Statutory Approvals Committee – minutes

Centre 0102 (Guys Hospital)

Pre-implantation Genetic Diagnosis (PGD) application for

Glycogen Storage Disease, Type 4 (GSD4), OMIM #232500

Thursday, 30 March 2017

HFEA, 10 Spring Gardens, London, SW1A 2BU

Committee members	Margaret Gilmore (Chair) Anne Lampe Anthony Rutherford	
Members of the Executive	Dee Knoyle Erin Barton	Secretary Governance Manager
External adviser	Dr Alison Male	
Legal Adviser	Sarah Ellson	Fieldfisher
Observers		

Declarations of interest

- Members of the panel 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 the Licence Committee Meeting on 25 August 2011 which approved Glycogen Storage Disease type 1A as a condition for which PGD can be applied.
- Minutes of the Licence Committee Meeting on 11 September 2008 which approved Pompe Disease (also known as Glycogen Storage Disease type 2A) as a condition for which PGD can be applied.

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 Glycogen Storage Disease Type 4 (GSD4), OMIM #232500 is consistent with the Peer Review.

1.3. The committee noted that the Genetic Alliance opinion provided a patient's 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. It noted that Glycogen Storage Disease type 1A and type 2A are on the approved list.

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 and there is a 25% chance of having an affected child in each pregnancy, if each parent has a relevant mutation.

1.8. The committee noted that the condition demonstrates 100% penetrance and the onset of symptoms is from birth.

1.9. The committee noted that GSD4 has 5 subtypes which form a spectrum, with overlap between them. They show variable severity and different subtypes can be seen within a family.

1.10. The committee noted that the most severe subtype is 'fatal perinatal neuromuscular'. There is usually polyhydramnios (excess amniotic fluid), reduced fetal movements, hydrops (fluid within the baby's tissues, abdomen and around the lungs and heart) and arthrogryposis (joint contractures). Affected babies die in the neonatal period, often from respiratory failure as the lungs are underdeveloped as a result of reduced fetal movement, and weak chest muscles. Babies with 'congenital neuromuscular' subtype have profound hypotonia (floppiness), and develop dilated cardiomyopathy and usually die within the first year of life from heart and/or respiratory failure. 'Childhood neuromuscular' subtype is often less severe and can range from mild to severe, and death can occur in childhood or early adulthood.

1.11. The committee noted that the commonest subtype is ' classic (progressive) hepatic'. Often babies are normal at birth but soon after present with failure to thrive (unable to gain weight properly), hepatomegaly (enlarged liver) and liver dysfunction which progresses to liver failure. This can cause abdominal pain, sleepiness and feeling generally unwell, bleeding due to reduced blood clotting, which can be from varices - dilated blood vessels in the oesophagus. They become hypotonic and develop dilated cardiomyopathy which can progress and cause heart failure. Usually children die by the age of 5, unless they have a liver transplant. However, even if transplanted there is still high mortality and morbidity related to the transplant, or other features of GSD4, especially dilated cardiomyopathy. 'Non-progressive hepatic' present similarly but the liver dysfunction doesn't progress and may improve. Neuromuscular abnormalities and dilated cardiomyopathy may occur.

1.12. All subtypes of GSD4 significantly reduce quality of life and death in early childhood is frequent (see above).

1.13. The committee noted that there is no curative treatment for the condition.

1.14. The committee noted the inspectorate's recommendation to consider the approval of Glycogen Storage Disease Type 4, (GSD4) to be included on the PGD List. The committee agreed to consider the application on this basis.

2. Decision

2.1. The committee considered that the condition is serious. All subtypes of GSD4 significantly reduce quality of life and death in early childhood is frequent. In the most severe subtype babies die in the neonatal period, often from respiratory failure as the lungs are underdeveloped.

2.2. Liver failure may cause abdominal pain, nausea, sleepiness, feeling generally unwell, bleeding, including from oesophageal varices and confusion and cognitive impairment in hepatic encephalopathy. Usually children die by the age of 5, unless they have a liver transplant, however there is high morbidity related to the transplant.

2.3. Heart failure from dilated cardiomyopathy may cause breathlessness and fatigue and hypotonia results in failure to reach motor milestones. The committee considered how distressing these symptoms are for the child and their family and that intensive supportive care is required.

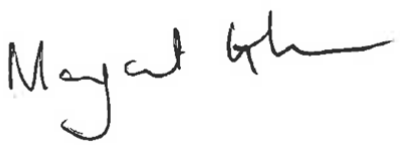
2.4. The committee had regard to its explanatory note and noted that on the basis of the information presented, given the condition's worst symptoms, it was satisfied that there is a significant risk that a person with the abnormality will have or develop a serious physical or mental disability, a serious illness or any other serious medical condition. The committee was therefore satisfied that the condition meets the criteria for testing under paragraph 1ZA(1)(b) and (2) of Schedule 2 to the Act.

2.5. The committee agreed to authorise the testing of embryos for Glycogen Storage Disease Type 4, (GSD4) OMIM #232500.

3. Chair's signature

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

Signature



Name

Margaret Gilmore

Date

30 March 2017