Statutory Approvals Committee – minutes

Centre 0102 (Guys Hospital)

Pre-implantation Genetic Diagnosis (PGD) application for Congenital hypomyelinating neuropathy 3 (CHN3), OMIM #618186

Thursday, 17 December 2020

HFEA, 2nd Floor, 2 Redman Place, London E20 1JQ via Teams Meeting

Committee members	Margaret Gilmore (Chair) Emma Cave Anne Lampe Ruth Wilde	
Members of the Executive	Moya Berry Catherine Burwood	Committee Officer Licensing Manager
Specialist Adviser	Dr. Alison Male	
Legal Adviser	Tom Rider	Fieldfisher - LLP

Declarations of interest:

- Members of the committee declared that they had no conflicts of interest in relation to this item.

The committee had before it:

- 9th edition of the HFEA Code of Practice.
- Standard licensing and approvals pack for committee members.

The following papers were considered by the committee:

- Executive summary
- PGD Application form
- Redacted peer review
- Genetic Alliance statement
- Phenotype of CNTNAP1: a study of patients demonstrating a specific severe hypomyelinating neuropathy with survival beyond infancy, KJ Lowe et al, 2018

1. Consideration of application

1.1. The committee welcomed the advice of its specialist adviser, Dr. Alison Male, who confirmed that the condition was as described in the papers.

1.2. The committee noted that the description in the PGD application for Congenital hypomyelinating neuropathy 3 (CHN3), OMIM #618186, is consistent with the peer review.

1.3. The committee noted that the condition being applied for is not on the list of approved PGD conditions.

1.4. The committee noted that the Genetic Alliance statement provided a perspective on the impact of the condition on patients, their families and carers.

1.5. The committee had regard to its decision tree. The committee noted that the centre is licensed to carry out PGD. The committee was also satisfied that the centre has experience of carrying out PGD and that generic patient information about its PGD programme and associated consent forms had previously been received by the HFEA.

1.6. The committee noted that the proposed purpose of testing the embryos was as set out in paragraph 1ZA(1)(b) of Schedule 2 of the Act, i.e. 'where there is a particular risk that the embryo may have any gene, chromosome or mitochondrion abnormality, establishing whether it has that abnormality or any other gene, chromosome or mitochondrion abnormality'.

1.7. The committee noted that Congenital hypomyelinating neuropathy 3 (CHN3), OMIM #618186, is inherited in an autosomal recessive manner, which means there is a 25% chance of an embryo being affected by the condition in each pregnancy if each parent has a relevant mutation.

1.8. The committee noted the penetrance is unknown.

1.9. Congenital hypomyelinating neuropathy 3 (CHN3), OMIM #618186, is characterised by the onset of neuromuscular impairment in utero. Affected individuals present with severe hypotonia at birth, causing respiratory insufficiency or inability to swallow or feed properly. Affected individuals may die in infancy or early childhood.

1.10. There is no cure for the condition. Treatments aim to promote survival from infancy to early childhood and include respiratory support with tracheostomy. All individuals are significantly impacted and will have significant medical needs in their lifetime.

1.11. The committee noted the executive's request to consider Congenital hypomyelinating neuropathy 3 (CHN3), OMIM #618186, for inclusion on the list of conditions approved for PGD. The committee agreed to consider the application on this basis.

1.12. The committee also noted the recommendation of the peer reviewer to consider two other types of conditions for inclusion on the list for which PGD can be applied. These conditions are Congenital hypomyelinating neuropathy type 1, OMIM #605253 and Congenital hypomyelinating neuropathy 2, OMIM #618184.

1.13. Congenital hypomyelinating neuropathy 1, OMIM #605253 is clinically indistinguishable from Congenital hypomyelinating neuropathy 3 (CHN3), OMIM #618186 in its presentation (autosomal recessive), although only the peripheral nerves are affected, and cognition is usually normal.

1.14. Congenital hypomyelinating neuropathy 2, OMIM #618184 is inherited in an autosomal dominant manner and presents with early onset hypotonia, severely delayed motor development and muscle weakness. The severity is variable with some patients presenting at birth with contractures and respiratory insufficiency, whereas others may achieve walking. However, even if those with the condition are able to walk, they may require assistance with the aid of a walker or crutches and a wheelchair. The facial nerve and other cranial nerves can be affected, causing facial weakness and curvature of the spine in some. Cognition is normal.

2. Decision

2.1. The committee considered that, in the worst-case scenario, Congenital hypomyelinating neuropathy 3 (CHN3), OMIM #618186, is a rare life-limiting neuromuscular condition that develops in utero and presents at birth. There is no cure for the condition and affected individuals can die in infancy or early childhood. Those who do survive may be unable to sit or walk and have profoundly impaired psychomotor development and developmental delay. There is no cure for the condition and the committee considered the potential physical and devastating impact on the quality of life of those affected with the condition.

2.2. The committee considered that, in the worst-case scenario, Congenital hypomyelinating neuropathy 1, OMIM #605253 and Congenital hypomyelinating neuropathy 2, OMIM #618184 both present with severely delayed motor development and muscle weakness that can present at birth and lead to death in infancy.

2.3. The committee had regard to its explanatory note and confirmed that, on the basis of the information presented, it was satisfied that there is a particular risk that an embryo may have the abnormality in question and that there is a significant risk that a person with such an abnormality will, given the condition's worst symptoms, have or develop a serious physical disability, a serious illness or any other serious medical condition.

2.4. The committee was therefore satisfied that the following conditions meet the criteria for testing under paragraph 1ZA(1)(b) and (2) of Schedule 2 of the Act.

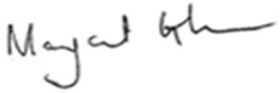
2.5. The committee agreed to authorise testing for:

- Congenital hypomyelinating neuropathy 1 (CHM1), OMIM #605253
- Congenital hypomyelinating neuropathy 2 (CHN2), OMIM #618184
- Congenital hypomyelinating neuropathy 3 (CHN3), OMIM #618186

3. Chairs signature

3.1. I confirm this is a true and accurate record of the meeting.

Signature



Name
Margaret Gilmore

Date
14 January 2021