Statutory Approvals Committee – minutes

Centre 0102 (Guy's Hospital)

Pre-implantation Genetic Diagnosis (PGD) application for

Crigler-Najjar Syndrome Type 1 (CN1), OMIM #218800

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 Crigler-Najjar Syndrome Type 1 (CN1), OMIM #218800 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 CN1 is a rare genetic metabolic disorder in which the body cannot properly clear bilirubin from the body. CN1 is caused by mutations of the UGT1A1 gene, which produces an enzyme which converts unconjugated to conjugated bilirubin, which can be excreted from the blood via the kidneys. Bilirubin is an orange-yellow bile pigment that is mainly a waste product of the natural breakdown of old or worn out red blood cells by the liver. CN1 is a very severe medical condition and affected individuals can die in childhood due to kernicterus (a type of brain damage that can result from high levels of unconjugated bilirubin). The trademark finding of CN1 is a yellowing of the skin, mucous membranes and whites of the eyes (jaundice) shortly after birth, which does not clear within three weeks.

1.9. The committee noted that other symptoms of this condition include lack of energy (lethargy), vomiting, and/or unsatisfactory feeding. Infants are at risk of developing kernicterus, potentially a life-threatening neurological condition in which toxic levels of bilirubin accumulate in the brain, causing damage to the central nervous system. Kernicterus can result in milder symptoms such as clumsiness, difficulty with fine motor skills and underdevelopment of the enamel of teeth, or it can result in severe complications such as hearing loss, problems with sensory perception, convulsions, and slow, continuous, involuntary, writhing movements (athetosis) of the arms and legs or the entire body.

1.10. The committee noted that treatment is not curative. Symptoms can be managed by lowering the level of bilirubin in the blood. Early treatment is imperative in CN1 to prevent the development of kernicterus during the first few months of life. The mainstay of treatment is aggressive phototherapy, in which the individual must lie with their skin exposed to bright light, wearing eye protection, for up to 10-12 hours per day. Phototherapy converts bilirubin into products which can be excreted via the liver and kidneys. The effectiveness of phototherapy declines as children age and skin thickens.

1.11. The committee noted that liver transplantation is the only definitive treatment for individuals with CN1. Livers for transplantation are however not readily available, lifetime immunosuppressive therapy is needed post operatively and the procedure is not without significant risks. Gene therapy is still only at the stage of clinical trial.

1.12. The committee noted the inspectorate's request to consider whether Crigler-Najjar Syndrome Type 1 (CN1), OMIM #218800 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, Crigler-Najjar Syndrome Type 1 (CN1), OMIM #218800 is a serious condition. CN1 affects one of the main organs, the liver and the age of onset is shortly after birth. The condition can cause death in early childhood due to brain damage as a result of toxic levels of bilirubin accumulated in the brain. The committee noted the burden of symptoms and severe complications such as hearing loss, involuntary movements of the arms and legs or the entire body. Affected individuals may have delayed speech and language development, intellectual disability, seizures and tremors. The condition is life threatening.

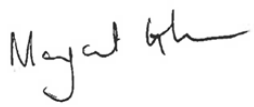
2.2. The committee noted the restrictive nature of effective treatment such as phototherapy and that gene therapy treatment is in the early stages of development. A liver transplant, which involves major surgery, is the only definitive treatment, however organs are not readily available. Without a successful liver transplant the impact on the quality of life of affected individuals is severe.

2.3. 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 Crigler-Najjar Syndrome Type 1 (CN1), OMIM #218800 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