Statutory Approvals Committee – minutes

Centre 0101 (CARE Nottingham)

Pre-implantation Genetic Diagnosis (PGD) application for Myoclonic Epilepsy of Unverricht-Lundborg Disease (ULD-EPM1), OMIM #254800

Thursday, 28 June 2018

HFEA, 10 Spring Gardens, London, SW1A 2BU

Committee members	Margaret Gilmore (Chair) Bobbie Farsides (Deputy Chair) Anne Lampe Ruth Wilde Anthony Rutherford	
Members of the Executive	Dee Knoyle Bernice Ash Paula Robinson Catherine Burwood Richard Chamberlain	Committee Secretary Committee Secretary (Observer) Head of Planning and Governance (Observer) Senior Governance Manager (Observer) Temporary Committee Clerk (Observing for Induction)
Specialist Adviser	Dr Alan Fryer	
Legal Adviser	Tom Rider	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

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 Myoclonic Epilepsy of Unverricht-Lundborg Disease (ULD-EPM1), OMIM #254800 is consistent with the peer review.

1.3. The committee noted that Genetic Alliance 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 in each pregnancy, if both parents have a relevant mutation.

1.8. The committee noted that ULD-EPM1 is a rare form of progressive myoclonus epilepsy caused by homozygous or compound heterozygous changes (point mutations / dodecamer repeat expansions) in the CSTB gene. The condition is characterised by periods of involuntary muscle jerking or twitching (myoclonus) increasing in frequency and severity over time. ULD-EPM1 is typically diagnosed between the ages of 5-15 years. Affected individuals are prone to periodic bouts of myoclonus brought on by physical exertion, stress, light or other stimuli. These episodes can lead to muscle rigidity, convulsions and total loss of consciousness. The episodes can be severe enough to interfere with walking and everyday activities.

1.9. The committee noted that the symptoms of this condition include involuntary muscle jerking, muscle rigidity, twitching (myoclonus) increasing in frequency and severity over time, convulsions, loss of consciousness, incoordination, ataxia, dysarthria (difficulty speaking), depression and decline in intellectual ability. The disease course is inevitably progressive, however, the rate of deterioration, especially in terms of walking capacity appears to vary even within the same family. Disease severity also varies among affected individuals within a family with apparently similar repeat-size expansions. It appears to be 100% penetrant. There can be variability in age of onset and rate of progression which may be connected to the length of the dodecamer repeat, as well as the nature of the mutation on the second allele.

1.10. The committee noted that ULD-EPM1 is a progressive neurodegenerative disorder requiring life-long surveillance and various forms of anti-epileptic medications. Generalised tonic-clonic seizures are usually controlled with treatment, but myoclonic jerks may become severe, appear in series, and inhibit normal activities. Treatment options are not curative. Clinical management involves lifelong surveillance to evaluate the efficacy of the drug therapy with respect to stabilising the condition and reducing medication side effects. The socio-psychological effect of living with repeated seizures affecting everyday living can severely impact an individual's ability to lead a normal healthy life, leading to a diminished quality of life. One third of individuals with ULD-EPM1 become wheelchair bound. Life expectancy has increased from 24-30 years to near normal life, depending on how well individuals respond to medication, physiotherapeutic and psychosocial support.

1.11. The committee noted the inspectorate's request to consider whether Myoclonic Epilepsy of Unverricht-Lundborg Disease (ULD-EPM1), OMIM #254800, should be approved for inclusion on the PGD List. The committee agreed to consider the application on this basis.

2. Decision

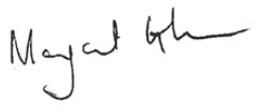
2.1. The committee considered that, in the worst case scenario, Myoclonic Epilepsy of Unverricht-Lundborg Disease (ULD-EPM1), OMIM #254800 is a serious condition given it is a progressive disabling condition which causes seizures, disabling myoclonus, and ataxia. The committee noted that the age of onset could be as early as six years old. There is no curative treatment for this condition and individuals require lifelong anti-epileptic medication and not all affected respond in the same way. Affected individuals also experience a decline in intellectual ability as well as physical ability. The committee considered the impact on the quality of life and day to day living with the condition which causes involuntary muscle jerking or twitching and may result in the individual becoming wheelchair bound.

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 Myoclonic Epilepsy of Unverricht-Lundborg Disease (ULD-EPM1), OMIM #254800 meets the criteria for testing under paragraph 1ZA(1)(b) and (2) of Schedule 2 of the Act and agreed to authorise testing.

3. Chair's signature

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

Signature



Name

Margaret Gilmore

Date

30 July 2018