Statutory Approvals Committee – minutes

Centre 0102 (Guy's Hospital)
Pre-implantation Genetic Diagnosis (PGD) application for Tyrosine Hydroxylase Deficiency, OMIM #605407

Thursday, 13 December 2018

HFEA, 10 Spring Gardens, London, SW1A 2BU

Committee members	Margaret Gilmore (Chair) Bobbie Farsides (Deputy Chair) Anne Lampe Anthony Rutherford Emma Cave	
Members of the Executive	Dee Knoyle Catherine Burwood Paula Robinson	Committee Secretary Senior Governance Manager (Observer) Head of Planning and Governance (Observer)
Legal Adviser	Eve Piffaretti	Blake Morgan LLP
External adviser	Dr Jenny Carmichael	
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
- Email from the centre

1. Consideration of application

1.1. The committee welcomed the advice of its Specialist Adviser, Dr Jenny Carmichael who confirmed that the condition was as described in the papers with one exception, the reference to types 1, 2 and 3 represents the variability of severity of the disease and there is one OMIM number #605407 which covers all levels of severity.

1.2. The committee noted that the description in the application for PGD for Tyrosine Hydroxylase Deficiency OMIM #605407 is consistent with the peer review.

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

1.4. The committee noted that the Genetic Alliance opinion provided a patient perspective and supported the application.

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 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. The condition is 100% penetrant.

1.8. The committee noted that the condition manifests by infancy. Symptoms may include progressive infantile encephalopathy leading to severe physical and intellectual disability, fetal distress in utero, feeding difficulties, hypotonia (reduced muscle tone), dystonia, irritability/lethargy crises and growth retardation. Brain dysfunction means there could be a profound impact on the quality of life, potential early death and severe intellectual disability. The condition can cause a lack of coordination and various movement disorders, which are progressive requiring a wheelchair for mobility. Some affected individuals may have delayed motor skills, intellectual disability, stiff muscles affecting posture, droopy eyelids, attention deficit disorder, speech problems and mental health issues, as well as autonomic nervous dysfunction resulting in stomach reflux, and dysregulation of blood sugar, blood pressure and body temperature. Life-long medical and developmental support is necessary.

1.9. The committee noted that symptom management is dependent upon severity and will need regular on-going review by paediatric and adult neurologists. Treatment can successfully manage the disease in some cases and affected individuals may lead relatively symptom-free lives with minimal problems. Tyrosine hydroxylase deficiency is treatable in some cases with Levodopa therapy, however there is some sensitivity to its side effects, e.g. significant dyskinesia (disorders of movement). Individuals have variable response to Levodopa and in some the medication can take several years to take effect. Although Levodopa treatment in early childhood can prevent some manifestations of the disorder there are no clinical trials reported on its use in early infancy.

1.10. The committee noted that there is no curative treatment for this condition.

1.11. The committee noted the inspectorate's request to consider whether Tyrosine Hydroxylase Deficiency OMIM #605407 should be approved for inclusion on the list of conditions approved for PGD. The committee agreed to consider the application on this basis.

2. Decision

2.1. The committee considered that, in the worst case scenario Tyrosine Hydroxylase Deficiency OMIM #605407 is a serious progressive debilitating disease which manifests by infancy and could result in early death. The condition causes severe mental and physical disability. Affected individuals may have intellectual impairment and complex behaviour problems, and movement disorder which can severely limit mobility requiring some individuals to use a wheelchair. There is no curative treatment for this condition and affected individuals require lifelong medical support. The quality of life of affected individuals may be severely impacted.

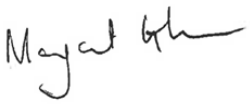
2.2. Tyrosine hydroxylase deficiency is treatable in some cases with Levodopa therapy, however the side effects of this drug, starting early on in life with increased doses over time, can be significant and there are no trial reports on its use in early infancy

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 Tyrosine Hydroxylase Deficiency OMIM #605407 meets the criteria for testing under paragraph 1ZA(1)(b) and (2) of Schedule 2 of the Act and agreed to authorise testing.

3. Chairs signature

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

Signature



Name

Margaret Gilmore

Date

17 January 2019