



Reply

## Reply to a Comment Paper on the Published Paper by Canta, A. et al: “Calmangafodipir Reduces Sensory Alterations and Prevents Intraepidermal Nerve Fibers Loss in a Mouse Model of Oxaliplatin Induced Peripheral Neurotoxicity”—*Antioxidants* 2020, 9, 594

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The comments sent by Stehr, Lundstom and Karlsson with reference to our article “Calmangafodipir reduces sensory alterations and prevents intraepidermal nerve fiber loss in a mouse model of oxaliplatin-induced peripheral neurotoxicity” are very interesting, since they suggest possible mechanisms of action of the compound, which might contribute to its protective action.

However, we performed the study with a different aim, which was to search a thoroughly characterized mouse model for pathological evidence of calmangafodipir’s efficacy.

This approach was prompted by the clinical observation of its neuroprotective activity in oxaliplatin-treated patients, based on patient reported outcome (PRO) measures. The use of PROs is strongly supported by international regulatory agencies, but in clinical trials it is hardly possible to achieve pathological confirmation of the results. This might raise concerns over the objective extent of the perceived effect reported by patients and graded only using PRO measures.

As a consequence of our study design and its endpoint, we did not plan to collect biological samples that might be used for mechanistic studies on calmangafodipir activity, which might be the topic of specific new studies.

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