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REPLY TO LETTER

# Reply to: The need for evidence-based treatment decisions in spinal muscular atrophy type 0

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Dear Prof Kessler,

Thank you for giving the possibility to comment to the letter sent by Erbas and Gusset[1] in reply to our case report describing treatment of a patient affected by the most severe form of spinal muscular atrophy with prenatal onset (type 0).[2]

We were pleased to see that the patient/family perspective on this topic is very much in line with the conclusions of our case report. We fully share their concern that little is still known about the possible efficacy of the new therapies in patients with the most severe form of SMA with prenatal onset. The three cases briefly reported by Erbas and Gusset in the table suggest a possible better response than that seen in our case and we hope that there will be a full report of those cases with more details on onset, timing of need of ventilation, nutritional support, and other aspects. This would help to better characterize both the severity of the cases before treatment and the full extent of the possible response to treatments in patients who may have different presentation and severity.

We fully support the statement that treatment decision should be made at the individual level, together with the involved family and in full transparency. As clinicians, however, we also feel that on the basis of the existing data the amount of information available to the families at the time of making a decision is still very limited and controversial and that we should be cautious in supporting an indiscriminate full access to the therapies to the severely affected patients. We often face families of severely affected infants having unrealistic expectations on the possible efficacy of treatment in their children, basing their hopes on the successful results obtained in more typical type I SMA infants that cannot be replicated in the most severe cases. Even in the more positive experience of treatment reported in the letter, these children do require invasive ventilation and do not resemble the treated infants with less severe forms. Another note of caution and concern is that the most severe forms are also more likely to have a more severe phenotype with multiorgan involvement and may therefore also have a different safety profile and increased risk compared to the less severe type I infants.

We therefore also encourage, in agreement with Erbas and Gusset, the publication of other existing cases of treated type 0 patients to improve our knowledge on efficacy and safety and the ability to make decisions that at the moment is based on anecdotal cases.

## References

1. Erbas J, Gusset N. The need for evidence based treatment decisions in spinal muscular atrophy type 0. Ann Clin Transl Neurol.
2. Tiberi E, Costa S, Pane M, et al. Nusinersen in type 0 spinal muscular atrophy: should we treat? Ann Clin Transl Neurol. 2020;7:2481-2483.