Tuesday 16 June 2020 as from 5:30PM
VIRTUAL/ONLINE SYMPOSIUM

www.paradigms-symposium.be
Dear Colleagues and friends,

On behalf of the ParadigMS Foundation and the Belgian Study Group for Multiple Sclerosis (BSGMS), it is our honour to welcome you to the fifth ParadigMS Symposium. Adapting in a positive spirit to the new normal the 5th ParadigMS Symposium is a fully virtual symposium.

We invite you to make the best use of the opportunities offered by the digital tools: submitting your questions and comments beforehand via Slido and participating in the polling, interacting via the chat during the workshops and plenary, listening to the simultaneous translation offered via Interprefy, ....

It will be an innovative symposium that we hope will be a great learning experience.

Our scientific programme offers workshops on progressive MS and NMO spectrum disorders. Two topics that were high on the agenda of the 2019 ECTRIMS meeting in Stockholm.

We are also grateful that our international colleagues, Nikolaos Grigoriadis (Greece) and Carlo Pozzilli (Italy) accepted our invitation to speak at the symposium on biomarkers in MS and epidemiology of MS respectively.

We invite you to actively engage in this interactive and fully digital learning experience and look forward to your feedback and ideas for future symposia.

Over the years, we have kept the core of the programme the same with national and international key notes combined with networking opportunities and added means to increase interaction and engagement. We are happy that last years’ workshops were very much appreciated and repeat this format again this year. As a novelty, we activated our interactive tool Slido since early February already, allowing you to submit your input even before the start of the 5th ParadigMS Symposium. This year, the main organisational innovation we offer is the remote simultaneous translation of the plenary session.

Wishing you an interesting evening!

PROF. BÉNÉDICTE DUBOIS
President of the Belgian Study Group for Multiple Sclerosis

PROF. BART VAN WIJMEERSCH
Immediate Past-President of ParadigMS Foundation
**JOIN THE CONVERSATION**

Submit your questions/ comments/ biggest challenges on the symposium topics and participate in polls.

1. Join via [www.slido.com](http://www.slido.com)  
2. Event code F805

**TRANSLATION**

You can follow the translation of the plenary session in Dutch or French. Download the free [Interprefy App](https://www.interpret.world/login=ParadigMS-2020) from App store or Google Play. Search “Interprefy” or scan the QR code.

1. Connect to Wi-Fi  
2. Connect your earphones to your smartphone and open the Interprefy App  
3. Enter the token: ParadigmMS-2020  
4. Choose your language.  
5. Then press CONNECT

If disconnected, please press CONNECT again.

<table>
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<th>Time</th>
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| 17:00 - 17:30| Welcome, testing your connection and submitting your questions  
Master of ceremony: Stéphanie Coerten |
| 17:30 - 19:00| **Workshop 1**  
*Progressive forms of Multiple Sclerosis: pathogenesis and treatment options*  
Carlo Pozzilli (Italy)  
Bart Van Wijmeersch (UHasselt) |
| 19:00 - 19:45| **Workshop 2**  
*NMO spectrum disorders: clinics, diagnosis and treatment options*  
Nikolaos Grigoriadis (Greece) |

**PLENARY (LIVE STREAMED)**

<table>
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<th>Time</th>
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| 18:00 - 19:30| Welcome, testing your connection and submitting your questions  
Master of ceremony: Stéphanie Coerten |
| 19:30 - 19:45| **Welcome and introduction**  
Guy Laureys (UGent)  
Bart Van Wijmeersch (UHasselt) |
| 19:45 - 20:15| **Biomarkers in MS**  
Nikolaos Grigoriadis (Greece) |
| 20:15 - 20:45| **Epidemiology of MS**  
Carlo Pozzilli (Italy) |
| 20:45 - 21:15| **Q&A and panel discussion** |

(*) Simultaneous translation from English into French and Dutch.
NIKOLAOS GRIGORIADIS

Professor in Neurology, Aristotle University of Thessaloniki

Head of the MS Centre and the Laboratory for Experimental Neurology and Neuro-immunology at AHEPA University Hospital

Nikolaos Grigoriadis graduated from the Faculty of Medicine of the Aristotle University of Thessaloniki. He did his PhD thesis and residency in Neurology in the same institution. He has been specialized in clinical and experimental Neuroimmunology and CNS immunopathology in a number of research centers and institutions abroad. He is now Professor of Neurology at the Aristotle University of Thessaloniki and Head of the of the B’ Dept of Neurology, AHEPA University Hospital. the MS Centre and the Laboratory of Experimental Neurology and Neuroimmunology (www.neuroimmunology.gr). Professor Grigoriadis is member of various international scientific committees such as the European School of Neuroimmunology, ParadigMS, the subcommittee of ENS for Multiple Sclerosis, the ECTRIMS committee (until 2010).

Co-founder and Secretary of the Hellenic Academy of Neuroimmunology (www.helani.gr). He is President of the Hellenic Neurological Society. He is Ad Hoc reviewer in more than 40 international scientific journals, co-ordinator in more than 40 multicenter clinical trials for MS and principal investigator in collaborative research projects for experimental cell therapies in CNS autoimmune demyelination. His field of interests are: Neuroimmunology; Multiple sclerosis; experimental models of autoimmune diseases (EAE etc); neurodegeneration; immunomodulation; cell therapies. He has published more than 180 papers in peer reviewed journals. He has been awarded several times for his scientific work.

BART VAN WIJMEERSCH

Professor at the University of Hasselt
Immediate past president of ParadigMS
Neurologist-immunologist specialising in multiple sclerosis
Chief physician at the MS and Rehabilitation Centre in Overpelt

Bart Van Wijmeersch is a neurologist specialized in Multiple Sclerosis. He is medical director of the Rehabilitation and MS Center in Pelt where he leads the multidisciplinary MS-team. Furthermore, he is an associate professor of Neurology at the University of Hasselt, affiliated with the Biomedical Institute, where he’s involved in pre-clinical as well as the clinical research on MS at the biomedical institute (BIOMED). He has a supporting role in all the immunological research on blood- and CSF samples of persons with MS and in EAE-animal models, as well as in the rehabilitation research at REVAL. Immunological, Biomarker, MRI, Electrophysiological and Rehabilitation research in MS come together in this way. He has an educational role in the faculty of medicine and physiotherapy.

He’s a member of the Belgian Study Group of Multiple Sclerosis, first President of ParadigMS and a member of advisory boards of different pharmaceutical companies with interest in Multiple Sclerosis.

As acknowledgment of his scientific work, he received an honorary award of the Flemish government in the summer of 2019.
CARLO POZZILLI

Professor in Clinical Neurology in the Neurology department at “La Sapienza” University in Rome
Director of the Multiple Sclerosis (MS) Centre at Ospedale Sant’Andrea, University of Rome

Carlo Pozzilli studied at the University of Rome “La Sapienza”. He then moved to the Hammersmith Hospital in London, UK, to take up a research post in 1980. In 1983, he became a Board Certified Neurologist at the University of Rome. In 1986 obtained a research grant in Neuroimaging at the Tohoku University, Sendai Japan. In 1987, he was awarded a PhD in Clinical Neurosciences by the University of Rome, where he became Full Professor in 2006. In 2002 he funded and become Director of the Multiple Sclerosis (MS) Center of Ospedale Sant’Andrea, University of Rome which is his actual position. Professor Pozzilli’s fields of interest include the clinical aspects and treatment of MS; he has published more than 350 papers and reviews on these subjects. Professor Pozzilli is a member of several National and International Societies. He has participated as a first investigator in at least 250 multicentre clinical trials on patients with MS. He was also member of the Steering Committee and Advisory Board in several multicentre trials.

VINCENT VAN PESCH

Clinical head of Saint-Luc University Hospital
Chief researcher of the Neurochemistry unit (Institute for Neurosciences, UClouvain)

Vincent van Pesch is mainly involved in the diagnosis and treatment of neuro-immunological disorders, among which Multiple Sclerosis, with over 1000 patients followed. He is also involved in clinical neurophysiology and responsible for interpreting neurochemistry and neuro-immunological tests. He is involved in the international MSBase registry. His main research interests include biomarkers for MS and other neurological disorders, immunology of MS and more recently the role of microRNAs and extracellular vesicles in MS. He has published over 100 peer-reviewed articles.

Multiple Sclerosis (MS) is a chronic inflammatory demyelinating disease of the central nervous system (CNS) and causes neurological impairment and disability. Progressive MS (PMS) is characterized by a continuous clinical deterioration without recovery. Patients who initially present with PMS are termed primary progressive (PPMS), while those who evolve to PMS after initially presenting with RRMS are termed secondary progressive (SPMS). Active patients experience superimposed inflammatory episodes (occurrence of clinical relapses at least once annually and/or enlarged, new or contrast enhancing T2 lesions). Non-active patients do not have clinical relapses and MRI activity (e.g., gadolinium enhancing MRI lesions, new or enlarging T2 lesions) since 1 year.

Our knowledge of PMS has increased significantly in the last few decades. A key discovery was that the pathophysiological hallmark of progression is ongoing intrathecal inflammation, behind a closed blood–brain barrier, leading to the continuing metabolic failure of neurons and axons. This finding has led to several clinical trials and research programmes that evaluate the use of disease-modifying treatments (DMTs) in the progressive forms of MS. Although there is no difference between secondary and primary progressive MS pathologically, a relapsing phase of the disease precedes SPMS clinically, and therefore the development of SPMS may be amenable to prevention. The risk of SPMS has been studied widely and is often very closely related to the bad prognostic factors of MS. The risk of SPMS increases with age, duration of illness and worsening disability, and decreases with improving disability. Bad prognostic signs on clinical, imaging, functional and biological grounds have been associated clearly with increased disability over time, and with the risk of SPMS. Furthermore, DMTs may delay the onset of secondary progression.

Although there are multiple approved drugs for the treatment of RRMS, current treatments have limited therapeutic benefit in PMS patients, especially the non-active population. In active PPMS patients, Ocrelizumab can be prescribed. Ocrevus is a humanized monoclonal antibody that selectively depletes CD20-expressing B cells. The initial 600 mg dose is administered as two separate intravenous infusions; first as a
300 mg infusion, followed 2 weeks later by a second 300 mg infusion. Subsequent infusions are administered as a single 600 mg intravenous infusion every 6 months. Siponimod is indicated for SPMS. Siponimod is a sphingosine 1-phosphate receptor (S1P) modulator which selectively binds the S1P1 and prevents lymphocytes from entering the lymph nodes and the central nervous system (CNS). The approval was based on results of the EXPAND study, a randomised, double-blind, placebo-controlled trial which compared the safety and efficacy of Siponimod to a placebo. Considering the lack of other treatment options, PMS patients are prescribed DMT agents off-label as well as symptomatic treatments (e.g., fampridine) to improve their quality of life.

**NMO SPECTRUM DISORDERS: CLINICS, DIAGNOSIS AND TREATMENT OPTIONS**

**NIKOLAOS GRIGORIADIS**

Diagnostic errors may still common in Multiple Sclerosis (MS). In a number of cases where T2 lesions are identified in MRI may be considered as MS lesions resulting in inappropriate, sometimes harmful therapeutic interventions for the patient. Mono- or multi-focal symptoms consistent with inflammatory demyelinating disease, are subject to differential diagnosis. Neuromyelitis optica spectrum disorders (NMOSD) are autoantibody mediated chronic inflammatory diseases. Serum antibodies (Abs) against the aquaporin-4 water channel lead to recurrent attacks of optic neuritis, myelitis and/or brainstem syndromes. In addition, in some patients with symptoms of NMOSD, Abs against myelin-oligodendrocyte-glycoprotein (MOG) though not AQP4 are detectable. These clinical syndromes are now frequently referred to as “MOG-encephalomyelitis” (MOG-EM).

The two groups of disorders may have similar symptoms though distinct clinical courses or lesion distribution throughout central nervous system (CNS) as indicated by the MRI findings. A central component of diagnostics in NMOSD and MOG-EM is the detection of the correspondent serum Abs. Differential diagnosis from other conditions with similar symptoms such as sarcoidosis or MS and other CNS disorders should be performed on the basis of relevant laboratory test. In NMOSD as well as in MOG-EM, acute attacks are usually treated with 1,000 up to 2000 (in some cases) mg intravenous methylprednisolone (IVMP) for 3–5 days with complete or almost complete recovery in 50% and 17–35% of IVMP treated MOG-EM and NMOSD attacks, respectively. In case of poor response, treatment escalation with plasma exchange (PLEX) is indicated. Long term therapy includes immunosuppression to reduce disease activity and to avoid further attacks. However, in the absence of placebo controlled trials, treatment choice is based on case reports, observational studies etc. Thus, Azathioprine, Rituximab, Mycophenolate Mofetil, low dose Prednisone/Prednisolone may be among the currently used therapeutic options. On the contrary, Treatment with medications indicated for MS such as interferon-beta, glatiramer acetate, fingolimod, alemtuzumab, natalizumab, and dimethyl fumarate is known to have no effects in NMOSD / MOG-EM or may even be proven harmful. Evidently, it is of importance to establish the right diagnosis before any decision making for treatment.

**VINCENT VAN PESCH**

The diagnostic criteria of Neuromyelitis Optica Spectrum Disorders (NMOSD) have considerably evolved during the past 20 years, allowing for more precise and earlier diagnosis. Along with increasing knowledge regarding the pathology of this broadening disease entity, there have been significant advances in therapeutic strategies. This workshop will review current diagnostic criteria of NMOSD, highlight key clinical and radiological features distinguishing MS from anti-aquaporin-4 and anti-MOG-mediated disease and discuss NMOSD diagnostic pitfalls. An update on existing and future treatments as well as treatment algorithms will be provided. The workshop will be illustrated by clinical cases.
**Biomarkers in MS**

**NIKOLAOS GRIGORIADIS**

Multiple Sclerosis is an autoimmune, multifactorial disorder with its main hallmarks the persistent neuroinflammation and chronic neurodegeneration. Despite its extensive study, the lack of reliable and specific biomarkers for the disease makes it difficult to achieve differential diagnosis and delays early treatment. The disease is also characterized by high heterogeneity, a factor that complicates the process of finding suitable biomarkers. A number of biomarkers such as the anti-Aquaporine 4, the anti-MOG Abs are among those currently being used for the differential diagnosis of CNS demyelinating processes, the anti-JCV Abs for the safe administration of DMTs, particularly natalizumab (NTZ) treatment together with the anti-NTZ neutralizing Abs in case of treatment failure are well established for the daily clinical practice. Interestingly enough, there is increasing evidence indicating that the plasma neurofilament light chain (pNfL) concentrations in relapsing remitting multiple sclerosis (RRMS) may be a valuable biomarker reflecting the neurodegenerative process which underlies the corresponding disability progression. Moreover, recent reports provide evidence that the choice of disease modified treatment in RRMS is significantly associated with degree of reduction in pNfL, which supports a role for pNfL as a drug response marker. In addition, all “omics” approaches are high throughput, data-driven, and holistic methodologies and metabolomics in particular may be used for the discovery of biomarkers. Metabolomics use the means of cutting-edge technologies, like NMR and MS, in the analysis of high throughput data and following the requirements of personalized medicine aims to a patient-tailored healthcare. Also, seeks to capture the complexity of metabolic networks, create a personalized metabolomic profile for the disease and the final goal is to identify metabolites that can be used as candidate biomarkers in daily clinical practice. Those biomarkers will contribute not only in prognostic evaluation but also as a mean of monitoring the disease or treatment efficacy.

The implementation of soluble as well as novel imaging biomarkers may complement current clinical and imaging monitoring. However, the road map to establish a molecule as potential biomarker in a complex disease such as MS is a long one. On the other hand, it may be the only way to develop a precision medicine approach in the overall management of the disease.

**Epidemiology of MS**

**CARLO POZZILLI**

Multiple sclerosis (MS) is a major cause of neurological disability with a considerable socioeconomic burden. This presentation provides an overview of recent estimates of the worldwide prevalence and incidence rates, of changes in the distribution MS by age and sex, as well as looking at some recent advances in understanding of environmental epidemiology and the natural history of MS.

Although MS is present in all regions of the world, the incidence and prevalence is higher in some countries than in others. This is occurring in populations at high risk (such as Sardinia) and in those at low risk (such as Norway), suggesting that, whatever the causative factors of MS may be, their influence appears to increase.

In addition, an increase in the female/male ratio has been demonstrated over time in many countries around the world.

One of the most striking indicators of a potential environmental role has always been considered to be the gradient of MS prevalence with latitude.

Susceptibility to MS is complex, with evidence supporting both genetic and environmental factors, with genetic effects shaping the population risk for MS. A major supporting factor for a genetic effect is the positive family history of MS observed in 20% of all patients of European descent and estimates of MS heritability (the proportion of phenotypic variance attributable to heritable factors)range from 25 to 76%. Although epidemiological studies provide evidence of a genetic basis, the specific gene or genes remain elusive.

A large number of environmental or lifestyle factors have been identified to play a role in MS including smoking, pre-pubertal diet, childhood obesity, pollution, exposure to the Epstein-Barr virus and low exposure to sunlight (mediated through vitamin D insufficiency). A number of studies support a significant role for hypovitaminosis D as a risk factor for multiple sclerosis. Additional research is needed to conclusively prove which factors are important in increasing the risk of MS.
This symposium is an initiative of the ParadigMS Private Foundation in collaboration with the Belgian Multiple Sclerosis Study Group.

**ParadigMS (2015, Berlin)** is an independent and non-profit international group of Multiple Sclerosis experts dedicated to improving Multiple Sclerosis patient care by translating state-of-the-art science into practical education at local and national level. ParadigMS offers offline and online trainings in all aspects of MS care in both Europe and the Middle East.

More information: [www.paradigms.foundation](http://www.paradigms.foundation)

The Belgian Study Group for Multiple Sclerosis (BSGMS) is a non-profit organisation formed in 1957 with the goals to favour and develop in Belgium, in collaboration with the Fondation Charcot Stichting, the study of the nature and more specifically the treatment of Multiple Sclerosis through various disciplines and to contribute to medical training in the domain of Multiple Sclerosis.

More information: [www.bsgms.org](http://www.bsgms.org)

**ACCREDITATION**

Both workshops and the plenary session of the symposium are being evaluated by the joint committee of neurology of RIZIV/INAMI for accreditation (number 20006396).

YOUR LOGIN TO THE VIRTUAL SESSION(S) WILL BE VALID FOR ACCREDITATION. THE ORGANISERS WILL PROVIDE THE LIST TO THE RIZIV/INAMI.

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Our mission is clear: we are pioneers in neuroscience. Millions of people around the world are affected by multiple sclerosis, Alzheimer’s disease, Parkinson’s disease and amyotrophic lateral sclerosis. Many people suffer from less common diseases such as spinal muscular atrophy.

We believe that no other disease area holds as much need or as much promise for medical breakthroughs as neuroscience.

Our scientific expertise and courage to take risks make us leaders in the research and development of medicines to transform neuroscience to benefit society.

Recognizing the challenges facing health care systems today, we collaborate with regulatory authorities, health care providers and payers, so that those in need can access our medicines.

Biogen-42123. February 2020
With over 20 years of experience in MS, we remain committed to finding solutions for patients’ unmet needs by advancing care and providing innovative treatments.

This year, come join us at AAN to learn about:

- How BTK inhibition promotes myelin repair in models of demyelination
- The impact of cladribine tablets on pathological B and T cell subsets, and inflammatory and neurodegeneration biomarkers in blood and CSF
- How disease progression improves in CLARITY and CLARITY Extension
- How serum neurofilament light chain levels are reduced with IFN β-1a treatment in patients with a first clinical demyelinating event.

as well as discover our poster selected for the Grande Finale of the science innovation lunch, on immune cell reconstitution after treatment with cladribine tablets using deconvolution algorithms.

As always, count on our teams to keep you abreast of the latest data that matter to your practice!
YOUR FEEDBACK IS IMPORTANT TO US!

Do send us your feedback on the symposium. Even more importantly, we are curious to hear your future training needs: what topics should we cover, what formats would you most appreciate?

Go to our survey via this QR code and submit your ideas. We will share the results afterwards.

ParadigMS is grateful to the sponsors, who support the event without any involvement in the programme and the content of the Symposium.

Platinum: Biogen, Merck, Roche, Celgene, Bristol Myers Squibb

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