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Effect of Edaravone in Patients with advanced Amyotrophic Lateral Sclerosis

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Introduction

In 2017, the FDA approved Edaravone as a neuroprotective agent to slow the progression of Amyotrophic Lateral Sclerosis (ALS). The precise mechanism of Edaravone in the treatment of ALS is not known, but its therapeutic effect is considered to be done by its antioxidant properties. The former clinical trials have been performed on ALS patients in less advanced status only (Japan ALS severity classification grade 1-3; forced vital capacity (FVC) in ratio to normal predicted value (FVCPred%) of ≥60%). In the previous clinical trials published in 2014, the average change in ALSFRS score was -5.7 ± 0.85 decline, and the next study presented only at the 2016 conference showed a decrease in average ALSFRS score -6.52 ± 1.78. Therefore we included more advanced ALS patients with a FVCPred% of less than 60% to study the efficacy of Edaravone in these patients.

Case report

Since January of 2017 to June of 2018, 19 patients were enrolled in the Edaravone treatment. 60 mg of Edaravone is administered daily intravenously for the first 14 days which is followed by 14 days of rest. In the second to sixth cycles, the same dose of Edaravone is given for 10 days in every cycle, with a 14-day rest period between each cycles. Eleven patients finished the treatment of 6 cycles, 2 patients were dropped out and 3 patients are still continuing the treatment. Among the 11 patients who finished the total 6 cycles, 7 patients (M:F=5:2, mean age = 58.6±8.8 years) had FVCPred% of less than 60% at initial. These seven patients started the Edaravone infusion approximately 2.17±1.58 years after symptom onset and 0.99±1.02 years after diagnosis. For all subjects, pulmonary function(FVC and peak cough flow), ALS functional rating scale (ALSFRS) and manual muscle test were checked at the beginning and end of the Edaravone infusion for every cycle. We also performed the regular laboratory tests to screen drug-related adverse outcomes. The mean ALSFRS score was 30.1 ± 8.1 at baseline and 24.7 ± 5.4 after 6 cycles of Edaravone administration. The mean change in ALSFRS score from baseline was -7.2 ± 6.6. The mean baseline FVC Pred% in the sitting position was 36.1 ± 12.4 and it became 25.7 ± 12.7 after therapy. The mean baseline FVC

Pred% and after 6 months of treatment in the supine position was 28.3 ± 5.5 and 22.5 ± 8.9 respectively. Not any major drug-related side effects were found.

Conclusion

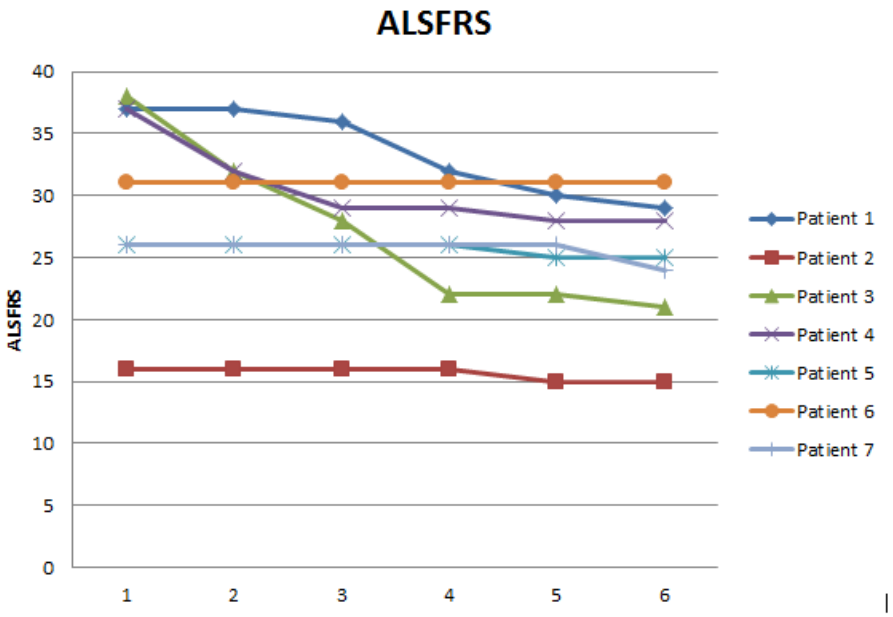
The mean change in ALSFRS scores of patients with more advanced ALS was significantly reduced compared to the values reported in previous clinical trials. We can conclude that Edaravone can be successfully treated in ALS patients with a FVCPred% of less than 60%. Nowadays, we are enrolling more patients, following up serial ALSFRS scores and pulmonary function parameters, aiming to compare the efficacy of Edaravone depending on the types of onset and on the Methods of therapies(combined with exercise therapy Vs. Edaravone alone).

Table 1. FVC and ALSFRS score in each patient under Edaravone therapy

	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5	Patient 6	Patient 7
Age (years) at	65	52	58	63	42	63	67
Sex	F	F	M	M	M	M	M
Type	Limb	Limb	Bulbar	Limb	Limb	Limb	Limb
FVC sitting $_{Pred}$ (%) - initial	56.8	21.0	25.4	27.7	40.0	44.6	37.0
FVC sitting $_{Pred}$ (%) - endpoint	41.6	9.3	23.3	16.7	33.1	40.1	15.8
delta FVC sitting $_{Pred}$ (%)	-15.2	-11.7	-2.1	-11.0	-6.9	-4.5	-21.2
FVC supine $_{Pred}$ (%) - initial	36.7	21.0	25.2	25.4	32.8	31.9	25.2
FVC supine $_{Pred}$ (%) - endpoint	36.8	10.6	20.7	15.7	28.2	27.2	18.0
delta FVC supine $_{Pred}$ (%)	0.1	-10.4	-4.5	-9.7	-4.6	-4.7	-7.2
ALSFRS total - initial	37.0	16.0	38.0	37.0	26.0	31.0	26.0
ALSFRS total - endpoint	29.0	15.0	21.0	28.0	25.0	31.0	24.0
delta ALSFRS total	-8.0	-1.0	-17.0	-9.0	-1.0	0.0	-2.0

Abbreviation : F:Female; M:Male; FVC:forced vital capacity; ALSFRS:Amyotrophic lateral sclerosis functional rating scale

Figure 1. Changes of ALSFRS score at each cycle of Edaravone therapy



Four ALS patients with forced vital capacity (FVC) in ratio to normal predicted value (FVC_{Pred}%) of < 60% finished the Edaravone treatment of total 6 cycles. ALS functional rating scale scores of each patient at each cycle depicted in the figure (mean±SD change in ALSFRS score from baseline to after therapy was -7.2±6.6).