SUMMARY OF THE HABILITATION THESIS

The interdisciplinary approach of neurological patients in critical condition- biological therapies in neuro-immunological disorders

Author: Associate Professor ROMAN-FILIP CARMEN CORINA,M.D,PhD.

Institution:"Lucian Blaga" University of Sibiu

Clinical Medicine Department, Discipline of Neurology

This thesis briefly presents my personal preoccupations regarding the scientific, professional and academic development after obtaining the title of Doctor of Medicine, awarded in 2006 by the "Carol Davila" University of Bucharest, where I defended my doctoral thesis with the title: *"Clinical and laboratory study of endocrine-reproductive dysfunction in epileptic women"*under the coordinator Prof.Dr.Ovidiu Bajenaru, president ad vitam of the Romanian Society of Neurology.

In the field of **scientific research,** after obtaining the PhD title, I extended my research interests, mainly in the field of epilepsy, but also in other scientific fields (neuroimmunediseases, neurodegenerative diseases, cerebrovascular diseases).

In the area of epilepsy, being part of a multidisciplinary research team (along with the colleagues from the Intensive Care Unit and the Biochemistry and Pharmacy Department), I have monitored patients with status epilepticus and cluster seizures, aiming at clinical evolution, patients' response to treatments with new molecules indicated in the therapy of epileptic status and frequent seizures, valproic acid,respectively levetiracetam; the results of these researches being presented as posters and published as abstracts at 6 international congresses, and 3 ISI papers published in extenso as the first author. Also, in this field of research, I am the director of an ongoing research grant in which we study, in a multidisciplinary team (neurology, biochemistry, psychology), the implications of chronic hyponatremia in the elderly patient on cognitive decline and epilepsy. In the field of epilepsy, I have been main investigator in 6 national / international multicentre clinical studies.

In severe neuroimmune pathologies (myasthenia gravis, Guillain-Barre syndrome, myelitis, neuromyelitisoptica, stiff-person syndrome, multiple sclerosis), together with the colleagues from the Intensive Care Unit and from the Department of Biochemistry and Pharmacy

within “Lucian Blaga” University of Sibiu, we followed the evolution and response to plasmapheresis and double-filtration plasmapheresis, the therapeutic alternative to high doses of immunoglobulins administered intravenously in a group of patients with severe forms of these pathologies; The potential mechanism of action of this procedure is to eliminate some of the mediators of inflammation, autoantibodies, serum complement and cytokines (the patient’s plasma is removed and replaced with human albumin or fresh frozen plasma).The neurological disorders, in which plasmapheresis is accepted as the first line treatment, are the Guidelin-Barré syndrome, myasthenia gravis in severe crisis (in association with immunosuppressants and cholinesterase inhibitors), chronic inflammatory demyelinating polyneuropathy (CIDP), corroborated with corticotherapy and in fulminant forms of Wilson’s disease. Plasmapheresis is accepted as a second-line therapy in: Lambert-Eaton myasthenic syndrome, flare-up relapsing-remitting multiple slecrosis (RRMS),if the patient does not respond to corticosteroids; it is also indicated in ADEM and NMO that do not respond to high doses of corticosteroids.Double-filtration plasmapheresis (DFPP) ,has the same plasmapheresis indications, which is a newer technique in which plasma is not removed entirely, but only antibodies, using special filters. From the study group of severe neuroimmune diseases cases, I have published 2 articles in extenso, case presentations, in international journals indexed ISI with IF; 4 articles in extenso in B+ journals, according to the classification of the National Council for Scientific Research in Higher Education (CNCSIS), I have presented 5 poster papers at national conferences and 2 are accepted to be presented and published within the European Neurology Academy in Amsterdam, June 2017. In this field of severe neuroimmune pathology, I am also a member in an ongoing scientific research grant, led by the “Lucian Blaga” University of Sibiu (coordinated by Sibiu Intensive Care Unit), in which we will follow the therapeutic response to plasmapheresis/ double-filtration plasmapheresis, and the quality of life of patients with myasthenia gravis in severe forms correlated with the serologic values of the immunological biomarkers of the disease (acetylcholine receptor antibodies, anti-MUSK antibodies commonly used, and anti LRP4 antibodies, anti-titin antibodies, anti-Kv1.4 antibodies, antiarrhydrin antibodies, anti-muscle fibers antibodies, newer antibodies used in research, biomarkers of myasthenia gravis).

My scientific activity, after obtaining the title of Doctor of Medicine, is found in numerous publications: a) **first author of 4 monographs/courses,** published in CNCSIS recognized publishing houses; b) **main author of 10 articles in extenso published in ISI journals with IF** c) **18 works in extenso** in CNCSIS B + journals, d) I have actively participated in congresses / conferences / national and international courses, where I presented **46 posters** (as main author and co-author).

The research activity was carried out within two research projects, **2 grants won as a project director,** and **3 grants in which I am a member of research teams**. I was also the main investigator in **13** international / national **multicentre clinical studies** concluded.

Regarding **the professional and academic achievements** gained after obtaining the title of Doctor of Medicine, I participated in 6 international training courses (for one of the courses, I have won a scholarship with a paper on epilepsy therapy - Eilat Israel Sept.2011); I have

obtained competence in electroencephalography, (exam at "Carol Davila" University of Medicine and Pharmacy, 2010), Master in Health Management, "Lucian Blaga" University of Sibiu, 2010; In 2013, I obtained the title of Associate Professor of Neurology Discipline - Lucian Blaga University of Sibiu, and since 2013, I have been Coordinator for Neurology Residents; the residents in neurology presenting under my guidance scientific papers in the form of posters at the National Neurology and Epilepsy Conferences, 12 in the last 3 years, winning the 2nd prize at the National Epilepsy Conference 2016, respectively the third prize at the National Neurology Conference, 2017. Internationally, in 2016, under my direct guidance, 2 residents were accepted with scholarships to present 2 poster papers at the European Neurology Academy in Copenhagen, June 2016. In 2016 (28.10.2016),I organized the interdisciplinary workshop at the "Lucian Blaga" University of Sibiu, (addressed mainly to resident physicians in neurology intensive care, emergency medicine), with the theme: „Neurological emergencies", accredited by the College of Physicians.

Regarding my future plans for my professional development, I aim at: **The interdisciplinary approach of the neurological patient in critical condition,** extending and equipping the Intensive Care Unit of the clinic (through interdisciplinary collaboration), for the monitoring of critically ill neurological patients (patients in coma, status epilepticus, autoimmune encephalitis, post-hypoxic-ischemic encephalopathies, severe neuroimmune diseases) by determining from serum and cerebrospinal fluid, the biomarkers specific to these diseases), for specific treatment and accurateassessment of prognosis and evolution. These studies will lead to specialized scientific publications that will improve the visibility of the discipline and the university.

Sibiu, June 2017 **Associated Professor Corina Roman-Filip, PhD, M.D**