

## Late-breaking Abstracts

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Late Breaking News: General

### OPR-200

#### Erenumab Versus Topiramate for the Prevention of Migraine: Results of a Randomised Active-controlled Double-dummy Trial

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**Background and aims:** Erenumab (erenumab-aooe in the US) is a fully human monoclonal antibody that inhibits the calcitonin gene-related peptide (CGRP) receptor and approved by the Food & Drug Administration and European Medicines Agency as the first medication specifically developed for migraine prevention. HER-MES is the first Head-to-head study of Erenumab against topiramate-Migraine study to assess tolerability and efficacy in a patient-centered Setting (NCT03828539).

**Methods:** In this 24-week double-blind, double-dummy treatment epoch (DBTE), a German cohort of 777 adult migraine patients with  $\geq 4$  monthly migraine days (MMD) received either erenumab 70mg or 140mg/month subcutaneously (investigator's choice) and an oral placebo or a subcutaneous placebo and the maximum tolerated dose of oral topiramate (50–100 mg/day; control group). The primary endpoint of tolerability was assessed by the rate of treatment discontinuation due to adverse events (AEs). The secondary endpoint addressing efficacy was assessed by the proportion of patients achieving  $\geq 50\%$  reduction from baseline MMD over Months 4, 5, and 6.

**Results:** Both primary and secondary endpoints were met, showing a significant difference between erenumab and topiramate. During the DBTE, 10.6% of patients receiving erenumab and 38.9% of patients receiving topiramate discontinued study treatment due to AEs. Additionally, the 50% responder rate was significantly higher for erenumab compared to topiramate.

**Conclusion:** The results of this first head-to-head trial of a therapy targeting the CGRP pathway compared to a preventive standard-of-care therapy will provide guidance for clinical decision-making for the preventive treatment of migraine.

**Disclosure:** This study was funded by Novartis. Detailed author disclosures will be provided in the oral/poster presentation.

### OPR-201

#### Onasemnogene Apeparvovec for Presymptomatic Infants with Spinal Muscular Atrophy and 2 Copies of SMN2: A Phase III Study

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**Background and aims:** Patients with spinal muscular atrophy type 1 (SMA1), a neurodegenerative disease, never achieve independent sitting and either die or require permanent ventilation by 2 years of age if untreated. This Phase III study (SPRINT) investigated the efficacy and safety of onasemnogene apearvovec in presymptomatic patients at risk of SMA1.

**Table 1. Demographics and Baseline Clinical Characteristics in SPRINT Two-Copy Patients**

	All Patients (N=14)
Mean ± SD (range) age at baseline, days	20.6 ± 7.9 (8–34)
Mean (SD) gestational age at birth, weeks	38.2 (1.4)
Mean (SD) age at diagnosis, days <sup>a</sup>	7.2 (4.8)
Mean (SD) weight at baseline, kg	3.6 (0.39)
Sex, n (%)	
Male	4 (28.6)
Female	10 (71.4)
Race, n (%)	
White	7 (50.0)
Other	4 (28.6)
Black or African American	1 (7.1)
Asian	2 (14.3)
American Indian or Alaska Native	0
Native Hawaiian or other Pacific Islander	0
Ethnicity, n (%)	
Not Hispanic or Latino	10 (71.4)
Hispanic or Latino	4 (28.6)
Informative family history of ≥1 sibling(s) with SMA, n (%)	6 (42.9)
Method of SMA diagnosis, n (%)	
Prenatal testing	5 (35.7)
Newborn screening	9 (64.3)

<sup>a</sup>n=9 patients diagnosed after birth

**Methods:** 14 presymptomatic patients with biallelic SMN1 deletions and two SMN2 copies were enrolled. Primary endpoint was independent sitting for ≥30 seconds (Bayley-III #26) by 18 months. Secondary endpoints were survival (no death/permanent ventilation) at 14 months and maintaining body weight (≥3<sup>rd</sup> WHO percentile) without feeding support at any visit. Safety evaluations included adverse events (AEs), concomitant medications, physical examinations, vital signs, cardiac indices, and laboratory data. End-of-study data were analysed.

**Table 2. Primary and Secondary Results in SPRINT**

	Onasemnogene abeparvovec 1.1 x 10 <sup>14</sup> vg/kg (N=14)	PNCr (N=23)
<b>Primary endpoint: Independent sitting ≥30 seconds at any visit up to 18 months of age<sup>b,c,d,e</sup></b>		
n (%)	14 (100.0)	0 (0)
97.5% CI	76.8, 100.0	
p-value	<0.0001	
<b>First secondary endpoint: Event-free survival at 14 months of age<sup>d,f,g</sup></b>		
n (%)	14 (100.0)	6 (26.1)
Difference from PNCr		
Difference	73.9	
95% CI for difference	44.7, 91.6	
p-value	<0.0001	
<b>Second secondary endpoint: Maintenance of weight (≥3<sup>rd</sup> WHO percentile without feeding support at any visit up to 18 months of age<sup>d,h,i</sup></b>		
n (%)	13 (92.9%)	0 (0)
97.5% CI	66.1, 99.8	
p-value	<0.0001	
Does not receive nutrition through mechanical support	14 (100.0)	
Maintains weight consistent with age at all visits	13 (92.9%)	

CI, confidence interval; PNCr, Pediatric Neuromuscular Clinical Research; WHO, World Health Organization.

<sup>a</sup>A one-sided exact binomial test was used to test the null hypothesis of a p≤0.1% at significance level of 0.025.

<sup>b</sup>The corresponding 97.5% CI was estimated by the exact method for binomial proportions.

<sup>c</sup>Milestone is confirmed by independent central review.

<sup>d</sup>Versus Pediatric Neuromuscular Clinical Research (PNCr) natural history data for SMA1 (n=23).

<sup>e</sup>Bayley Scales Item #26.

<sup>f</sup>Formal testing for the primary and secondary efficacy endpoints was performed using a hierarchical approach to protect against Type I error as follows. First, the primary endpoint of independent sitting ≥30 seconds was assessed. If the analysis of the primary endpoint was determined to be statistically significant (p<0.025), then formal testing of the first secondary endpoint, percentage of patients that survived and did not require permanent ventilation, was conducted. If the analysis of this secondary endpoint was determined to be statistically significant (p<0.05), then formal testing of the second secondary endpoint, maintenance of weight ≥3<sup>rd</sup> WHO percentile without feeding support at any visit up to 18 months of age, was conducted. The analysis of the second secondary endpoint was determined to be statistically significant if p<0.025.

<sup>g</sup>Event-free survival at 14 months of age includes patients who did not die, did not require permanent ventilation, and did not withdraw from the study by 14 months of age.

<sup>h</sup>Exact 95% CI and corresponding p-value calculated from a two-sided Fisher's exact test with a significance level of 0.05 for the comparison between onasemnogene abeparvovec and PNCr data.

**Results:** All primary and secondary endpoints were statistically significant (p<0.001). All patients sat independently (11/14 within WHO-MGRS developmental window), all survived without permanent ventilation, and 13 (93%) maintained body weight without feeding support. No patient used nutritional/respiratory support (including cough assist) during the study. Eleven patients stood (Bayley-III #40) and 9 walked (Bayley-III #43) (7/11 and 5/9 within WHO-MGRS developmental windows, respectively). All patients had AEs; pyrexia, upper respiratory tract infection, constipation were most common. Ten (71%) had at least one treatment-related AE. No serious AEs were considered related by investigator.

**Conclusion:** Onasemnogene abeparvovec was efficacious and well-tolerated in the treatment of presymptomatic patients at risk of SMA1. All patients survived without nutritional/respiratory support; all sat independently, most within the normal developmental window. No new safety signals were identified during this study.

**Table 3. Treatment-emergent Adverse Events**

	Patients with Two Copies of SMN2 (N=14)
Any TEAE, n (%)	14 (100)
TEAEs related to study treatment, n (%)	10 (71.4)
Serious TEAEs, n (%)	5 (35.7)
Serious TEAEs related to study treatment, n (%)	0
TEAEs leading to study discontinuation, n (%)	0
TEAEs leading to death, n (%)	0

TEAE, treatment-emergent adverse event; SMN2, survival motor neuron 2 gene.

**Disclosure:** The study (ClinicalTrials.gov identifier: NCT03505099) was supported by Novartis Gene Therapies, Inc.

## OPR-202

**Dexamethasone versus Surgical Treatment for Chronic Subdural Hematoma: The DECSA trial**

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**Background and aims:** The optimal treatment for symptomatic chronic subdural hematoma is unclear. We conducted a phase III multicenter, randomized trial to compare the effect of dexamethasone therapy with surgical evacuation on functional outcome.

**Methods:** Symptomatic patients with a chronic subdural hematoma, with symptom severity defined as Markwalder Grading Scale (MGS) 1 to 3, were eligible for the study. We randomly assigned patients in a 1:1 ratio to a 19-day oral dexamethasone tapering course or surgical evacuation through burr-hole craniostomy. The primary outcome was functional outcome as expressed by the modified Rankin scale (ranging from 0 (no symptoms) to 6 (death)), at 3 months after start of treatment, analysed with adjusted proportional odds regression. Secondary end points were quality of life, MGS and Glasgow Outcome Scale-Extended scores, failure of treatment, duration of hospital stay, complications, and mortality.

**Results:** We enrolled 252 patients; 127 were assigned to dexamethasone therapy and 125 to surgery evacuation. No conclusive data are available yet at the time of abstract submission deadline (May 17th, 2021), since the final follow-up and subsequent database lock took place recently (May 2021). The results will therefore be presented at the meeting.

**Conclusion:** The DECSA trial provides decisive insight in the effectiveness of dexamethasone therapy compared with surgical evacuation on functional outcome in symptomatic patients with a chronic subdural hematoma.

**Disclosure:** Nothing to disclose.

## OPR-203

**The Treatabolome flags treatable genes and variants: an emerging concept**

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**Background and aims:** Although next generation sequencing (NGS) has drastically improved diagnosis for patients with rare diseases, access to knowledge of existing effective treatments is still sparse and often unclear. To alert the treating clinicians about patients with treatable conditions at the time of reviewing NGS results, the Treatabolome, a computer-readable and interoperable knowledge-based linking treatable variants with the evidence for the treatment, has been set up. The idea is to have the therapeutic information for each gene and variant-specific treatment in an online freely available database and make it interoperable with clinical diagnosis support tools, allowing that information to be provided simultaneously with the diagnosis.

**Methods:** The methodology to accrue the Treatabolome database's content is to conduct systematic literature reviews (SLR) and generate uploadable FAIR datasets.

**Results:** Following published methodology paper's directives, datasets have been produced via SLR led by disease experts for Congenital Myasthenic Syndromes, Muscle Channelopathies, Hereditary Peripheral Neuropathies, Laminopathies, Genetic Parkinson Disease and in the pipeline are datasets for Leigh's Disease and Early-Onset Ataxias.

**Conclusion:** This project is part of Solve RD (solve-rd.eu), initiated with 4 European Reference Networks for rare neuromuscular diseases, rare neurological diseases, rare congenital malformation and syndromes with intellectual and other neurodevelopmental disorders and rare genetic tumour risk syndromes. Still, we now want to expand the concept to the remaining 24 networks, make it available outside of the European space, and enrich it with additional SLR and corresponding datasets for other rare disease conditions, particularly neuromuscular disorders.

**Disclosure:** No conflicts of interest.

## OPR-204

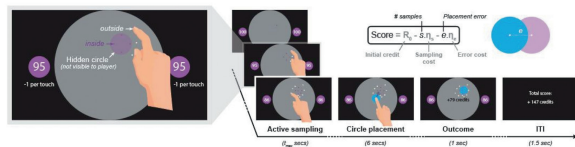
**Hypersensitivity to uncertainty in subjective cognitive impairment**

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**Background and aims:** Subjective cognitive impairment (SCI) is a clinical diagnosis describing self-reported deficits in cognition without objective clinical evidence of cognitive impairment at diagnosis. Many SCI patients often suffer from other neuropsychiatric syndromes such as depression and anxiety which have been hypothesised to account, at least in part, for their cognitive symptoms. Despite this strong association between SCI and neuropsychiatric features, the cognitive and brain mechanisms underlying SCI are still poorly understood.

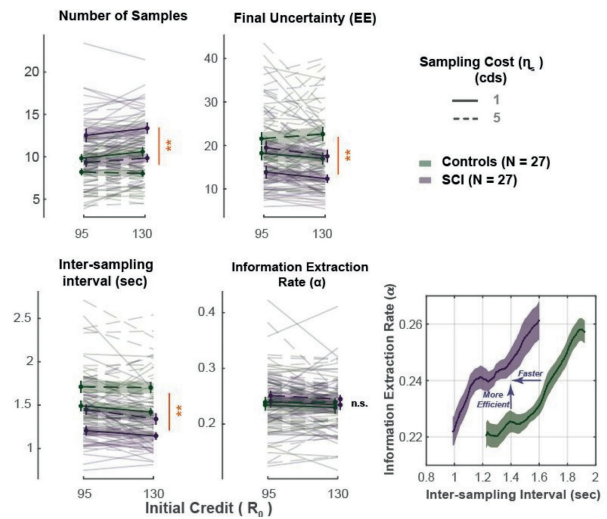
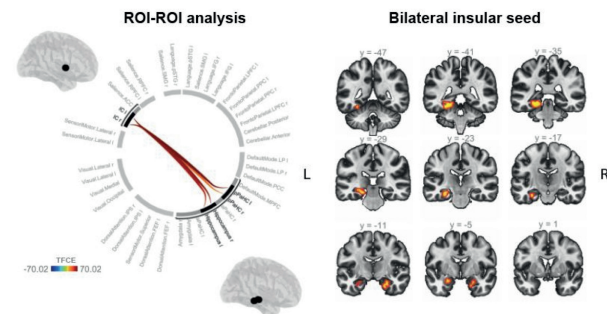
**Methods:** 27 SCI patients along with 27 healthy matched controls performed an information sampling task and completed self-report questionnaires of anxiety and depression. Resting-state functional MRI (r-fMRI) scans were obtained from 23 patients and 25 controls.



**Active information gathering task** with large and complex sampling space. In our paradigm, people search spatially for a hidden circle, by touching screen areas, before committing to an answer. The hidden circle is 5.80% the size of the arena. They win credits as a function of the number of samples used ( $R_s = s \times n_s$ ), and the precision of their response ( $e \times n_e$ ). Paradigm from Pettit et al (in press) *Nature Hum Behaviour*.

**Experimental paradigm**

**Results:** Across different conditions, SCI patients sampled more and faster, thereby obtaining more information than controls. Remarkably, however, despite this speedy sampling behaviour, SCI patients were able to sample as efficiently as controls. I.e., they broke the speed-efficiency trade-off that otherwise characterises sampling for information on the task. Hypersensitivity to uncertainty indexed by this extensive rapid-and-efficient sampling behaviour correlated with the severity of affective burden dimension that includes depression and anxiety. Analysis of r-fMRI revealed that hypersensitivity to uncertainty, as well as affective burden score, were both associated with stronger insular-hippocampal connectivity. A causal mediation analysis revealed that hypersensitivity to uncertainty mediated the aforementioned association between insular-hippocampal connectivity and severity of affective burden.

**Extensive and faster sampling in SCI****Increased insular-hippocampal connectivity in SCI**

**Conclusion:** These results suggest that altered uncertainty processing is a key mechanism underlying the psychocognitive manifestations in SCI and implicate a specific brain network that might be a possible target for future treatments.

**Disclosure:** None

## OPR-205

## Associations of antiepileptic drugs, pharmacoresponse with magnetic resonance imaging in temporal lobe epilepsy

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**Background and aims:** The use of antiepileptic drugs (AEDs) might alter metabolic and structural Magnetic Resonance Imaging (MRI) of temporal lobe epilepsy (TLE). However, the inclusion of AEDs effects in the analysis of MRI data is challenging. A biclustering algorithm was adopted to mine coherent patterns in MRI associated with AED administration and clinical data.

**Methods:** Clinical (pharmacoresponse, hippocampal atrophy side, major depression, AED-regimen, antidepressant medication) and MRI features (ipsi- and contralateral hippocampal volume [Hvol] and n-acetylaspartate, myo-inositol, glutamate, and choline [markers of neuronal damage, gliosis, and membrane turnover, respectively]) were extracted from 128 patients with unilateral TLE. Patients and features were simultaneously grouped by means of the In-Close5 biclustering algorithm, with a chi-squared pruning filter, aiming at mining pharmacoresistant or pharmacoresponse classes. The selected biclusters have at least one AED and one MRI feature, so that biclusters with more features were preferred. We obtained z-scores using the values of 50 controls.

**Results:** The biclusters of interest are listed in Table 1. Only ipsilateral changes were related to both classes of pharmacoresponse. Interestingly, a bicluster involving pharmacoresponsive patients grouped individuals with reduced myo-inositol, including four pharmacoresistant patients, instead of the expected increased levels of myo-inositol.

Table 1. A list of relevant mined biclusters considering patients and their corresponding features. Notice the existence of several biclusters grouping solely AED-resistant patients, and few hybrid biclusters composed of AED-resistant and AED-responsive patients, but with a highly-predominant class.

N	Features			Patients
	Clinical Feature	Associated AED	MRI change z-score (group mean ± SD)	Distribution of the patient labels
1	Polytherapy	CLB	NAA < -3 SD (0.66 ± 0.07)	15 AED-resistant
2	Polytherapy	CBZ	NAA < -3 SD (0.68 ± 0.06)	11 AED-resistant
3	Polytherapy	CBZ	NAA < -3 SD (0.68 ± 0.05) Myo-Ins > 3 SD (1.489 ± 0.2)	10 AED-resistant
4	Polytherapy	CBZ+CLB	NAA < -3 SD (0.68 ± 0.06) Myo-Ins > 3 SD (1.5 ± 0.22)	8 AED-resistant
5	Polytherapy	CLB	NAA < -3 SD (0.68 ± 0.06) Myo-Ins > 4 SD (1.54 ± 0.24)	10 AED-resistant
6	Polytherapy; depression	CLB	Hvol < -3 SD (2311.40 ± 183.9)	8 AED-resistant
7	Polytherapy; Left-AH	CLB	NAA < -3 SD (0.66 ± 0.1)	8 AED-resistant
8	Polytherapy	CBZ	Myo-Ins > 3 SD (1.5 ± 0.17)	13 AED-resistant 3 AED-responsive
9	Polytherapy	CLB	Myo-Ins > 3 SD (1.48 ± 0.19)	15 AED-resistant 4 AED-responsive
10	Polytherapy	VLP	Hvol < -3 SD (2378.9 ± 321.5)	8 AED-resistant
11	Polytherapy	CLB	NAA < -3 SD (0.66 ± 0.09)	8 AED-resistant
12	Polytherapy	TPM	NAA < -3 SD (0.66 ± 0.09)	8 AED-resistant
13	Polytherapy; major depression	CLB	Hvol < -3 SD (2311.4 ± 183.9)	8 AED-resistant
14	-----	CBZ	Myo-Ins < -3 SD (0.86 ± 0.1)	9 AED-responsive 4 AED-resistant
15	Contralateral hippocampal loss	CBZ	Hvol < -2 SD (2768 ± 267.9)	7 AED-responsive 1 AED-resistant

Legend: AED, Antiepileptic Drugs; MRI, Magnetic Resonance Imaging; CLB, Clobazam; CBZ, Carbamazepine; HA, hippocampal atrophy; VLP, Valproate; TPM, Topiramate; SD, Standard Deviation; NAA, N-acetyl-aspartate; Myo-Ins, Myo-inositol; Hvol, Hippocampal volume (values in mm<sup>3</sup>). Values of the control group (n = 50) used for comparisons: hippocampal volume (mean ± SD) 4128.7 ± 600.8 mm<sup>3</sup>; NAA 0.974 ± 0.105; Myo-inositol 1.144 ± 0.111.

**Conclusion:** Pharmacoresistant and pharmacoresponsive TLE patients were properly grouped considering (1) significant ipsilateral metabolic and structural changes, (2) common clinical features and (3) AEDs in use. Being an enumerative approach devoted to revealing all consistent associations in a dataset, biclustering might be a useful technique to uncover possible associations of AEDs with MRI alterations.

**Disclosure:** This study was funded by institutional grants PIBIC-SAE UNICAMP/ FAPESP 2013/07559-3.

## Late Breaking News: COVID-19/ Neuro-immunology

### OPR-206

#### COVID-19 risk factors in people with multiple sclerosis treated with ocrelizumab

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**Background and aims:** As of December 2020, >200,000 people with multiple sclerosis (pwMS) have been treated with ocrelizumab. Understanding risk factors for developing symptomatic COVID-19 in this population is important.

**Methods:** Confirmed/suspected COVID-19 cases in ocrelizumab-treated pwMS were identified from 10 ongoing clinical trials as of 27 November 2020. Multi-variable logistic regression models were used to evaluate risk factors associated with symptomatic COVID-19 and serious vs on-serious disease. A qualitative analysis of post-marketing cases was also undertaken.

**Results:** 193 (4.9%) cases of COVID-19 were identified in 3,974 patients; 29.5% (n=57/193) were serious and 29.0% (n=56/193) had  $\geq$  comorbidity (Table). Comorbidities were associated with COVID-19 (1 comorbidity: odds ratio [OR]=1.68, 95% confidence interval [CI] [1.15, 2.47], p=0.01;  $\geq$ 2 comorbidities: OR=2.25, 95% CI [1.09, 4.66], p=0.03). There was a trend for a higher likelihood of serious COVID-19 with age >50 years (OR=1.88, 95% CI [0.77, 4.55], p=0.16) and Expanded Disability Status Scale (EDSS) score of  $\geq$ 6 (OR=2.72, 95% CI [0.82, 8.96], p=0.10). The same risk factors were identified by qualitative analysis of post-marketing data on a more diverse population of ocrelizumab-treated pwMS (613 COVID-19 cases as of 30 November 2020).

	Symptomatic COVID-19 (N=193)	Serious COVID-19 (N=57)
<b>Total number of patients with at least one comorbidity</b>	<b>56 (29.0%)</b>	<b>23 (40.4%)</b>
<b>Vascular disorders</b>	<b>35 (18.1%)</b>	<b>16 (28.1%)</b>
Hypertension	32 (16.6%)	13 (22.8%)
Essential hypertension	2 (1.0%)	2 (3.5%)
Peripheral arterial occlusive disease	1 (0.5%)	1 (1.8%)
<b>Metabolism and nutrition disorders</b>	<b>15 (7.8%)</b>	<b>6 (10.5%)</b>
Type 2 diabetes mellitus	7 (3.6%)	4 (7.0%)
Obesity	6 (3.1%)	3 (5.3%)
Diabetes mellitus	2 (1.0%)	0
Hyperglycaemia	2 (1.0%)	1 (1.8%)
Type 1 diabetes mellitus	1 (0.5%)	0
<b>Respiratory, thoracic and mediastinal disorders</b>	<b>15 (7.8%)</b>	<b>6 (10.5%)</b>
<b>Cardiac disorders</b>	<b>4 (2.1%)</b>	<b>1 (1.8%)</b>

\*Reported cases were defined as symptomatic, as the vast majority of cases in our database are reported as such and no systematic collection of positive tests in asymptomatic patients has been implemented.

Table. Comorbidities known to be associated with more severe COVID-19 in symptomatic\* and serious COVID-19 cases

**Conclusion:** For symptomatic cases, logistic regression suggests that comorbidities may increase the likelihood of symptomatic COVID-19 in ocrelizumab-treated pwMS. For serious cases, a descriptive comparison of the risk factors was in line with those reported in general and MS registry populations; this is also supported by the pharmacovigilance data. Logistic regression analysis identified age and EDSS level as the most important factors for serious outcomes.

**Disclosure:** Sponsored by F. Hoffmann-La Roche Ltd; writing and editorial assistance was provided by Articulate Science, UK.

## OPR-207

### Impact of Ofatumumab on Immune Responses Post-vaccination in RMS Patients: ALITHIOS Vaccination Sub-study Design

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**Background and aims:** Ofatumumab, a fully human anti-CD20 monoclonal antibody, is indicated for the treatment of relapsing multiple sclerosis (RMS) in adults. Data on humoral response post-vaccination in ofatumumab-treated patients is currently limited. This study evaluates the effects of ofatumumab on humoral responses to selected vaccines and keyhole limpet haemocyanin (KLH) neo-antigen.

**Methods:** This is an optional, open-label, single-treatment arm, vaccination sub-study embedded in the ongoing umbrella extension Phase 3b ALITHIOS study (NCT03650114). Participants will continue to receive ofatumumab 20mg subcutaneously every 4 weeks along with the tetanus toxoid (TT) vaccine, 13-valent conjugate pneumococcal vaccine (13-PCV), 23-valent pneumococcal polysaccharide vaccine (23-PPV), KLH (in a sub-set of participants within the US), and the 2020-21 or 2021-22 seasonal influenza vaccine. Primary endpoint is the proportion of patients with a positive antibody response to the TT vaccine 8 weeks post-vaccination. Secondary endpoints include, among others, the proportion of patients with an antibody response to the TT vaccine at 4 weeks and to 13-PCV and 23-PPV at 4 and 8 weeks post-vaccination; mean titres of anti-KLH antibodies 4 weeks post-vaccination; and a main antibody responder analysis for influenza vaccines. The study plans to enrol ~145 patients.

**Results:** First patient first visit was in September 2020, with first interim results expected by Q2 2022. Full study design details will be presented at the congress.

**Conclusion:** This study will provide a greater understanding of the effect of B-cell depletion by ofatumumab on immune responses post-vaccination and will help to guide physicians treating RMS patients with ofatumumab when considering primary and secondary immunisation.

**Disclosure:** The study was supported by Novartis Pharma AG, Switzerland. Detailed author disclosures will be provided in the subsequent presentation.

## OPR-208

### Analysis of post-treatment relapse activity in the phase 3 OPTIMUM study of ponesimod compared with teriflunomide

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**Background and aims:** Cases of exacerbation of multiple sclerosis (MS) disease activity have been reported after discontinuation of S1P-receptor modulators. Here we report on post-treatment relapse activity in the OPTIMUM study of ponesimod.

**Methods:** In this phase-3 study, patients with relapsing MS were randomized (1:1) to 20mg ponesimod or 14mg teriflunomide once-daily for up to 108 weeks. Patients who stopped treatment prematurely or after completing the treatment period were asked to participate in a safety follow up (approximately 30 days after the last dose) and a post-treatment observation period (from last dose up to 108 weeks after randomization) and were included in this analysis.

**Results:** Of the 1,124 (1,133 randomized) patients with post-treatment observation in the OPTIMUM study (ponesimod: 559; teriflunomide: 565), 8 ponesimod and 14 teriflunomide patients experienced 23 post-treatment relapses within 182 days of last dosage of study drug. Available post-treatment follow-up during this period was similar for both treatment arms: mean (median [range]), days: ponesimod: 31.6 (17 [1–182]) and teriflunomide: 30.8 (17 [1–182]). Post-treatment relapses for ponesimod (3 confirmed, 4 unconfirmed, 2 unknown) occurred between 6 and 168 days without any pattern of latency or severity. The post-treatment annualized relapse rate (ARR) did not exceed the on-treatment ARR for ponesimod (0.186 and 0.246, respectively; includes non-confirmed relapses). Relapse activity in patients with post-treatment relapses is presented in Figure.

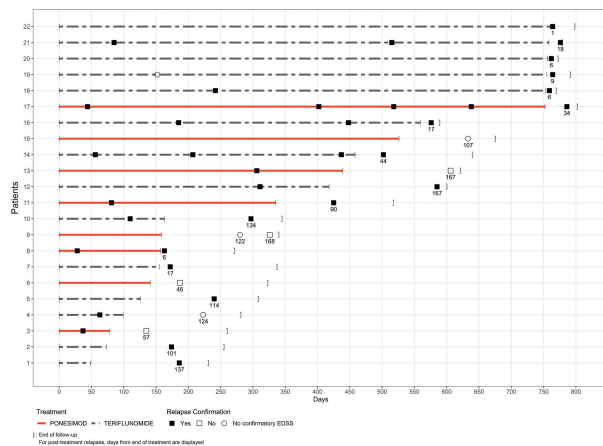


Figure. Patients with post-treatment relapse within 182 days from end of treatment

**Conclusion:** These prospectively obtained post-treatment observation data in patients who stopped poniesmod treatment in the OPTIMUM study, do not support increased early post-treatment relapse activity as compared to activity on treatment.

**Disclosure:** LK's institution (University Hospital Basel) has received research support from Actelion, Bayer HealthCare, Biogen, BMS, Genzyme, Janssen, Merck, Novartis, Roche, Sanofi, Santhera, TG Therapeutics.

## OPR-209

### Single-cell profiling of myasthenia gravis identifies a pathogenic T cell signature

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**Background and aims:** Myasthenia gravis (MG) is an autoimmune disease characterized by impaired neuromuscular signaling due to autoantibodies targeting the acetylcholine receptor. Although its auto-antigens and effector mechanisms are well defined, the cellular and molecular drivers underpinning MG remain elusive.

**Methods:** Here, we employed high-dimensional single-cell mass and spectral cytometry of blood and thymus samples from MG patients in combination with supervised and unsupervised machine-learning tools to gain insight into the immune dysregulation underlying MG.

**Results:** By creating a comprehensive immune map, we identified two dysregulated subsets of inflammatory circulating memory T helper (Th) cells. These signature ThCD103 and ThGM cells populated the diseased thymus, were reduced in the blood of MG patients, and were inversely correlated with disease severity. Both signature Th subsets rebounded in the blood of MG patients after surgical thymus removal, indicative of their role as cellular markers of disease activity.

**Conclusion:** Together, this in-depth analysis of the immune landscape of MG provides valuable insight into disease pathogenesis, suggests novel biomarkers and identifies new potential therapeutic targets for treatment.

**Disclosure:** None

## OPR-210

Abstract withdrawn



## OPR-211

**The impact of COVID-19 on short and intermediate mortality in patients with dementia.**

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**Background and aims:** Dementia and cognitive decline are not conclusive risk factors for severe outcome of the coronavirus disease 2019 (COVID-19). We aimed to determine whether the presence of dementia is associated with higher in-hospital mortality in patients with COVID-19.

**Methods:** We conducted an open-cohort observational study Stockholm in participating hospitals for older adults from pandemic start until January 8th, 2021. In total, we identified 4,715 patients, out of which 480 (10.2%) patients had diagnosis of both COVID-19 and dementia, 2,362 (50.1%) had COVID-19 and were dementia-free and 1,873 (39.7%) had dementia without COVID-19. Patients' age, sex, oxygen saturation, comorbidities, and medication prescription (cardiovascular and psychotropic medication) were registered at admission. First and second wave of COVID-19 pandemic were defined. The hazard ratios (HR) with 95% confidence intervals (CI) of in-hospital mortality associated with dementia were obtained using proportional hazards regression with time since entry as time scale.

**Results:** After adjustment, dementia was independently associated with 59% higher in-hospital mortality among COVID-19 patients compared to patients who were dementia-free at admission [HR 1.59 (1.26–2.01)]. In addition, the prescription of antipsychotic medication was associated with substantially higher mortality, however only in patients who were dementia-free [2.79 (2.05–3.81); vs dementia 1.32 (0.84–2.09)].

**Conclusion:** Dementia is an independent risk factor for short-term mortality in patients hospitalized due to COVID-19. Our results may help identify high-risk patients in need of more specialized care when infected with COVID-19.

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