead of a monography. The large variability of care among European countries is one of the head conclusions of both publications. The advantages and disadvantages of the different health system are thus identified, revealing practices with a need of a potential improvement. An example for Bulgarian health system is given, where there is a fast and easy access to specialized medical tests (CT, PET/CT, etc.) and to tertiary care specialist. A disadvantage of the Bulgarian system is the lack of specialized cancer centers, leading to a decrease in the quality of the treatment care. The elaboration of a conceptual model of a functioning specialized center, valid for all countries is a clinical contribution of national and international significance.

6. Management of breast cancer – 10 publications (articles 2, 3, 5, 6, 12, 21 – 24, B 7)

The international experience that Dr. Konsoulova has in oncologic gynecology is obvious. It is though clear the scientific and clinical interest that she has in the field of breast cancer in both women and men. The listed articles in this area discuss provide a multitude of scientific theoretical research and clinical contributions. Key factors, relevant for the difference in survival of patients with breast cancer are identified. Analyses of national and international databases are undertaken and they discuss differences in many parameters (as survival, rates of diagnostic biopsy prior treatment, volume of surgery, rates of neoadjuvant treatment, chemo- or endocrine therapy, etc.). The scientifically proven data for value of different systemic therapies (neoadjuvant or endocrine therapy, etc.) are also discussed, based on own national data. Different factors with predominant scientific and practical contribution on survival improvement of breast cancer patients in Bulgaria are identified.

7. Translational medicine and biomarkers – 13 publications (articles 1, 6, 8, 13-17, 19, 20 B1, 3, 12)

After the successful defense of the PhD thesis for educational and scientific degree “Doctor of Medicine”, Dr. Konsoulova continues working in the field of the translational research. The work in different cancer localizations as colon and breast cancer identify potential biomarkers with predictive and prognostic significance.

Besides the theoretical importance of the identification of key molecules, participating in different cell signaling pathways, relevant for the development and the progression of the tumors, the research led to the discovery of biomarkers that could be subject to a further prospective research and validation.

8. Immunotherapy – 3 publications (articles 7, 10, 11)

The listed publications focus on the modern and in fast development immune therapy. Of note is to emphasize that the listed publications are original and one of them (article 7) is a part of an international peer-review edition, published in English where the applicant is the sole author. The summary on the role and the types of immune response as well as its measurement are discussed within the context of malignant melanoma. The immune strategies and the prospective study and summary of clinical data led to a change in the oncological management in this oncological localization. The newly registered just weeks before checkpoint inhibitors are discussed with comprehension and details,

precising their potential role in the further clinical use. The definition and the structuring of the first Bulgarian evidence-based algorithms for malignant melanoma management, are a major scientific contribution of the publication.

The dynamically evolving immune therapy is a key component of the anticancer treatment in the medical oncology, which is continuously growing and this confirms the validity and significance of the scientific contribution of the above listed publications.

IV. INTERPRETATION OF THE SCIENTIFIC CONTRIBUTIONS OF THE APPLICANT

The scientific presence in the Bulgarian oncology of Dr. Assia Konsoulova is evident and is featured by actual focus, methodological competence, analytical capacity and clinical significance.

V. EDUCATIONAL ACTIVITY

The applicant has presented a certificate for a 4-year teaching practice as a regular assistant in Bulgarian and English language that was done at the Department of Introduction to the Internal medicine at the Medical University - Varna. She also worked for 5 years (2007 / 2008 and from 2010 to 2014 incl.) as a part-time assistant. She participated in lecture programs for different topics with physicians, specializing Internal Medicine and Medical Oncology or on individual training.

VI. MEDICAL ACTIVITIES

Until 11 Dec 2020, Dr. Assia Konsoulova-Kirova has a total of work professional as a physician of more than 14 years: 9 months and 1 day as a physician in an outpatient clinic, 11 years, 3 months and 22 days at the Multidisciplinary Hospital or Active treatment "Sveta Marina"- Varna, and 1 year, 10 months and 10 days at the CCC – Burgas. As Internal medicine specialist, the applicant has practice of over 9 years, whereas as a Medical oncologist specialist – over 5 years.

VII. PARTICIPATION IN SCIENTIFIC SOCIETIES

Dr. Konsoulova is a member of the Bulgarian physician alliance, the European respiratory society (ERS), as well as to other specialized societies in Oncology:

- Bulgarian association for dermato-oncology (BADO);
- Bulgarian oncological scientific society;

- Young oncologists club, Bulgaria (member of the ethical commission);
- American society of Clinical oncology (ASCO);
- European society for medical oncology (ESMO);
- European school of Oncology (ESO);
- College of the European school of Oncology (ESCO).

CONSLUSION:

Having considered all of the above, I assume that the treatment, diagnostic, research and the teaching activities are above the minimal requirements for the acquisition of the academic position of “Associate professor” at „University Prof. Dr. Assen Zlatarov“– Burgas”. I consider that Dr. Assia Andrianova Konsoulova-Kirova, DM is eligible for the position of “Associate professor”.

I recommend to the Respected scientific board to vote positively and to delegate the **academic position “Associate professor”** in the field of Higher education **7. Health and sports**; professional sphere **7.1. Medicine**, scientific specialty „Internal medicine“ to **Dr. Assia Konsoulova-Kirova, DM**.

03 Feb 2021

Prof. Dr. Konstantin Ramshev, DM