Stem Cell Therapy in Neuromuscular Diseases

Statement by the TREAT-NMD Project Ethics Council, February 2014

Summary

- Previous PEC guidance on stem cells remains valid.
- Stem cells are still not a proven treatment for neuromuscular diseases.
- To become a proven treatment, they must first undergo rigorous clinical trials to prove they are both safe and effective.
- Such trials should be well-designed and be approved by regulators; "n = 1" trials or other individual applications do not fall within this category.
- Direct offers of unproven so-called 'treatments' to families are unethical and cannot be endorsed by the PEC.
- Although a promising area, much more research is required before stem cells can be considered a safe and effective treatment for humans.
- The PEC encourages families to contact the TREAT-NMD Secretariat if they have further questions.

Full Statement

Stem cell therapy is an issue that has been considered by the PEC on a number of occasions in the past [1]. These have included a question submitted to the PEC regarding "stem cell tourism" [2] and a statement in relation to SMA Type 1 children [3]. A series of resources have also been posted on the TREAT-NMD website in relation to these issues [4], particularly in the areas of "Hope versus hype" [5] and cord blood banking [6]. The conclusions presented in those documents are still valid.

However, stem cell research remains an active topic, with discussion amongst patients and families about new findings in this area of research. The PEC therefore believes it is important to revisit this issue and state the current situation for the benefit of the community, and particularly to emphasise that **stem cells are still not a proven treatment** for neuromuscular diseases.

In particular there is no evidence of beneficial effect of stem cells when administered systemically (i.e. for diseases in which there is the intent to obtain improvement in many different muscle groups, such in muscular dystrophies, following an administration in the bloodstream) nor when administered directly into the spinal fluid for spinal muscular atrophy. Research into the use of autologous stem cells in oculopharyngeal muscular dystrophy (OPMD), following their direct injection in some of the swallowing muscles, is more advanced and promising than in other conditions, but even in this specific case it is still at an early experimental stage.

For a potential stem cell therapy to become a viable treatment, it must be demonstrated to be both safe and effective. To enable this, research on stem cells should adhere to clinical trial good practices, with appropriate approval from regulatory authorities. It should be conducted in such a way that something can be learned from the trial, with a rigorous scientific rationale and a realistic pathway for further development.

The first clinical trials, such as those currently ongoing for mesangioblasts, are at the 'safety test' stage with the number of cells transplanted being far below what would be expected to lead to clinical improvement. Because stem cells are by their nature cells with a huge potential to divide, safety tests are a crucial step in the development to exclude (for example) cancer formation. At the moment, it is not only unknown whether treatment with stem cells will be effective, but it is also unknown whether they are safe. As the previous PEC guidance states, "using an intervention where the risks are unknown or not made known, and without the evidence for benefit makes it impossible to make an informed choice" [2].

Given these uncertainties, **the PEC considers that it is not appropriate to offer such an intervention to an individual patient outside a controlled clinical trial**. In fact, offering it to patients risks creating a misconception that stem cells are a legitimate 'treatment' in spite of a lack of evidence. The problems associated with administering an intervention to an individual (a so-called 'n=1 trial') in a progressive disease such as Duchenne muscular dystrophy have been addressed by Annemieke Aartsma-Rus, who notes that these are not trials in the correct sense of the word, but rather are "the administration of potentially harmful substances to a patient in the (possibly unjustified) hope that it might help, but without evidence that there are reasonable chances that it will" [7]. This applies to stem cells as it does to exon-skipping and other experimental therapies.

Furthermore, there have been instances where unproven 'stem cell treatments' have been offered to patients directly. In some cases, families have been charged considerable amounts of money for procedures which have not been shown to be efficacious and may indeed be harmful. The recent revelations around the framework related to work performed by the Stamina Foundation in Italy provide just one example of the need for significant caution to be exercised about those claiming to offer 'stem cell therapies' [8]. Nevertheless, despite these excesses, stem cells still represent innovative and promising approaches as illustrated by clinical trials that have started in the last decade, but more research will be necessary before this will translate into safe therapies for humans [9, 10]

The TREAT-NMD Alliance is keen to support patients and their families, and encourages anyone with questions about possible treatments to contact the TREAT-NMD Secretariat in the first instance.

References

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[2] PEC Question 7: Unproven Stem Cell Therapy, http://www.treat-nmd.eu/resources/ethics/questions-received/#7

[3] "Concerns over stem cell therapy for SMA type 1 children", statement by President of SMA Europe, TREAT-NMD Website, http://www.treat-nmd.eu/resources/ethics/stem-cell-sma/

[4] "Stem Cells", TREAT-NMD Website, http://www.treat-nmd.eu/resources/ethics/stem-cell/

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