FDA Approves Radicava (Edaravone) as treatment for MND/ALS

The U.S. Food and Drug Administration announced on the 6th of May 2017 that it has granted approval to MT Pharma America to begin marketing Edaravone as a treatment for MND/ALS. The approval of Edaravone marks the first new treatment to be approved for MND/ALS by the FDA since Rilutek (Riluzole) was approved in 1995.

WHAT IS EDARAVONE?

Edaravone is a U.S. FDA approved intravenous infusion treatment option developed originally for the treatment of stroke by Japanese pharmaceutical company Mitsubishi Tanabe Pharma Corporation. The drug is believed to act as a free radical scavenger and prevent oxidative stress damage to neurones. The pharmaceutical company turned its attention to MND/ALS initially in 2002 and worked through several clinical trials of the drug in patients diagnosed with the disease right up until the definitive Phase 3 trial in 2011-2014 was completed. In this pivotal trial, Edaravone treatment was shown to slow the decline in physical function in a sub-group of MND/ALS patients as measured by the ALS Functional Rating Scale-Revised (ALSFRS-R), a validated rating instrument for monitoring the progression of disability in patients with MND/ALS.

IS EDARAVONE A CURE? HOW MEANINGFUL A TREATMENT IS IT?

No, Edaravone is not a cure and it is only likely to be of benefit to some people with MND/ALS.

Every person diagnosed with MND/ALS experiences a different rate of disease progression and differing patterns of spread. This likely reflects, to some degree, differing disease biology that exists from patient to patient which may mean that only certain patients will respond to any given medication or treatment. In the studies performed by the drug company using Edaravone this was certainly the case, with early results from the trials actually showing no benefit of Edaravone treatment when all MND/ALS patients treated on the trials were analysed together. However, when the investigators looked closer at the data, a certain subset of patients did appear to respond to the drug compared to placebo.

In the definitive trial to analyse this effect in the identified subset of patients, it was shown that Edaravone was of benefit to people early on in the disease course (within 2 years of diagnosis), who had well preserved lung function (FVC > 80%), and whom had relatively well preserved overall physical function at the time of starting treatment (demonstrated by the patients having greater than or equal to 2 points in each of the categories measured in the ALSFRS-R).
WHAT DATA LED TO EDARAVONE’S APPROVAL?

The definitive Phase 3 clinical trial that led to the approval of Edaravone was the MCI186-19 trial (click here to read more). This study assessed the safety and efficacy of Edaravone compared to placebo in 137 people with MND/ALS matching the sub-group characteristics mentioned (within 2 years of diagnosis, FVC > 80%, and greater than or equal to 2 points in each of the ALSFRS-R measurement tool). Following a 12 week pre-observation period where patients were observed to determine their pre-treatment baseline individual MND disease rate of decline, eligible patients were randomised 1:1 to receive Edaravone 60mg intravenously or placebo during a six-month double-blind placebo controlled phase. The primary endpoint the investigators assessed was monitoring the change in ALSFRS-R score from baseline to six months.

What does all that mean?

1:1 Randomised: this means that participants were randomised to receive either Edaravone or placebo, with 50% of patients on each arm of the study.

Placebo: non-drug compound, visually identical to trial drug and given to the patient in the exact same way as the trial drug.

Double-Blind: this means that neither the patient or the doctor giving the drug knew whether the drug being given to the patient was the placebo or the trial medication.

Primary endpoint: this is the main question or measurement that the investigators are interested in while doing the trial. In this case it is the change in ALSFRS-R score. Although rates of MND/ALS progression can vary significantly between patients, research shows people with MND/ALS lose an average of one point per month on the ALSFRS-R scale.

What were the Results?

![Graph of physical function at 6 months mean change in ALSFRS-R score from baseline least square mean ± standard error]

At completion of the trial the data demonstrated that patients who received Edaravone for six months experienced the following, relative to those who received placebo:

A statistically significant reduction in the rate of decline in physical function by **33 per cent** (or 2.49 ALSFRS-R points) p=0.0013, in this sub-group of MND/ALS patients.

In regards to safety, it was found that the most common adverse reactions that occurred in greater than 10 percent of patients receiving Edaravone was increased bruising, problems walking (gait disturbance), headache, inflammation of the skin (eczema), and rash (contact dermatitis).
HOW DO I GET ACCESS TO EDARAVONE?

Currently, Edaravone is not available to Australians living with MND/ALS. The announcement by the U.S. FDA of its approval for the use of Edaravone however, is a big step forward in getting this medication to patients diagnosed with MND/ALS in Australia.

There is likely to be some delay involved in the process of getting the drug approved in Australia as to ensure the drug is safe and worthwhile, the Australian Therapeutics Goods Administration (TGA) will need to do its own analysis of the data from the clinical trials before approving the drug. Work will then begin on getting the drug subsidised for patients on the Pharmaceutical Benefits Scheme (PBS).

It is worth noting again that if approved for use in Australia, it is likely to be approved for patients who are most likely to benefit from the drug as identified by the sub-group analyses and the definitive Phase 3 clinical trial - that is patients within 2 years of diagnosis, with a lung capacity of >80%, and with relatively well preserved physical function as determined by having at least 2 or more points for each category on the ALSFRS-R scale when beginning treatment.

Fight MND is determined to see Edaravone approved for treatment of MND/ALS in Australia, and we will work tirelessly with the TGA and Australian Government to make this happen.

"The team at Fight MND are very excited by this news. This is the first new MND-specific treatment developed in over 20 years", said Dr Ian Davis, Fight MND Founder and Research Sub-Committee chair. "Fight MND will now work hard to get this new medication to Australia for MND patients here to access, and we hope that this announcement signals a new beginning in the fight against this devastating disease. Our determination for funding new effective treatments is unwavering, and we are hopeful that people living with MND will have even more therapies available to them in the near future."