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Neuroprotective therapy both for acute ischemic stroke and ALS

Edaravone is a free radical scavenger, which is the first clinical drug for neuroprotection in the world which has been approved from 2001 in most ischemic stroke patients in Japan, and some of China and India. Edaravone scavenges hydroxyl radicals both in hydrophilic and hydrophobic conditions, and is especially useful in thrombolytic therapy with tissue plasminogen activator (tPA). Combination therapy of Edaravone with tPA greatly increased survival of stroke animals, reduced infarct size, and inhibited molecular markers of oxidative damage in lipid, protein and DNA. Use of Edaravone greatly reduced hemorrhagic transformation accompanied by tPA treatment, and may also extend therapeutic time window with tPA therapy for more than 4.5 hrs in human stroke patients for preserving neurovascular unit (NVU). An intensive Edaravone therapy for 3 days now showed a favorite recovery in 3 European countries. Amyotrophic lateral sclerosis (ALS) is a progressive and fatal neurodegenerative disease caused by selective death of motor neurons. Among our own 390 ALS patients, 4.1% show familial ALS (FALS), in which 50% is associated with missense mutations of SOD1, 25% were TDP43 and FUS mutations, and 6.3% is an optineurin mutation. Although the underlying mechanism of ALS has not yet been fully clarified, several reports have implicated the involvement of oxidative stress under selective death of motor neurons in both ALS patients and animal models. A recent multicenter prospective double-blind placebo-control clinical trial with edaravone for ALS patients conducted in Japan showed a positive effect for delaying the clinical score (ALS FRS-R) during the course of examination (24 weeks). Serious or critical adverse effect was not noted in this clinical trial. Of particular was that this clinical benefit of edaravone was shown as an add-on therapy after anti-glutamatergic riluzole. These data strongly suggest a potential underlying mechanism of oxidative stress in ALS and a clinical delay by a free radical scavenger. These translational studies on a free radical scavenger Edaravone allowed governmental permissions both for acute ischemic stroke after 2001 and for ALS after 2015. Edaravone was approved for ALS at 2015 in Japan, 2016 in Korea, and 2017 in USA.

Recent Publications

1. Abe K et al., (1988) Strong attenuation of ischemic and postischemic brain edema in rats by a novel free radical scavenger. Stroke 19: 480-485.
2. Abe K et al., (2017) Safety and efficacy of edaravone in well-defined patients with ALS: a randomised, double-blind, placebo-controlled trial. Lancet Neurol. 16: 505-512.
3. Kaste M, Murayama S, Ford GA, Dippel DW, Walters MR and Tatlisumak T (2013) MCI-186 study group. Safety, tolerability and pharmacokinetics of MCI-186 in patients with acute ischemic stroke: new formulation

and dosing regimen. Cerebrovascular Dis. 36:196-204.

4. Abe K, Itoyama Y, Sobue G, Tsuji S, Aoki M, Doyu M, Hamada C, Kondo K, Yoneoka T, Akimoto M and Yoshino H (2014) Confirmatory double-blind, parallel-group, placebo-controlled study of efficacy and safety of edaravone (MCI-186) in amyotrophic lateral sclerosis patients. Amyotroph Lateral Scler Frontotemporal Degeneration 15: 610-617

Biography

Koji Abe is currently a Professor and Chairman of Neurology at Okayama University Medical School in Japan. He graduated MD from Tohoku University School of Medicine, and then got PhD title from Tohoku University under direction of Professor Kyuya Kogure. He has been publishing more than 350 papers on cerebral blood flow and metabolism and neurodegenerative diseases. His research interests cover many important fields of neurology especially in the mechanism of ischemic brain damage, gene and stem cell therapy, neuroprotection, and neuroimaging. He is the Past President of the International Society of Cerebral Blood Flow and Metabolism (CBFM), and organized World CBFM meeting in Osaka in 2007 and Japan-Asia CBFM meeting Okayama city in 2014. He is currently serving Presidents of both Vas-Cog Japan and Vas-Cog Asia societies.

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