Abstract
Book

20th

State of the Art

Symposium

Swiss
Multiple Sclerosis
Society

The 20th State of the Art Symposium

«Experimental Therapies in Multiple Sclerosis»

Dear Colleagues,

On behalf of the Swiss Multiple Sclerosis Society and its Scientific Advisory Board it is our distinct pleasure to invite you to the 20th State of the Art Symposium.

Multiple Sclerosis (MS) presents as a very heterogeneous disease considering its underlying mechanisms and its clinical presentation. Response to treatments is equally variable. Thus there is continuous search for improved treatment strategies. The 20th State of the Art Symposium is therefore dedicated to discussing these **«Experimental Therapies in Multiple Sclerosis»**.

In the plenary morning sessions of the State of the Art Symposium six experts in the field will address individual topics within the theme of the Symposium. After a discussion on anti-viral therapies for the treatment of MS by **Gavin Giovannoni, Andreas Lutterotti** will discuss novel approaches for MS-treatment. **Aiden Haghikia** presents the influence of gut bacteria and nutrition on the development of MS. The first morning session will conclude with the highly valuated traditional update on current treatment options for MS by **Ludwig Kappos.**

The second morning session will be entirely dedicated to stem cell therapy in MS by the format of a podium discussion, which is novel to the State of the Art Symposium. After short statements favoring and questioning stem cell therapy given by **Roland Martin** and **Per Soelberg Sørensen,** respectively, both experts will be available for a podium discussion.

The afternoon session, with two sets of two parallel workshops, will address specific topics relevant to the daily practice. In Workshop A the speakers will present **«Patients' Needs for Personalized Treatment»** including first insights into the Swiss MS Registry and the Swiss MS Cohort Study. Workshop B is dedicated to the discussion of **«Neuroprotection in MS». «Apps and Video Games for MS Training»** will be discussed in Workshop C, while Workshop D will introduce **«Advances in the Fight against PML».**

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 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; Tobias Derfuss, Basel; Renaud Du Pasquier, Lausanne;
Christian Kamm, Lucerne; Patrice Lalive, Geneva; Sven Schippling, Zurich; Chiara Zecca, Lugano

Organisation

Swiss Multiple Sclerosis Society and its Scientific Advisory Board

Contact

Swiss Multiple Sclerosis Society, Josefstrasse 129, CH-8031 Zurich
symposium@multiplesklerose.ch, www.ms-state-of-the-art.ch

Credits

The Swiss Neurological Society will award **5 credit points**.
The Swiss Society of General Internal Medicine (SGAIM/SSMIG/SSGIM) will award **4.5 credit points**.

A special thanks to our sponsors

The Symposium is kindly supported by: Almirall AG, Biogen Switzerland AG, Celgene GmbH, Merck (Schweiz) AG, Novartis Pharma Schweiz AG, Roche Pharma (Schweiz) AG, Sanofi Genzyme und TEVA Pharma AG.

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Speakers (Lectures)

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Blizard Institute

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Prof. Per Soelberg Sørensen, Copenhagen (DK)
Rigshospitalet and University of Copenhagen
Danish Multiple Sclerosis Center

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Programme

Saturday, January 27th, 2018

Chairpersons	**Session 1:** Prof. Britta Engelhardt, Bern PD Dr. Christian Kamm, Lucerne
	Session 2: Prof. Sven Schippling, Zurich Dr. Chiara Zecca, Lugano
09.30 – 10.00	Welcome with Coffee and Gipfeli
10.00 – 10.10	Dr. Christoph Lotter, Zurich **Welcome from the Swiss MS Society**
10.10 – 10.35	Prof. Gavin Giovannoni, London (GB) **The Charcot Project: Anti-viral Therapies for Treating MS**
10.35 – 11.00	Prof. Andreas Lutterotti, Zurich **New Approaches to MS-Treatment**
11.00 – 11.25	Prof. Aiden Haghikia, Bochum (DE) **Gut Bacteria and Nutrition**
11.25 – 11.50	Prof. Ludwig Kappos, Basel **Update on New Therapies**
11.50 – 12.15	Coffee Break
12.15 – 12.30	Prof. Roland Martin, Zurich **HSCT – an Option for Patients with Aggressive Disease?**
12.30 – 12.45	Prof. Per Soelberg Sørensen, Copenhagen (DK) **HSCT – not the first Choice**
12.45 – 13.00	**Podium Discussion** **on Hematopoietic Stem Cell Transplantation** with Prof. Per Soelberg Sørensen and Prof. Roland Martin
13.00 – 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

Prof. Gavin Giovannoni

The Charcot Project: Anti-viral Therapies for Treating MS

There is increasing evidence to support the hypothesis that multiple sclerosis (MS) is either caused, or triggered, by an infectious agent, probably a virus.

The most compelling evidence points to Epstein-Barr Virus (EBV) as there is now overwhelming evidence that infection with EBV is essential to development of MS. Therefore, it appears that it is not possible to have adult MS without having previously been infected with EBV. However, the corollary is not true, so having EBV infection does not always lead to MS. Importantly, developing infectious mononucleosis (IM) increases your risk of developing MS. These observations underpin the MS prevention strategy of developing effective antiviral treatments and/or vaccines to treat IM and or prevent EBV infection, respectively.

How EBV causes MS is a moot point. One hypothesis involves the dysregulation of B and T-cells and underpins the trial of using cytotoxic T-cells targeting EBV-infected B-cells in MS. There is also a large amount of circumstantial evidence that disease-modifying therapies in MS may target memory B-cells, the cell population that host the EBV virus. Could effective MS therapies all be working via an EBV mechanism? EBV may be linked to Human Endogenous Retroviruses (HERVs). Following mapping of the human genome, scientists discovered that 8% of our genome is composed of viral DNA, which includes HERVs. It has been observed that EBV can up-regulate (activate) these HERVs, which could explain the key role that EBV plays in the pathogenesis of MS.

Using the NHS hospital statistics we have shown that HIV infection protects you from developing MS. We think this may be due to the use of highly-active antiretroviral therapies to treat HIV that may work against HERVs. The latter hypothesis underpinned our recently completed raltegravir trial in patients with active relapsing MS.

Prof. Gavin Giovannoni, London (GB)
Queen Mary University London
Blizard Institute

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1. Fachinformation Sativex® www.swissmedicinfo.ch
2. Novotna A et al, A randomized, double-blind, placebo-controlled, parallel-group, enriched-design of Nabiximols (Sativex®), as add-on therapy, in subjects with refractory spasticity caused by multiple sclerosis. Eur J Neurol 2011; 18 (9): 1122–31
3. Coghe G et al, Walking improvements with Nabiximols in patients with multiple sclerosis, J Neurol 2015; 262 (11): 2472–7

Gekürzte Fachinformation Sativex® Z: 1 Sprühstoss à 100 µl enthält 2,7 mg Delta-9-Tetrahydrocannabinol (THC) und 2,5 mg Cannabidiol (CBD). **I:** Symptomatische Behandlung von Patienten mit mittelschwerer bis schwerer Spastik aufgrund von Multipler Sklerose. Die Anwendung von Sativex® ausserhalb der zugelassenen Indikation bedarf einer Bewilligung des Bundesamtes für Gesundheit (BAG). **D:** Bis zu 12 Sprühstösse pro Tag. Dosisfindung abhängig vom Schweregrad der Symptomatik und in Absprache mit behandelndem Arzt. **KI:** Überempfindlichkeit gegenüber Cannabisextrakten oder einen der Hilfsstoffe gemäß Zusammensetzung; Suizidalität oder Suizidgedanken; bekannte oder vermutete (Familien-)Anamnese von Schizophrenie oder anderen Psychosen und erheblichen psychiatrischen Störungen; schwere Persönlichkeitsstörung oder andere erhebliche psychiatrischen Störung, mit Ausnahme von Depressionen in Verbindung mit Multipler Sklerose; Stillzeit. **VM:** Anwendung einer zuverlässigen Verhütungsmethode während der Anwendung und 3 Monate darüber hinaus (Männer und Frauen bzw. deren Partner); nicht anwenden während Schwangerschaft; nicht empfohlen bei Kindern und Jugendlichen unter 18 Jahren sowie schweren Herz-Kreislauf-Erkrankungen; häufig Schwindelanfälle insbesondere zu Beginn der Behandlung, erhöhtes Sturzrisiko; klinische Überwachung bei Beeinträchtigung der Leber- oder Nierenfunktion; Vorsicht bei Anamnese von Epilepsie, rezidivierenden Krampfanfällen sowie Suchtmittelmissbrauch. **Warnhinweise:** additive Wirkung mit Muskelrelaxantien möglich; psychiatrische Symptome; bei Desorientierung (oder Verwirrung), Halluzinationen, Wahnvorstellungen, vorübergehenden psychotischen Reaktionen sowie Suizidgedanken sollte Behandlung mit Sativex® umgehend abgebrochen werden mit sorgfältiger Überwachung bis zum vollständigen Nachlassen der Symptome; Reaktionen an der Anwendungsstelle; Screeningtests auf Drogenmissbrauch liefern positive Befunde; Auslandsreisen (Rechtsstatus von Sativex® länderspezifisch unterschiedlich). IA: Anwendung zu den Mahlzeiten erhöht THC-C_{max}- und THC-AUC-Werte um das 1,6 bzw. 2,8-fache, CBD-C_{max}- bzw. CBD-AUC-Werte um das 3,3- bzw. 5,1-fache. Gleichzeitige Behandlung mit CYP3A4-Inhibitoren (z.B. Ketoconazol, Ritonavir, Clarithromycin) erhöhte THC-C_{max}- bzw. THC-AUC-Werte um das 1,2- bzw. 1,8-fache, CBD-C_{max}- bzw. CBD-AUC-Werte um das 2- bzw. 2-fache. Gleichzeitige Behandlung mit CYP3A4-Induktoren (z.B. Rifampicin, Carbamazepin, Johanniskraut) reduzierte THC-C_{max}- bzw. THC-AUC-Werte um 40 % bzw. 20 %, Hauptmetaboliten um 85 % bzw. 87 % und CBD um 50 % bzw. 60 %. Laut in-vitro-Daten inhibitorische Wirkung von CBD auf p-Glykoprotein im Darm nicht ausgeschlossen. Vorsicht deshalb bei gleichzeitiger Behandlung mit Digoxin und anderen Arzneimitteln, die als Substrate für p-Glykoprotein dienen. Vorsicht bei Hypnotika, Sedativa und Arzneimitteln mit potentiell sedierender Wirkung (additiver Effekt hinsichtlich Sedierung und Muskelrelaxation möglich). Interaktionen mit Alkohol möglich (Beeinträchtigung von Koordination, Konzentration und Reaktionsfähigkeit). **Schwangerschaft:** Keine ausreichenden Daten zum Einfluss von Sativex® auf menschliche Reproduktion. Während der Therapie und 3 Monate darüber hinaus müssen Frauen im gebärfähigen Alter und zeugungsfähige Männer (bzw. deren Partner) eine zuverlässige Verhütungsmethode anwenden. Sativex® sollte nicht während der Schwangerschaft verwendet werden. Während der **Stillzeit ist Sativex® kontraindiziert**. **UW:** *Sehr häufig:* Müdigkeit (12 %), Schwindelanfälle (25 %). *Häufig* (1–10 %): Anorexia (inklusive verminderter Appetit), erhöhter Appetit, Depressionen, Desorientierung, Dissoziation, euphorische Stimmung, Amnesie, Gleichgewichtsstörungen, Aufmerksamkeitsstörungen, Dysarthrie, Dysgeusie, Lethargie, Gedächtnisstörungen, Schläfrigkeit, Verschwommenes Sehen, Vertigo, Verstopfung, Diarrhoe, Mundtrockenheit, Glossodynie, Mundschleimhautaphten, Nausea, Unbehagen und Schmerzen in der Mundhöhle, Erbrechen, Schmerzen an der Anwendungsstelle, Asthenie, Unbehagen, Trunkenheitsgefühl, Malaise, Sturz. UW < 1 %: siehe www.swissmedicinfo.ch. **P:** Packungen zu 3 Sprayflaschen à 10 ml [A+]. **Zulassungsinhaberin:** Almirall AG, Alte Winterthurerstr. 14, 8304 Wallisellen. Ausführliche Informationen siehe www.swissmedicinfo.ch. Stand der Information Dez 2015.

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Prof. Andreas Lutterotti

New Approaches to MS-Treatment

The treatment landscape of multiple sclerosis (MS) is increasing and continuously offering additional options for MS patients and their physicians. Although the efficacy of many novel therapies is improving, some of the therapeutic advances come at the cost of safety and tolerability. Other important aspects of the disease, such as disability progression secondary to neurodegeneration, are not efficiently targeted by current therapeutic approaches.

New treatment strategies aim to target more specifically the deleterious immune response via induction of antigen-specific immune tolerance. These approaches offer the opportunity of a highly specific intervention without altering the normal immune system and thus providing a favorable safety profile. Several new approaches are directed towards prevention of disability progression through different neuroprotective strategies. Choosing the adequate trial design and outcome parameter will be crucial for successful clinical development.

New approaches to MS treatment will hopefully improve patient care and add to the understanding of the disease.

Prof. Andreas Lutterotti, Zurich
University Hospital Zurich
Department of Neurology

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Prof. Aiden Haghikia

Gut Bacteria and Nutrition

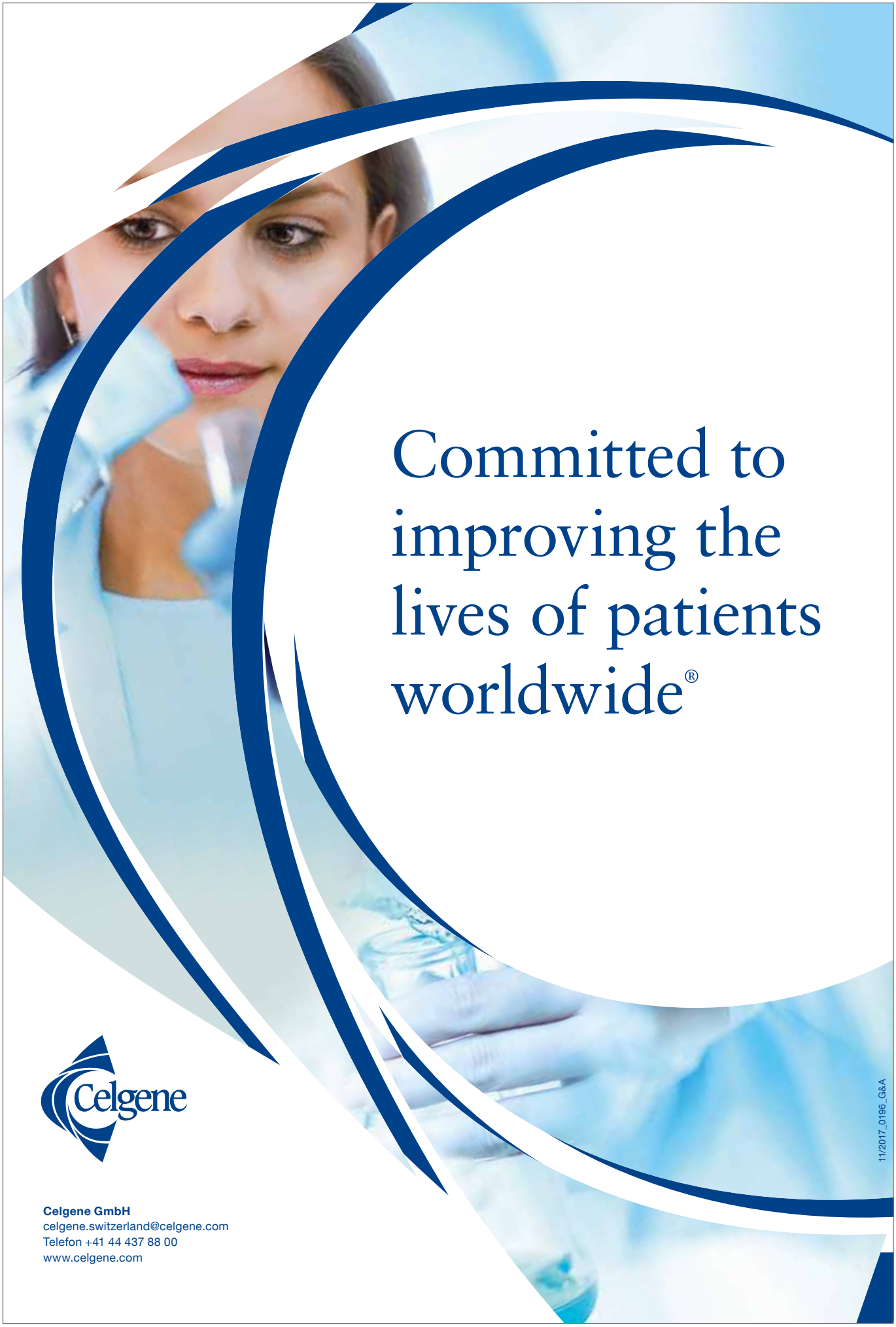
We recently showed the possible involvement of dietary fatty acids in multiple sclerosis (MS). In the animal model of MS, the experimental autoimmune encephalomyelitis (EAE), fatty acids as microbial byproducts modulate the gut associated immune system. While short chain fatty acids like propionic acid (PA) increased regulatory T cell (Treg) differentiation in vitro and ameliorate the course of EAE, long chain fatty acids (LCFA) foster T helper (Th) 17 differentiation and worsen clinical symptoms of EAE. Furthermore, we demonstrated that the microbiome composition during EAE was altered by LCFA-enriched diet which led to a shift in relative abundance of bacterial phyla.

We subsequently investigated the effect of orally applied PA on immune cell-phenotype, -function and corresponding cytokine parameters as well as individual microbiome composition and diversity of MS patients and healthy volunteers in a proof-of-concept study.

PA has been approved as food additive without safety concerns by European and American Food Safety Agencies. This study was performed at the Ruhr-University Bochum with a cohort of 90 MS patients (under diverse disease modifying treatments) and 30 healthy controls (HC). PA was administered at 500mg twice daily for 14 to up to 2 years. Immune phenotyping as well as functional in vitro assay were performed to study the immunomodulatory potential of PA. Furthermore we analyzed the individual microbiome by 16s ribosomal RNA sequencing of stool samples, which were collected before and during PA treatment.

PA was well tolerated with no reported side effects during the study period. Immune phenotyping displayed a significant reduction in pro inflammatory Th1 and Th17 cells after 14 days of PA intake, which was more prominent in MS patients. Concomitantly, Treg levels were increased after PA treatment. Additionally, we observed a significant increase in Treg modulatory capacities during PA treatment in MS patients. We also observed significant differences in the microbiome of MS patients versus healthy controls. Furthermore, MS patients displayed a significant reduction in the microbiome diversity, and differential clustering in MS subtypes. The retrospective evaluation of the clinical course of MS patients supplemented with PA suggests an additionally beneficial effect of PA on disease progression and relapse rate. In our current study, we translate our initial findings from the animal model to MS, and verify the influence of dietary fatty acids on the systemic immune response in humans as well as the importance of individual microbiome in association with MS. Hence, our findings suggest PA as a possible immune-modulatory supplement for application as add-on treatment to currently approved first line MS drugs.

Prof. Aiden Haghikia, Bochum (DE)
Ruhr-University Bochum, St. Josef-Hospital
Department of Neurology



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Prof. Ludwig Kappos

Update on New Therapies

2017 has been a year of both consolidation and innovation:

After successful phase III studies, Ocrelizumab is entering the stage in more and more countries, changing the way we are approaching both relapsing and primary progressive MS.

Second generation S1P modulators as Siponimod (relapsing and secondary progressive MS) or Ozanimod (relapsing MS) are queuing up for approval.

Cladribine, a lymphocyte selective cytostatic agent, is also entering the field after initial concerns regarding safety were alleviated.

In the still underdeveloped area of therapeutic options against neurodegeneration or promoting remyelination two new compounds, Ibudilast and Clemastine entered with promising phase II proof of concept results.

On the negative side, the indication for Daclizumab was restricted because of very seldom but severe hepatic adverse events. In a recent phase III study Laquinimod failed in fulfilling the expectations in relapsing MS. With systematic longterm extensions of controlled clinical trials and large observational studies, we learned more about the respective effectiveness and risk management of the second and third generation higher efficacy compounds and also about the integration of advanced and quantifiable clinical assessments, including electronic devices and neuropsychological tests with imaging measures to guide therapeutic decisions in daily care. Neurofilament light levels in serum have emerged as a valuable additional biomarker for therapeutic studies but hopefully also for individualized choices.

Prof. Ludwig Kappos, Basel
University Hospital Basel
Department of Neurology

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1. PRISMS Study Group. Randomised double-blind placebo-controlled study of interferon beta-1a in relapsing/remitting multiple sclerosis. PRISMS (Prevention of Relapses and Disability by Interferon beta-1a Subcutaneously in Multiple Sclerosis) Study Group. Lancet 1998 Nov 7;352(9139):1498-1504. **2.** PRISMS Study Group. PRISMS-4: Long-term efficacy of interferon-beta-1a in relapsing MS. Neurology 2001 Jun 26;56(12):1628-1636. **3.** Kappos L, et al. Long-term subcutaneous interferon beta-1a therapy in patients with relapsing-remitting MS. Neurology 2006 Sep 26;67(6):944-953. **4.** Kappos L, et al. Factors influencing long-term outcomes in relapsing-remitting multiple sclerosis: PRISMS-15. J Neurol Neurosurg Psychiatry 2015 Nov;86(11):1202-1207. **5.** Schwid S, Panitch HS. Full results of the Evidence of Interferon Dose-Response-European North American Comparative Efficacy (EVIDENCE) study: a multicenter, randomized, assessor-blinded comparison of low-dose weekly versus high-dose, high-frequency interferon beta-1a for relapsing multiple sclerosis. Clin Ther 2007 Sep;29(9):2031-2048. **6.** Fachinformation Rebif®, www.swissmedicinfo.ch, September 2015. **7.** SPECTRIMS Study Group. Randomized controlled trial of interferon- beta-1a in secondary progressive MS: Clinical results. Neurology 2001 Jun 12;56(11):1496-1504. **8.** Veugelers P, et al. Disease progression among multiple sclerosis patients before and during a disease-modifying drug program: a longitudinal population-based evaluation. Mult Scler 2009 Nov;15(11):1286-1294. **9.** De Stefano N, et al. Efficacy and safety of subcutaneous interferon β-1a in relapsing-remitting multiple sclerosis: further outcomes from the IMPROVE study. J Neurol Sci 2012 Jan;312(1-2):97-101. **10.** Uitdehaag BM, et al. The changing face of multiple sclerosis clinical trial populations. Curr Med Res Opin. 2011 Aug;27(8):1529-1537. **11.** Kurtzke JF. Rating neurologic impairment in multiple sclerosis: an expanded disability status scale (EDSS), Neurology. 1983 Nov;33(11):1444-52. **12.** De Stefano N, Comi G, Kappos L, et al. Efficacy of subcutaneous interferon β-1a on MRI outcomes in a randomised controlled trial of patients with clinically isolated syndromes. J Neurol Neurosurg Psychiatry 2014 Jun;85(6):647-653.

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Prof. Roland Martin

HSCT – an Option for Patients with Aggressive Disease?

Autologous hematopoietic stem cell transplantation (aHSCT) and hematopoietic stem cell transplantation in general have first been used in 1958, and 1990 E. Donnall Thomas was awarded the Nobel Prize in Physiology for the discovery of bone marrow transplantation. Since the middle of the 1990ˢ aHSCT has been pursued as a treatment for a number of severe autoimmune diseases, and most prominently among these, for multiple sclerosis (MS). Over the last more than two decades variations of transplant regimens with different intensities have been tested in well over 2'000 MS patients. Individual treatment experiences, small case series and mid-size to larger clinical trials have been conducted in the last 10 years. During this time the safety of aHSCT has steadily improved, and a better understanding was developed as to which patients are the best candidates, which is the best regimen and what the mechanism/s of action of aHSCT are. Several prospective studies have been conducted, although a large phase III trial similar to those that have been performed for the approved medications in MS is still missing, mainly from the reasons that there is no commercial interest in aHSCT and that public funding could therefore never be raised.

According to the current state of knowledge aHSCT is likely superior in efficacy to all existing medications for MS. Transplant-related mortality has dropped to below 0.5% in the last 5 years. The BEAM-ATG regimen or a regimen combining cyclophosphamide with T cell depletion are the most frequently used procedures for abrogation of the immune system, and data from our own laboratory has shown that a new T cell repertoire is established after aHSCT as its main mechanism of action. Patients with highly active relapsing-remitting MS, below 50 years of age, with a disability below 6 and within 10 years after diagnosis are the best candidates for aHSCT. Recent data supports that aHSCT can also be considered for some patients with progressive MS, as long as certain criteria are fulfilled.

Regarding the availability of aHSCT, this treatment is currently not available for MS patients although aHSCT is a routine treatment for several hematological and oncological diseases and also approved for an autoimmune disease, systemic sclerosis. In Sweden, aHSCT is reimbursed for the treatment in MS, and we are currently applying for reimbursement in Switzerland as well. The presentation will summarize the current state of using aHSCT in MS.

Prof. Roland Martin, Zurich
University Hospital Zurich
Department of Neurology

Eine Kapsel Normalität – jeden Tag[1–4#]

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* GILENYA® ist zur Behandlung von Patienten mit schubförmig remittierend verlaufender Multipler Sklerose (RRMS) zur Reduzierung der Schubhäufigkeit und zur Verzögerung des Fortschreitens der Behinderung indiziert.
# Bei der abgebildeten Person handelt es sich um keine Multiple Sklerose-Patientin, sondern um ein Model.

1 Ziemssen T et al. 4 years PANGAEA: A 5-year non-interventional study of safety, effectiveness and pharmacoeconomic data for fingolimod patients in daily clinical practice – effectiveness update, poster presented at 68th American Academy of Neurology (AAN) annual meeting, April 15–21, 2016, Vancouver, BC, Canada, P072. **2** Ziemssen T et al. 4 years PANGAEA: Effectiveness update of a 5 year non-interventional study on the daily use of fingolimod in Germany, poster presented at 32nd Congress of the European Committee for Treatment and Research in Multiple Sclerosis, September 14–17, 2016, London, United Kingdom, P1223. **3** Fox E et al. Outcomes of switching directly to oral fingolimod from injectable therapies: Results of the randomized, open-label,multicenter, Evaluate Patient OutComes (EPOC) study in relapsing multiple sclerosis. Mult Scler Realt Disord 2014 (3), 607–619. **4** Crayton H et al. Realworld patient retention and satisfaction on fingolimod versus platform injectable disease modifying therapies in early relapsing–remitting multiple sclerosis: results from PREFERMS, poster presented at 68th American Academy of Neurology (AAN) annual meeting, April 15–21, 2016, Vancouver, BC, Canada, P167. **5** Swissmedic, Zulassungen, GILENYA®, verfügbar unter: https://www.swissmedic.ch/zulassungen/00153/00189/00200/00927/index.html?lang=de, zuletzt eingesehen am 28. Dezember 2016. **6** Cohen JA et al. Fingolimod versus intramuscular interferon in patient subgroups from TRANSFORMS. J Neurol. 2013;260(8): 2023–32. **7** Khatri B et al. TRANSFORMS Study Group. Comparison of fingolimod with interferon beta-1a in relapsing-remitting multiple sclerosis: a randomised extension of the TRANSFORMS study. Lancet Neurol. 2011;10(6): 520–529. **8** Kappos L et al. for FREEDOMS Study Group. A placebocontrolled trial of oral fingolimod in relapsing multiple sclerosis. N Engl J Med. 2010;362(5): 387–401. **9** GILENYA® (Fingolimod) Fachinformation, Stand der Information: März 2016, www.swissmedicinfo.ch. **10** Zecca C et al. Real-life long-term effectiveness of fingolimod in a Swiss relapsing-remitting multiple sclerosis cohort. Poster presented at: 32nd Congress of the European Committee for Treatment and Research in Multiple Sclerosis; September 14–17, 2016; London, UK, poster 1219. **11** Derfuss T et al. The ACROSS study: Long-term efficacy of fingolimod in patients with RRMS (follow-up at 10 years). Poster presented at: 32nd Congress of the European Committee for Treatment and Research in Multiple Sclerosis; September 14–17, 2016; London, UK, poster 1219. **12** Novartis Q3 and 9M 2016 Condensed Interim Financial Report, verfügbar unter: https://www.novartis.com/sites/www.novartis.com/files/2016-10-interim-financial-report-en.pdf, zuletzt eingesehen am 28. Dezember 2016. **13** Cohen J et al. Ongoing safety and effectiveness: An interim analysis of long-term fingolimod treatment, poster presented at 68th American Academy of Neurology (AAN) annual meeting, April 15–21, 2016, Vancouver, BC, Canada, P3.057 **14** Seifer G et al. Cardiac Safety Profile of the First Dose Observation. III Interim Analysis (181 patients) of the Argentinean Registry of Patients Treated with Fingolimod (REAL Study), poster presented at 68th American Academy of Neurology (AAN) annual meeting, April 15–21, 2016, Vancouver, BC, Canada.

Z: Kapseln zu 0.5 mg Fingolimod. **I:** Behandlung von Patienten mit schubförmig remittierend verlaufender multipler Sklerose (MS) zur Reduzierung der Schubhäufigkeit und zur Verzögerung des Fortschreitens der Behinderung. **D:** 0.5 mg 1x täglich oral • Überwachung nach Erstgabe von Gilenya • *Spezielle Pat.-Gruppen:* s. www.swissmedicinfo.ch **KI:** Myokardinfarkt, instabile Angina pectoris, Schlaganfall/TIA, akut dekompensierte Herzinsuffizienz, Herzinsuffizienz NYHA-Klasse III/IV • Schwere Herzrhythmusstörungen • AV-Block 2. Grades vom Typ Mobitz II oder ein AV-Block 3. Grades oder Sick-Sinus-Syndrom, sofern nicht Schrittmacher-versorgt • QTc-Intervall ≥500 ms bei Baseline • Bestehendes Immundefizienzsyndrom • Erhöhtes Risiko für opportunistische Infektionen • Schwere aktive Infektionen oder aktive chronische Infektionen • Aktive maligne Erkrankungen • Mittlere und schwere Leberinsuffizienz/Leberzirrhose (entsprechend Child-Pugh-Klasse B und C) • Bestehendes Makulaödem • Kinder und Jugendliche • Schwangerschaft und Stillzeit • Überempfindlichkeit gegenüber Fingolimod oder einem der Hilfsstoffe. **VM:** Überwachung nachErstgabe von Gilenya: *Bei allen Patienten:* 6-stündige Überwachung auf Symptome einer Bradykardie sowie auf atrioventrikuläre Überleitungsstörungen; kardiale Überwachungsmassnahmen: stündliche Messungen Puls und Blutdruck, 12-Kanal-EKG vor Behandlungsbeginn und nach Überwachung, Möglichkeit einer kardiologischen Notfallbehandlung, kontinuierliche (Echtzeit-) EKG-Überwachung empfohlen. *Bei Auftreten von symptomatischen Bradyarrhythmien in den ersten 6 Stunden:* Überwachung bis zum vollständigen Abklingen der Symptome. *Wenn Herzfrequenz 6 Stunden nach Ersteinnahme den niedrigsten Wert erreicht:* kardiales Monitoring bis zur Erholung der Herzfrequenz (mind. jedoch um 2 Stunden verlängern). *Wenn im EKG 6 Stunden nach der 1. Dosis Herzfrequenz <45 Schläge/Min, persistierender neuer AV-Block 2. Grades oder höhergradiger AV-Block, QTc Intervall ≥500 ms oder wenn ein AV-Block 3. Grades zu jedwedem Zeitpunkt auftritt:* Verlängerung des kardialen Monitorings mind. über Nacht. *Falls nach der 1. Dosisgabe medikamentöse Behandlung aufgrund von Bradyarrhythmien notwendig ist:* Beobachtung über Nacht in einer med. Einrichtung und bei der 2. Dosis gleiche Überwachungsstrategie wie nach der 1. Dosis. Für bestimmte Pat.-Gruppen Gilenya nur dann erwägen, wenn der erwartete Nutzen die potentiellen Risiken überwiegt. *Patienten unter Betablockern, Calciumkanalblockern und anderen Substanzen die die Herzfrequenz reduzieren:* Generell von einer Behandlung mit Gilenya absehen • *Bei Patienten mit signifikanter QTc-Verlängerung vor Behandlungsbeginn oder zusätzlichen Risikofaktoren für das Auftreten einer QT-Verlängerung:* vor Behandlungsbeginn eine/n Kardiologen/in konsultieren und geeignetes kardiales Monitoring festlegen. • Regelmässige Blutbildkontrollen: Aktuelles, grosses Blutbild (inkl. Differentialblutbild) vor Einleitung der Behandlung, in Monat 3 und danach regelmässig (mind. jährlich), sowie bei Anzeichen einer Infektion. Bei Gesamtlymphozytenzahl <0.1x10^9/l Behandlung pausieren. Bei Gesamtlymphozytenzahl <0.2x10^9/l Differentialblutbild mind. alle 3 Monate. Bei schweren aktiven Infektionen oder aktiven chronischen Infektionen mit Behandlung abwarten. Bei Infektionen während der Therapie geeignete diagnost. und therapeut. Massnahmen, v.a. bei Viren der Herpesgruppe. Gleichzeitige Anwendung einer antineoplastischen, immunsupprimierenden oder immunmodulierenden Therapie vermeiden, Behandlung mit Corticosteroiden nach klinischem Ermessen. Seit Markteinführung wurden Fälle progressiver multifokaler Leukenzephalopathie (PML) dokumentiert. Auf Symptome bzw. MRT-Befunde achten, die auf PML hindeuten. Bei Verdacht auf PML Behandlung unterbrechen, bis PML ausgeschlossen werden kann. Seit Markteinführung sind einzelne Fälle von Kryptokokkeninfektionen einschliesslich Kryptokokkenmeningitis berichtet worden. Patienten mit Verdacht auf eine Kryptokokkenmeningitis sollten umgehend diagnostisch beurteilt werden. Wird eine Kryptokokkenmeningitis diagnostiziert, ist eine geeignete Behandlung einzuleiten. • Anwendung von attenuierten Lebendimpfstoffen vermeiden. Varizella-Zoster-Virus Antikörperbestimmung und Impfung von antikörpernegativen Patienten • Augenärztliche Untersuchung vor Beginn und nach 3 bis 4 monatiger Therapie. Visusuntersuchungen alle 6 Monate. Regelmässige ophthalmologische Untersuchungen bei Patienten mit Diabetes mellitus, Uveitis und Makulaödem • Bestimmung der Leberwerte vor Beginn und 1, 3, 6, 9 und 12 Monate nach Beginn der Therapie, im weiteren Verlauf periodisch. Bei wiederholtem Nachweis von >5x Transaminasenerhöhung: Gilenya absetzen bis sich Werte normalisiert haben. Vermeiden von zusätzlicher Einnahme von lebertox. Substanzen, nicht behandeln bei Leberzirrhose, Leberinsuffizienz, und bei Hepatitis B Infektionen • Blutdruck regelmässig kontrollieren • Bei Verdacht auf posteriores reversibles Enzephalopathie Syndrom Gilenya absetzen • Pulmonologische Untersuchung bei symptomatischen Patienten • Basalzellkarzinome traten unter der Behandlung mit Gilenya auf. Eine regelmässige dermatologische Überwachung ist empfohlen. • Bei der Umstellung von anderen immunsuppressiven oder immunmodulierenden Therapien auf Gilenya ist Vorsicht geboten. Bei Natalizumab und Teriflunomid Halbwertszeit berücksichtigen. Umstellung von Alemtuzumab nicht empfohlen • Überwachung auf Infektionen bis zu 2 Monate nach Absetzen der Therapie fortsetzen • Weitere Einzelheiten s. www.swissmedicinfo.ch. **IA:** Antineoplastische, immunsuppressive oder immunmodulierende Therapien (inkl. Kortikosteroide) • Umstellung von lang wirkenden Immuntherapeutika (Natalizumab, Teriflunomid oder Mitoxantron) • Attenuierte Lebendimpfstoffe und andere Impfstoffe • Betablocker, Calciumkanalblocker mit verlangsamender Wirkung auf die Herzfrequenz oder andere Substanzen, die die Herzfrequenz verlangsamen können • Ketoconazol • Carbamazepin. Weitere Einzelheiten s. www.swissmedicinfo.ch **UW:** *Sehr häufig:* Grippale Virusinfektionen, Sinusitis, Kopfschmerzen, Durchfall, Rückenschmerzen, erhöhte Leberenzyme, Husten • *Häufig:* Bronchitis, Herpes Zoster, Tinea Versicolor, Basalzellkarzinom, Bradykardie, atrioventrikuläre Blocks, Schwindel, Migräne, Asthenie, Ekzem, Pruritus, erhöhte Bluttriglyzeride, Atemnot, Verschwommensehen, Hypertonie, Leukopenie, Lymphopenie • *Gelegentlich:* Pneumonie, Makulaödem • *Selten und sehr selten* s. www.swissmedicinfo.ch. **P:** Kapseln zu 0.5 mg: 28* und 98*. Verkaufskategorie: **B.** *Kassenzulässig. Weitere Informationen finden Sie unter www.swissmedicinfo.ch. April 2016 V9. Novartis Pharma Schweiz AG, Risch; Adresse: Suurstoffi 14, 6343 Rotkreuz, Tel. 041 763 71 11.

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Prof. Per Soelberg Sørensen

HSCT – not the first Choice

During the last decades we have witnessed an evolution in disease-modifying drugs (DMDs) for treatment of relapsing-remitting multiple sclerosis (RRMS). These treatments have been increasingly effective, in particular the introduction of the therapeutic monoclonal antibodies, natalizumab and alemtuzumab.

Intense immunosuppression followed by autologous haematopoietic stem cell transplantation (HSCT) has been used to treat patients with MS for more than 2 decades. Recent studies have reported very positive results, in particular in highly active patients in early course of MS. Although the treatment-associated mortality of HSCT has decreased in recent years, in particular when low intensity non-myeloablative conditioning with cyclophosphamide was applied, overall it is still counted in percentages.

Treatment with the monoclonal antibodies natalizumab and alemtuzumab in particular may match the efficacy of the most recent series of HSCT. In the CARE-MS 1 study 61% of patients treated with alemtuzumab with NEDA-3 after 2 years had still NEDA-3 after 5 years without additional therapy. Ocrelizumab or cladribine therapy results in NEDA-3 in 48% or 47%, respectively, after 2 year's treatment.
The treatment-associated mortality in JC virus antibody negative patients treated with natalizumab and in patients treated with alemtuzumab using risk minimization programmes is below one per thousand, and the newly approved therapies, ocrelizumab and cladribine, seem to have very favourable risk-benefit profiles.

A controlled trial comparing HSCT with an effective DMD is warranted, but may not achievable.

Hence, intensive immunosuppression with HSCT should remain a third-line therapy. Patients failing a first-line therapy should be offered treatment with an effective second-line therapy before HSCT. However, patients failing more than one DMD should be offered the choice of HSCT without any unnecessary delay.

Prof. Per Soelberg Sørensen, Copenhagen (DK)
Rigshospitalet and University of Copenhagen
Danish Multiple Sclerosis Center

Roche

Bei schubförmiger Multipler Sklerose (RMS)
Wann wird eine **hochwirksame** Therapie[1] am meisten benötigt?

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der MRI-Aktivität im Vergleich zu hochdosiertem Interferon beta-1a[2,3]

ÜBERLEGENE KLINISCHE ERGEBNISSE
Reduzierte Schubrate und reduziertes Risiko für Behinderungsprogression im Vergleich zu hochdosiertem Interferon beta-1a[2,3]

ÄHNLICHES VERTRÄGLICHKEITS-PROFIL
im Vergleich zu hochdosiertem Interferon beta-1a[2-4]

INFUSION ALLE 24 WOCHEN§
Keine JCV- oder kardiovaskulären Tests sowie kein Monitoring zwischen den Infusionen notwendig[2]

JCV = John Cunningham Virus. *Mit 600 mg Ocrelizumab i. v. alle 24 Wochen verglichen mit hochdosiertem Interferon beta-1a (44 µg dreimal wöchentlich) bei Patienten mit schubförmiger MS.[3] §Nach der Anfangsdosis mit zwei 300-mg-Infusionen an Tag 1 und Tag 15. **Referenzen:** 1. Vargas DL et al. Update on disease-modifying therapies for multiple sclerosis. J Investig Med. 2017 Jan 27. pii: jim-2016-000339. doi: 10.1136/jim-2016-000339. 2. OCREVUS Fachinformation, www.swissmedicinfo.ch 3. Hauser SL et al. Ocrelizumab versus interferon β-1a in relapsing multiple sclerosis. N Engl J Med. 2017;376(3):221-234. 4. Hauser SL et al. Ocrelizumab versus interferon β-1a in relapsing multiple sclerosis (Supplementary appendix). N Engl J Med. 2016. http://www.nejm.org/doi/suppl/10.1056/NEJMoa1601277/suppl_file/nejmoa1601277_appendix.pdf. Accessed January 3, 2017.

OCREVUS® (Ocrelizumab). Rekombinanter humanisierter monoklonaler (Anti-CD20-) Antikörper. **I:** Erwachsene Patienten mit aktiven schubförmigen Verlaufsformen der Multiplen Sklerose (MS). Erwachsene Patienten mit primär progredienter Multipler Sklerose (PPMS) zur Verlangsamung der Krankheitsprogression und zur Reduzierung der Verschlechterung der Gehgeschwindigkeit. **D:** *Anfangsdosis:* 600 mg auf zwei separate i.v. Infusionen zu jeweils 300 mg im Abstand von zwei Wochen. *Nachfolgende Dosen:* Einzeldosis von 600 mg alle 6 Monate. *Prämedikation:* Methylprednisolon 100 mg i.v. oder Äquivalent und ein Antihistaminikum vor jeder Infusion. **KI:** Überempfindlichkeit gegen Ocrelizumab oder einen der Hilfsstoffe, schwere Herzinsuffizienz (NYHA-Stadium IV), schwere Immunsuppression, aktive Infektion, bestehende aktive maligne Erkrankungen mit Ausnahme von kutanem Basalzellkarzinom, Therapiebeginn während der Schwangerschaft. **VM:** *Infusionsbedingte Reaktionen:* Bei Patienten mit schweren pulmonalen Symptomen (Bronchospasmus, Asthma-Exazerbation) Infusion sofort und dauerhaft abbrechen; ein erniedrigter Blutdruck kann während jeder OCREVUS-Infusion auftreten, daher Unterbrechung antihypertensiver Behandlung 12 Stunden vor und während jeder Infusion in Betracht ziehen. *Überempfindlichkeitsreaktionen:* können auftreten, in der Regel aber nicht während der ersten Infusion. In diesem Fall Infusion sofort und dauerhaft stoppen. *Infektionen:* Bei aktiver schwerer Infektion (z. B. Tuberkulose, Sepsis, opportunistische Infektionen) oder eingeschränkter Immunabwehr (z. B. stark reduzierte CD4 oder CD8 Zellzahl) nicht verabreichen. Bei aktiver Infektion mit der OCREVUS-Infusion zuwarten, bis die Infektion abgeheilt ist. In den klinischen Studien mit OCREVUS sind bislang keine PML-Fälle aufgetreten. Falls eine PML auftritt, ist die Behandlung dauerhaft abzubrechen. HBV-Screening bei allen Patienten vor Behandlungsbeginn mit OCREVUS durchführen. *Immunsuppressiva:* mit Ausnahme von Kortikosteroiden zur symptomatischen Behandlung von Schüben keine Empfehlung gleichzeitiger Anwendung von anderen Immunsuppressiva und OCREVUS. *Impfungen:* Impfstatus von Patienten überprüfen und die gültigen Impfempfehlungen für Schutzimpfungen vor der Behandlung mit OCREVUS beachten, Impfungen mindestens 6 Wochen vor der ersten OCREVUS-Anwendung abschliessen. *Fahrtüchtigkeit:* Einfluss der Prämedikation mit Antihistaminika beachten. **IA:** Es wurden keine formalen Arzneimittel-Interaktionsstudien durchgeführt. Ein Risiko für Interaktionen mit gleichzeitig angewendeten Arzneimitteln kann nicht ausgeschlossen werden. **SS/St:** OCREVUS während einer Schwangerschaft nicht anwenden, es sei denn, der mögliche Nutzen für die Mutter überwiegt gegenüber dem möglichen Risiko für den Fötus. Das Stillen während der Ocrelizumab Therapie einstellen. **UAW:** *Sehr häufig:* Infusionsbedingte Reaktionen, Infektion der oberen Atemwege, Nasopharyngitis, Influenza, verminderte IgM-Serumspiegel. *Häufig:* Bronchitis, Sinusitis, Gastroenteritis, virale Infektion, oraler Herpes, Infektion der Atemwege, Zellulitis, Herpes Zoster, Konjunktivitis, Husten, Katarrh, verminderte IgG-Serumspiegel. **P:** 1 Durchstechflasche zu 10 ml enthält 300 mg Ocrelizumab. **Abgabekat.:** A. **Stand:** Juni 2017. Weitere Informationen entnehmen Sie bitte der publizierten Fachinformation (www.swissmedicinfo.ch).

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Prof. Per Soelberg Sørensen

Prof. Roland Martin

Podium Discussion on Hematopoietic Stem Cell Transplantation

Since HSCT is a topic discussed quite controversially, two renowned experts will gather for a podium discussion: Roland Martin will propagate the benefits, while Per Soelberg Sørensen will underline the risks involved in this therapy. The audience is encouraged to actively participate and ask questions.

Prof. Per Soelberg Sørensen, Copenhagen (DK)
Rigshospitalet and University of Copenhagen
Danish Multiple Sclerosis Center

Prof. Roland Martin, Zurich
University Hospital Zurich
Department of Neurology

Workshops
Saturday, January 27th, 2018

Clinical Case Management
These four workshops focus on aspects relevant to the daily management of MS patients.

14.15 – 15.00 **Workshop A: «Patients' Needs for Personalised Treatment»**
PD Dr. Jens Kuhle, Basel and PD Dr. Viktor von Wyl, Zurich
- P4 Medicine in MS: Predictive, Preventive, Personalized & Participatory
- Swiss MS Registry: Bringing Patients' Perspectives into P4 Medicine
- Swiss MS Cohort Study: A Cornerstone for Swiss P4 Medicine
- Case Study: Towards a Biomarker for Personalised Treatment Decisions

Workshop B: «Neuroprotection in MS: Medical Needs and already existing Opportunities»
Prof. Roland Martin, Zurich and Prof. Nicole Schaeren-Wiemers, Basel
- Neuroprotection for which Forms of MS and at which Stage?
- Off-label use of existing Neuroprotective Compounds
- Are there any endogenous Neuroprotective Mechanisms known in MS?
- A View from the Molecular and Cellular Side of the Central Nervous System

15.00 – 15.20 Coffee Break

15.20 – 16.05 **Workshop C: «Apps and Video Games for MS-Training»**
Dr. Marcus D'Souza, Basel and Dr. Tim Vanbellingen, Lucerne
- Sensorless Movement Monitoring
- Exergaming
- Tablet-App based Training, a Possibility for Tele-Rehab
- Video-Game Virtual Reality Dextery Training

Workshop D: «Advances in the Fight against PML»
Dr. Ivan Jelcic, Zurich and Prof. Renaud Du Pasquier, Lausanne
- Novel Insights into Antibody Responses in PML
- Development of targeted Immunotherapy for PML - a realistic Possibility?
- Too much of a good Thing: the Fight against PML versus the Risks of IRIS

16.05 Farewell Apero

PD Dr. med. Jens Kuhle

PD Dr. sc. Viktor von Wyl

Workshop A

«Patients' Needs for Personalised Treatment»

The P4 Medicine concept calls for a paradigm shift by not simply treating a disease but to «maximize wellness» for patients. Along these lines, the four «Ps» stand for predictive, preventive, personalized and participatory health care. Although frequently used in the context of Genomics (and other –omics disciplines), the P4 Medicine concept also lends itself to a broader application in multiple sclerosis (MS) care and maintenance of wellness. Yet, the P4 Medicine concept is not without challenges, which, for the most part, are not only technical but also social. For example, some physicians may still be skeptical towards the participatory aspects of P4, which implies stronger involvement of persons with MS (PwMS) in decision making and recognition of their expertise regarding their own well-being.

In this workshop, we will argue that Switzerland is in a unique position to study the implementation and outcomes of MS P4 Medicine by combining data from the Swiss Multiple Sclerosis Registry (SMSR) and the Swiss Multiple Sclerosis Cohort Study (SMSC). The SMSR is a participatory, nationwide, longitudinal, observational study that mostly relies on self-reported information from PwMS, although some clinical data are collected for validation purposes. Since its launch in June 2016, the SMSR has recruited 1'600 participants and received nearly 3'000 surveys (including follow-up assessments). Major goals of the SMSR are to estimate the number of persons with MS living in Switzerland, and to comprehensively describe the life circumstances and clinical MS course of PwMS.

By contrast, the SMSC has a stronger emphasis on collection of high-quality clinical information. It is a prospective cohort of MS patients with standardized collection of demographic, clinical, MRI data and body fluids that can be used to develop prognostic indicators and biomarkers of disease evolution and therapeutic response. Meanwhile 1'168 patients have been recruited between June 2012 and August 2017. 4'775 visits with a median follow-up of 35 months have been performed and serum, plasma and whole blood samples collected at 4,724 individual time-points. In addition, 2'753 brain MRI scans have been acquired according to a standardized MRI protocol.

Recently, the SMSC has achieved an important step towards a breakthrough in treatment personalization by assessing the predictive value of serum neurofilament (NfL) measurements for therapy outcomes. The results indicate that this exclusively neuronally expressed protein has the potential to be employed in clinical routine as a sensitive and clinically meaningful blood biomarker to monitor tissue damage and the effects of therapies in MS. Building upon these encouraging findings, we will discuss how the collaboration between the SMSR and SMSC could contribute to the impact of routine NfL measurements on the other three dimensions of P4 Medicine and on the patients' well-being in general.

PD Dr. Jens Kuhle, Basel
University Hospital Basel
Neurologic Clinic and Policlinic

PD Dr. Viktor von Wyl, Zurich
University of Zurich
Epidemiology, Biostatistics & Prevention Institute

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Prof. Roland Martin

Prof. Nicole Schaeren-Wiemers

Workshop B

«Neuroprotection in MS: Medical Needs and already existing Opportunities»

Chronic injury of the CNS in MS is attributed primarily to ongoing inflammation and neurodegenerative mechanisms such as chronic demyelination and axonal damage, which lead in the long run to progressive neurological deficits. It became more and more evident that CNS damage cannot be prevented by using only immunomodulatory drugs, and there is a need for neuro- and myelin-protective therapies in MS.

Neuroprotection aims to prevent irreversible damage of myelin, oligodendrocytes and their axons, which are very vulnerable to the toxic (micro-)environment occurring in the MS brain. Neuroprotective strategies aim at different pathomechanisms including oxidative stress, ion imbalance, energy failure due to mitochondrial damage and metabolic changes, as well as remyelination to name a few. Substantial progress has been made regarding the basic mechanisms of remyelination and how to influence the above mechanisms. Some of these strategies are now being developed for clinical use or have already entered testing in clinical trials. We expect that this field will expand in the near future.

For patients and neurologists it is of interest that neuro- or myelin-protective activities have already been shown for several drugs that are in clinical use and approved for other indications either in animal models, in vitro systems or early phase clinical testing. We will discuss the off-label use of these. The aim is to impede progressive degenerative processes and support endogenous neuroprotective mechanisms in MS which would improve the quality of life of MS patients. It might be that neuroprotective therapies do not directly target disease specific processes; still they target endogenous repair mechanisms and can be useful for other neurodegenerative diseases as well.

Prof. Roland Martin, Zurich
University Hospital Zurich
Department of Neurology

Prof. Nicole Schaeren-Wiemers, Basel
University Hospital Basel,
Department of Biomedicine
University of Basel, Neurobiology Laboratory

TEVA Pharma

COPAXONE® Z: 1 Fertigspritze enthält 40 mg/ml Glatirameracetat, Mannitol, Aqua ad iniectabilia. **I:** Behandlung der schubförmigen multiplen Sklerose (MS). COPAXONE® ist nicht indiziert bei primär oder sekundär progredienter MS. **D:** Empfohlene Dosierung bei Erwachsenen: 40 mg COPAXONE®, entsprechend einer Fertigspritze, als dreimal wöchentliche s.c. Injektion im Abstand von mind. 48h. Kinder resp. Jugendliche und ältere Patienten sowie spezielle Dosierungsanweisungen siehe Arzneimittelinformation. **KI:** Bekannter Hypersensibilität gegenüber Glatirameracetat oder Mannitol. **V:** Ausschliesslich s.c. injizieren, Regelmässige Kontrolle von Patienten mit Herzkrankheiten oder Niereninsuffizienz. **UW:** Sehr häufig: Infektion, Influenza, Angst, Depression, Kopfschmerzen, Vasodilatation, Dyspnoe, Übelkeit, Rash, Arthralgien, Rückenschmerzen, Asthenie, Brustschmerzen, Reaktionen an der Injektionsstelle, Schmerzen Häufig: Bronchitis, Gastroenteritis, Herpes simplex, Otitis media, Rhinitis, Zahnabszess, Candida-Mykose der Vagina, benigne Neoplasien der Haut, Neoplasien, Lymphadenopathie, Hypersensibilität, Anorexie, Gewichtszunahme, Nervosität, Geschmacksstörungen, spastisch erhöhter Muskeltonus, Migräne, Sprachstörungen, Synkope, Tremor, Diplopie, Funktionsstörungen der Augen, Ohrenschmerzen, Herzklopfen, Tachykardie, Husten, saisonale Rhinitis, anorektale Funktionsstörungen, Obstipation , Zahnkaries, Dyspepsie, Dysphagie, Darminkontinenz, Erbrechen, abnormaler Leberfunktionstest, Ekchymose, Schwitzen, Juckreiz, Störung der Haut, Urtikaria, Nackenschmerzen, Harndrang, häufiges Harnlassen, Harnretention, Schüttelfrost, Gesichtsödem, Atrophie an der Injektionsstelle, lokale Reaktionen, peripheres Ödem, Ödem, Fieber. **IA:** Sind nicht systematisch untersucht worden. **Liste:** B. Weiterführende Informationen siehe Arzneimittelinformation www.swissmedicinfo.ch. Teva Pharma AG, Kirschgartenstrasse 14, 4010 Basel, www.tevapharma.ch. [4017]

12/2017

Dr. Marcus D'Souza

PD Dr. Tim Vanbellingen

Workshop C

«Apps and Video Games for MS-Training»

Multiple sclerosis (MS) is a chronic and heterogeneous disease associated with long-term disability, negatively influencing quality of life of the patients. Tracking the course of MS is challenging. New training methods such as virtual reality (VR) training and tablet-based tools seem to be promising to further enhance body functions, therefore contributing to better quality of life (QoL) in patients with MS. Video-game-based training might be a feasible tool to improve manual dexterity in MS patients. For more consistent tracking of motor dysfunction in MS, the «Assess MS system» provides a sensor-less capture of movements. This machine learning algorithm based system might be used in a home setting, allowing more frequent monitoring of neurological dysfunction in an interactive manner.

This workshop will demonstrate latest developments with regard to tablet App based and Video-game based training in MS. It will also provide an overview of tools attempting to track the course of MS, taking into account the patient's and doctor's perspectives.

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Prof. Renaud Du Pasquier

Dr. Ivan Jelcic

Workshop D

«Advances in the Fight against PML»

Progressive multifocal leukoencephalopathy (PML) is due to the reactivation of the polyomavirus JC (JCV), which infects oligodendrocytes, and to a lesser extent astrocytes and neurons, leading to severe demyelination. This JCV reactivation occurs in the setting of immunosuppression (HIV/AIDS; hemopathies, chemotherapies, etc.), but can also occur in MS patients who are not immunosuppressed. In the latter case, PML occurs in the context of disease modifying treatment (DMT), in particular natalizumab. Some cases also occurred in patients on fingolimod and dimethyl-fumarate.

The cellular immune response plays a key role in preventing the onset of PML and, once the disease has started, in limiting the extent of infection. However, by definition, such a response can often not take place in immunosuppressed patients. Thus, everything must be done to reconstitute the JCV-specific immune response in PML patients. However, sometimes this response is too brisk or too strong, with massive influx of T cells to the brain, an inflammatory response which in itself can be deleterious. This condition is named Immune Reconstitution Inflammatory Syndrome (IRIS).

For a long time, the contribution of JCV-specific humoral immunity to controlling asymptomatic infection throughout life and to eliminating JCV from the brain has been poorly understood. JCV-specific antibody responses have been primarily identified as surrogate markers for PML and thus are usually measured to stratify the patients at risk of developing PML. A number of recent data now provided novel insights into peripheral and intrathecal JCV-specific antibodies in PML and PML-IRIS. Most notably, PML patients revealed significant «recognition holes» in their antibody responses against PML-associated JCV VP1 variants. Immune reconstitution then leads to a rise of CSF antibody titers, particularly to broadened antibody responses against PML-associated JCV VP1 variants and elimination of the virus. Approaches to boost immunity against JCV in PML patients by vaccinating actively with JCV VP1 protein or

peptides resulted not only in substantially reduced CSF viral load and slower progression of PML, but also broadened the humoral response against JCV VP1 variants. Based on these data, highly potent neutralizing JCV VP1-specific antibodies were generated which represent promising candidates for the development of a passive immunization of PML patients.

This workshop should provide tools to understand the concept of JCV-specific cellular and humoral immune responses, why immunotherapeutic approaches for PML may be feasible and help to discriminate between classical PML and PML-IRIS. Such a recognition is important as treatments differ.

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We thank you for your participation and wish you a safe journey home.

See you next year at the
21th State of the Art Symposium,
Saturday, January 26th, 2019.

Best regards
Swiss Multiple Sclerosis Society

MS Swiss Multiple Sclerosis Society

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