Response to Elia *et al.* 'Tauroursodeoxycholic acid in the treatment of patients with amyotrophic lateral sclerosis'

M. Michaud[a,b], C. Gauchet[c] and C. Dray[d]

[a]*CHU Toulouse, Service de Médecine Interne et Gérontologie,* [b]*Université de Toulouse, Faculté de Médecine,* [c]*CHU Toulouse, Direction de la Recherche et de l'Innovation, and* [d]*Inserm, U1048, Toulouse, France*

Correspondence: M. Michaud, Post Urgence Gériatrique, Pavillon Sénac, Hôpital Purpan, Place Dr Baylac, 31049 Toulouse Cedex, France (tel.: +33 561 77 92 88; fax: +33 561779927; e-mail: martin.michaud85@gmail.com).

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Dear Editor,

We have read with attention the original paper by Elia *et al.* [1] about tauroursodeoxycholic acid (TUDCA) in the treatment of patients with amyotrophic lateral sclerosis (ALS).

The choice of TUDCA as a potential treatment of ALS is justified by potential neuroprotective and anti-cytotoxic effects of TUDCA. Regarding this point we do think that the role of endoplasmic reticulum (ER) stress in the pathophysiology of ALS could have been developed in this paper.

ER is responsible for the folding, post-translational modification and trafficking of many transmembrane and secretory proteins [2]. Accumulation of unfolded and misfolded proteins leads to ER stress, also called unfolded protein response. Unfolded protein response is initially a physiological response to restore ER homeostasis. In contrast, when the ER stress is not resolved apoptosis pathways are triggered.

In animal models of ALS, an excessive ER stress activation has been observed [3]. Moreover, ER stress has been observed in spinal cord tissues of patients suffering from sporadic ALS [4–6]. As ER stress can induce oxidative stress, apoptosis and autophagy, targeting ER stress is a potential therapeutic direction in several diseases, including ALS [7,8]. Indeed, there is a growing interest in TUDCA and its potential therapeutic effects. Elia *et al.* suggest that the beneficial effect of TUDCA is mediated by mitochondrial dysfunction. We advocate that a main point with TUDCA is its ability to reduce ER stress. Studies report that TUDCA could be an anti-apoptotic agent for a number of other neurodegenerative diseases (Alzheimer's disease, Parkinson's disease and Huntington's disease) and metabolic diseases (diabetes, obesity, stroke, acute myocardial infarction) [9].

Finally, a measurement of ER stress levels in peripheral blood mononuclear cells of patients in both groups (TUDCA and placebo) would have been interesting [10].

Disclosure of conflicts of interest

The authors declare no financial or other conflicts of interest.

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