It was a pleasure to be able to organise and Chair The British Association for the study of the Liver (BASL) Special interest group (SIG) in Wilsons Disease(WD) on 24th Nov 2023 held at St Ethelburga's Centre for Reconstruction and Peace Venue, London. I am delighted to have taken over the SIG chair and batton last year from Dr Bill Griffiths, Cambridge and excited to be steer the ship. The SIG meeting was kindly supported by Institute of Liver Studies, King's College Hospital, London

The SIG WD meeting was our first 1st face to face meeting since the pandemic with 29 attendees, 8 speakers including multidisciplinary members from Neurology, Psychiatry, Genetics, Pathology, Trace elements, NIHR, Wilson's Disease Support Group-UK, trainees, Adult and Paediatric Hepatology, and Nuclear medicine.

Here is a short summary of the meeting:

Prof Aftab Ala, (Kings and Royal Surrey) Rare Liver disease and Wilsons disease SIG chair set the scene and discussed the **unmet needs in Wilson's disease** and priorities in diagnosis, management and need to work collaboratively in networks across UK though the specialist centres

Dr Rupert Purchase University of Sussex, presented the science behind cuproptosis (copper induced cell death) highlighting the role and function of mitochondria, oxidation pathways and role of Cu^{+} and Cu^{2+}.

A **national audit** was proposed by Aftab Ala, Prof Oliver Bandmann (Sheffield) and Dr Bill Griffiths and jointly presented with Dr James Liu Yin (Kings) around current practise in Wilson's disease and ongoing use of BASL guidance amongst clinicians. It is anticipated the electronic short audit will be disseminated to SIG members at the specialist centres in Q2 2024. James Liu Yin, Bill Griffiths (Cambridge), Aftab Ala and Oliver Bandmann will be core group developing the audit for final distribution and update at the next SIG meeting

A summary of **new emerging generic trientine formulations** licenced by the MHRA including national and international productions and different dose base were summarised by Dr Rupert Purchase, It is anticipated that there will be updates in pricing and formulations from NHS England in Spring-Summer 2024

The relationship between **Wilson's disease and psychiatric presentation is poorly understood and yet remains a common association** – Dr David Okai (Maudsley, SLaM) described key links with neural networks. The Kings/Maudsley group are planning a future pilot study using dried blood spot and novel *ATP7B* peptide as marker of Wilson's disease in a "high risk" population planned at King's College Hospital and the Maudsley hospital.

Wilson's Disease - Skin Associations was presented by Dr James Liu Yin on behalf of the King's Group. This association is somewhat underestimated. There is increasing recognition of skin related side effects due to long term chelator treatment and the possible implications of overtreatment and approach to management were discussed. The potential importance of monitoring was emphasised supported by publication in Lancet Gastroenterology and Hepatology. Yin JL, Salisbury J, Ala A. Skin changes in long-term Wilson's disease. *Lancet Gastroenterol Hepatol.* 2024 Jan;9(1):92.

Genetics and Wilsons disease. Dr Bill Griffiths presented an interesting case study that was discussed highlighting key issues and points around genetic testing for ATP7B and its utility in diagnosis. He described a sibling trio with ATP7B and exploring dilemmas in watch and wait, liver biopsy, and/or treating. We discussed the importance of SIG in discussing the challenging cases.

Dr James Liu Yin presented 'Wilson's disease **highlights from the American Association for the Study of Liver Disease (AASLD) annual conference 2023**. Oral presentations included updates on dried blood spot testing of newborn babies in Washington state, clinical data on the use of Methanobactin for Wilson's disease, comparison of non-caeruloplasmin copper by protein speciation and 24hr urinary copper excretion results from the CHELATE trial and work investigating other biochemical pathways in the development of liver disease in ATP7B deficient animal models.

(v)Setting up and developing **Patient and Public Involvement and Engagement (PPIE)** in Wilson's Disease and guiding clinical trials – Invaluable experience from NIHR PPIE group Lead James Ratcliff and working with Wilsons disease support group. There was discussion of the value of PPIE in the study of rare diseases –especially Wilson's disease. His talk described the importance of listening to peoples' lived experiences when making decisions on the direction of clinical research and how patients can help set the priorities for physicians and researchers.

PET imaging in Wilson's Disease – update on Total Body PET. Emerging evidence of PET technology in management of Wilson's Disease outlined by Prof Phil Blower, King's College London. Comparison was made with Denmark and normal subjects using copper 64-PET in improved understanding of mechanisms of drugs in the treatment of Wilson's disease

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Current UK clinical studies in Wilson's Disease

1. UNITED study- Pharmacokinetics study in Trientine 2HCL (Adults and Paediatrics)

2. Open label, Multicentre, Prospective Study to Characterize the Pharmacokinetics and Pharmacodynamics of *Cufence* (Trientine Dihydrochloride) and to Investigate the Efficacy and Safety in Wilson's Disease Patients

3. Randomized, double-blind, placebo-controlled, seamless, adaptive Phase 1/2/3 clinical study of UX701 in patients with Wilson disease (ULTRAGENYX – King's College recruiting)

4. A Phase I/II Study of VTX-801 in Adult Patients with Wilson's Disease (GATEWAY)

5. International Wilson's Disease Patient Registry (iWilson Registry)

Up and coming clinical trials in Wilson's Disease

1.*ArborMed* Therapeutics. Phase 1 – In set up
Efficacy and Safety of *Methanobactin* in normal human and Wilson's Disease patients. 2025 Set up.

2. *Orphalan.* A Phase I, Single Centre, Randomised, Interventional, Open-Label, Cross-Over Study to Evaluate the Pharmacokinetics (PK) and the Safety and Tolerability of a Total Daily Dose of 900mg of TETA 4HCL 2024-2025.

3. Developing the use of optical coherence tomography to assess Kayser Fleischer rings in Wilson's disease. Proof of concept work – single centre. James Liu Yin, Samira Anwar, Frank Proudlock, Simon Taylor, Aftab Ala, Investigator led, supported by Orphalan. NIHR CRN portfolio adopted 2024.

Previous completed clinical trials in Wilson's Disease

1. Copper Concentration & Histopathologic Changes in Liver Biopsy in Participants With Wilson Disease Treated With ALXN1840. Phase 2 *(Submitted for consideration of publication 2024)*

2. Copper and Molybdenum Balance in Participants with Wilson Disease Treated With ALXN1840. Phase 1 and 2 *(Submitted for consideration of publication 2024)*

NHS England and Wilson's Registry

- Ongoing work with NHSe and National Congenital Anomaly and Rare Disease Registration Service (NCARDS) with a focus towards case assortment, hospital episode statistics data and outcomes including hepatocellular carcinoma, prevalence, and prescribing data. Dr James Liu Yin (Specialist Registrar) is taking over the work done by Dr O Mohammed.

We look forward to organising another meeting around June/July 2024 and hope we can update you on activities. In the meantime, please do reach out to with items you wish to be presented at next meetings including cases.

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