

To the Chairman of the Scientific Jury

Statement

by: Assoc. Prof. Dr. Antonio Ivanov Antonov, MD, PhD

Head of the Hematology Clinic,
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on the dissertation for the award of the educational and scientific degree "PhD"

Professional field: 7. Health and Sports, 7.1 Medicine

Scientific specialty: "Hematology and Blood Transfusion"

Author: Dr. Yavor Anzhelov Petrov

Scientific organization: Medical University "Prof. Dr. Paraskev Stoyanov" Varna

Topic: "Role of the lymphocyte populations after allogeneic transplantation of hematopoietic stem cells."

Scientific supervisor: Prof. Dr. Ilina Dimitrova Micheva, MD, PhD

Order on the composition of the Scientific Jury No. P-109-332/28.07.2025 of the Rector of MU-Varna

Structure of the dissertation:

The dissertation is written according to generally accepted requirements and consists of ten sections, while respecting textual proportions.

The content covers 79 pages with 19 tables and 52 figures. The tables and figures are clear, well adapted and explained.

The bibliography covers a total of 386 titles in Latin only.

Thematic relevance of the dissertation:

In recent years, the treatment of malignant hematological diseases has been revolutionized due to a better understanding of key moments in the pathogenesis and pathophysiology of this group of life-threatening diseases.

These achievements have led to the development and introduction into practice of a new type of targeted and immune therapies, which have radically changed treatment approaches.

Regardless of the successes, allogeneic hematopoietic stem cell transplantation (allo-SCT) continues to be a curative therapy for high-risk malignant hematological diseases.

The main challenges facing every transplantation team are the risks associated with disease recurrence and possible and often life-threatening complications.

Finding the right individual strategy for each patient to deal with graft versus host disease (GVHD), infectious complications and the restoration of the immune system is of decisive importance.

Modulating the effects on the immune system and the formation of a new immune defense are the basis of the final success.

On the other hand, the dynamic assessment and monitoring of the different lymphocyte subpopulations is of fundamental importance for making important therapeutic decisions.

The present scientific work studies the changes in the immunoregulation of recipients at fixed points in the post-transplantation period and their importance for forming the final prognosis.

The topic is current, disputable and studies the relationship between various transplantation factors and the restoration of the immune system with the development of new anti-infective and anti-tumor immunity.

National studies on this topic are limited.

Literature review:

The presented review is spread over 44 pages. It summarizes but examines in detail the main factors important for the post-transplantation restoration of the immune system: donor selection, stem cell source, conditioning regimens, infectious complications.

The pathogenesis of the main immunological complication associated with allo-SCT – the graft-versus-host disease (GVHD), which is a major cause of mortality in the post-transplant period, is

also presented. Later, the stages of immune recovery of the different cell subpopulations are described, as are the severe immune dysregulation in the early post-transplant period and the infectious complications associated with it.

The structure of the review corresponds to the topic of the dissertation work. It presents and systematizes the current ideas on the problem.

Goal and objectives:

The main goal is formulated specifically and clearly.

The research tasks are 5, assessing different aspects of the remodeled immune system.

I consider the formulated goal and research tasks to be very well structured.

Methodology of the dissertation work:

The analysis included 89 adult patients, balanced by gender, who received allogeneic hematopoietic stem cell transplantation for the period 2017 - 2023 in the Department of Hematopoietic Stem Cell Transplantation at the Hematology Clinic at the University Hospital "St. Marina" in Varna.

The largest group of patients was with acute myeloid leukemia – 54 (60.6%), followed by those with acute lymphoblastic leukemia – 16 (18%), Non-Hodgkin lymphomas – 5 (5.6%), Hodgkin lymphoma 5 (5.4%), Aplastic anemia – 6 (6.7%), Plasma cell leukemia 1 (1.1%), BPDCN 2 (2.1%), CML – 1 (1.1%).

The main method of study was multiparameter flow cytometry of peripheral blood on day 100, 180 and day 270. The studies were performed in the Laboratory of Clinical Immunology at the University Hospital "St. Marina" EAD, Varna

The statistical analysis was performed with the IBM SPSS Statistics software, version 22 and other appropriate statistical methods enabling reliable data analysis.

Results:

The results reflect the changes found in the overall recovery of the immune system and individual lymphocyte subpopulations on days 30, 100 and 180 after allo-SCT. They follow the sequence of the research tasks set.

They describe the influence of significant transplantation factors and post-transplant complications.

They are illustrated with clear figures and tables.

I accept the described results as meeting the set goals and objectives.

Discussion:

The discussion examines the obtained results in detail by analyzing the importance of some transplantation factors for immune recovery and comparing them with the results of similar studies.

The dependence of immune recovery on the main diagnosis, gender, intensity of the conditioning regimen, and type of HSC are discussed as expected. These results confirm the data of different research groups. The need for dynamic assessment of individual lymphocyte subpopulations in different time periods is considered.

The established relationship between the development of GVHD and lower levels of CD3+CD4+ cells on days 100 and 180 and CD3+CD8+ cells on days 180 and 270 is discussed.

Data from the literature on the role of infectious complications in the dysregulation of posttransplant immunity and as a prerequisite for the development of complications such as GVHD are confirmed.

The discussion ends with the identification of various innovative methodologies for faster immune recovery and improving the outcome of transplantation in general.

Conclusions:

The conclusions are well-formed, summarize the results obtained and follow the tasks set in the dissertation.

I accept all of them as sufficiently reliable and well-reasoned. They have an important practical focus.

Contributions of the dissertation:

The contributions are expectedly organized into 3 groups.

The first group notes 3 original contributions evaluating the role of transplantation factors, complications, survival and recovery of immune subpopulations in the post-transplantation period after allo-SCT.

Contributions of a scientific and practical nature are logical and particularly essential for the formation of practical approaches for post-transplantation follow-up of patients and create opportunities for selective intervention at certain stages.

Contributions of a confirmatory nature are also well defined.

In summary, I accept both the contributions formulated by the author and the proposed abstract, which meets the necessary requirements.

Conclusion:

The dissertation on the role of immune recovery and lymphocyte subpopulations after allogeneic hematopoietic stem cell transplantation is a topical, practically oriented and significant work. It meets the scientometric criteria according to the regulations for academic development of MU-Varna for awarding the scientific and educational degree "PhD".

I make a recommendation to the Scientific Jury to award the scientific and educational degree "PhD" in the scientific specialty "Hematology and Blood Transfusion" to Dr. Yavor Anzhelov Petrovv.

Date: 08.09.2025

Assoc. Prof. Dr. Antonio Antonov MD PhD