PEER REVIEW

from Prof. Zhasmina Mihaylova Milanova, MD, PhD

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Subject: Dissertation on the topic: "The relationship between distress and time perception in cancer patients" of the full-time PhD student - Dr. Dragomir Svetozarov Stoyanov, for awarding the educational and scientific degree "DOCTOR (PhD)" in professional field 7.1 Medicine, scientific specialty "Oncology",code 03.01.46.
Scientific Supervisor: Assoc. Prof. Nikolay Vladimirov Conev, MD, PhD

I. Administrative evaluation

Dr. Dragomir Stoyanov, a resident in the Clinic of Medical Oncology at the University Hospital "St. Marina" - Varna, Department of "Oncology" at MU-Varna, is enrolled in a full-time doctoral program on 16.07.2018 with the topic "The relationship between distress and time perception in cancer patients" - scientific supervisor Assoc. Prof. Nikolay Vladimirov Conev, MD, PhD, with order № P-109-435 / 16.07.2018 of the Rector of the Medical University "Prof. Dr. Paraskev Stoyanov" - Varna.

By decision of department meeting of the Department of Oncology - MU-Varna, Faculty of Medicine - Protocol 14 / 01.10.2020 the scientific work of Dr. Stoyanov "The relationship between distress and time perception in cancer patients" was approved and

proposed for defense. By order № P-109-422 / 22.10.2020 of the Rector of MU-Varna the dissertation thesis was directed for defense and a five-member scientific jury was elected.

II. Brief biographical data

Dr. Dragomir Svetozarov Stoyanov graduated from the High School of Mathematics "Dr. Petar Beron" - Varna with a degree in Mathematics and Informatics. In 2017 he obtained a degree in Medicine at the Medical University - Varna, graduating with full honors and was awarded the Golden Hippocrates Award. During his medical study, he attended the Clinic of Medical Oncology at the University Hospital St. Marina – Varna as a volunteer for a period of three years (2015-2017). He started working as a resident in the Clinic of Medical Oncology at the University Hospital St. Marina - Varna and as a part-time assistant at the Department of Propaedeutics of Internal Medicine. In 2018 he was appointed as a full-time assistant and doctoral student at the same department. In 2020 he was reappointed with the formation of the Department of Oncology.

Dr. Stoyanov is the author of 4 full-text publications, 2 of which are in peer-review journals. There are 2 participations with abstract entries published in the Annals of Oncology and the Journal of Clinical Oncology.

Dr. Stoyanov is a member of the European Society of Medical Oncology (ESMO).

III. Evaluation of the dissertation thesis

1. Relevance of the topic

The dissertation is focused on the large group of patients with cancer. Globally, according to data for 2018, the newly diagnosed cases of cancer are 18.1 million, and deaths due to cancer are 9.6 million. According to various studies, between 20% and 52% of cancer patients have significant levels of distress, and 30% to 40% of them suffer from mood disorders (affective disorders). In recent years, more and more attention has been paid to the fact that cancer is not only a medical problem, but also a social one. Social support, social functioning, relationships with others, the effect of the

diagnosis on patients' families are identified as problems in all age groups, regardless of gender and specific histological subtype and tumor localizations. Early detection of patients with high levels of distress is key to the subsequent development of a treatment plan. Timely detection and treatment of distress helps to improve the quality of life of patients and their families, improves compliance to prescribed treatment and the overall prognosis of the disease. In this aspect, the method proposed in the dissertation for assessment of the perception of time is an original predictive marker for distress in patients with malignancies. This method is easy to perform and it achieves satisfactory accuracy in discriminating low and high levels of distress.

2. General characteristics of the thesis

The dissertation is designed in accordance with the requirements of the Law on the Development of Academic Staff in the Republic of Bulgaria, namely - it is presented in a volume of 135 pages, of which: "Introduction" - 2 pages, "Literary Review" - 52 pages, "Aim and objectives of the study" - 1 page, "Hypotheses" - 1 page, "Materials and methods" - 6 pages, "Results" - 24 pages, "Discussion" - 11 pages, "Summary" - 1 page, "Conclusions" - 2 pages, "Contributions" - 1 page, " Publications and participations in scientific forums related to the dissertation " - 2 pages, "Appendices" - 2 pages. The dissertation is illustrated with 6 tables and 24 figures. The bibliography includes 309 titles, of which 2 in Cyrillic and 307 in Latin.

The scientific work of the doctoral student is structured with a proper sequence and volume of chapters. The information is properly visualized with appropriately selected graphic methods - figures, graphs, tables.

The abstract consists of 72 pages and fully corresponds to the text of the dissertation.

3. Aim and objectives

The aim of the dissertation thesis is clearly formulated, specific and feasible:

„*To investigate the relationship between time perception and levels of distress in patients with malignant solid tumors*"

The set 8 objectives are logically related to the aim and give grounds to assume that by mastering and applying the methodology of scientific research, they will be successfully completed.

4. Methods of research

- A prospective study was conducted among 262 patients who have been treated at the Clinic of Medical Oncology at the University Hospital Sveta Marina EAD - Varna;
- The study was conducted in the period from August 2016 till December 2017;
- Inclusion and exclusion criteria are defined to select suitable patients for the study;
- The methods for assessment of distress levels and perception of time and statistical design are described correctly.

5. Results

The obtained results are original and are the result of the research work of the doctoral student. The results are presented in three separate subsections:

- Descriptive analysis of the studied group of patients;

- Correlation analysis between time perception, distress levels and patient characteristics;

- Predictors of high levels of distress.

The results are professionally illustrated with tables and figures. Their description is according to the standard requirements for the dissertation.

6. Evaluation of the dissertation thesis and the contributions

The doctoral student Dr. Dragomir Stoyanov presented the conclusions and contributions in several sections, formulating 12 clear conclusions. Some of the more significant conclusions are:

- more than 51.9% of patients with malignant solid tumors in the studied sample have high levels of distress (measured with NCCN's Distress Thermometer) which is consistent with worldwide data. This could negatively impact their quality of life, treatment process and prognosis;

- The following factors are associated with a greater risk of significantly higher distress levels: subjective prospective estimation of one-minute time interval ≤ 40 seconds, age < 62 years, ECOG performance status = 1, lung cancer and breast cancer;
- Women exhibited significantly higher levels of distress than men;
- Patients with fast time estimation of one-minute time interval (i.e. patients with slow subjective feeling of passage of time) have significantly higher distress levels than patients with slow time estimation;
- Assessment of time perception by prospective estimation of one-minute time interval can be used as an ultrashort screening tool for distress level assessment with sensitivity of 62.5% and specificity of 53.2% (AUC = 0.60).

Significant contributions:

- For the first time worldwide, a relationship between distress levels in cancer patients (assessed with NCCN's Distress Thermometer) and perception of time (assessed with prospective one-minute time estimation test) was demonstrated.

- For the first time worldwide, correlations between demographic and clinicopathological characteristics of cancer patients, their distress levels and their perception of time were identified.

- For the first time worldwide, assessment of time perception by prospective estimation of one-minute time interval is proposed as a novel ultrashort screening tool for distress in cancer patients. This tool has an advantage because it avoids stigmatizing terms and it potentially has a higher rate of completion among patients.

IV. Scientific production

The scientific production of the candidate, related to the topic of the dissertation, includes 4 publications. Two of them are in international journals with an impact factor. The doctoral student has 2 participations with abstract presentation of the results of the dissertation work at international forums.

V. Conclusion

The dissertation thesis of Dr. Dragomir Stoyanov is an in-depth and meaningful study of "The relationship between distress and time perception in cancer patients." The design of the study is scientifically sound. Appropriate scientific methods are applied and well explained.

As a member of the Scientific Jury, I consider that the presented scientific work is up-to-date, precisely made and with significant contributions to oncology science and clinical practice. My assessment is based on the content of the dissertation, in which the doctoral student proves that he has mastered the methodology of scientific research and that he is able to apply it. All this gives me reason to convincingly suggest to the members of the scientific jury to vote positively for the acquisition of the scientific and educational degree "DOCTOR (PhD)" in the scientific specialty "Oncology" by Dr. Dragomir Stoyanov.

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With best regards:

/Prof. Zhasmina Mihaylova, MD, PhD/