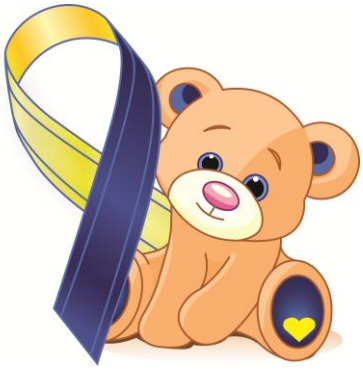

OMSLife Foundation

and

Dancing Eye Syndrome Support Trust

present

The Eleventh International Workshop on Opsoclonus Myoclonus Ataxia Syndrome Clinical and Basic Science

Leonardo Royal Hotel Oxford, Godstow Rd, Wolvercote, Oxford OX2 8AL, United Kingdom

10th – 12th April 2025

THE WORKSHOP

This is the 11th International OMS workshop to be held at Leonardo Royal Hotel in Oxford. Formerly known as Dancing Eye Syndrome workshops, they are an opportunity to bring together clinicians and scientists with a special interest in the condition. Parents and patients contribute first -hand experience of the lives of children with OMS.

The organisation of the workshop is thanks to the dedication of the members of the OMS scientific steering committee.

The workshop is being sponsored jointly by The OMSLife Foundation and Dancing Eye Syndrome Support Trust.

Thank you to the Leonardo Royal Hotel for providing such a conducive venue for this kind of meeting.

Thank you to everyone who has given up their time to come and participate in this workshop.

www.dancingeyes.org.uk

www.omslifefoundation.org

Thursday 10th April

1600: Tea and Welcome

1630: SESSION 1: UPDATES, PROGRESS AND INITIATIVES
Chair: Ming Lim

Welcome:-

Andrea Klein - *OMS History: with tribute to Marcel Kinsbourne*

Ming Lim - *OMS introduction and summary of last workshop*

Ian Grummitt - *OMS Charter, membership and election: progress since last year*

Clinical Studies:-

Mark Gorman, Rebecca MacRae - *Prognosis, treatment, and mechanisms in an international pediatric-onset opsoclonus myoclonus ataxia syndrome (POOMAS) study: an update*

Abstract:

Gudrun Schleiermacher, Benoit Dumont - *Opsoclonus Myoclonus Syndrome/ Dancing Eye Syndrome (OMS/DES) in Children With and Without Neuroblastoma (NBpos and NBneg)Opsoclonus Myoclonus Syndrome/Dancing Eye Syndrome (OMS/DES) in Children With and Without Neuroblastoma (NBpos and NBneg)*

Abstract:
OMAS is a rare paraneoplastic syndrome. In children, it is associated with neuroblastoma in over 50% of cases. The OMS/DES study was conducted to evaluate the efficacy of a standardized escalating treatment schedule on disease remission and long-term neuropsychological outcome. We conducted a prospective multi-national clinical trial recruiting children between 6 months to 8 years old with newly diagnosed OMAS. We included 101 patients (median 21 months), 66 with neuroblastoma. Escalating treatment is an efficient strategy to treat OMAS patients avoiding treatment-related toxicities. No significant difference in OMAS score at diagnosis was observed, indicating that the severity of symptoms alone is not sufficient to predict treatment response.

Gary Cutter - *Adaptive trial designs in rare disorders*

Abstract:
Adaptive designs are not new and may not even be innovative. They are done for efficiency. In rare diseases sample sizes are always an issue. Longer trials don't compensate for lack of sample size and the desire to move faster is always present. Use of biomarkers and preferably surrogate outcomes can speed the time of investigation. Examples of older adaptive and futility designs are discussed as well as the risk and benefits of platform designs. Some general pitfalls of entrance criteria, ethical decisions in design of trials and the use of medical records to get around trials are also presented

---

1930: Conference Dinner – Oriel Suite

Friday 11th April

0830: SESSION 2: THERAPEUTICS
Chair: Mark Gorman

Tim Lotze, Ming Lim - *Vamorolone: Can it be a treatment for OMAS?*

Abstract:
Vamorolone is a first-in-class steroidal anti-inflammatory drug, designed to lack an 11-carbon oxygen group (hydroxyl or carbonyl) that is 1 of 5 molecular contact sites with the glucocorticoid receptor. In vitro pharmacology and now clinical studies have shown that Vamorolone retains the anti-inflammatory activity of steroid drugs, while lacking the adverse effects (AEs) associated with these drugs (stunting of growth, bone morbidities, muscle atrophy) in these models. The talk will review the data from Duchene Muscular Dystrophy and explore the potential for use in a range of neuroinflammatory conditions including OMAS.

Wendy Mitchell, Cheryl Hemingway - *Smorgasbord of challenging cases*

Abstract:
Various cases presented for open discussion:

- Cheryl Hemingway – Treatment resistance
- Andrea Klein -
- Lizzie Wilson – OMS Post NB
- Kavita Thakkar
- Prerna Kumar
- Benoit Dumont – Treatment resistance
- Wendy Mitchell
- “the cat with OMS”

1030: Coffee

1100: SESSION 3: BIOMARKERS

Chair: Wendy Mitchell

Thais Armangue - ***Detection of novel autoantibodies in children with OMS***

Abstract:

Opsoclonus–myoclonus-ataxia syndrome (OMAS), is a rare autoimmune disorder that typically affects previously asymptomatic children between 1 and 3 years of age,[1] although it can also occur in teenagers and adulthood.[2,3] This condition typically presents with a characteristic eye movement disorder and myoclonus, along with ataxia, irritability, and sleep disturbances. Approximately 50% of pediatric cases are paraneoplastic associated with neuroblastoma.[4] In addition, although an autoimmune etiology is suspected, the exact pathogenic mechanism remains unknown.[5] An antibody-mediated mechanism has been hypothesized, supported by evidence of clonal B-cell expansion in the cerebrospinal fluid (CSF) of these patients and their favorable response to immunotherapy, including rituximab.[6–8] Although both onconeuronal antibodies (anti-Hu, anti-Ri) and neuronal surface antibodies (HNK1, glycine receptor) have been found in a percentage of paraneoplastic OMAS patients,[5,9,10] efforts to identify a common target antigen have not yet succeeded[11] and no antibodies have been found in idiopathic cases. We will review previous, current and "future" techniques applied for antibody discovery in OMAS.

Mark Gorman - ***KCTD14: A Newly Identified Autoantigen in OMAS – Implications for Diagnosis and Treatment***

Abstract:

Opsoclonus-myoclonus-ataxia syndrome (OMAS) is a rare neuroimmune disorder without defined autoimmune responses. Using a high-throughput protein array, we identified KCTD14 as a novel autoantigen in patients with OMAS. Radioligand binding assay revealed 10/21 (48%) patients with OMAS in the discovery cohort had antibodies to KCTD14 as compared to 0/16 of healthy control donors (P=0.0017, Fisher's exact test). Validation of KCTD14's role as a neuronal autoantigen was conducted via *in silico* expression analysis, immunoblotting, cell fractionation, electron microscopy, and biochemical approaches. These findings establish KCTD14 as an autoantibody target in OMAS, providing insights into disease pathogenesis and potential diagnostic or prognostic biomarkers.

Taisuke Yamauchi - ***Comprehensive Identification of Novel Autoantibody Candidates in Opsoclonus-Myoclonus Ataxia Syndrome Using Proteome-Wide Screening Platforms***

Abstract:
Opsoclonus-myoclonus ataxia syndrome (OMAS) is a rare neuroinflammatory disorder, likely autoimmune in origin, but its specific autoantibody targets have not been well characterized. OMAS remains a diagnostic and therapeutic challenge due to its rarity, limited biomarker availability, and variability in clinical presentation. In this study, we performed a comprehensive analysis of cerebrospinal fluid (CSF) from patients with OMAS using three complementary, proteome-wide screening approaches: human proteome microarrays, Phage ImmunoPrecipitation Sequencing (PhIP-seq), and Liquid Chromatography–Tandem Mass Spectrometry (LC-MS/MS). Each method enabled broad detection of candidate autoantibodies, facilitating a comprehensive exploration of the autoantibody repertoire in OMAS. From this integrated strategy, we identified several novel candidates of autoantibody not previously reported to be associated with OMAS. Further validation studies are underway. Our findings contribute to a deeper understanding of the OMAS immunopathology and may serve as a basis for future research for etiology or biomarker discovery.

Ann Yeh - ***Eye tracking and its structural and functional correlates in OMAS***

Abstract:
Ongoing cognitive abnormalities in children with a history of OMAS have been well documented. Eye tracking is a novel technology that can be used to identify anatomical and functional correlates of disease. Previous studies have implicated altered circuit dynamics in the brainstem reticular formation to account for the uncontrolled saccades associated acutely with opsoclonus in OMAS. Specifically, disruption of intrinsic membrane properties of excitatory and inhibitory burst neurons that drive the extraocular motoneurons is hypothesized to underlie saccade oscillations, and this intracellular mechanism has been successfully modeled. Using eye tracking, we have found ongoing circuit abnormalities in children with a history of OMAS. This talk will outline eye tracking abnormalities detected in this population and identify correlates with cognitive metrics. Details of an ongoing multi-site study of eye tracking in children with OMAS with be shared.

Sally George[1] and Matthias Fischer[2] - ***Investigating the underlying biology of OMS associated neuroblastoma***

Abstract:

[1]Group Leader, Institute of Cancer Research and Honorary Consultant Paediatric Oncologist, The Royal Marsden Hospital, London, UK
[2]Department of Experimental Pediatric Oncology, University Children's Hospital, and Center for Molecular Medicine of Cologne (CMMC), Medical Faculty, University of Cologne, Cologne, Germany

The favorable oncological outcome and the neurological symptoms in OMS-associated neuroblastoma are thought to be elicited by anti-tumor antibodies cross-reacting with cerebellar cells. We here sought to evaluate this hypothesis by determining the genetic features of OMS-associated neuroblastoma, the spatial organization and maturation stages of tumor infiltrating B cells (TIBs), and the characteristics and specificities of antibodies produced by TIBs. OMS tumors had a low mutational burden, suggesting the presence of few neo-epitopes. Nonetheless, these tumors frequently harbored mature tertiary lymphoid structures, containing germinal center B cells and T follicular helper cells, unlike non-OMS tumors. Single-cell analysis uncovered enrichment of B cells of various maturation stages in OMS tumors. Germinal center B cell clones in OMS tumors underwent somatic hypermutation, immunoglobulin class switching, and maturation into plasma and memory B cells. We identified several antibodies derived from these B cell clones with high binding affinity to neuroblastoma cell antigens, which are currently being characterized.

1300: LUNCH

1400: SESSION 4: SYMPTOMS AND OUTCOMES

Chair: Cheryl Hemingway

Yasmin Khakoo, Scott Milligan - ***Children Sleep Habits Prior, During, and After Active OMAS: An Initial Analysis (OMSLife Registry)***

Abstract:

Authors: Khakoo Y[1], Dias B, Hauptman A[2], Milligan KL[3], Rossor T[4], Schofield H[5], Michaelis M[6]
Affiliations: [1]Memorial Sloan Kettering Cancer Center, New York NY USA, [2]Kennedy Krieger Institute, Baltimore MD USA, [3]Principled Research Resources, Belfast ME USA, [4]Evelina London Children's Hospital, London UK, [5]Children's Hospital of Philadelphia PA USA, [6]The OMSLife Foundation, Cypress TX USA

Background & Objective: Sleep disturbances are common in individuals with OMAS, persisting variably even during remission. This study aims to characterize sleep behaviors before, during, and after active OMAS to inform care strategies and identify potential long-term consequences of the disease.

Methods: Between August 2024 to Jan 2025, caregivers of 121 children with active (n=28) or in remission (n=93) OMAS completed an abbreviated Children's Sleep Habit Questionnaire (CSHQ), made available through a secure online portal. Each caregiver

completed the questionnaire up to 3 times, based on recall of pre-, active, and post-OMAS. Questions fell into 8 domains (bedtime resistance, sleep delay, sleep anxiety, night wakings, parasomnias, disordered breathing, daytime sleepiness) and each question had a response scale of 0 (never) to 4 (always).
Results: Differences in mean scores were indicated for 14/15 questions in comparing pre- and active OMAS,13/15 between active and post-OMAS, and 4/15 across pre-, active, and post-OMAS. Nearly all distributions observed were multi-modal.
Conclusions: Aggregate survey responses suggest that sleep habits are largely suboptimal during active OMAS compared to pre- and post-OMAS. Given the multi-modal distributions observed for most questions, further assessments will be needed to identify subsets that may be impacted during and after active OMAS.
References:
Owens J.A., Spirito A., McGuinn M. The Children's Sleep Habits Questionnaire (CSHQ): Psychometric properties of a survey instrument for school-aged children. Sleep. 2000;23:1043–1051. doi: 10.1093/sleep/23.8.1d.
Smith-Hicks C, Wright D, Kenny A, Stowe RC, McCormack M, Stanfield AC, Holder JL Jr. Sleep Abnormalities in the Synaptopathies-SYNGAP1-Related Intellectual Disability and Phelan-McDermid Syndrome. Brain Sci. 2021 Sep 17;11(9):1229. doi: 10.3390/brainsci11091229. PMID: 34573249; PMCID: PMC8472329.

Scott Milligan - *Development of a real-world evidence (RWE) roadmap to advance OMAS understanding & advocacy*

Abstract:
Background & Objective: Readily-available healthcare data and AI advancements have enabled patient advocacy groups (PAGs) to become hubs for data-driven research. Our objective is to establish a strategic plan for using real-world evidence (RWE) to benefit those affected by Opsoclonus Myoclonus Ataxia Syndrome (OMAS).
Methods: The roadmap will be informed by research agendas of PAGs with natural history registries (n=188, The Roadmap Project). Research objectives will be gathered from people affected by OMAS (patient, caregiver, family member), advocates, and researchers directly or via structured online forms. Data acquisition approaches will be primary collection (registry, surveys), consented health records, and/or consented tokenization of patient identifiers. Publication plans will consider all healthcare stakeholder audiences.
Results: The RWE roadmap will have defined objectives, methods, and dissemination plans, among which is the creation of a standardized data repository for use by academic researchers.
Conclusion: This strategic plan will advance OMAS understanding & advocacy by leveraging RWE and facilitating collaborative research initiatives.
Reference: Korsunska, A., Bolden, S. E., Repasky, M., Zuccato, M., Fajgenbaum, D. (2023) The ROADMAP Project. https://www.everycure.org/roadmap

---

Mark Gorman, Rebecca MacRae - *Whole Genome Sequencing and HLA typing in OMAS*

Abstract:

Background: Prior studies suggest a genetic contribution to opsoclonus-myoclonus ataxia syndrome (OMAS) but are limited.
Methods: We enrolled patients diagnosed with OMAS ≤ 18 years at a pediatric neuroimmunology clinic in Boston, USA, using the 2004 Genoa Criteria. WGS was conducted for the patients and their biological parents (when available), with one case including an unaffected twin. *De novo* germline variants (DNVs) in probands were identified and validated, and analyses of structural variants (SVs), recessive variants in neuroimmune-associated genes, and high-resolution HLA typing were performed.
Results: Our study included 42 probands, 23 of whom had neuroblastoma. We found 12 confirmed DNVs in protein-coding regions in nine (21.4%) probands. Ten patients (23.8%) had rare homozygous or compound heterozygous variants known to alter protein function, affecting 11 genes. However, no clearly disease-causing variants were identified. The *HLA-DRB1*01* allele was observed in 27 out of 84 (32.1%) alleles in the probands, significantly higher than that in the general population (Chi-square test, $p < 0.0001$). The *HLA-DOB*01:01* was very common (86%) and was compared to a prior study.
Conclusions: This first genome sequencing study reveals potential genetic contributors to OMAS, implicating polygenic predisposition with *HLA-DRB1*01:01* and *HLA-DOB*01:01* as possible genetic risk factors.

Mark Gorman, Mike Michaelis - *Inaugural Findings on OMSLife Registry*

Abstract:
Background: Most prior studies of opsoclonus-myoclonus-ataxia syndrome (OMAS) are limited in size due to its rarity. Patient-reported registries may overcome this challenge.
Methods: Retrospective analysis of data entered by parents of patients with OMAS into nine online surveys created by OMSLife Foundation and NORD assessing demographics, symptoms at onset, triggers, time of diagnosis, treatment, and additional therapies.
Results: 194 patients were enrolled. There was a female predominance (54%) and high rate of parental autoimmunity (31%). Age at onset peaked between 12 and 18 months overall. Initial misdiagnosis occurred in nearly 50% and tumor discovery was delayed in

18 patients, but overall median time to correct diagnosis was 25 days. Most patients (56%) received combination immunomodulatory therapies, and nearly all underwent supportive therapies.
Conclusions: Patient- and parent-powered research is feasible in OMAS and created the second largest published cohort of pediatric patients with OMAS. Results were similar to other large cohorts and also validated findings from prior case reports and smaller case series.

1600: Tea

1630: Session 5: Spectrum of OMAS: an international perspective
Chair: Ming Lim

Naveen Sankhyan - ***Neurodevelopmental outcomes following OMAS: An Indian perspective***

Abstract:
The presenter will briefly review the available literature from India on OMAS outcomes. The cognitive, behavioural, motor, and language outcomes in children with OMAS collected at the presenter's institute prospectively will be elaborated. Data of 42 children treated with immunomodulation for at least 12 months starting with at least 2 drugs will be presented. Data on drugs used, relapses, and course of illness will be presented. Factors associated with poor cognitive outcomes will be discussed. Common parental concerns included misarticulation, language delay, and other issues that were observed will be discussed further. Finally, lessons learnt and how they will impact care of children with OMAS will be discussed.

Naveen Sankhyan - ***Infections associated OMAS: Do we need to approach differently?***

Abstract:
While OMAS is a prototype of a childhood paraneoplastic neurological syndrome, not all OMAS cases are tumor-associated. Some children develop OMAS as a post-infectious phenomenon, and even more rarely, in association with acute viral and bacterial infections. In this talk, the presenter will discuss the occurrence of OMAS in the setting of various infections, reviewing the available literature. Emphasis will be placed on the management of infection-associated OMAS and how it might differ from

other forms. The goal is to provide a comprehensive overview of OMAS related to infections and discuss effective management strategies.

Renata Paolilo - *Clinical presentation and outcome of OMAS: A Brazilian perspective*

Abstract:
Opsoclonus-myoclonus-ataxia syndrome (OMAS) is a rare immune-mediated neurological disorder associated with cognitive impairment. This presentation will highlight findings from a Brazilian multicenter cohort of 27 patients followed for a median of 1.7 years. Most cases had a paraneoplastic etiology, with tremor and ataxia being the most common initial symptoms. Less than 20% of patients achieved remission and most experienced multiple relapses. Poor outcomes at the last follow-up were associated with disease course and treatment. These findings underscore the challenges of managing OMAS, particularly in resource-limited settings, reinforcing the need for early recognition and intervention to improve patient outcomes.

Taisuke Yamauchi - *Clinical presentation and outcome of OMAS: A Japanese perspective*

No Abstract

Naveen Viswanatha - *Pablove grant considerations*

Abstract:
For nearly 20 years, Naveen has worked at Google, where he is a Director of Product Management. He resides in NorCal with his wife, Crystal, and their 2 amazing daughters Keira and Akemi. At just 18 months, Keira was diagnosed with Neuroblastoma and Opsoclonus-Myoclonus Syndrome (OMS) – an extremely rare autoimmune disease caused by an immune reaction to her cancer. Passionate advocates and change-makers, The Viswanathas began fundraising and pedaling for The Pablove Foundation 11 years ago. They have funded 8 Powered by Pablove research projects focused on OMS.

1930: Conference Dinner - Oriel Suite

Saturday 12th April

0900: Session 6: Behavioural Issues and OMAS
Chair: Aaron Hauptman

Aaron Hauptman, Hannah Schofield - ***Moving Forward in the Neuropsychiatric Care and Neuropsychological Assessment of Individuals with OMAS***

Abstract:
Neuropsychological and neuropsychiatric effects of OMAS are broadly accepted as core components to the disease, but are not well-characterized and have been minimally studied to date. In this symposium, we introduce and define both the field of neuropsychology and neuropsychiatry. We then provide an update on the current OMAS literature in both disciplines. We provide a brief discussion of current findings on behavioral healthcare grounded in survey data from the NORD registry. Using this identification of gaps in current knowledge, we propose next steps in diagnostic and treatment guidelines for neuropsychological and neuropsychiatric assessment and care including recommendations for behavioral health clinicians, families, and other providers. We will use the opportunity to gather data from the assembled experts on current neuropsychiatric and neuropsychological standards of care, next steps in data gathering, and attainable research goals.

Objectives:

- Review existing literature and guidance for neuropsychiatric care of patients with OMAS
- Review existing literature and guidance for neuropsychological assessment of patients with OMAS
- Describe outstanding needs and gaps in knowledge regarding neurobehavioral and neuropsychological outcomes of OMAS
- Discuss opportunity to develop guidelines for neuropsychiatric and neuropsychological care for patients with OMAS

1230: Summing up session

1300: Lunch and farewell
Steering committee to meet over lunch