Pat Ahlquist reports on the 31st International Symposium on ALS/MND

Attending international palliative care research conferences every few years has been a highlight of my working life, but I could never justify taking time off to go to the Association's excellent Annual International Symposium on ALS/MND. They were due to meet in Montreal in December 2020 but early in the year decided to change to a virtual platform. Brian Dickie and his team then worked incredibly hard and created an extremely successful virtual symposium, and this time I could join in! They even allowed catch-up viewings online until the end of January.

Over 3 days, more than 1800 delegates from 48 countries took part. Lectures and presentations from leading world experts were followed by ample time for questions and over 400 e-posters could be looked at, with 'lightening explainer' videos to summarise the research with specific sessions when the presenters could present and discuss their work in real time. It was humbling and inspiring to see how much is being done to discover the causes of MND and thereby find targeted treatments. The international community is really working together and there was a lot of evidence of the benefits from this collaboration, and of co-operation with researchers in parallel fields.

One fascinating lecture was by Prof. Tanzi from Harvard, who was talking about neuroinflammation across neurodegenerative diseases. His work has been mainly on Alzheimer's and aging but provides valuable insights into how abnormal amyloid-β protein deposits in the cells cause inflammation and cell death. They have even developed 3-D neural cell cultures, growing in a dish, derived from human stem cells. This enables them to quickly test the effects of drugs on cell damage in Alzheimer's and MND, and make much more rapid progress.

The increased speed of research was also highlighted by Prof. Al-Chalabi from King's in London when he spoke at the preconference symposium hosted by Cytokinetics. Platform trial designs (a new concept) are enabling much more efficient evaluation of multiple interventions with the ability to keep trials running and adapt them for new discoveries from within and outside the trial. New diagnostic criteria, tools that measure the rate of progression and genetic profiling are also helping to stratify trials so that specific drugs can be targeted more accurately. The eventual future really does seem to be in Precision Medicine and a much more personalised approach to treatment.

One type of precision based medical therapy is anti sense oligonucleotides (ASOs), and I learnt a lot from a presentation by Prof. Chio of the University of Turin. ASOs are short, synthetic, single-stranded nucleic acids that attach to mRNA and modulate protein expression. He presented very encouraging data from exploratory clinical trials of an ASO drug called Tofersen. It reduces the production of the dangerous SOD-1 protein in people who have that genetic mutation and seems to significantly slow the rate of clinical decline. Results of the Phase 3 trial are expected later this year. Another ASO drug for the C9ORF72 mutation is now in phase 1 trials.

People having these drugs have to have lumbar punctures every month but one presentation even offered hope that targeted ultrasound may help drugs cross the blood brain barrier more effectively, though clinical trials with this for MND are only just starting.

The results of three large Phase 3 trials were presented at the meeting. These have been really well explained on the Research Blog of the MNDA website (https://mndresearch.blog). Unfortunately the trials of NurOwn (using stem cells) and levosimenden (repurposing a cardiac drug) did not meet their primary

endpoints to show an impact of treatment. However the NurOwn study has a lot more work to do and their CSF biomarker data showed interesting results to work on. Also the levosimenden trial showed a trend towards slower progression in some people and they are hoping that the open label trial extension, reporting later this year, will throw more light on that. The trial results of an oral drug called AMX0035 were much more promising with at least a 6 month survival benefit. The extension trial data is still awaited and it is still an experimental compound without regulatory approval, but I'm sure we will be hearing more about it soon.

I must confess to not reading all 400 posters, but a few from the Sheffield research group caught my eye. They already support the useful website Home - myBreathing (mymnd.org.uk) which is targeted at people living with MND. They presented research on the best ways of providing NIV, inequities across the UK and the development of their new NIV toolkit website for health care professionals. Along with others they also presented information on the use of digital remote monitoring and telemedicine clinics. It was clear that one of the benefits of the pandemic is that it has accelerated development and assessment of the benefits of virtual clinics which could really reduce the future burden of clinic attendance, especially for those involved in clinical trials.

Sitting at my computer, attending the Symposium, I have watched how basic scientists, clinicians and drug companies are all working together, irrespective of international boundaries. It truly is an exciting era of MND research and my lasting impression was one of hope for the future. If you want to find out more do look at the MNDA website and their interactive Periodic Table of Research. (Periodic Table of MND Research | International Symposium on MND/ALS (mndassociation.org)) .