18th STATE OF THE ART

SYMPOSIUM of the Swiss Multiple Sclerosis Society  www.multiplesklerose.ch

PROGRAMME | ABSTRACTS SATURDAY, JANUARY 30TH, 2016

KKL Luzern, Culture and Convention Centre

COMORBIDITIES AND ENVIRONMENTAL FACTORS INFLUENCING MULTIPLE SCLEROSIS

supports research
Dear colleagues,

On behalf of the Swiss Multiple Sclerosis Society and its Scientific Advisory Board it is our pleasure to invite you to the 18th State of the Art Symposium.

Recent epidemiological studies demonstrate that in addition to genetic factors environmental factors influence susceptibility to Multiple Sclerosis (MS) and might additionally influence the disease course. The plenary morning session of the 18th State of the Art Symposium entitled «Comorbidities and Environmental Factors influencing Multiple Sclerosis» is thus to a large degree dedicated to this topic. Four internationally well-known experts have accepted our invitation and will present recent advances in this field. Tomas Olsson will highlight how environmental factors in combination with MS risk genes might influence MS in individual patients. Matthias Mehling will address the effects of immunomodulatory therapies on vaccinations in MS patients, but also touch upon the risk of developing MS following a vaccination. In addition Kerstin Hellwig will report on the influence of pregnancy and oestrogens, while Joost Smolders will discuss the role of vitamin D on the course of MS. The morning will continue with an update on the Swiss MS Registry and the Swiss MS Cohort Study provided by Viktor von Wyl and Jens Kuhle, and will conclude with a presentation of Ludwig Kappos on the changing treatment algorithms of MS integrating the new drugs on the market.

The afternoon session, with two sets of two parallel workshops, will bring to discussion topics relevant in daily practice. The speakers will show the Impact of PML Risk in the treatment of MS (workshop A), explain the benefit of Biomarkers in MS disease course and treatment personalization (workshop B), highlight agents that might promote Neuroprotection (workshop C) and discuss the relevance of measuring Brain Atrophy in clinical practice (workshop D).

Updated information about the Symposium can be found on www.ms-state-of-the-art.ch

In the name of the organisers and speakers, we sincerely hope that the programme meets with your interest and that you will be able to attend and actively take part in the discussions.

We wish you an interesting symposium.

Prof. Dr. Britta Engelhardt
President of the Scientific Advisory Board

Patricia Monin
Director of the Swiss MS-Society
GENERAL INFORMATION

Venue
KKL Luzern, Europaplatz 1, CH-6005 Lucerne
www.kkl-luzern.ch

Programme committee
Britta Engelhardt, Bern; Claudio Gobbi, Lugano; Tobias Derfuss, Basel; Christian Kamm, Bern; Patrice Lalive, Geneva; Renaud Du Pasquier, Lausanne

Organisation
Swiss MS-Society and its Scientific Advisory Board

Contact
Swiss MS-Society, Josefstrasse 129, CH-8031 Zürich
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Credits
The Swiss Neurological Society will award 5 credit points.
The Swiss Society of General Internal Medicine (SGIM/SGAM) will award 4.5 credit points.

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PROGRAMME

Chairpersons

Session I:  Prof. Britta Engelhardt, Bern CH  
            PD Dr. Myriam Schluep, Lausanne CH  
Session II: Prof. Nicole Schaeren-Wiemers, Basel CH  
            Prof. Renaud Du Pasquier, Lausanne CH

09.30-10.00 Welcome with Coffee and Gipfeli

10.00-10.10 Dr. Christoph Lotter, Zurich CH  
Welcome from the Swiss MS-Society

10.10-10.40 PD Dr. Kerstin Hellwig, Bochum DE  
Pregnancy and Oestrogens

10.40-11.10 Prof. Tomas Olsson, Stockholm SE  
Lifestyle Factors in MS – Interactions with MS Risk Genes

11.10-11.40 Dr. Matthias Mehling, Basel CH  
MS and Vaccinations

11.40-12.10 Coffee Break

12.10-12.35 Dr. Joost Smolders, Nijmegen NL  
Environmental Factors – Vitamin D

12.35-12.50 Dr. Viktor von Wyl, Zurich CH and PD Dr. Jens Kuhle, Basel CH  
Swiss MS Registry and Swiss MS Cohort Study

12.50-13.15 Prof. Ludwig Kappos, Basel CH  
New Drugs and changing Treatment Algorithms

13.15-14.15 Lunch

14.15-15.00 Workshops A and B

15.00-15.20 Coffee Break

15.20-16.05 Workshops C and D

16.05 Farewell Apero
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Department of Clinical Neuroscience
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CWZ MS Center, Department of Neurology

Dr. Viktor von Wyl, Zurich CH
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Speakers (Workshops)

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Department of Neurology
Multiple sclerosis is a common neurological disease mainly affecting young women in their reproductive age. Why the susceptibility for most autoimmune diseases such as MS is higher in women than in men is not completely understood. Interestingly, the risk of developing MS seems to be increasing in females during the last few decades. This timespan is too short to explain the increase by genetic factors. Environmental factors (fewer children, more smoking amongst women, exogen hormonal factors, diet?) might play a role.

The course of MS is also influenced by hormonal factors. Most well known is the powerful reduction of relapses during pregnancy – more effective than any available treatment for MS – followed by an increase of disease activity postpartum. Exclusive breastfeeding with its distinct hormonal changes leads to a moderate relapse risk reduction in the first 6 months after birth.

Unfortunately smaller clinical trials failed to show a meaningful effect on the postpartum relapse risk with high dose progesteron; estriol – an estrogen exclusively produced during pregnancy – led to a relapse reduction, paradoxically not reflected in the development of new T2 lesions. Attempts to pharmaceutically imitate the power of pregnancy have unfortunately not been successful yet. This talk will focus on the interactions of endogenous and exogenous hormonal changes on susceptibility and prognosis of multiple sclerosis.
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LIFESTYLE FACTORS IN MS – INTERACTIONS WITH MS RISK GENES

There is solid evidence for variants of genes and lifestyle / environmental factors influencing the risk for multiple sclerosis (MS), each of which has low or modest impact on the disease. Gene-environment interactions may be important. Detailed knowledge on these may allow more precise therapy and prevention. The epidemiological and genetic fields have mostly operated separately. We combine these in a nation-wide study on incident MS cases (now 3500) and matched population based controls (4400).

So far we have evaluated lifestyle / environmental factors; like smoking (OR~1.6), exposure to organic solvents (OR~1.5), use of oral tobacco (OR~0.5), lack of sun exposure / vitamin D (OR~1.5), Epstein Barr virus (EBV) infection (OR~2), high EBNA1 fragment serology (OR~4), obesity (OR~2 at age 20) and night shift work (OR~1.7 before age of 20).

We studied interaction with the strongest MS risk genes: HLA DRB1*15:01 and HLA A2 status.

Smoking interacted with carriage of HLA-DRB1*15 and absence of HLA-A*02. The risk of developing MS was substantially increased among smokers with both genetic risk factors (OR 13) compared to non-smokers with neither of these factors, similar to organic solvent exposure. Similar interactions prevailed with measures of EBV infection, obesity at age 20, while there were no interactions between sun exposure habits / vitamin D levels, night shift work and HLA MS risk genes.

Hypothetically, inflammatory irritation in the lung in context with MS risk genes may trigger MS. These immune reactions will be important to study. Furthermore, upcoming studies of MS genetics should take lifestyle / environmental factors into account.
Als eines der weltweit führenden Biotechnologie-Unternehmen engagiert sich Biogen in der Erforschung, Entwicklung, Herstellung und im Vertrieb innovativer Therapeutika. Wir sind bestrebt, mit modernen Therapien die Lebensqualität der Patienten und deren Familien nachhaltig zu verbessern.
Vaccinations are of fundamental importance for preventing communicable infectious diseases in humans. In individuals with MS vaccinations reduce the risk of relapses related to infections.

Notwithstanding this, concerns on vaccinations in the context of MS are regularly raised by patients and also in the media for various reasons. Recurring questions are, whether vaccinations can trigger MS-relapses or even induce the disease onset by molecular mimicry or polyclonal bystander activation of autoreactive lymphocytes. Are vaccinations under specific immune-therapies safe and also efficacious? With a focus on these questions this talk will review important aspects of vaccinations in individuals with MS.
Die Schubratenreduktion als primärer Endpunkt in den Zulassungsstudien TEMSO und TOWER betrug 31,5 % bzw. 36,3 %. Unterschiedliche Werte zwischen Zulassungsstudien und Post-hoc Analyse der gepoolten Daten beider Zulassungsstudien aufgrund unterschiedlicher Fragestellungen und statistischer Voraussetzung.

1 Schübe, die zu einer nicht vollständigen neurologischen Regenerierung führen (beurteilt durch den Prüfarzt)
2 im Vergleich zu Placebo

6 Weitere Informationen entnehmen Sie bitte der Aubagio® Fachinformation unter www.swissmedicinfo.ch.

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*Die Schubratenreduktion als primärem Endpunkt in den Zulassungsstudien TEMSO und TOWER betrug 31,5 % bzw. 36,3 %. Unterschiedliche Werte zwischen Zulassungsstudien und Post-hoc Analyse der gepoolten Daten beider Zulassungsstudien aufgrund unterschiedlicher Fragestellungen und statistischer Voraussetzung.

1 Chöbe, die zu einer nicht vollständigen neurologischen Regenerierung führen (beurteilt durch den Prüfarzt) im Vergleich zu Placebo
5 Weitere Informationen entnehmen Sie bitte der Aubagio® Fachinformation unter www.swissmedicinfo.ch.


A poor vitamin D status has been associated with an increased risk of developing multiple sclerosis (MS). In subjects with MS, a low circulating vitamin D status has been associated with several adverse disease outcomes such as an increased risk of relapses, a higher EDSS-score and an increased risk of disease activity on MRI. In MS patients visiting our outpatient clinic, higher circulating levels of the vitamin D metabolite 25-hydroxyvitamin D (25(OH)D) were associated with a higher risk of remaining relapse-free the subsequent 3 years. EDSS-progression was not predicted by 25(OH)D levels. However, relapsing remitting MS (RRMS) patients with a rapid transition towards progressive MS displayed lower 25(OH)D levels at diagnosis than matched patients with a prolonged RRMS phase.

Although the causality of these associations is not consolidated, the prospect of a disease modulating effect of vitamin D supplementation in MS is tempting. To assess this hypothesis, we designed a randomized controlled clinical trial (RCT) on vitamin D supplementation as add-on therapy in Interferon Beta-treated RRMS patients. In vitro and in experimental models of MS, the active metabolite of vitamin D is a potent immune regulatory molecule. It is believed that an immune regulatory role of vitamin D in vivo may underlie the earlier reported associations of vitamin D status with disease outcomes of MS. We explored correlations between relevant immunological outcomes and 25(OH)D levels in cross-sectional studies and finally assessed an effect of vitamin D supplementation on these outcomes in a sub-study of the earlier mentioned RCT.

Preliminary results will be discussed in this lecture. We conclude that vitamin D supplementation may modulate the disease course of MS, yet definitive results of RCT’s are needed to translate associations to therapeutic interventions. Results of several RCT’s are expected and may provide more clearness in the near future.
Referenzen

Gekürzte Fachinformation Rebif®/Rebif® multidose/Rebif® RebiDose®
Interferon beta-1a ADNr. I: Patienten mit einem ersten klinischen, auf Multiple Sklerose (MS) hinweisenden neurologischen Ereignis bei Ausschluss anderer Diagnosen und glz. hohem Risiko für das Auftreten einer schubförmigen MS. Schubförmige MS. D: i.Allg. 44/uni2009/uni00B5g, dreimal pro Woche subkutan. KI: Behandlungsbeginn während der Schwangerchaft, Überempfindlichkeit gegen einen Inhaltsstoff, schwerwiegende Depressionen und/oder Suizidgefährdungen. V: Thrombotische Mikroangiopathie, Depressive Störungen, Krampfleiden, nicht adäquat therapierte Epilepsie, Angina pectoris, kongestive Herzinsuffizienz, Arhythmien, schwere Hypersensitivitätsreaktionen, Hautläsionen an Injektionsstelle, schwere Nieren-/Leberinsuffizienz, schwerwiegende Leberfunktionsstörungen, Nephrotisches Syndrom, akute Myelosuppression, Alkoholisches Leiden, maligne Infektionen, vorübergehende Veränderungen der Leberenzyme, ggf. Schildrüsenfunktionsstörung. IA: Medikamente mit engem therapeutischen Breite und/oder Metabolisierung über CYP450 wie Antiepileptika oder Antidepressiva. UAW: Grippeähnliche Symptome, Entzündungen, Hautreaktionen und Schmerzen an der Injektionsstelle, Kopfschmerzen, Myalgien, Arthralgien, Müdigkeit, Fieber, Anstieg der Leberfunktionswerte, Pruritus, Ausschläge, Urtikaria, Akne, Neutropenie, Lymphopenie, Leukopenie, Luesinfektionen, Anämie, Durchfall, Erbrechen, Übelkeit, Depression, Schlafstörungen, Dyspnoe. P: Rebif 8.8/uni00B5g/0.2 ml und 22/uni00B5g/0.5 ml Fertigspritzen: 6+6 (Startpackung*); 22/uni00B5g/0.5 ml oder 44/uni00B5g/0.5 ml Fertigspritzen: je 12*. Rebif multidose Patronen zu 66/uni00B5g/1.5 ml oder 132/uni00B5g/1.5 ml: je 4*. Rebif RebiDose 8.8/uni00B5g/0.2 ml und 22/uni00B5g/0.5 ml Fertigspritzen: 6+6 (Startpackung*); 22/uni00B5g/0.5 ml oder 44/uni00B5g/0.5 ml Fertigspritzen: je 12*. (*/uni2009/kassenzulässig). Für detaillierte Informationen siehe www.swissmedicinfo.ch. MA15 12/2015 d/f

Merck (Schweiz) AG, Chamerstrasse 174, CH-6300 Zug, Tel. +41 41 729 22 22, www.merck.ch
Together, the Swiss MS Registry (SMSR) and the Swiss MS Cohort Study (SMSC) create a very unique study base for highly innovative national and international MS research. The SMSC is a clinic-based, observational study that started recruiting in June 2012. Currently, over 900 MS patients seen at seven Swiss MS centers are enrolled. The SMSC collects longitudinal, high-quality clinical data, biosamples and MRI scans. Follow-up data are obtained every 6 or 12 months and include assessments of EDSS scores by certified examiners, serum, plasma and whole blood samples and optional cranial MRI. Research objectives entail investigations into MS progression, search for and validation of biomarkers, as well as evaluations of safety and efficacy of MS therapies.

The SMSR pursues a citizen-science approach and is open to all persons with a confirmed MS diagnosis. Enrollment will start in June 2016, and participation will be possible via the internet or by paper questionnaires. From the start, persons with MS were involved in the planning and development of the SMSR. Interactive tools such as online voting and feedback systems, patient diaries, and discussion forums will be offered to maintain the engagement of the MS community with the SMSR. Data collections span a wide range of topics from nutrition, coping with MS, physiotherapy, or mental health through longitudinal surveys, as well as clinical information on MS by medical record abstraction.

Topical overlaps exist between the SMSR and the SMSC in the collection of clinical data, and these are intended. Both databases are designed for mutual compatibility, and informed consent procedures involve the option of data exchanges between the studies for double enrollees. Moreover, the inclusive nature of the SMSR offers the possibility to engage less-studied persons with MS in research (e.g. persons with severe disabilities or those who are not in care at MS centers), thereby complementing the more clinic-centered, but well documented SMSC population.

In summary, the close partnership between the two studies ensure the creation of maximal synergies and benefits for persons with MS and other stakeholders. Together, the SMSR and the SMSC strive to advance Swiss MS research by providing comprehensive, high quality data and a unique platform for nested studies.
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Referenzen:
NEW DRUGS AND CHANGING TREATMENT ALGORITHMS

In the last years we have witnessed an accelerated development of new compounds for the treatment of relapsing multiple sclerosis. New oral treatments and monoclonal antibodies (already approved or in the process of approval by health authorities) did not only improve tolerability and thus convenience, but have also shown superiority in direct head-to-head comparisons with well established compounds for first-line treatment.

Results of recent controlled trials and systematic observational studies concerning both efficacy and side-effects / risks underline the need for valid criteria, if not for prediction then at least for early assessment of treatment response as a basis for therapeutic choices. In addition, recent progress challenges the up to now preferred therapeutic algorithms for staged treatment escalation and underlines the necessity to evaluate such escalation algorithms against early induction treatment. Finally, latest evidence suggests that emerging treatments may also have direct beneficial effects on the progressive plan of the disease.

After a short review of most recent clinical trial results the lecture will cover actual and emerging criteria for treatment decisions in daily practice and resulting algorithms.
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D: Injektion s.c. an wechselnden Injektionsstellen, 20 mg täglich.
KI: Hypersensibilität gegenüber Inhaltsstoffen, Schwangerschaft.
IA: Überempfindlichkeitsreaktionen, Nierenfunktion niereninsuffizienter Patienten regelmäßig überprüfen.
UAW: Schwindel, Depression, Angst, erhöhte Muskelspannung, Polyurie, Polydipsie, Dyspnöe, Nausea, Obstipation, Diarrhoe, Rash, Schweit, Arthralgien, Reaktionen an der Injektionsstelle, Kopfschmerzen.
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Progressive multifocal leukoencephalopathy (PML) is a severe infectious disease of the central nervous system that is caused by reactivation of the JC virus in people carrying the virus, which are around 50% of the population. PML occurs almost exclusively in immunosuppressed individuals and is associated with several disease modifying treatments (DMTs) in multiple sclerosis (MS).

PML may cause death or severe disability and therefore must be considered in the choice of treatment in MS. This workshop aims to give an overview of PML risk in MS and its implication on treatment.
Given the growing therapeutic armamentarium with potential severe adverse drug reactions (sADR), there is a clear medical need for the establishment of new biomarkers. These need to address a) differential diagnosis, b) heterogeneity of the disease, c) optimized patient selection for a given treatment and d) markers of the risk to develop sADR.

In this workshop we will review the stepwise approach to CSF analysis in the differential diagnosis. This is especially important since our understanding of the defining disease pathogenesis remains incomplete and no specific markers are currently available to confirm the disease. Additional biomarkers characteristic for differential diagnoses (e.g. AQP IV, MOG-antibodies) and potential surrogate markers of the disease (e.g. EBV serology, VitD, KIR 4.1 antibodies) will be discussed. Current status of research on response biomarkers will be reviewed, e.g. chitinase 3 like 1 and neurofilaments that may help to monitor therapeutic decisions in MS in future. Finally, markers that may assist in the risk stratification of sADR such as PML will be addressed (e.g. Anti JCV-antibody, lymphocyte counts, CD62L).

Upon completion of this workshop the participant will have an overview on the value of established biomarkers for clinical practice as well as development and controversies surrounding experimental markers.
Neuroprotection is an important unmet medical need in MS both at the early stages, but particularly once patients begin to enter the chronic progressive stages.

We will give a brief introduction into the topic with respect to mechanisms of the «degenerative» aspects of MS and how neuroprotection can be achieved, highlight which substances that are approved for other indications have already shown promise as neuroprotective agents in MS, and finally give an outlook on approaches that are being pursued for future therapies.
Local and global atrophy measurements provided by structural magnetic resonance images (MRI) may provide a clinical marker of neurodegeneration in multiple sclerosis patients.

In workshop D, we will first present a summary of the literature showing how MRI-based atrophy metrics correlate with patients clinical outcome and response to therapy. We will then make a brief introduction of the most common methods used to quantify brain volume changes over time in MS research. And we will discuss the advantages and disadvantages of providing atrophy metrics to radiologist and neurologist using the methods currently available in research settings. Last, we will attempt at summarizing the future steps towards «clinically meaningful» atrophy measurements in clinical practice.
WE THANK YOU FOR YOUR PARTICIPATION
AND WISH YOU A SAFE JOURNEY HOME.

SEE YOU NEXT YEAR AT THE
19TH STATE OF THE ART SYMPOSIUM,
SATURDAY, 28TH JANUARY 2017.

BEST REGARDS
SWISS MULTIPLE SCLEROSIS SOCIETY