Statutory Approvals Committee - minutes

Centre 0201 (Edinburgh Assisted Conception Unit)

Preimplantation Genetic Diagnosis (PGD) application for TBCK related developmental disorder hypotonia, infantile, with psychomotor retardation and characteristic facies 3 (IHPRF3), OMIM #616900

Date:	29 April 2021
Venue:	Microsoft Teams Meeting
Committee Members:	Margaret Gilmore (Chair) Emma Cave Anne Lampe Ruth Wilde Jason Kasraie
Specialist Adviser:	Jenny Carmichael
Legal Adviser:	Darryn Hale – DAC Beachcroft LLP
Members of the Executive:	Moya Berry - Committee officer Catherine Burwood - Licensing Manager
Observers:	Julia Chain - HFEA Chair (Induction) Tim Child - HFEA Authority Member (Induction) Neil Ward - Mills & Reeve LLP (New Legal Adviser) (Induction)
Apologies:	No apologies were received for the meeting
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:

- HFEA Code of Practice 9th edition
- Standard Licensing and Approvals Pack

The following papers were considered by the committee:

- Executive Summary
- PGD Application form
- Redacted Peer review
- Genetic Alliance (UK) Statement
- 2018-08-30 Statutory Approvals Committee Minutes- Multiple Congenital Anomalies Hypotonia Seizures type 3 (MCAHS3) OMIM #615398

1. Consideration of application

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

1.2. The committee noted that the description in the PGD application for TBCK related developmental disorder hypotonia, infantile, with psychomotor retardation and characteristic facies 3 (IHPRF3), OMIM #616900, 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 condition, TBCK related developmental disorder hypotonia, infantile, with psychomotor retardation and characteristic facies 3 (IHPRF3), OMIM #616900 is also known as Hypotonia, infantile, with psychomotor retardation and characteristic facies 3 (IHPRF3), OMIM #616900. As the OMIM website entry lists Hypotonia, infantile, with psychomotor retardation and characteristic facies 3 (IHPRF3), OMIM #616900 as the primary name of the condition, the condition, for the purposes of this application, will be termed Hypotonia, infantile, with psychomotor retardation and characteristic facies 3 (IHPRF3), OMIM #616900.

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

1.6. 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.

1.7. 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'.

1.8. The committee noted that Hypotonia, infantile, with psychomotor retardation and characteristic facies 3 (IHPRF3), OMIM #616900, 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.

1.9. The committee noted that the penetrance of the condition is 100%.

1.10. Hypotonia, infantile, with psychomotor retardation and characteristic facies 3 (IHPRF3), OMIM #616900, is characterised by delayed psychomotor development. Affected children have reduced muscle tone that often results in feeding difficulties and can cause breathing difficulties

in severe cases. Affected children often have few or no words. Epileptic seizures are common. Some affected children have a progressive disorder with loss of previously acquired abilities.

1.11. There is no treatment for this condition and most affected children have both severe intellectual and physical disability.

1.12. The committee noted the executive's request to consider Hypotonia, infantile, with psychomotor retardation and characteristic facies 3 (IHPRF3), OMIM #616900, for inclusion on the list of conditions approved for PGD. The committee agreed to consider the application on this basis.

1.13. 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 and agreed to consider the application on this basis.

1.14. The conditions Hypotonia, infantile, with psychomotor retardation and characteristic facies 1 (IHPRF1), OMIM #615419 and Hypotonia, infantile, with psychomotor retardation and characteristic facies 2 (IHPRF2), OMIM #616801 are of a similar phenotype and clinical presentation to Hypotonia, infantile, with psychomotor retardation and characteristic facies 3 (IHPRF3), OMIM #616900. The conditions are inherited in an autosomal recessive manner, which means there is a 25% chance of an embryo being affected by the conditions in each pregnancy if each parent has a relevant mutation. Penetrance is also likely to be 100%. Most cases present at birth or soon after with severe hypotonia (decreased muscle tone) and developmental delay is severe in all subtypes. Types 1 and 2 sometimes show regression of any skills that have developed. Most affected individuals remain non-verbal. Seizures occur in all sub-types, as does visual impairment, the need for gastrostomy feeding, ventilation and limited lifespan.

2. Decision

2.1. The committee considered that, in the worst-case scenario, Hypotonia, infantile, with psychomotor retardation and characteristic facies 3 (IHPRF3), OMIM #616900, is a progressive neurodevelopmental disorder with onset at birth or in early infancy. There is no treatment for the condition and most affected individuals will suffer severe intellectual and physical disability with very poor psychomotor development, poor communication, and a lack of mobility. Those affected may also suffer with epilepsy and visual impairment. The committee considered the serious implications for, and the potential severe impact, on the quality of life of those affected by the condition.

2.2. The committee also considered the conditions, Hypotonia, infantile, with psychomotor retardation and characteristic facies 1 (IHPRF1), OMIM #615419 and Hypotonia, infantile, with psychomotor retardation and characteristic facies 2 (IHPRF2), OMIM #616801. These conditions can present from birth and in the worst-case scenario those affected show severe delayed physical and intellectual development, limited speech development, seizures and usually an inability to walk unaided.

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 conditions' worst symptoms, have or develop a serious physical disability, a serious illness, or any other serious medical condition.

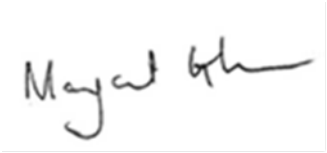
2.4. The committee was therefore satisfied that the following conditions meet the criteria for testing under paragraph 1ZA(1)(b) and (2) of Schedule 2 of the Act. The committee agreed to authorise testing for:

- Hypotonia, infantile, with psychomotor retardation and characteristic facies 1 (IHPRF1), OMIM #615419
- Hypotonia, infantile, with psychomotor retardation and characteristic facies 2 (IHPRF2), OMIM #616801
- Hypotonia, infantile, with psychomotor retardation and characteristic facies 3 (IHPRF3), OMIM #616900

3. Chair's signature

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

Signature



Name

Margaret Gilmore

Date

1 June 2021