COPPER-ATSM CLINICAL TRIAL FOR MND

The first clinical trial of copper-ATSM as a potential treatment option for motor neuron disease (MND) will start in 2016. The trial is sponsored by Collaborative Medicinal Development, Pty Ltd. (CMD). Importantly, Cu-ATSM therapy was developed in Australia, the first-in-man clinical study is being performed in Australia, and the sponsor is an Australian company (CMD). An overview of the research that has been performed to date, the rationale for why this compound may be an effective treatment, and the status of the clinical trial is briefly summarized in the following paragraphs.

A brief history of the research
The drug is copper-ATSM. Its chemical name is diacetylbis(4-methylthiosemicarbazonato)copper\textsuperscript{II} but is often abbreviated to Cu-ATSM or Cu\textsuperscript{II}(atsm). In 2005, Anthony White, Kevin Barnham and Paul Donnelly at The University of Melbourne began discussing the potential to treat neurodegenerative disease by using Cu-ATSM.

Skipping forward to 2008, for the first time copper-ATSM was given to mice that develop symptoms that mimic human MND. About 10\% of all MND cases are familial, which means the disease-causing genes can be passed on from parent to child. Mutations in the gene for superoxide dismutase-1 (SOD1) account for a large proportion of familial MND. The mice most commonly used to study MND in the laboratory develop MND-like symptoms because they too have a mutated form of SOD1. They are often called mutant SOD1 mice.

Although the first study to test copper-ATSM in mutant SOD1 mice took many months to complete, the outcomes were clear: treating with copper-ATSM protected motor neurons in the spinal cord, improved the animals’ MND-like symptoms, and extended lifespan of the mice. These outcomes were published in 2010 and heralded the beginning of an expanded research effort designed to answer one important question: what is the full therapeutic potential for copper-ATSM as a treatment for MND?

Subsequent research revealed more provocative observations, including:

1. Copper-ATSM is more effective in mutant SOD1 mice than riluzole (the only approved treatment for MND)
2. The benefits of Cu-ATSM in the mutant SOD1 mice are evident even when the treatment starts after the mice have developed overt MND-like symptoms.
3. Copper-ATSM is effective when administered orally.
4. In some mouse models of MND, the benefit of Cu-ATSM were especially compelling (http://www.alzforum.org/news/research-news/copper-rescue-als-mice)

Can Cu-ATSM treat the majority of people with MND who don’t have a SOD1 mutation (sporadic MND)?
Unfortunately, there is no animal model for sporadic MND. However, in 2015 Peter Crouch and colleagues at the University of Melbourne and the Florey Institute presented studies performed on MND-affected tissues obtained from people who died because of sporadic MND. These studies showed important similarities to mice that responded to Cu-ATSM and suggests that Cu-ATSM may have activity in both sporadic and familial MND.

Moving from the laboratory into the clinic
Despite some interesting challenges, the experimental Cu-ATSM molecule has been developed into a pharmaceutical for human administration. The study can begin after the clinical trial is approved by the appropriate regulatory and ethics committees. Clinical trial sites will be in Sydney and Melbourne. Once the trial is approved by regulatory authorities, details will be posted on www.clinicaltrials.gov.