Statutory Approvals Committee – minutes

Centre 0102 (Guy's Hospital)

Pre-implantation Genetic Diagnosis (PGD) application for

Nemaline Myopathy type 8, OMIM #615348

Thursday, 24 May 2018

HFEA, 10 Spring Gardens, London, SW1A 2BU

Committee members	Margaret Gilmore (Chair) Bobbie Farsides (Deputy Chair) Anne Lampe	
Members of the Executive	Bernice Ash Dee Knoyle Paula Robinson Catherine Burwood Mhairi West	Committee Secretary Committee Secretary (Observer) Head of Planning and Governance (Observer) Senior Governance Manager (Observer) Inspector (Observer - Induction)
Specialist Adviser	Dr Ed Blair	
Legal Adviser	Sarah Ellson	Fieldfisher 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 UK Statement
- 2017-10-26 SAC Minutes - PGD Nemaline Myopathy ACTA 1 OMIM #161800
- 2015-02-25 SAC Minutes - PGD for Nemaline myopathy type 2 OMIM #256030

1. Consideration of application

1.1. The committee welcomed the advice of its Specialist Adviser, Dr Ed Blair who confirmed that the condition was as described in the papers.

1.2. The committee noted that the description in the application for Nemaline Myopathy type 8, OMIM #615348 is consistent with the peer review.

1.3. The committee noted that the Genetic Alliance opinion provided a patient perspective and 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 pattern which means there is a 25% chance of an embryo being affected with the condition, if each parent has a relevant mutation.

1.8. The committee noted that Nemaline Myopathy is a muscle disorder characterized by weakness of all skeletal muscles (myopathy) throughout the body, but most severe in the face, neck, trunk and muscles close to the centre of the body (shoulder and pelvis muscles). The muscle weakness causes swallowing and feeding difficulties, and respiratory insufficiency leading to respiratory failure. Nemaline Myopathy, type 8 is a severe early onset myopathy caused by an abnormality in the KHLH40 gene. Affected foetuses have no spontaneous movement in utero during pregnancy and may have contractures – permanent shortening of muscles – from early in the new born period. These children have difficulty in swallowing, making feeding very difficult, and also have severe gastroesophageal (acid) reflux. Together, these complications, which may be present from birth, mean that the children do not thrive.

1.9. Symptoms of the condition include foetal akinesia or hypokinesia (decreased foetal movement), weak muscles in face, neck, trunk, upper arms, contractures, fractures, scoliosis (spine has a sideway curve), respiratory insufficiency and failure, swallowing difficulties which are apparent at birth and delayed motor development.

1.10. Nemaline myopathy occurs in multiple types varying according to causative mutation, age of onset and severity, although there is overlap of symptoms. The genetic basis of some types is unknown. Nemaline Myopathy type 8 is one of the more severe types with presentation in the early neonatal period. The condition is 100% penetrant in a foetus which inherits two causative mutations.

1.11. The panel noted that treatment available is not curative. It requires a multi-disciplinary approach. Respiratory infections require fast and aggressive treatment, and possibly the need for a mechanical ventilator at night. Patients need good nutrition and possibly special feeding techniques. Orthopaedic assessments for muscle contractures and scoliosis with physiotherapy and speech therapy are required. Children have breathing difficulty due to involvement of the muscles in the diaphragm and chest wall, and therefore require respiratory support. Many children also have poor heart muscle function – cardiomyopathy. Most children die in infancy.

1.12. The committee noted the inspectorate's request to consider whether Nemaline Myopathy type 8, OMIM #615348 should be approved for inclusion on the PGD List. The committee agreed to consider the application on this basis.

2. Decision

2.1. The committee considered that, in the worst case scenario, Nemaline Myopathy type 8, OMIM #615348 is serious given that it can cause cardiomyopathy and respiratory failure, resulting in death in early infancy. The committee considered this a devastating condition which can have severe effects on the quality of life of those with the condition and their families.

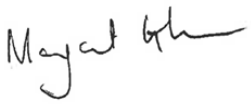
2.2. The committee had regard to its explanatory note and confirmed that, on the basis of the information presented, it was satisfied that there is a particular risk that an embryo may have the abnormality in question and that there is a significant risk, given the condition's worst symptoms, that a 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 Nemaline Myopathy type 8, OMIM #615348 meets the criteria for testing under paragraph 1ZA(1)(b) and (2) of Schedule 2 of the Act.

2.3. The committee agreed to authorise testing for Nemaline Myopathy type 8, OMIM #615348.

3. Chair's signature

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

Signature



Name

Margaret Gilmore

Date

19 June 2018