

Is statistical significance sufficient for recommending the use of a drug for ALS patients? Yes

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In general, motor neuron diseases like SMA and ALS are severe diseases which were previously thought to be untreatable. The experience of successful treatment of SMA children with antisense oligonucleotides has demonstrated that treatment can be convincingly successful. Therefore, the argument that clinical effects of pharmacological treatments of motor neuron diseases must be clearly visible, is easy to understand. But I think that this argument is an overreaction and premature. Not all subforms of MND can be defined by a definite cause like alterations in the SMN1 gene. Sporadic diseases are still defined by their complex formal and mechanistic pathogenesis and therefore we have to anticipate that therapeutic progress is slow in these sporadic patients and will occur in steps. Also, patients without defined risk factors such as a genetic cause need to be treated. Therefore, we should not abandon small steps of progress as shown in current clinical trials. We have to tell patients which advantages a given treatment may have although only a small statistical effect may be present. The final decision on the treatment must be made by the well-informed patient; for example 3-4 months more as achieved by a treatment without side effects may be valuable for many. There is also another reason to accept small steps of progress beyond this pragmatic one: a comparatively small statistic effect might serve as the proof of a new concept, which includes the subsequent conduct of dose/effect studies, the exploration of promising intervention pathways and the introduction of similar drugs. Therefore, statistically significant effects are not only valuable for patients accepting them, but also for future ALS and – SMA research.