Statutory Approvals Committee – minutes

Centre 0102 (Guys Hospital)

Pre-implantation Genetic Diagnosis (PGD) application for Familial Haemophagocytic Lymphohistiocytosis Type 3 (FLH3), OMIM #608898 and Familial Haemophagocytic Lymphohistiocytosis Type 4 (FLH4), OMIM #603552

Thursday, 25 July 2019

HFEA Foyle Meeting Room, Level 1, 10 Spring Gardens, London, SW1A 2BU

Committee members	Margaret Gilmore (Chair) Bobbie Farsides (Deputy Chair) Emma Cave Tony Rutherford	
Members of the Executive	Moya Berry Catherine Burwood	Committee Secretary Licensing Manager (Observer)
Specialist Adviser	Peter Turnpenny	
Legal Adviser	Jane Williams	Mills & Reeve LLP

Declarations of interest

- Members of the committee declared that they had no conflicts of interest in relation to this item.
- Apologies were noted from Rachel Cutting (Committee Member)

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 UK statement
- Statutory Approvals Committee Minutes - 30 October 2014 - PGD for Familial Haemophagocytic Lymphohistiocytosis, OMIM # 613101
- Licence Committee Minutes - 1 March 2012 - PGD for Familial Haemophagocytic Lymphohistiocytosis 5, OMIM #603553

1. Consideration of application

1.1. The committee welcomed the advice of its specialist adviser, Professor Peter Turnpenny, who confirmed that the conditions were as described in the papers.

1.2. The committee noted that the description in the PGD application for Familial Haemophagocytic Lymphohistiocytosis type 3 (FHL3), OMIM #608898 and Familial Haemophagocytic Lymphohistiocytosis type 4 (FHL4), OMIM #603552 were consistent with the peer review.

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

1.4. The committee noted that the Genetic Alliance UK statement provided a perspective on the impact of the conditions 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 both FHL3 and FHL4 are inherited in an autosomal recessive pattern, 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.

1.8. The committee noted the penetrance of both conditions is 100%.

1.9. FHL3 and FHL4 are diseases characterised by white blood cells that develop uncontrollably in response to infection and destruction of blood-producing cells in the bone marrow. The conditions usually occur early in childhood and lead to sudden illness with prolonged fever and enlargement of the spleen, with low red blood cell and platelet levels. The over-reaction of the immune system damages organs, including the brain, and has been reported to lead to leukaemia and lymphoma. Once the conditions progress, other symptoms include convulsions, mobility deterioration, muscle stiffness or laxity, loss of vision and coma. If these conditions are left untreated, most children will die within two months of symptom onset and, for many affected children, the onset is in infancy.

1.10. There is no cure for the conditions and treatment focuses on managing the disease through chemotherapy, immunotherapy, and stem cell transplantation. The five-year survival rate of the condition is around 10% with treatment, and the treatments themselves have risks to those affected.

1.11. The committee noted the executive's request to consider Familial Haemophagocytic Lymphohistiocytosis type 3 (FHL3), OMIM #608898 and Familial Haemophagocytic Lymphohistiocytosis type 4 (FHL4), OMIM #603552 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 executive's request for the change of name of the condition Familial Haemophagocytic Lymphohistiocytosis, OMIM #603553, which is currently on the PGD list on the HFEA website and agreed to change the condition's name to Familial Haemophagocytic Lymphohistiocytosis type 2 (FHL2), OMIM #603553.

2. Decision

2.1. The committee considered that, in the worst-case scenario, Familial Haemophagocytic Lymphohistiocytosis type 3 (FHL3), OMIM #608898 and Familial Haemophagocytic Lymphohistiocytosis type 4 (FHL4), OMIM #603552 are very serious life-limiting conditions that can be fatal in early childhood. There is a serious risk of children developing leukaemia or lymphoma and the treatments used to manage the disease can have serious side effects. The committee considered the severe effect on the quality of life of those affected by these conditions.

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 abnormalities 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.

2.3. 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:

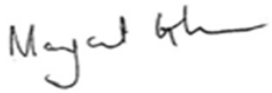
- Familial Haemophagocytic Lymphohistiocytosis type 3 (FHL3), OMIM #608898
- Familial Haemophagocytic Lymphohistiocytosis type 4 (FHL4), OMIM #603552

2.4. The committee also confirmed that Familial Haemophagocytic Lymphohistiocytosis OMIM #603553 should be listed on the PGD list as Familial Haemophagocytic Lymphohistiocytosis type 2 (FHL2), OMIM #603553.

3. Chairs signature

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

Signature



Name
Margaret Gilmore

Date
14 August 2019