Statutory Approvals Committee – minutes

Centre 0119 (Birmingham Women's Hospital)

Pre-implantation Genetic Diagnosis (PGD) application for Mitochondrial Complex 1 Deficiency caused by mutation in the NDUFS4 gene, OMIM #602694

Thursday, 29 June 2017

Church House Westminster, Dean's Yard, Westminster SW1P 3NZ

Committee members	Margaret Gilmore (Chair) Anne Lampe Ruth Wilde Bobbie Farsides	
Members of the Executive	Bernice Ash Paula Robinson	Secretary Head of Planning & Governance
External adviser	Dr Alan Fryer	
Legal Adviser	Ros Foster	Browne Jacobson LLP
Observers		

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:

- 8th 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 opinion
- Minutes of two previous Statutory Approval Committee decisions

1. Consideration of application

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

1.2. The committee noted that the description in the application for Mitochondrial Complex 1 Deficiency caused by mutation in the NDUFS4 gene, OMIM #602694 is consistent with the Peer Review.

1.3. The committee noted that while the Genetic Alliance opinion was given for Mitochondrial Complex 1 Deficiency in general, rather than specifically for the condition resulting from mutation in the NDUFS4 gene, the Executive was of the view that it was relevant as the peer reviewer had noted that the severity of Complex 1 deficiency was extremely variable but that the deficiency resulting from the NDUFS4 mutation was associated with more severe outcomes such as death in infancy. The Genetic Alliance supported the application.

1.4. 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.

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

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 the condition is inherited in an autosomal recessive manner which means there is a 25% chance of having an affected child in each pregnancy, if each parent has a relevant mutation.

1.8. Mitochondrial Complex 1 Deficiency, caused by a mutation in the NDUFS4 gene, has been seen to be lethal in early neonatal life in some cases. The condition appears to be fully penetrant.

1.9. The committee noted that, in the worst case scenario, an affected individual would demonstrate hypotonia (floppiness) within a few days of birth, and a lack of attentiveness or visual and auditory response. Subsequently the infant would fail to thrive with worsening hypotonia. The head size would fail to increase in size and microcephaly would develop. In addition, the heart may develop a form of hypertrophic cardiomyopathy (thickening of the heart muscle) which can be severe enough to cause circulatory collapse. Seizures and epilepsy are also likely and death may occur within a few weeks of birth.

1.10. The committee noted that even milder cases presenting in the post-neonatal period have a similar pattern of neurodegeneration and organ failure, leading to death in late infancy or early childhood.

1.11. The committee noted there is currently no curative treatment for Mitochondrial Complex 1 Deficiency. The condition is infantile onset and early death often occurs: affected individuals may have a poor quality of life. Not only do affected children fail to thrive but they also fail to demonstrate normal neurodevelopment.

1.12. The committee noted the inspectorate's request to consider whether Mitochondrial Complex 1 Deficiency caused by mutation in the NDUFS4 gene, OMIM #602694 should be approved for inclusion on the PGD List. If approved, the condition would be named as Mitochondrial Complex 1 Deficiency caused by mutation in the NDUFS4 gene, OMIM #602694 which is consistent with the information published by OMIM. The committee agreed to consider the application on this basis.

2. Decision

2.1. The committee considered that Mitochondrial Complex 1 Deficiency caused by mutation in the NDUFS4 gene, OMIM #602694 is serious given the early onset and the impact on quality of life of this condition, including hypertrophic cardiomyopathy, effects on communication abilities, severe impact on life expectancy and the lack of a cure. The committee considered the impact on the family caring for affected individuals.

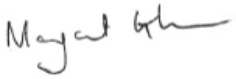
2.2. The committee had regard to its explanatory note and noted that on the basis of the information presented, given the condition's worst symptoms, it was satisfied that there is a significant risk that a person with the abnormality will have or develop a serious physical or mental disability, a serious illness or any other serious medical condition. The committee was therefore satisfied that the condition of Mitochondrial Complex 1 Deficiency caused by mutation in the NDUFS4 gene, OMIM #602694 does meet the criteria for testing under paragraph 1ZA(1)(b) and (2) of Schedule 2 of the Act.

2.3. The committee agreed to authorise the testing for Mitochondrial Complex 1 Deficiency caused by mutation in the NDUFS4 gene, OMIM #602694.

3. Chair's signature

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

Signature



Name

Margaret Gilmore

Date

25 July 2017