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A.A. Sanabria-Sanchinel[a], E.S. Pérez-Almengor[a], M. Guasch-Jiménez[a], A. Principe[a,b], M. Ley[a,b,*], R.A. Rocamora-Zúñiga[a,b]

[a] *Unidad Multidisciplinar de Epilepsia, Servicio de Neurología, Hospital del Mar, Barcelona, Spain*
[b] *IMIM (Instituto de Investigaciones Médicas del Hospital del Mar), Barcelona, Spain*

* Corresponding author.
E-mail address: mley@parcdesalutmar.cat (M. Ley).

https://doi.org/10.1016/j.nrleng.2020.10.004
2173-5808/

Treatment of patients with spinal muscular atrophy 5q: towards a new protocol☆

Tratamiento de pacientes con atrofia muscular espinal 5q: hacia un nuevo protocolo

Dear Editor:

In recent years, significant advances have been made in the treatment of spinal muscular atrophy (SMA) through the development of disease-modifying treatments.[1] The first treatment available in clinical practice is nusinersen, an anti-sense oligonucleotide that increases production of the SMN protein by the *SMN2* gene, and should be administered intrathecally. The drug was approved based on the results of 2 pivotal trials: ENDEAR, for type 1 SMA,[2] and CHERISH, for type 2 and 3 SMA.[3] In 2018, the Spanish Ministry of Health published a pharmacological and clinical protocol for the use of nusinersen to treat patients with muscular atrophy, based on a therapeutic positioning report gathering the evidence available until 2017.[4] This protocol has been used as a guideline to establish an efficient and equitable approach within the Spanish National Health System, both in terms of access to treatment and proper monitoring.

However, more accurate information on the long-term effects of this treatment has been obtained over the past 3 years,[5,6] as well as information from populations not initially included in the pivotal trials, such as presymptomatic and adult patients.[7,8] We also now have further information on the natural history of the condition, particularly on the development of motor assessment scales for type 2 and 3 SMA.[9–12] Furthermore, new treatments including risdiplam[13] and onasemnogene abeparvovec (Zolgensma®) will become available in the coming months.[14]

It is therefore particularly important to review the current therapeutic positioning, from the perspective of clinical practice and from that of the healthcare system. On the one hand, the review should address the clinical criteria for, among other things, favouring earlier treatment onset (when treatment is more efficacious), including during the presymptomatic stage of the disease; adapting therapeutic objectives to the functional status of each patient; better defining the indications in adolescent and adult patients; and monitoring the simultaneous use of other treatments. On the other hand, follow-up protocols should focus on improvements in patients' functional status and quality of life, beyond the observable changes in the motor scales used in every visit. Furthermore, this follow-up should be adjusted in line with the increasing evidence on the low frequency of some adverse effects, avoiding unnecessary and especially invasive tests in some populations, such as infants with type 1 SMA, and the possible occurrence of events associated with the neophenotypes resulting from treatment (for example, scoliosis). Finally, treatment with-

☆ Please cite this article as: Gómez-Andrés D, Martínez-Moreno M, Vázquez-Costa JF. Tratamiento de pacientes con atrofia muscular espinal 5q: hacia un nuevo protocolo. Neurología. 2021;36:636—637.

drawal criteria should be adjusted according to new data on the natural history of the condition, considering the objectives established for each patient based on their clinical situation prior to treatment onset. In summary, the new protocol should follow a patient-oriented approach enabling the personalisation of therapeutic objectives and the assessment of risks in consensus with the patient, within a pre-established framework. A multidisciplinary group of Spanish paediatric neurologists, neurologists, and rehabilitation physicians with experience in SMA, together with patients' representatives, is currently working on a consensus document providing recommendations on inclusion and exclusion criteria and assessment of the response to new treatments in patients with SMA. We hope that these recommendations will be of assistance in designing a new protocol that maximises the benefit and minimises the risks of the new treatments.

Conflicts of interest

JFVC has received lecture honoraria and consulting fees from Biogen and Roche. He works as a researcher in projects funded by FUNDAME, Biogen, and Roche.

DGA has received research funding from PTC Therapeutics, lecture honoraria from PTC Therapeutics, Biogen, and Shire, and consulting fees from Biogen; he is also a shareholder in Aura Robotics S.L.

MMM has received lecture honoraria from Biogen, Roche, and Avexis.

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D. Gómez-Andrés[a,b], M. Martínez-Moreno[c,d], J.F. Vázquez-Costa[e,f,g,*]

[a] *Grupo de Trabajo de Enfermedades Neuromusculares de la Sociedad Española de Neurología Pediátrica, Barcelona, Spain*
[b] *Unidad de Enfermedades Neuromusculares Pediátricas, Neurología Pediátrica, Hospital Universitario Vall d'Hebron, Barcelona, Spain*
[c] *Sección de Rehabilitación Infantil, Servicio de Medicina Física y Rehabilitación, Hospital Universitario La Paz, Madrid, Spain*
[d] *Sociedad Española de Rehabilitación Infantil, Madrid, Spain*
[e] *Centro de Investigación Biomédica en Red de Enfermedades Raras (CIBERER), Valencia, Spain*
[f] *Unidad de Enfermedades Neuromusculares, Departamento de Neurología, Hospital Universitario y Politécnico La Fe, Valencia, Spain*
[g] *Departamento de Medicina, Facultad de Medicina, Universitat de València, Valencia, Spain*

* Corresponding author.
E-mail address: juan.vazquez.neuro@gmail.com (J.F. Vázquez-Costa).

https://doi.org/10.1016/j.nrleng.2020.10.005
2173-5808/