POSITION STATEMENT

Development and approval of drugs to treat motor neurone disease

Background

ALS/MND associations globally are excited and enthusiastic about the new approaches and new drugs that are being tested for people with ALS/MND and are hopeful that one or more of these will become a therapy with substantial impact on slowing down or perhaps even stopping ALS/MND in the near future.

There is an urgency to find treatments for this disease which has such a rapid course and devastating impact. MND Australia supports and commends the many people and organisations committed to identifying promising treatments more rapidly through initiatives, funding and collaborations to improve clinical trial design and encourage the testing of promising compounds in phase II studies.

There is one medication approved for treatment of MND in Australia – riluzole (sold as Rilutek™ or APO-Riluzole). Riluzole probably prolongs median survival by two to three months. Research indicates that people who start taking riluzole early in their disease progression are more likely to remain in the milder stages of the disease for longer than those not taking riluzole.

Clinical trials

Clinical trials are research studies on people that determine whether drugs are safe and whether they work. They are divided into different stages, called phases. Drugs must perform well enough in each phase to be allowed to progress on to the next one. Typically, drugs must successfully complete a three-phase process before being approved by a country's health authority for widespread use.

Why do we need clinical trials?

Clinical trials in ALS/MND are taking place worldwide. In Australia, clinical trials are governed by national ethics guidelines and codes of conduct. Anyone taking part in a trial must be fully informed about the objectives of the research, what is expected of them and any risks and potential inconveniences that may be experienced during and after the trial. If you are thinking of being included in a trial, as part of the process of informed consent you should be given a participant information and consent form that contains details of the trial and your participation.

MND is a disease that can be quite different from one individual to the next. These differences in how MND progresses are particularly apparent when looking at small numbers of people for short periods of time. Therefore, well-controlled, relatively large studies are the best way to test whether a drug works. This was illustrated in the clinical trials of dexpramipexole. While results from a phase II trial of dexpramipexole found that the drug was safe and well tolerated in 102 people and showed a significant benefit, unfortunately the phase III trial of 943 people showed that dexpramipexole was not beneficial for people living with MND.

Supplying a drug broadly without a larger trial exposes people living with MND to possible side effects that may reduce their quality of life and risks making them worse. For example, excitement about lithium as a therapy for MND was followed by no effect (or worsening of symptoms) in subsequent studies.
A multinational group of neurologists, basic scientists, statisticians, patient advocates, representatives from the pharmaceutical industry, as well as regulatory agencies and patients with ALS/MND are currently revising, updating and expanding the Guidelines for Clinical Trials in ALS/MND. See draft guidelines.

Current clinical trials in Australia

The Australian New Zealand Clinical Trials Registry lists clinical trials including MND studies in Australia and New Zealand, as well as trials from across the globe that have been completed, are currently recruiting or are pending.

Expediting trials of drugs that treat serious and life-threatening diseases

In some countries, drug companies can apply to the health authority to request permission to speed up the development and availability of drugs that treat serious or life-threatening diseases.

In recent years, most drug development for ALS/MND has occurred in the United States.

Fast Track designation

The United States Food and Drug Administration (FDA) has granted Fast Track designation to the following drugs and therapy that have been developed to treat motor neurone disease (MND):

- tirasemtiv (Cytokinetics, Incorporated) – currently in Phase III trial
- NurOwn stem cell therapy (BrainStorm Cell Therapeutics) – preparations underway for Phase III trial
- GM604 (Genervon Biopharmaceuticals) – there is no independently verifiable data supporting the efficacy or safety of GM604. Read a review of GM604 by ALSUntangled
- Endavarone (Radicut) – New Drug Application (final stage of the development and approval process) has been submitted. Decision on the application is expected in July 2017.

Once a drug receives Fast Track designation, early and frequent communication between the FDA and the drug company is encouraged throughout the entire drug development and review process. The frequency of communication assures that questions and issues are resolved quickly, often leading to earlier drug approval and access by patients

Accelerated Approval designation

When studying a new drug, it can sometimes take many years to learn whether a drug actually provides a real effect on survival and on how a patient feels or functions. Mindful of the fact that it may take an extended period of time to measure a drug's intended clinical benefit the FDA has instituted the Accelerated Approval regulations that allow drugs for serious conditions to be approved more quickly.

Other ways to access trial drugs or therapies not yet licensed in Australia

The Australian Therapeutic Goods Administration (TGA) does not include accelerated approval pathways for drug development or availability.

Special Access Scheme
Individuals, following discussion with their neurologist, may be able to apply to access products that have been not yet been approved in Australia through the Special Access Scheme.

Off-label prescribing
Sometimes a medicine may be licensed for one condition, but could have the potential to be used to treat other conditions or illnesses. This is referred to as "off-label" use. An unlicensed medication may be prescribed by doctors if they think it is likely to be effective for their patient and any benefits outweigh potential side-effects or risks.

Personal importation scheme
Individuals can legally import most therapeutic goods for personal use under the Personal Importation Scheme. It is important to note that such therapeutic goods may not be approved for supply in Australia; this means there are no guarantees about their safety or quality.

MND Australia's Position

It can be difficult for people living with MND and their families to endure the wait for the development of an effective treatment and cure. MND Australia acknowledges the urgency to advance research to better understand MND and the desperate need for an effective treatment.

MND Australia believes any drug must have been proven to be safe and to improve health outcomes of people living with MND before it is made available for widespread use.

See also MND Australia's Position Statement on alternative and unproven therapies for people diagnosed with MND.

MND Australia is an active member of the International Alliance of ALS/MND Associations and is committed to keeping the Australian MND community up to date on any promising new therapies.

MND Australia's research arm – the MND Research Institute of Australia (MNDRIA) –promotes and funds only Australia's best MND research which has the greatest chance of making a difference for people with MND. MNDRIA supports a range of research including genetics, proteomics, cell biology, metabolism, immunology, environmental/epidemiology and healthcare.

MNDRIA has been the preeminent independent funder of MND research in Australia for over 30 years providing over $20 million to the best research across Australia. MNDRIA awarded $3.75 million for MND research commencing in 2017 and is committed to growing research spend each year.

On behalf of the MND Australia board

Signed: David Ali (President) **Dated: 27 February 2017**